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ORIGINAL RESEARCH

Rheumatic Heart Disease Burden

A Comparative Analysis between the United States and the European Union

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ABSTRACT

BACKGROUND Rheumatic heart disease (RHD) is a major challenge to global health, primarily in low- and middle-income countries. Even though RHD is rare in high-income countries, it still poses a health challenge, yet there is a lack of data on its impact within the highest-income regions.

OBJECTIVES The purpose of this study was to compare the epidemiology of RHD in the United States of America (USA) and the European Union (EU).

METHODS Data on RHD burden were collected using the Global Disease Burden Study 2021 using the Global Health Data Exchange query tool. Age-standardized rates of incidence (ASIR), prevalence (ASPR), death (ASDR), disability-adjusted life years (ASDALY), years lived with disability (ASYLD), and years of life lost (ASYLL) were collected. Estimated annual percentage change (EAPC) was calculated.

RESULTS In USA in 2021, the ASPR was 123.4/100,000 with a decreasing annual trend of 0.32% since 1993. Between 2021 and 1993, the ASIR decreased from 10.6 to 10.0/100,000 cases. In the EU in 2021, the ASPR was 49.7/100,000 cases, with an annual decreasing trend of 1.6% between 2021 and 1993. Between 2021 and 1993, the ASIR decreased from 7.43 to 4.6/100,000 cases. The changing prevalence and incidence in the US was primarily driven by Florida, Nevada, and Tennessee. There has been a reversal in the burden of RHD since 2007 in the USA. In both regions, there was a significant gender disparity with female predominance. The EU reported higher age-standardized disability-adjusted life years and age-standardized years of life losts than the USA.

CONCLUSIONS The varied trends underscore the complexity of RHD epidemiology and the need for region-specific strategies to address this persistent health challenge. (JACC Adv. 2024;3:101393) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

ASDR = age-standardized death rate

ASDALY = age-standardized disability-adjusted life year

ASIR = age-standardized incidence rate

ASPR = age-standardized prevalence rate

ASYLD = age-standardized year lived with disability

ASYLL = age-standardized year of life lost

EAPC = estimated annual percentage change

EU = European Union

GBD = Global Disease Burden

RHD = rheumatic heart disease

Rheumatic heart disease (RHD) is a major challenge to global health, primarily affecting young people leading to significant cardiovascular morbidity and mortality among these individuals.[1] Recurrent estimates suggest millions of individuals continue to live with RHD, with a high number of these cases going undetected due to the silent nature of the disease in its early stages.[2] RHD is common in low- and middle-income countries, highlighting social disparities and healthcare accessibility issues, such as limited access to penicillin and other antibiotic medications.[3] RHD remains less common in affluent areas and prevalent in regions with poor healthcare infrastructure and resources.[4] While RHD is rare in developed regions including Europe and North America, it still poses a significant health challenge in the United States of America (USA) with almost 350,000 deaths related to it in the last 5 decades.[5] In the USA, specific regions are seeing increasing mortality rates from RHD, particularly among populations with lower socioeconomic status and other health outcome disparities.[5] Additionally, there is a notable inconsistency in following secondary prevention guidelines with only 58% of patients receiving the recommended benzathine penicillin G, and nearly 20% undergoing treatment for a shorter than advised duration.[6] On the other hand, following 2014, there has been a noticeable increase in incidence within the European Union (EU) region.[7] This resurgence has been likely related to the ongoing refugee crisis and migrations of indigent peoples to higher gross domestic product per capita countries.[8] Although previously published studies have evaluated the burden of RHD in low-income countries, there is a lack of comprehensive analysis of RHD's impact within the highest-income regions, specifically the USA and the EU. Therefore, the purpose of this study was to compare RHD in the USA and EU, specifically examining the prevalence, incidence, death, disability-adjusted life years, years of life lost, and years lived with disability.

METHODS

Data on RHD burden was collected using the Global Disease Burden (GBD) Study 2021 using the Global Health Data Exchange query tool.[9] The GBD study methodology has been published before.[10-13] Published studies, organization websites, and primary data were provided by the database. RHD was identified by GBD code: B.2.1 and International Classification of Diseases-10th Revision (ICD-10) codes (I01 to I01.9, I02.0, and I05 to I09.9). Age-standardized rates of incidence (ASIR), prevalence (ASPR), deaths (ASDR), disability-adjusted life years (ASDALYs), years of life lost (ASYLLs), and years lived with disability (ASYLDs) between the USA and EU were collected. The years 1993 to 2021 were analyzed. Using Joinpoint Regression Analysis (Joinpoint Regression Program version 4.9.1.0 [National Cancer Institute, Bethesda, Maryland, USA]), we calculated estimated annual percent change (EAPC) and relative 95% confidence intervals to quantify the trends in ASIR, ASPR, ASDR, ASDALYs, ASYLDs, and ASYLLs. JointPoint Regression software analyses the trend by using the input trend data (i.e. ASPR, ASIR, ASDR over time) and constructs the simplest model by connecting several different line segments (joinpoints) on a logarithmic scale. The software begins by using the minimum number of joinpoints (zero joinpoints represent a straight line) and tests whether the addition of further joinpoints is statistically significant and should therefore be added to the model. The software uses a Monte Carlo permutation as a test for significance, which was established as a resulting P value <0.05. The program also calculates the EAPC for each line segment and its confidence interval.[14] An increasing trend of ASR is determined if both the EAPC value and its 95% CI >0. A decreasing trend of ASR is determined if both the EAPC value and 95% CI <0; other trends mean that ASR was stable over time. All graphical illustrations were created in R statistical software. Approval from an ethics committee was not necessary due to the use of publicly accessible information.

RESULTS

BURDEN IN THE UNITED STATES. In 2021, the USA had 714,196 (95% CI: 651,023-787,357) persons of all ages living with RHD, which represents a 55.3% increase compared to 1993. Of that, 405,676 (95% CI: 369,965-445,833) were females (with a 38.5% increase) and 308,519 (95% CI: 280,075-342,543) were males (with 84.9% increase). The total ASPR was 123.4/100,000 in 2021 with an overall decreasing annual trend of 0.32% (EAPC −0.32 [−0.50 to −0.15]; $P < 0.001$). In 2021, females had a higher ASPR of 127.2/100,000 than males with an ASPR of 119.6/100,000. The overall ASPR showed a notable decline from 1993 to 2007, dropping to 106.5 cases per 100,000 people with the highest declining annual change between 2000 and 2005 (EAPC −8.1; $P < 0.001$). However, since 2007, there has been a consistent upward trend, with an EAPC of 1.8

(2.2-10.9; $P < 0.001$) for 2016 to 2021 period. Both genders had similar trends during this 1993 to 2021 period.

Similar trends have been observed with absolute incidence number and ASIR. In 2021, there were 58.065 (95% CI: 51,949-64,324) new cases of RHD which was an increase of 70.2% compared to 1993 (96% in males versus 53.7% in females). Total ASIR has slightly decreased from 10.6/100,000 cases to 10.0/100,000 cases in 2021. Initially, ASIR showed an upward trajectory, reaching its highest rate in 2000 at 13.0/100,000. After 2000, there was a decreasing trend, with ASIR dropping to 8.3/100,000 by 2006. Since then, however, there has been an upward trend with an EAPC of 2.5 (2.1-2.9; $P < 0.001$) between 2016 and 2021.

In 2021, the absolute death number for both sexes have decreased since 1993 by 28.3% and was 5,078 (95% CI: 4,121-5.600). Females had a higher absolute number of deaths with 3,316 (95% CI: 2,663-3,679) compared to males with 1,762 (95% CI: 1,450-1,938) in 2021. ASDR has decreased from 2.1 to 0.8/100,000 with an overall decreasing trend of 3% (EAPC −3.0 [−3.4 to −2.7]; $P < 0.001$).

Similar trends were observed with DALYs and YLLs. ASDALY has decreased from 53.8 to 22.5/100,000 with an EAPC of 2.9% (EAPC −2.9 [−3.3 to −2.5;] $P < 0.001$), while ASYLLs decreased from 47.1 to 16.9/100,000 with an EAPC of 3.4% (EAPC −3.4 [−3.8 to −2.9]; $P < 0.001$). On the other hand, ASYLD was slightly decreased from 6.6 to 5.6/100,000 with EAPC of −0.49 (−0.6 to −0.3; $P < 0.001$). In 2021, ASDALY, ASYLLs, and ASYLDs were higher in females with 24.4/100,000, 18.5/100,000, and 5.9/100,000 cases, respectively (**Table 1**, **Figure 1**).

BURDEN IN THE EU REGION. In the EU, in 2021, the total number of prevalent cases was 446,691 (95% CI: 389,480-515,586) which is 6% lower than 1993. Similar to the USA, females had a higher prevalence in 2021 (273,866) than males (172,824). The overall ASPR has decreased from 79.1 to 49.7/100,000 cases with an annual decreasing trend of 1.6% (EAPC −1.6 [−1.71 to −1.55]; $P < 0.001$). Both genders had similar decreasing trends; however, ASPR in 2021 was primarily driven by female cases with a rate of 54.5/100,000 compared to males who had an ASPR of 43.8/100,000.

In 2021, there were 40,368 new cases of RHD (of which, 60.9% were females) which is 5.6% less compared to 1993. Overall ASIR has also decreased from 7.43 to 4.6/100,000 cases with an annual decreasing trend of 1.7% (EAPC −1.7 [−1.8 to −1.6]; $P < 0.001$) and it was higher in females (4.97/100,000) than males (4.1/100,00).

From 1993 to 2021, the absolute death number for both males and females decreased by 17.9% (from 7,586-6,226) and 16.8% (from 14,861 to 13,372), respectively. However, overall number of deaths remained higher than the USA and was significantly higher in females (13,372) than males (6,226). The ASDR has also decreased for both genders, from 3.7 to 1.6/100,000 with an EAPC of −2.8 (−3.1 to −2.4; $P < 0.001$). Females had a higher ASDR (1.7) than males (1.4) in 2021.

The number and age-standardized rates of DALYs, YLDs, and YLLs have decreased, in both males and females. In 2021, ASDALYs and ASYLLs were higher in the EU than the USA, with 31.9/100,000 (EAPC −3.7; [−3.9 to −3.4]; $P < 0.001$) and 29.1/100,000 (EAPC −3.8 [−4.1 to −3.6]; $P < 0.001$) cases, respectively. Conversely, ASYLDs for both genders were lower than the USA with 2.8/100,000 cases in 2021 and an overall decreasing annual change of 1.4% (EAPC −1.4 [−1.5 to −1.3]; $P < 0.001$) (**Table 1**, **Figure 1**).

SUBANALYSIS OF THE USA STATES AND EU COUNTRY REGIONS. In 2021, the states with the highest ASPR were Florida (186.5/100,000), Nevada (185.3/100,000), and Tennessee (184.7/100,000). Among these states, ASPR was higher among females in Florida (190.9/100,000) and Tennessee (190.9/100,000) but higher among males in Nevada (188.6/100,00). Overall, all three states had an increasing annual trend of 0.2% (EAPC 0.2; $P = 0.03$), 0.6% (EAPC 0.6; $P = 0.001$), and 0.2% (EAPC 0.2; $P = 0.09$), for Florida, Tennessee, and Nevada, respectively. From 2017 to 2021, Nevada had the highest increase in annual trends with an EAPC of 6.0 (5.2-6.9; $P < 0.001$). Conversely, Oregon (67.6/100,000), Iowa (75.1/100,000), and Delaware (78.6/100,000) had the lowest ASPR in 2021, but all three counties had started to show increasing annual trends since 2017 with EAPC of 2.6 (2.3-2.8; $P < 0.001$), 3.8 (3.4-4.3; $P < 0.001$), and 2.9 (2.5-3.2; $P < 0.001$). Interestingly, in the same period, New York had the highest decreasing annual trend in the USA by 3.3% (EAPC −3.3; $P < 0.001$). The highest and the lowest ASIR were found in the same states as mentioned above. The highest ASDR was in females in Utah (1.9/100,000) and Idaho (1.7/100,000). The lowest ASDR was seen in males in the District of Columbia (0.4/100,000), followed by males in New York (0.5/100,000) and males in Massachusetts (0.6/100,000). The highest ASDALYs were observed in females from Utah and Alaska, both with 41.1/100, respectively (**Figure 2**, Supplementary material).

In 2021, in the EU, the highest ASPR was observed among females in Latvia (189.4/100,000), Lithuania

TABLE 1 Age-Standardized Rates in the USA and EU, 1993-2021

GBD Region	Measure	Age-Standardized Rate (per 100,000) 1993 Both	Females	Males
United States of America	Incidence	10.60 (9.14-12.31)	11.66 (10.06-13.53)	9.46 (8.14-11.11)
	Prevalence	111.36 (96.25-126.22)	153.04 (131.10-178.91)	119.77 (103.08-140.31)
	Deaths	2.05 (1.88-2.14)	2.37 (2.15-2.49)	1.60 (1.52-1.66)
	DALYs	53.76 (50.60-57.01)	62.18 (58.21-65.86)	43.19 (40.70-45.86)
	YLLs	47.13 (44.62-48.70)	54.75 (51.56-56.72)	37.53 (36.21-38.66)
	YLDs	6.63 (4.18-9.63)	7.43 (4.69-10.77)	5.66 (3.57-8.24)
European Union	Incidence	7.43 (6.85-8.08)	8.29 (7.65-9.02)	6.39 (5.88-6.93)
	Prevalence	71.62 (63.56-79.83)	89.68 (80.74-100.74)	65.09 (57.65-73.34)
	Deaths	3.69 (3.46-3.83)	4.03 (3.76-4.21)	3.08 (2.98-3.17)
	DALYs	93.83 (90.54-96.68)	99.75 (95.64-103.30)	84.16 (81.85-86.66)
	YLLs	89.60 (86.63-91.96)	94.92 (90.83-98.10)	80.71 (78.67-82.71)
	YLDs	4.23 (2.81-6.04)	4.82 (3.20-6.87)	3.45 (2.27-4.89)

TABLE 1 Continued

GBD Region	Age-Standardized Rate (per 100,000) 2021 Both	Females	Males	EAPC 1993-2021 (95% CI)[a] Both	Females	Males
United States of America	10.03 (9.05-11.03)	10.21 (9.22-11.23)	9.89 (8.93-10.93)	−0.1 (−0.3 to −0.1)[b]	−0.1 (−0.3 to −0.1)[b]	0.2 (0.06-0.4)
	123.44 (112.81-135.61)	127.15 (116.53-139.05)	119.57 (109.25-131.60)	−0.32 (−0.50-0.15)	−0.3 (−0.5 to −0.2)	0.07 (−0.8-0.2)[b]
	0.83 (0.68-0.91)	0.92 (0.75-1.01)	0.69 (0.57-0.76)	−3.0 (−3.4 to −2.7)	−3.2 (−3.5 to −2.8)	−2.8 (−3.1 to −2.3)
	22.56 (19.63-25.07)	24.35 (21.31-26.87)	20.31 (17.23-22.88)	−2.9 (−3.3 to −2.5)	−3.2 (−3.6 to −2.7)	−2.5 (−2.9 to −2.0)
	16.87 (14.42-18.26)	18.44 (15.99-19.86)	14.87 (12.39-16.19)	−3.4 (−3.8 to −2.9)	−3.6 (−4.1-3.1)	−2.9 (−3.4 to −2.5)
	5.68 (3.71-8.02)	5.90 (3.87-8.30)	5.44 (3.55-7.67)	−0.49 (−0.6 to −0.3)	−0.7 (−0.9 to −0.6)	−0.1 (−0.2-0.1)[b]
European Union	4.56 (4.16-5.07)	4.96 (4.52-5.52)	4.08 (4.55-3.71)	−1.7 (−1.8 to −1.6)	−1.8 (−1.9 to −1.7)	−1.6 (−1.7 to −1.5)
	49.66 (43.31-56.86)	54.46 (47.66-62.49)	43.78 (38.28-50.42)	−1.6 (−1.7-1.5)	−1.7 (−1.8 to −1.6)	−1.4 (−1.5 to −1.3)
	1.62 (1.39-1.76)	1.72 (1.43-1.90)	1.43 (1.29-1.53)	−2.8 (−3.1 to −2.4)	−2.9 (−3.2 to −2.5)	−2.6 (−2.9 to −2.2)
	31.88 (28.71-34.26)	32.62 (28.68-35.39)	30.13 (27.88-32.17)	−3.7 (−3.9 to −3.4)	−3.8 (−4.1 to −3.6)	−3.5 (−3.9 to −3.1)
	29.07 (25.83-31.04)	29.51 (25.66-31.96)	27.69 (25.52-29.28)	−3.8 (−4.1 to −3.6)	−4.0 (−4.3 to −3.7)	−3.6 (−3.9 to −3.2)
	2.81 (1.86-3.97)	3.11 (2.06-4.39)	2.44 (1.61-3.45)	−1.4 (−1.5 to −1.3)	−1.5 (−1.6 to −1.4)	−1.2 (−1.3 to −1.1)

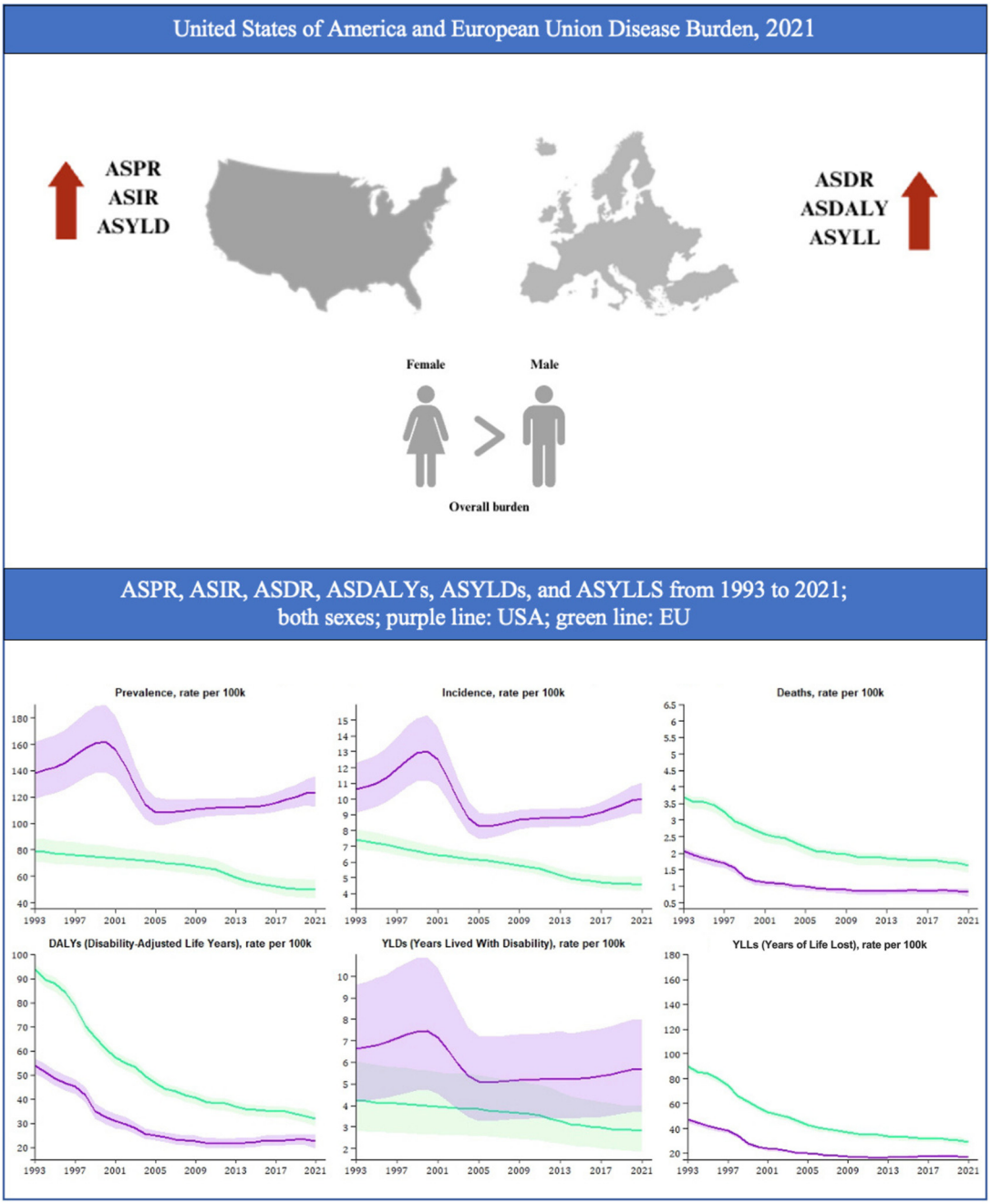
[a]An increasing trend of ASR is determined if both the EAPC value and its 95% CI >0. A decreasing trend of ASR is determined if both the EAPC value and 95% CI < 0. [b]Not statistically significant.

(179.9/100,000), and Estonia (176.8/100,000), while the lowest rates were reported in Sweden (14.6/100,000), Finland (14.7/100,000), and Malta (17.3/100,000), all in males. From 1993 to 2021, Finland and Malta experienced an overall annual decrease in the ASPR of 2.4% (EAPC −2.4 [−2.6 to −2.1]; $P < 0.001$) and 1.2% (EAPC −1.2 [−1.3-1.0]; $P < 0.001$), respectively. However, after 2015, both countries saw significant increases in annual trends, with Finland rising by 17.2% (EAPC 17.2; $P < 0.001$) and Malta by 6.0% (EAPC 6.0; $P < 0.001$). Similar ASIR trends were observed with the highest rates observed among females in Latvia (10.1/100,000), Lithuania (9.9/100,000), and Estonia (9.5/100,000). Conversely, the lowest ASIRs were found among males in Finland (1.2/100,000), females in Finland (1.6/100,00), and males in Sweden (1.7/100,000). The highest ASDR was observed among females in Cyprus (3.1/100,000), Germany (2.5/100,000), and Slovenia (2.4/100,000). Conversely, the lowest rates were recorded in males in Estonia (0.4/100,000), Sweden (0.5/100,000), and Ireland (0.6/100,000). Within the European Union, the highest ASDALYs were observed among females and males in Bulgaria (62.1 and 59.0/100,000), females in Cyprus (51.0/100,000), and females in Spain (42.3/100,000). In contrast, the lowest ASDALYs were reported among males and females in Ireland (11.7 and 19.3/100,000), males and females in Cyprus (33.8 and 44.1/100,000), and males and females in Slovenia (35.2 and 42.0/100,000) (**Figure 3**, Supplemental Tables 1 to 4).

DISCUSSION

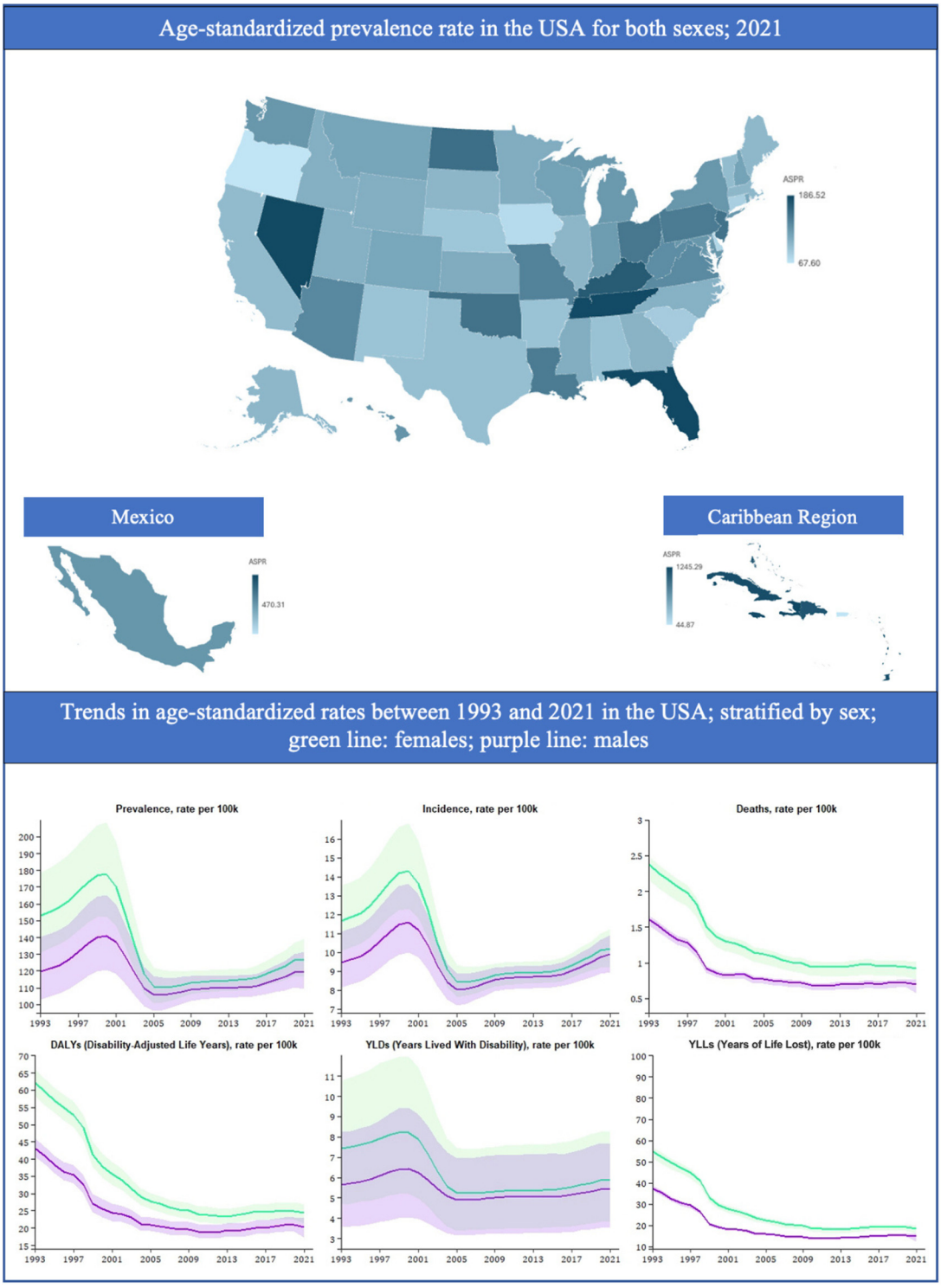
To the best of our knowledge, this is the first study comparing the burden of RHD between the USA and

FIGURE 1 **Overview of Burden in the United States of America and European Union, 1993 to 2021**



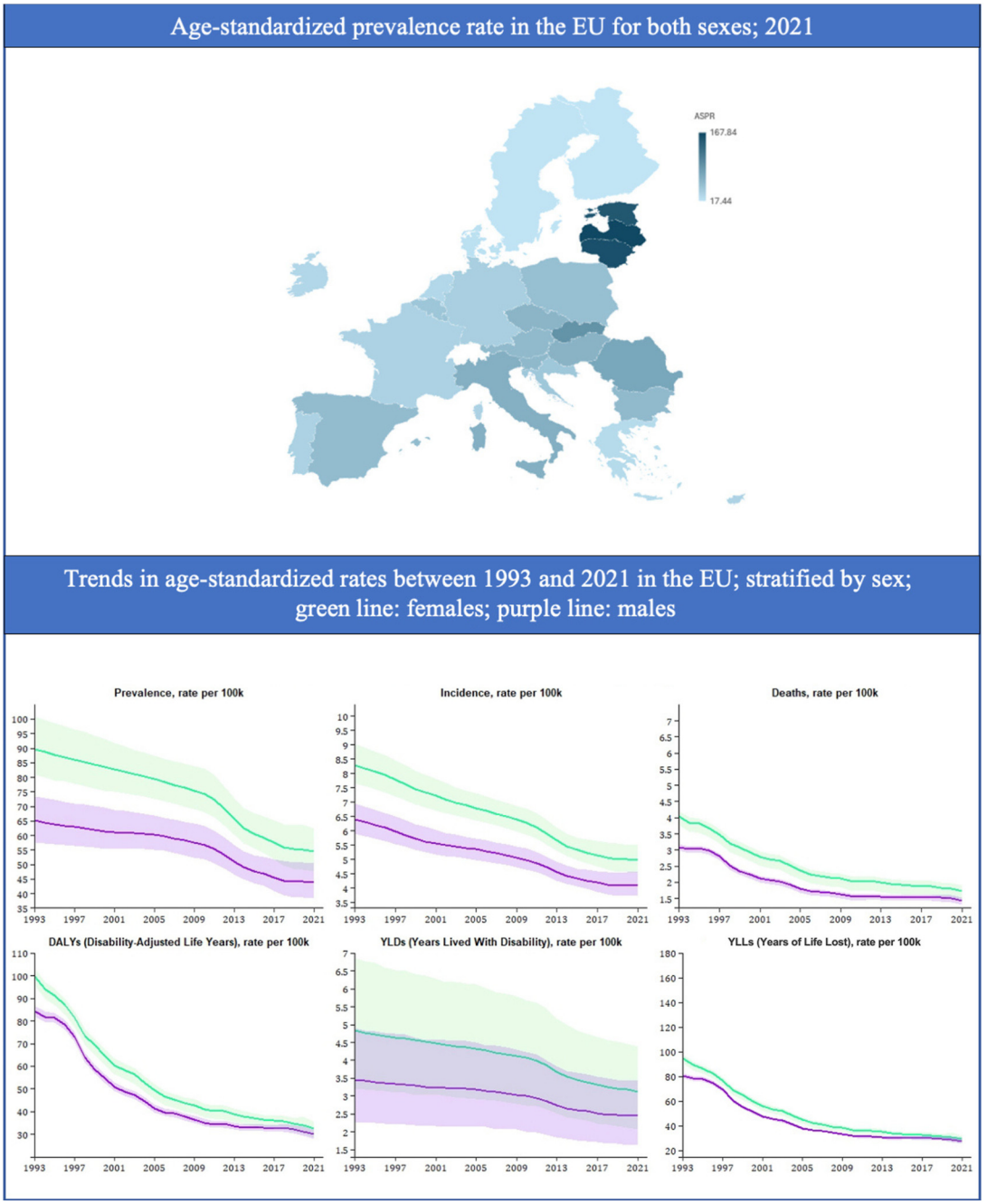
ASPR = age-standardized prevalence rate; ASIR = age-standardized incidence rate; ASDR = age-standardized death rate; ASDALYs = age-standardized disability-adjusted life years; ASYLLs = age-standardized years of life lost; ASYLDs = age-standardized years lived with disability.

FIGURE 2 ASPR in the USA, Caribbean Region, and Mexico in 2021 With Age-Standardized Trends From 1993 to 2021



ASPR = age-standardized prevalence rate.

FIGURE 3 ASPR in the EU



ASPR = age-standardized prevalence rate; EU = European Union.

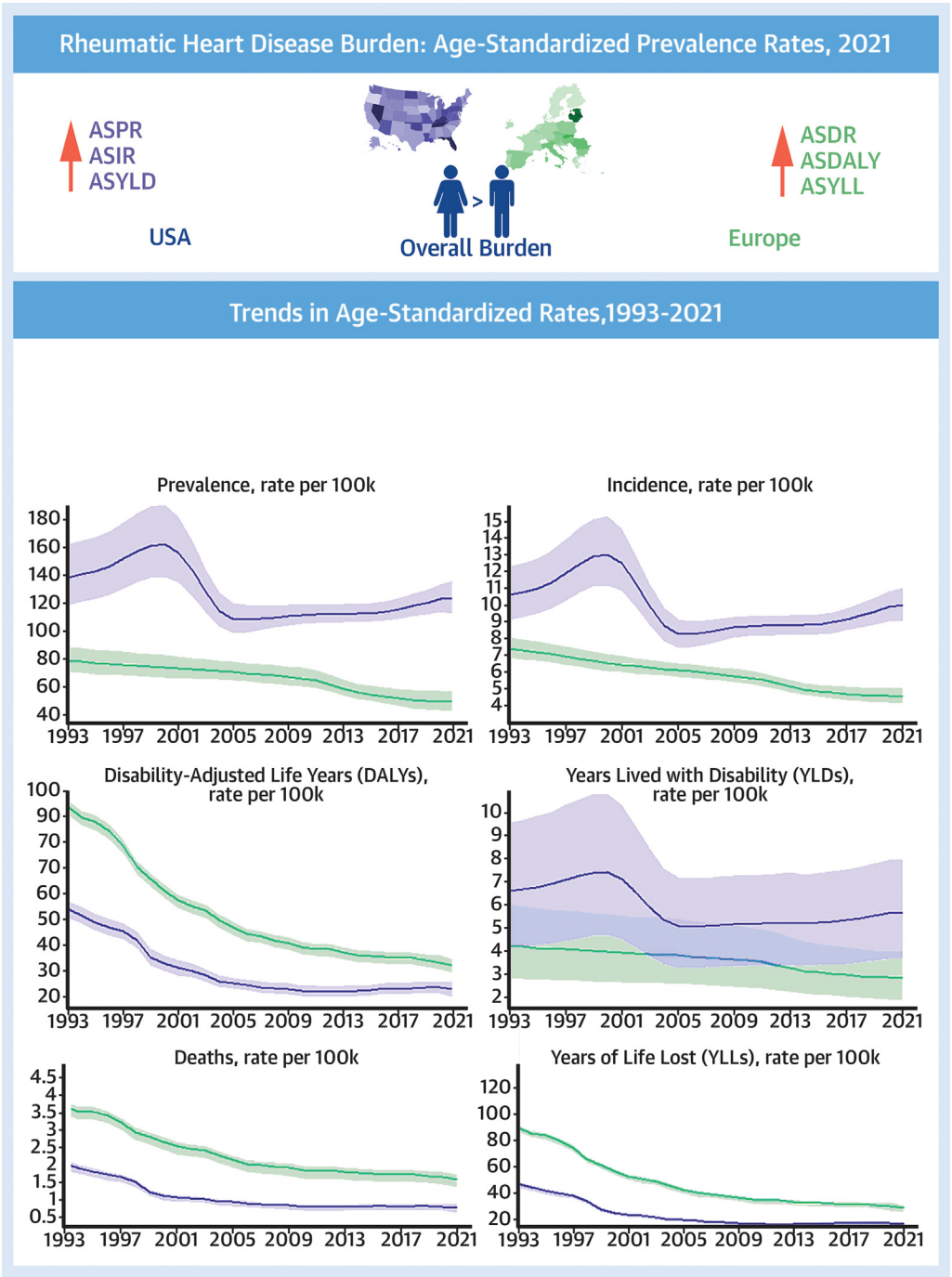
the EU. There is a burden divergence identified between these two regions. Our study has revealed several key findings. First, the USA had a higher and overall increasing prevalence and incidence than the EU. The burden of RHD in the USA was primary driven by highest burden in Florida, Nevada, and Tennessee. Second, after overall decline in prevalence and incidence in the last decade, the USA had a reversal in the burden of RHD with uprising trends since 2007. Third, the EU had reported higher death rates and higher

rate of DALYs and YLLs than the USA. Furthermore, we identified significant gender disparities in the burden of RHD across both regions. Interestingly, females had a higher burden of RHD in both regions with mild state/country variations but with overall significant female predominance. Lastly, there is a state- and country-level discrepancy, indicating that RHD is influenced by local healthcare policies, socioeconomic factors, and public health initiatives. The varied trends underscore the complexity of RHD epidemiology and the need for region-specific strategies to address this persistent health challenge (**Central Illustration**). Lower prevalence and incidence rates in the EU member states are likely related to robust healthcare systems that provide access to preventive care, early diagnosis, and timely treatment for RHD.[13-15] For example, nutrition and physical activity action plans implemented by the European healthcare systems from robust health policies aimed to improve healthcare access and reduce health disparities.[15] In Turkey, the declining patterns likely stemmed from the relocation of refugees prompted by domestic turmoil.[16] In Sweden, the Health in All Policies approach in Sweden integrates health considerations into all government policies, including housing, education, and employment. This holistic approach aims to reduce socioeconomic disparities and improve health outcomes, including those related to RHD.[17] In other countries of Central and Eastern Europe, the pronounced decreasing trends are most likely attributed to the EU's implementation of integrated and coordinated public health campaigns and education initiatives to raise awareness about RHD risk factors, symptoms, and preventive measures. For example, educational programs in schools and communities aim to educate children and families about the importance of streptococcal infection prevention and early treatment.[18] By aligning healthcare policies with public health objectives, the EU has been able to effectively address the underlying risk factors for RHD and reduce its prevalence and incidence. Despite the lower prevalence and incidence in the EU, ASDR, ASDALYs, and ASYLL were more pronounced in the EU than the US, but with overall decreasing trends. This is likely related to better access to antibiotics and availability of cardiac surgery improvement in living conditions and sanitation.[19-21] However, multiple European cities have identified increased mortality and morbidity in recent years, specifically in homeless population, which may have contributed to the higher ASDR, ASDALYs, and ASYLLs in 2021.[22-24] In November 2022, England experienced a significant outbreak of scarlet fever, with cases rising nearly fourfold. The potential causes of this surge include the start of the school year, which may have led to increased transmission rates, the emergence of macrolide-resistant bacterial strains, decreased herd immunity, various environmental factors, the lack of a vaccine, and the reduction of COVID-19 precautionary measures.[25] Latvia, Lithuania, and Estonia have the highest burden of RHD in the EU which is likely related with multiple factors including Soviet Union legacy, prioritizing treatment over prevention, economic transition, abundance of rural areas, and limited healthcare access and lower public awareness of disease.

In contrast, the unprecedented decade of immigration from 2000 to 2010 in the United States may have played a role in the persistent rise of RHD compared to the EU. The influx of immigrants during this period, particularly from regions with higher prevalence rates of RHD, could have contributed to an increased burden of the disease within the U.S. population.[26-28] This contrasts with the EU, where immigration patterns may not have been as pronounced during the same timeframe, potentially resulting in a lesser impact on RHD incidence rates.[29] Additionally, the US healthcare system faces challenges related to access, affordability, and fragmentation, which likely have hindered efforts to decrease RHD measures.[30,31] Disparities in healthcare access and coverage disproportionately affect marginalized communities, leading to gaps in preventive care and delayed diagnosis of RHD.[32-34] Moreover, overcrowding, poor housing conditions, improper health literacy, and other socioeconomic and environmental factors could lead to higher burden. These challenges contribute to the lack of a centralized approach to RHD prevention and management that has seemingly resulted in fragmented care delivery and inconsistencies in clinical practice. The fragmented nature of the US healthcare system has likely hindered coordination between healthcare providers and public health agencies, impeding the implementation of evidence-based strategies for RHD prevention and control.[35] Policy efforts to address RHD in the US have been limited compared to the EU, with insufficient investment in public health infrastructure, surveillance systems, and preventive interventions.[36,37]

The disparity in disease burden among different states in the USA may be influenced by several factors. These include the acceleration and diversification of immigration patterns, access to healthcare and the effectiveness of disease reporting system,

CENTRAL ILLUSTRATION **Rheumatic Heart Disease Burden in the United States of America and European Union**



Milutinovic S, et al. JACC Adv. 2024;3(12):101393.

Arrows indicate a higher age-standardized burden in the specific region. ASPR = age-standardized prevalence rate; ASIR = age-standardized incidence rate; ASDR = age-standardized death rate; ASDALYs = age-standardized disability-adjusted life years; ASYLLs = age-standardized years of life lost; ASYLDs = age-standardized years lived with disability.

population density, presence of specific migrant communities in different states, different socioeconomic and demographic characteristics, proportion of undocumented populations, etc. The number of people immigrating from Latin America is rapidly increasing.[38] "Border states" such as Florida, Texas, and California have the largest number of immigrants and have also experienced the greatest absolute growth in immigrant populations from 2010 to 2022.[27] Despite this, we found that Florida had a significantly higher burden of RHD than California, Arizona, and Texas. A potential explanation for the higher burden of RDH in Florida compared to others is the differing prevalence of RHD in immigrants' countries of origin. Specifically, RHD is much more prevalent in the Caribbean region than in Mexico.[8] Given that a significant portion of immigrants to Florida come from the Caribbean, including Cuba, while Mexican immigrants predominantly settle in Texas and California, this could account for the observed disparity in disease burden among these states. In 2021, most of the countries in Caribbean region had ASPR >1,000 per 100,000, including Haiti (1,245/100,000), Cuba (1,188/100,000), and Dominican Republic (1,140/100,000).[8] In contrast, Mexico reported a significantly lower prevalence of 470.3 per 100,000, which is less than half of most of the Caribbean countries.[8] Additionally, California and Texas host larger populations of undocumented immigrants compared to Florida, with 27% and 14% of the total undocumented immigrants in the U.S. residing in these states, respectively.[39] The undocumented status of these populations could result in reduced access to healthcare and decreased reporting of RHD, thus lowering burden of the disease. Interestingly, Tennessee and Nevada, despite not being border states, have reported a significantly higher burden of RHD than other states in the USA. Tennessee experienced a 36% increase in its immigrant population over the last decade, which could contribute to a higher number of RHD cases in the region.[38] Additionally, in 2018, almost 20% of Nevada's population were immigrants with 39% of those coming from Mexico.[40] Economic factors may also play a role; in 2022, 13% of Tennessee's and Nevada's population lived below the poverty line, potentially impacting access to healthcare and influencing disease prevalence.[41] Inadequate hygiene, overcrowded facilities, and subpar sanitation were present in 18.5% of the Nevada households.[42] Moreover, factors such as limited access to care, settlement of migrant communities, challenges in healthcare delivery in rural regions could further exacerbate these health disparities. There is a notable difference in the incidence of RHD by gender, been more common in woman.[43] Anatomical differences in regard to smaller chamber sizes in women and delayed diagnosis and treatment as a result from gender biases may account for such difference.[43]

Although high-income regions like the USA and EU have seen a rise in the burden of RHD, there remains a considerable gap compared to low- and middle-income countries. Globally, both the ASPR and ASIR have increased, but fortunately, ASDR has decreased over the past few decades. The global burden of RHD is largely driven by rising case numbers in Oceania, Southeast Asia, East Asia, and Sub-Saharan Africa.[44] It is important to note that the Caribbean region and several South American countries have experienced a significant increase in RHD cases over the past few decades. Worldwide increase in burden could potentially influence the local epidemiological trajectories in the high-income regions, particularly in regions with large immigrant populations from these areas, highlighting the need for continued vigilance and preventive measures in vulnerable communities.

STUDY LIMITATIONS. This study has several limitations. These may include data inconsistencies, limitations in data availability, or differences in diagnostic criteria and healthcare systems between the US and EU which have been refined over time. For future research, specific areas to explore include understanding the underlying reasons behind the observed trends in RHD prevalence and incidence. This includes examining healthcare infrastructure differences, access to preventive measures such as antibiotic prophylaxis, and cultural factors influencing disease awareness and management practices. Additionally, identifying effective interventions to reduce RHD burden is crucial. This may involve implementing targeted public health campaigns to raise awareness, improving access to healthcare services, and promoting early detection and management of streptococcal infections. Longitudinal studies assessing the effectiveness of these interventions and their impact on RHD rates over time would provide valuable insights for policymakers and healthcare professionals.

CONCLUSIONS

There are differences in the burden of RHD between the USA and the EU. Compared to the European Union, the USA has a higher prevalence, incidence, and morbidity. Identifying effective interventions to

reduce RHD burden remains crucial, specifically in Florida, Nevada, and Tennessee. This may involve implementing targeted public health campaigns to raise awareness, improving access to healthcare services, and promoting early detection and management of streptococcal infections. Addressing gender healthcare disparities may help decrease the gap in early diagnosis and treatment of RHD in women. Longitudinal studies assessing the effectiveness of these interventions and their impact on RHD rates over time would provide valuable insights for policymakers and healthcare professionals.

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PERSPECTIVE

COMPETENCY IN MEDICAL KNOWLEDGE: Rheumatic Heart Disease Burden is increasing in the United States of America. This is primarily driven by Florida, Nevada, and Tennessee.

TRANSLATION OUTLOOK: This study findings should inform policy makers to optimize and allocate resources on high-impacted states in the primary prevention of rheumatic heart disease.

REFERENCES

1. Ou Z, Yu D, Liang Y, et al. Global burden of rheumatic heart disease: trends from 1990 to 2019. *Arthritis Res Ther*. 2022;24(1):138. https://doi.org/10.1186/s13075-022-02829-3

2. Berhanu H, Mossie A, Morankar SN, Gemechu TD, Tegene E. Echocardiographic parameters and complication profiles among adult patients with rheumatic heart disease at Jimma Medical Center. *Vasc Health Risk Manag*. 2024;20:157-166. https://doi.org/10.2147/VHRM.S451957

3. Saxena A. Increasing burden of rheumatic heart disease in children: challenges persist despite a century of experience. *Int J Cardiol*. 2024;402:131828. https://doi.org/10.1016/j.ijcard.2024.131828

4. Hu B, Feng J, Wang Y, Hou L, Fan Y. Transnational inequities in cardiovascular diseases from 1990 to 2019: exploration based on the global burden of disease study 2019. *Front Public Health*. 2024;12:1322574. https://doi.org/10.3389/fpubh.2024.1322574

5. Salman A, Larik MO, Amir MA, et al. Trends in rheumatic heart disease-related mortality in the United States from 1999 to 2020. *Curr Probl Cardiol*. 2024;49(1 Pt C):102148. https://doi.org/10.1016/j.cpcardiol.2023.102148

6. de Loizaga SR, Arthur L, Arya B, et al. Rheumatic heart disease in the United States: forgotten but not gone—results of a 10-year multicenter review. *J Am Heart Assoc*. 2021;10:e020992. https://doi.org/10.1161/JAHA.120.020992

7. Ojha U, Marshall DC, Salciccioli JD, et al. Temporal trend analysis of rheumatic heart disease burden in high-income countries between 1990 and 2019. *Eur Heart J Qual Care Clin Outcomes*. 2024;10(2):108-120. https://doi.org/10.1093/ehjqcco/qcac083

8. Global Burden of Disease Collaborative Network. *Global Burden of Disease Study 2019 (GBD 2019) Results*. Seattle, United States: Institute for Health Metrics and Evaluation (IHME); 2020. https://vizhub.healthdata.org/gbd-results/

9. Global Burden of Disease Study 2019. (GBD 2019) data resources. Institute for health metrics and evaluation. Accessed August 31, 2023. https://ghdx.healthdata.org/gbd-2019

10. Institute for Health Metrics and Evaluation (IHME). *GBD compare data. Visualization*. Seattle, WA: IHME, University of Washington; 2015. Accessed August 31, 2023. http://vizhub.healthdata.org/gbdcompare

11. GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet*. 2023 Sep 30;402(10408):1132. https://doi.org/10.1016/S0140-6736(23)02044-5

12. GBD 2019 Mental Disorders Collaborators. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Psychiatr*. 2022;9(2):137-150. https://doi.org/10.1016/S2215-0366(21)00395-3

13. Sun J, Qiao Y, Zhao M, Magnussen CG, Xi B. Global, regional, and national burden of cardiovascular diseases in youths and young adults aged 15-39 years in 204 countries/territories, 1990-2019: a systematic analysis of Global Burden of Disease Study 2019. *BMC Med*. 2023;21(1):222. https://doi.org/10.1186/s12916-023-02925-4

14. Lv M, Jiang S, Liao D, Lin Z, Chen H, Zhang J. Global burden of rheumatic heart disease and its association with socioeconomic development status, 1990-2019. *Eur J Prev Cardiol*. 2022;29(10):1425-1434. https://doi.org/10.1093/eurjpc/zwac044

15. Timmis A, Vardas P, Townsend N, et al. European Society of Cardiology: cardiovascular disease statistics 2021. *Eur Heart J*. 2022;43(8):799. https://doi.org/10.1093/eurheartj/ehac064

16. Karadag SG, Sonmez HE, Demir F, et al. Rheumatic diseases in Syrian refugee children: a retrospective multicentric study in Turkey. *Rheumatol Int*. 2020;40(4):583-589.

17. Fredriksson M. Universal health coverage and equal access in Sweden: a century-long perspective on macro-level policy. *Int J Equity Health*. 2024;23(1):111. https://doi.org/10.1186/s12939-024-02193-5

18. Shimanda PP, Shumba TW, Brunström M, et al. Preventive interventions to reduce the burden of rheumatic heart disease in populations at risk: a systematic review. *J Am Heart Assoc*. 2024;13(5):e032442. https://doi.org/10.1161/JAHA.123.032442

19. Browne AJ, Chipeta MG, Haines-Woodhouse G, et al. Global antibiotic consumption and usage in humans, 2000-18: a spatial modelling study. *Lancet Planet Health*. 2021;5(12):e893-e904.

20. Vervoort D, Meuris B, Meyns B, Verbrugghe P. Global cardiac surgery: access to cardiac surgical care around the world. *J Thorac Cardiovasc Surg*. 2020;159(3):987-996.e6.

21. Quinn RW. Comprehensive review of morbidity and mortality trends for rheumatic fever, streptococcal disease, and scarlet fever: the decline of rheumatic fever. *Rev Infect Dis*. 1989;11(6):928-953.

22. Cady A, Plainvert C, Donnio P-, et al. Clonal spread of Streptococcus pyogenes emm44 among homeless persons, Rennes, France. *Emerg Infect Dis*. 2011;17(2):315-317. https://doi.org/10.3201/eid1702.101022

23. Bundle N, Bubba L, Coelho J, et al. Ongoing outbreak of invasive and non-invasive disease due to group A Streptococcus (GAS) type emm66 among homeless and people who inject drugs in England and Wales, January to December 2016. *Euro Surveill*. 2017;22(3):30446. https://doi.org/10.2807/1560-7917.ES.2017.22.3.30446

24. Dauby N, Miendje Deyi VY, Delforge V, et al. Streptococcus pyogenes infections with limited emm-type diversity in the homeless population of Brussels, 2016-2018. *Int J Infect Dis*. 2019;81:52-56. https://doi.org/10.1016/j.ijid.2019.01.026

25. Guy R, Henderson KL, Coelho J, et al. Increase in invasive group A streptococcal infection notifications, England, 2022. *Euro Surveill*. 2023;28(1):2200942. https://doi.org/10.2807/1560-7917.ES.2023.28.1.2200942

26. Bustamante AV, Chen J, Félix Beltrán L, Ortega AN. Health policy challenges posed by shifting demographics and health trends among immigrants to the United States. *Health Aff*. 2021;40(7):1028-1037. https://doi.org/10.1377/hlthaff.2021.00037

27. Batalova J, Blizzard B, Bolter J. *Frequently requested statistics on immigrants and immigration in the United States*. Migration Information Source; 2020.

28. Argeseanu Cunningham S, Ruben JD, Narayan KM. Health of foreign-born people in the United States: a review. *Health Place*. 2008;14(4):623-635. https://doi.org/10.1016/j.healthplace.2007.12.002

29. Estevens J. Migration crisis in the EU: developing a framework for analysis of national security and defense strategies. *Comp Migr Stud*. 2018;6(1):28. https://doi.org/10.1186/s40878-018-0093-3

30. Rice T, Rosenau P, Unruh LY, Barnes AJ, Saltman RB, van Ginneken E. United States of America: health system review. *Health Syst Transit*. 2013;15(3):1-431.

31. Pathman DE, Konrad TR, Dann R, Koch G. Retention of primary care physicians in rural health professional shortage areas. *Am J Publ Health*. 2004;94(10):1723-1729. https://doi.org/10.2105/ajph.94.10.1723

32. Qi M, Santos H, Pinheiro P, McGuinness DL, Bennett KP. Demographic and socioeconomic determinants of access to care: a subgroup disparity analysis using new equity-focused measurements. *PLoS One*. 2023;18(11):e0290692. https://doi.org/10.1371/journal.pone.0290692

33. Macias-Konstantopoulos WL, Collins KA, Diaz R, et al. Race, healthcare, and health disparities: a critical review and recommendations for advancing health equity. *West J Emerg Med*. 2023;24(5):906-918. https://doi.org/10.5811/westjem.58408

34. Joo JY. Fragmented care and chronic illness patient outcomes: a systematic review. *Nurs Open*. 2023;10(6):3460-3473. https://doi.org/10.1002/nop2.1607

35. Pastore S, De Cunto A, Benettoni A, Berton E, Taddio A, Lepore L. The resurgence of rheumatic fever in a developed country area: the role of echocardiography. *Rheumatology*. 2011;50(2):396-400. https://doi.org/10.1093/rheumatology/keq290

36. Marijon E, Mocumbi A, Narayanan K, Jouven X, Celermajer DS. Persisting burden and challenges of rheumatic heart disease. *Eur Heart J*. 2021;42(34):3338-3348. https://doi.org/10.1093/eurheartj/ehab407

37. Batalova J, Blizzard R, Bolter J. Frequently requested statistics on immigrants and immigration in the United States. *Migration Information Source*. 2020. Accessed May 27, 2021. https://www.migrationpolicy.org/article/frequently-requested-statisticsimmigrants-and-immigrationunited-states-2019

38. Budiman A. *Key findings about U.S. immigrants*. Washington (DC): Pew Research Center; 2020. Accessed May 20, 2021. https://www.pewresearch.org/fact-tank/2020/08/20/key-findings-about-u-s-immigrants/

39. U.S. Census Bureau. *2018 American Community Survey 1-Year Estimates. The American Immigration Council elected to use data from the 2018 survey. Note: "Foreign born" does not include people born in Puerto Rico or U.S. island areas or U.S. citizens born abroad of American parent(s)*. U.S. Census Bureau; 2018.

40. U.S. Census Bureau. *QuickFacts: Tennessee; Nevada*. U.S. Department of Commerce; 2024. Accessed May 6, 2024. https://www.census.gov/quickfacts/fact/table/TN,NV/HSG010222

41. Nevada Department of Health and Human Services. State health assessment 2022. Accessed May 6, 2024. https://dpbh.nv.gov/uploadedFiles/dpbhnvgov/content/About/AdminSvcs/DPBH-SHA-2022.pd

42. Coffey S, Roberts-Thomson R, Brown A, et al. Global epidemiology of valvular heart disease. *Nat Rev Cardiol*. 2021;18:853-864.

43. DesJardin JT, Chikwe J, Hahn RT, Hung JW, Delling FN. Sex differences and similarities in valvular heart disease. *Circ Res*. 2022;130(4):455-473.

44. Ghamari SH, Abbasi-Kangevari M, Saeedi Moghaddam S, et al. Rheumatic heart disease is a neglected disease relative to its burden worldwide: findings from global burden of disease 2019. *J Am Heart Assoc*. 2022;11(13):e025284. https://doi.org/10.1161/JAHA.122.025284

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APPENDIX For supplemental tables, please see the online version of this paper.