

## Original Article

# Understanding Cardiovascular Mortality and Disability in Central Asia: A GBD-Based Analysis and Forecast to 2050

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Received: Jan 19, 2026

Accepted: Jun 16, 2026

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Citation:

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## ABSTRACT

**Introduction:** Cardiovascular diseases (CVDs) remain the leading cause of mortality and disability in Central Asia. This study analyzes trends in CVD burden across nine countries from 1990 to 2021, identifies major subtypes, explores sex and country-level disparities, and forecasts trends through 2050.

**Methods:** We used data from the Global Burden of Disease (GBD) 2021 study to assess age-standardized death rates (ASDRs) and age-standardized disability-adjusted life years (ASYRs) for CVDs and their subtypes in Armenia, Azerbaijan, Georgia, Kazakhstan, Kyrgyzstan, Mongolia, Tajikistan, Turkmenistan, and Uzbekistan. Forecasts were generated using GBD reference and alternative risk-reduction scenarios.

**Results:** In 2021, the average ASDR for CVDs in the region was 436.1 per 100,000 population, nearly twice that for respiratory infections and tuberculosis. Ischemic heart disease (IHD) and stroke accounted for 89% of total CVD deaths. Turkmenistan reported the highest ASDR (552.2 per 100,000), while Armenia reported the lowest (314.8 per 100,000). Kazakhstan had the highest stroke-related ASDR at 163.0 per 100,000. Men experienced 1.5 times higher ASDR (538.2 vs. 365.7 per 100,000) and ASYR (10966.6 vs. 6807.5 per 100,000) than women. While most countries reduced ASDRs from 1990 to 2021, Uzbekistan showed a 0.7% increase. Forecasts project a regional decline in ASDR by 2050 in both improved-risk-factor and reference scenarios.

**Conclusion:** CVDs remain the dominant health burden in Central Asia. Evidence-based prevention, improved hypertension control, and health system strengthening are essential to achieving future gains and reducing premature cardiovascular mortality.

**Keywords:** Cardiovascular Disease; Central Asia; Global Burden of Disease; Age-Standardized Death Rate; Disability-Adjusted Life Years; Health Projections

## Introduction

Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality worldwide. Between 1990 and 2019, the number of people living with cardiovascular diseases nearly doubled, rising from approximately 271 million to 523 million (1). However, from 1990 to 2022, global deaths due to cardiovascular diseases declined by 34.9% (2). Despite advancements in prevention, diagnosis, and treatment, the global burden of CVDs continues to grow, driven by population aging, urbanization, and the persistence of modifiable risk factors such as hypertension, tobacco use, unhealthy diet, and physical inactivity. CVDs not only cause premature mortality but also lead to substantial disability (3), making them a major obstacle to sustainable development and health system resilience.

Among various metrics used to assess disease impact, age-standardized death rates (ASDRs) and disability-adjusted life years (DALYs) are essential for understanding the true burden of CVDs across populations (4). These indicators allow for meaningful comparisons across countries and over time, accounting for differences in population age structures. While DALYs capture the combined effect of mortality and non-fatal outcomes (5), death rates remain a particularly important indicator for assessing health system performance and identifying high-priority areas for intervention, especially for diseases like CVDs, where mortality represents a substantial share of total burden. According to the Global Burden of Disease (GBD) 2022 Study, ischemic heart disease had the highest age-standardized DALY rate (ASYR) globally, at 2,275.9 per 100,000 population (2). Moreover, Central

Asia (CA) recorded the highest age-standardized prevalence of cardiovascular diseases, with 11,342.6 cases per 100,000 people (2).

Although Central Asian countries are Kazakhstan, Kyrgyzstan, Uzbekistan, Tajikistan, and Turkmenistan, GBD also added Armenia, Georgia, and Mongolia to this list (6). Despite their geographic and historical interconnectedness, these countries exhibit distinct trends in CVD burden, shaped by varying health policies, access to care, and epidemiological risk profiles. CA remains underrepresented in global health research, and systematic evaluations of long-term trends in cardiovascular burden are scarce. Recently, Goh and colleagues estimated cardiovascular disease burden for Asian subregions including those in the Central Asian region (7). The primary objective of the study was to provide future regional estimates and trends of risk factors for cardiovascular disease for all of Asia, not a country specific analysis for the Central Asian region. In contrast, the current study provides a country specific analysis of CVD burden for 9 countries in the Central Asian region from 1990 to 2021, and a 5 year forecast until 2050 based on the GBD data.

This study aims to fill this gap by analyzing age-standardized death and DALY rates for all cardiovascular diseases in Central Asia from 1990 to 2021 using data from the Global Burden of Disease Study. In addition, we describe projections of the CVD burden in Central Asia through 2050 based on GBD forecast data. Understanding these dynamics is crucial for informing targeted, evidence-based interventions and shaping long-term health policy strategies to reduce the cardiovascular burden in the region.

## Materials and Methods

### Data source

This study utilized data from the GBD 2021 analysis to assess the global burden of cardiovascular diseases. We analyzed age-standardized mortality and DALY rates, and examined how these indicators varied by sex and region from 1990 to 2021. All datasets used in this study are extracted from the GBD 2021 Results Tool (<http://ghdx.healthdata.org/gbd-results-tool>), and no additional calculations of presented rates were not performed. GBD 2021 was the most recent and comprehensive release available at the time of data extraction and analysis.

### Classification of Cardiovascular Diseases

Cardiovascular diseases in this study were grouped into 12 categories: rheumatic heart disease, ischemic heart disease, stroke, hypertensive heart disease, pulmonary arterial hypertension, cardiomyopathy and myocarditis, atrial fibrillation and

flutter, aortic aneurysm, lower extremity peripheral arterial disease, endocarditis, non-rheumatic valvular heart conditions, and other cardiovascular and circulatory disorders. The complete GBD cause classification, including the associated ICD-9 and ICD-10 codes, along with specific methodological details, can be found in the GBD 2021 reports on cause-specific mortality and non-fatal health outcomes (8, 9).

### Measurement Approach

The disease burden was assessed using ASDRs and ASYRs across the selected region. Standardizing these rates was essential to remove confounding effects related to population structure, such as age and sex differences, enabling fair comparisons between regions. Age-standardized rates were calculated using the GBD world standard population. Rates per 100,000 population were reported with 95% uncertainty intervals (UIs). These UIs reflect the range of possible

values based on the variability in data inputs and modeling procedures; they are generated from 1,000 model runs, with the 95% UI defined by the 2.5th and 97.5th values. The percentage change in ASDRs and ASYRs from 1990 to 2021 was calculated using the formula:

$$\frac{ASDR \text{ or } ASYR_{1990} - ASDR \text{ or } ASYR_{2021}}{ASDR \text{ or } ASYR_{1990}} \times 100$$

### Disability-Adjusted Life Years

DALYs and mortality are key indicators commonly used in disease burden assessments. DALYs represent the total impact of disease by combining years lost due to premature death with years lived in less than full health due to illness or disability (9). One DALY represents one year of healthy life lost, and the overall DALY count reflects the gap between current health status and ideal health, where individuals live long, disease-free lives.

DALY is measured by combining the years of life lost due to premature death (YLLs) and years lived with disability (YLDs). The calculation follows the WHO methods for the global burden of disease estimates (10). The formula uses a simplified DALY measure, without age weighting or time discounting. YLL is determined by multiplying the number of deaths at a specific age by the standard life expectancy for that age, based on life tables. The calculation of YLD follows a prevalence-based approach, as used by WHO and GBD Studies. The formula for YLD involves multiplying the prevalence of a condition by its corresponding disability weight (DW) (10).

### Forecasting analysis

Future trends in trends in mortality due to cardiovascular diseases were assessed using long-term forecasts developed in the GBD 2021 forecasting framework. The forecasts were calculated by the Institute for Health Metrics and Evaluation (IHME). The framework relies on a multi-stage approach that integrates forecasts of sociodemographic and health-related determinants, such as age-specific fertility and educational attainment, along with exposure to key risk

factors, such as smoking, to project cause-specific mortality and YLLs (11).

We report mortality forecasts under the GBD reference scenario, which assumes current trends in health determinants continue, and the improved behavioral and metabolic risks scenario, which models the impact of gradually reducing exposure to modifiable risk factors such as tobacco use, poor diet, and high blood pressure through 2050. These scenarios are incorporated into the GBD forecasting framework and take into account future demographic, socioeconomic and risk factor trends. Each scenario incorporates age- and sex-specific population projections and accounts for the potential impact of demographic and environmental changes.

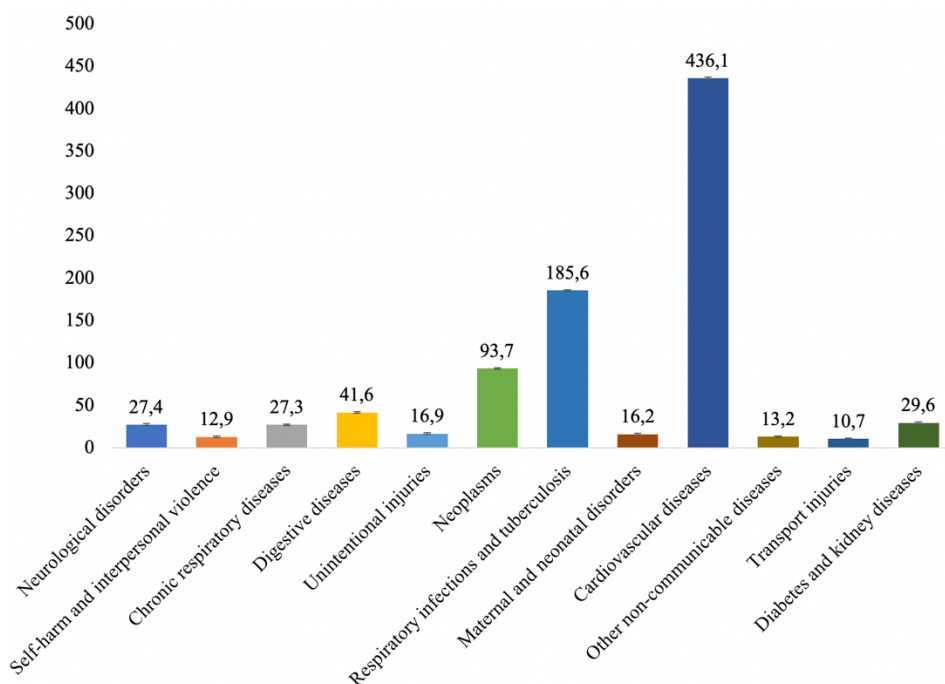
Uncertainty around forecasted estimates was quantified by propagating 500 draw-level simulations through the modeling pipeline, with final results presented as means with 95% UIs, derived from the 2.5th and 97.5th percentiles of the draws (11). This methodological structure ensures consistent, transparent, and comparable estimates of future CVD burden that can be used for scenario-based policy planning.

## Results

### Burden of CVD in Central Asia

The GBD study classifies non-communicable diseases (NCDs) into 12 broad categories, including CVDs, neurological conditions, neoplasms, chronic respiratory illnesses, diabetes and kidney diseases, digestive disorders, maternal and neonatal conditions, self-harm and interpersonal violence, unintentional injuries, transport-related injuries, respiratory

infections and tuberculosis, and other NCDs. Among these, CVD exhibited the highest ASDR in 2021, at 436.1 per 100,000 population (95% UI: 395.8-474.5), nearly double the corresponding rates for respiratory infections and tuberculosis (see Figure 1). In Central Asia, CVD was the leading cause of disease burden in that year.



**Figure 1.** The age-standardized death rate (ASDR) of 12 types of diseases in Central Asia in 2021.

Table 1 presents the ASDRs, ASYRs, and overall percentage change for total CVD and its 12 subtypes from 1990 to 2021. Between these years, both the ASDR and ASYR for CVD declined. In 2021, the

ASDR was 436.13 (95% UI: 395.75-474.54), and the ASYR was 8630.68 (95% UI: 7862.72-9433.91), compared to 512.88 (95% UI: 486.16-529.78) and 10668.11 (95% UI: 10266.44-10979.08), respectively, in 1990.

**Table 1.** The age-standardized rate of death (ASDR), disability-adjusted life years (DALYs), and total percent change of cardiovascular disease (CVD) and its 12 categories in Central Asia between 1990 and 2021.

Category	2021		1990		Total percentage change 1990-2021	
	ASDR	ASYR	ASDR	ASYR	ASDR	ASYR
Cardiovascular diseases	436.13 (395.75 - 474.54)	8630.68 (7862.72 - 9433.91)	512.88 (484.16 - 529.78)	10668.11 (10266.44 - 10979.08)	-0.15 [-0.22 - 0.08]	-0.19 [-0.26 - 0.12]
Ischemic heart disease	265.51 (240.67 - 290.42)	4864.49 (4415.55 - 5338.75)	320.47 (299.83 - 332.36)	6206.85 (5937.37 - 6407.43)	-0.17 [-0.25 - 0.10]	-0.22 [-0.29 - 0.14]
Stroke	124.06 (112.55 - 135.53)	2565.92 (2336.68 - 2798.31)	159.56 (150.66 - 165.89)	3504.49 (3351.69 - 3657.22)	-0.22 [-0.28 - 0.15]	-0.27 [-0.32 - 0.20]
Hypertensive heart disease	20.62 (17.75 - 23.92)	376.11 (320.94 - 441.92)	16.04 (13.85 - 18.83)	323.93 (284.08 - 368.09)	0.29 [0.01 - 0.57]	0.16 [-0.05 - 0.40]
Cardiomyopathy and myocarditis	13.87 (11.90 - 15.99)	413.46 (348.43 - 479.78)	4.95 (4.35 - 5.64)	156.66 (137.81 - 177.34)	1.80 [1.24 - 2.43]	1.64 [1.12 - 2.28]
Rheumatic heart disease	3.20 (2.79 - 3.66)	142.06 (120.70 - 167.98)	6.02 (5.44 - 7.07)	262.80 (238.03 - 294.99)	-0.47 [-0.58 - 0.36]	-0.46 [-0.54 - 0.37]

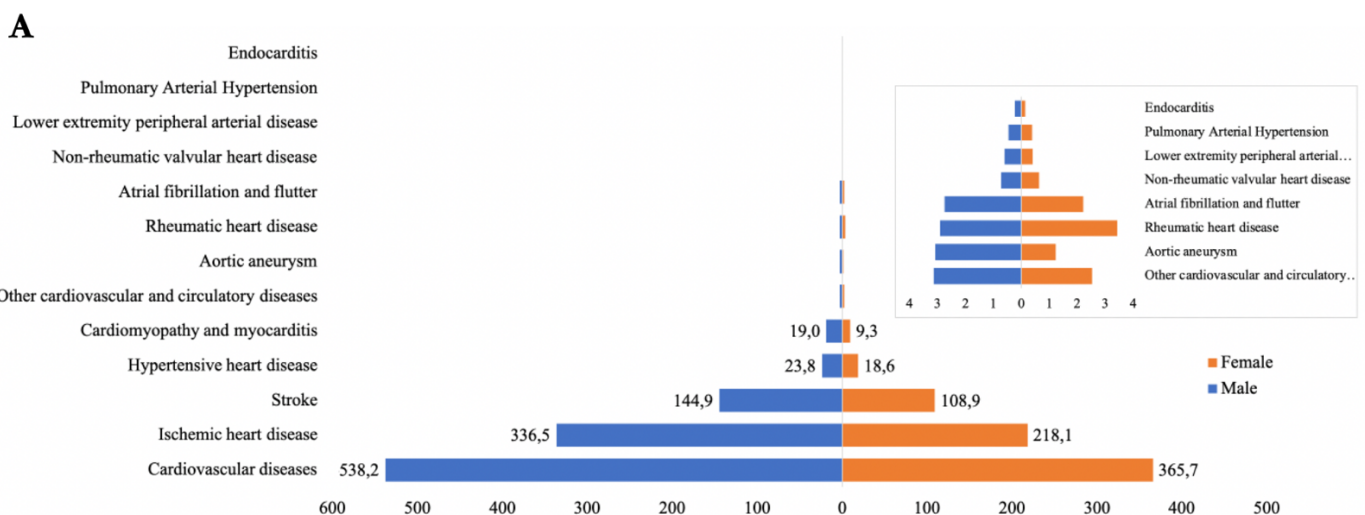
Category	2021		1990		Total percentage change 1990-2021	
	ASDR	ASYR	ASDR	ASYR	ASDR	ASYR
Atrial fibrillation and flutter	2.37 (2.09 - 2.60)	75.01 (59.90 - 95.50)	1.87 (1.61 - 2.19)	66.28 (51.57 - 86.71)	0.27 [0.07 - 0.47]	0.13 [0.06 - 0.22]
Aortic aneurysm	1.98 (1.77 - 2.21)	42.68 (37.78 - 47.93)	0.94 (0.81 - 1.13)	23.60 (20.78 - 27.99)	1.10 [0.71 - 1.51]	0.81 [0.47 - 1.16]
Non-rheumatic valvular heart disease	0.68 (0.60 - 0.76)	23.94 (19.42 - 29.98)	0.17 (0.14 - 0.19)	11.22 (8.04 - 16.17)	3.05 [2.32 - 3.99]	1.13 [0.84 - 1.59]
Lower extremity peripheral arterial disease	0.48 (0.41 - 0.55)	12.50 (9.59 - 16.93)	0.23 (0.19 - 0.29)	8.76 (6.09 - 13.19)	1.05 [0.62 - 1.55]	0.43 [0.25 - 0.69]
Pulmonary Arterial Hypertension	0.41 (0.34 - 0.48)	12.91 (10.61 - 15.60)	0.39 (0.31 - 0.47)	14.14 (11.27 - 16.45)	0.04 [-0.13 - 0.26]	-0.09 [-0.25 - 0.13]
Endocarditis	0.18 (0.15 - 0.20)	6.39 (5.57 - 7.29)	0.19 (0.18 - 0.22)	8.69 (7.62 - 10.21)	-0.11 [-0.25 - 0.05]	-0.26 [-0.39 - 0.12]
Other cardiovascular and circulatory diseases	2.79 (2.46 - 3.08)	95.20 (81.78 - 111.33)	2.04 (1.81 - 2.31)	80.67 (72.02 - 90.76)	0.37 [0.15 - 0.60]	0.18 [0.04 - 0.32]

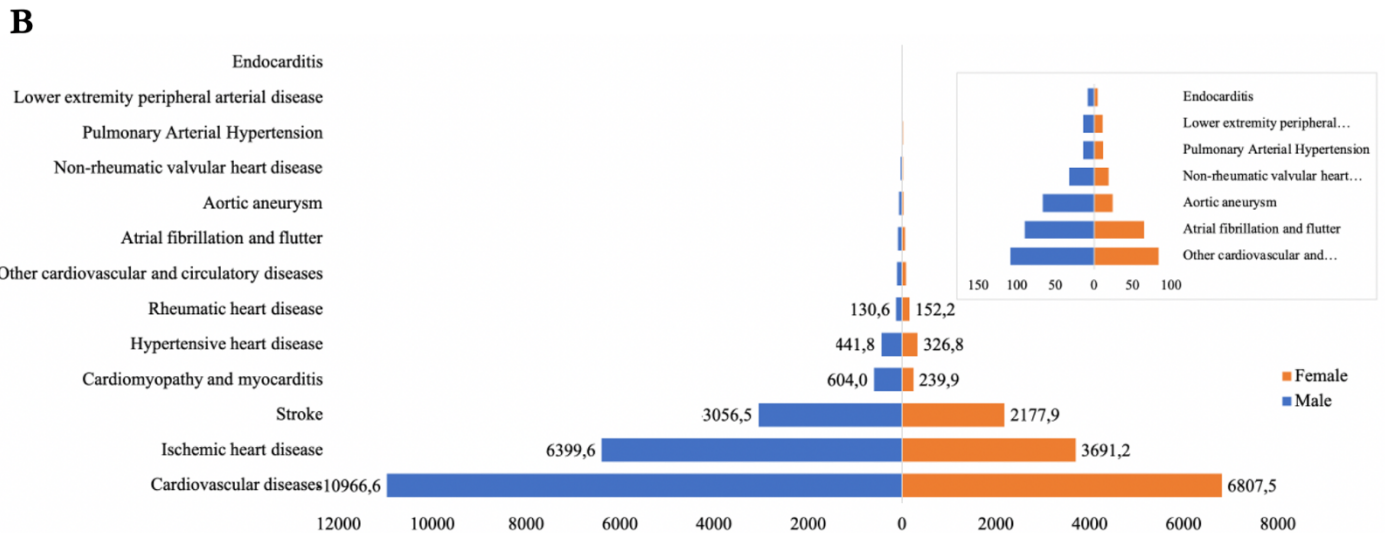
Ischemic heart disease and stroke remained the top contributors to CVD burden in 2021, accounting for 89% of the total ASDR (Table 1). Their respective ASDRs were 265.51 (95% UI: 240.67-290.42) and 124.06 (95% UI: 112.55-135.53), while their ASYRs were 4864.49 (95% UI: 4415.55-5338.75) and 2565.92 (95% UI: 2336.68-2798.31). Although the burden from most CVD subtypes declined between 1990 and 2021, a few showed an upward trend. Non-rheumatic valvular heart disease and cardiomyopathy experienced the largest relative increases in ASDR during this period - rising by 3.05% and 1.8%, respectively. Nevertheless, non-rheumatic valvular heart disease represented a

small fraction of the total CVD burden, contributing only 0.16% to the overall ASDR.

**Age-standardized CVD burden by gender**

As illustrated in Figure 2, the ASDR and ASYR for cardiovascular diseases were approximately 1.5 times greater in men than in women. In 2021, men in Central Asia had an ASDR of 538.16 per 100,000 population (95% UI: 492.78-583.90), while the ASDR among women was 365.74 (95% UI: 329.83-399.55) (Supplementary table 1). Similarly, ASYRs were higher in men at 10,966.59 (95% UI: 9981.13-11,976.28) than in women at 6,807.46 (95% UI: 6159.48-7438.62).





**Figure 2.** The rate of age-standardized of death (A) and disability-adjusted life years (DALYs) (B) of cardiovascular disease (CVD) and its 12 categories in Central Asia in 2021 by gender.

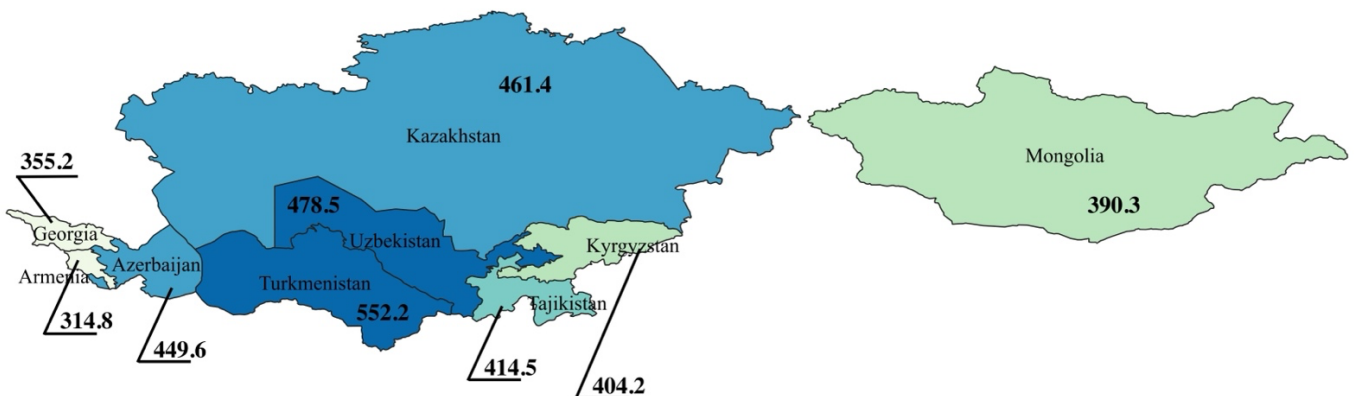
Among the 12 CVD subtypes, aortic aneurysm exhibited the most significant sex disparity. In men, the ASDR and ASYR for this condition were 3.08 (95% UI: 2.75-3.43) and 66.74 (95% UI: 58.94-75.55), respectively, whereas in women, the corresponding values were notably lower at 1.22 (95% UI: 1.07-1.39) and 24.25 (95% UI: 21.01-27.94). In contrast, rheumatic heart disease showed slightly higher ASDRs in women (3.43; 95% UI: 2.96-3.92) than in men (2.90; 95% UI: 2.54-3.29).

Ischemic heart disease and stroke were the leading contributors to CVD burden in both sexes, with consistently higher rates in men (Supplementary table 1). The ASDRs for ischemic heart disease and stroke in men were 336.53 (95% UI: 308.28-368.06) and 144.89 (95% UI: 131.18-158.75), respectively, while in women, these rates were 218.05 (95% UI: 195.72-238.69) and 108.86 (95% UI: 98.05-119.21). Corresponding ASYRs for men were 6399.61 (95% UI: 5807.8-7034.2) for

ischemic heart disease and 3056.46 (95% UI: 2769.64-3349.69) for stroke, compared to 3691.19 (95% UI: 3315.25-4051.95) and 2177.93 (95% UI: 1965.34-2392.43) in women.

**CVD burden in CA**

Figure 3 shows the ASDRs for CVDs in 2021 across nine Central Asian countries, based on estimates from the GBD study. Among these, four countries reported ASDRs above the regional average, with Turkmenistan recording the highest value at 552.2 per 100,000 population (95% UI: 453.6-672.8) (Figure 3). Uzbekistan, Kazakhstan, and Azerbaijan followed in terms of CVD-related mortality burden. A similar pattern was observed for ASYRs, with Turkmenistan again having the highest burden at 11,751.32 (95% UI: 9600.17-14,451.2), while Armenia had the lowest at 6,038.45 (95% UI: 5,491.88-6,673.52) (Supplementary table 2).



**Figure 3.** The map of CVD burden (age-standardized death rates per 100,000) in CA countries in 2021.

**Table 2.** The age-standardized death rate of CVD and its 12 categories for CA countries in 2021

	Turkme nistan	Republic of Uzbekistan	Republic of Kazakhsta n	Republic of Azerbaijan	Republic of Tajikistan	Kyrgyz Republic	Mongolia	Georgia	Republic of Armenia
Ischemic heart disease	343.7 (280.9 - 419.9)	339.5 (295.6 - 382.0)	235.9 (212.0 - 258.9)	306.1 (270.8 - 343.5)	244.9 (206.6 - 281.6)	274.4 (234.2 - 313.7)	219.6 (190.3 - 247.4)	124.2 (111.0 - 136.5)	209.8 (186.4 - 233.4)
Stroke	160.5 (128.7 - 194.0)	105.4 (92.2 - 121.5)	163.0 (144.2 - 183.1)	101.3 (85.3 - 120.1)	130.1 (105.4 - 154.8)	93.1 (79.4 - 107.4)	134.1 (109.1 - 159.6)	158.7 (141.1 - 176.1)	65.3 (57.3 - 72.9)
Hypertensive heart disease	20.9 (15.3 - 29.9)	19.6 (14.8 - 26.1)	9.23 (7.52 - 11.0)	20.4 (14.1 - 27.7)	33.5 (23.5 - 47.4)	17.7 (14.9 - 21.1)	9.01 (5.99 - 12.88)	44.8 (39.1 - 50.2)	15.0 (12.0 - 18.6)
Cardiomyopathy and myocarditis	15.8 (12.5 - 19.9)	2.29 (1.89 - 2.73)	41.8 (34.1 - 49.2)	14.2 (8.68 - 21.2)	1.20 (0.86 - 1.64)	9.88 (8.20 - 11.9)	15.8 (11.9 - 20.6)	6.30 (5.03 - 7.75)	4.64 (3.79 - 5.69)
Rheumatic heart disease	2.93 (2.18 - 3.90)	4.82 (3.93 - 5.74)	1.90 (1.46 - 2.35)	1.38 (0.83 - 1.99)	1.85 (1.38 - 2.48)	2.89 (2.35 - 3.59)	3.45 (2.86 - 4.10)	4.32 (3.69 - 5.07)	1.89 (1.36 - 2.32)
Atrial fibrillation and flutter	2.89 (2.27 - 3.76)	1.39 (1.18 - 1.60)	2.97 (2.57 - 3.34)	1.79 (1.39 - 2.21)	1.15 (0.92 - 1.44)	2.17 (1.82 - 2.49)	1.91 (1.49 - 2.44)	5.05 (4.37 - 5.62)	2.53 (2.18 - 2.86)
Aortic aneurysm	1.88 (1.42 - 2.67)	1.04 (0.85 - 1.28)	2.23 (1.79 - 2.71)	1.37 (0.93 - 2.08)	0.25 (0.18 - 0.34)	0.79 (0.63 - 0.96)	0.69 (0.53 - 0.89)	2.88 (2.43 - 3.35)	9.16 (7.61 - 10.8)
Non-rheumatic valvular heart disease	0.28 (0.22 - 0.37)	0.59 (0.48 - 0.73)	0.59 (0.49 - 0.69)	0.09 (0.07 - 0.14)	0.02 (0.01 - 0.03)	0.27 (0.22 - 0.33)	0.77 (0.61 - 0.97)	2.80 (2.42 - 3.21)	0.57 (0.48 - 0.67)
Lower extremity peripheral arterial disease	0.34 (0.25 - 0.47)	0.11 (0.09 - 0.14)	0.24 (0.19 - 0.29)	0.37 (0.17 - 0.71)	0.19 (0.12 - 0.33)	0.62 (0.51 - 0.74)	1.23 (0.78 - 1.87)	0.86 (0.72 - 1.00)	2.39 (1.99 - 2.83)
Pulmonary Arterial Hypertension	0.23 (0.17 - 0.31)	0.37 (0.29 - 0.46)	0.05 (0.04 - 0.06)	0.57 (0.36 - 0.85)	0.81 (0.53 - 1.09)	0.05 (0.04 - 0.06)	1.59 (0.91 - 2.05)	1.01 (0.79 - 1.27)	0.08 (0.06 - 0.09)
Endocarditis	0.26 (0.18 - 0.36)	0.14 (0.11 - 0.17)	0.33 (0.27 - 0.41)	0.03 (0.02 - 0.04)	0.03 (0.02 - 0.04)	0.12 (0.10 - 0.15)	0.22 (0.16 - 0.29)	0.28 (0.24 - 0.34)	0.09 (0.08 - 0.12)
Other cardiovascular and circulatory diseases	2.43 (1.83 - 3.21)	3.19 (2.64 - 3.80)	3.02 (2.56 - 3.51)	1.97 (1.33 - 2.69)	0.52 (0.38 - 0.71)	2.13 (1.79 - 2.54)	1.93 (1.43 - 2.59)	4.09 (3.48 - 4.72)	3.38 (2.82 - 3.95)

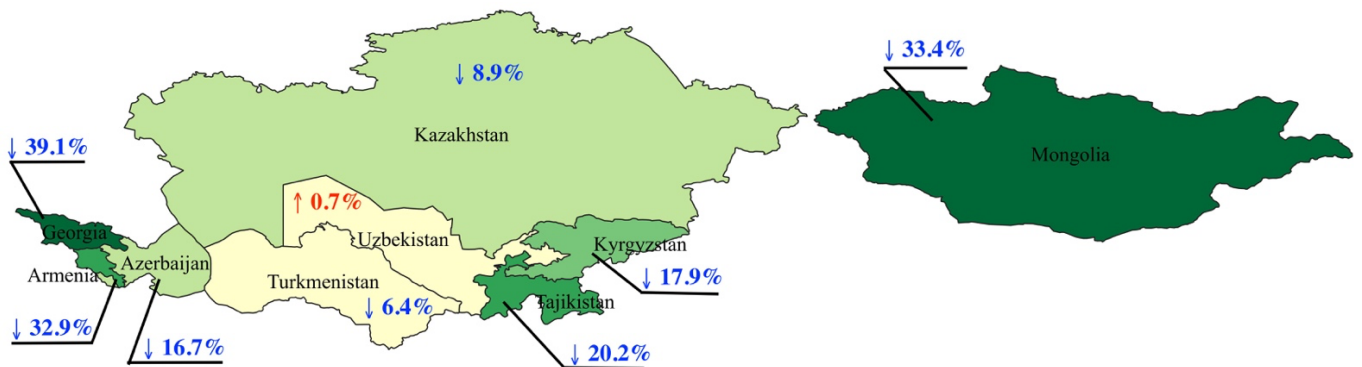
Table 2 presents the ASDRs for 12 categories of CVDs in CA in 2021. Across all countries, the highest burdens were attributed to ischemic heart disease, stroke, and hypertensive heart disease. However, in Kazakhstan and Mongolia, cardiomyopathy and myocarditis ranked third in terms of disease burden, with ASDRs of 41.8 (95% UI: 34.1-49.2) and 15.8 (95% UI: 11.9-20.6), respectively.

The highest ASDR for ischemic heart disease was observed in Turkmenistan (343.7; 95% UI: 280.9-

419.9), for stroke in Kazakhstan (163.0; 95% UI: 144.2-183.1), and for hypertensive heart disease in Georgia (44.8; 95% UI: 39.1-50.2). Notably, Kazakhstan and Mongolia reported substantially lower ASDRs for hypertensive heart disease than other Central Asian countries, at 9.23 (95% UI: 7.52-11.0) and 9.01 (95% UI: 5.99-12.8), respectively. The results of the percentage change in ASDRs and ASYRs from 1990 to 2021 are illustrated in Figure 4 and Supplementary Figure 1, respectively. Of the nine countries, Uzbekistan was the

only one to show a slight increase in ASDR, rising by just 0.7 (95% CI: -0.12 – 0.13). All other countries experienced a decline in both ASDRs and ASYRs over the study period. The most substantial reductions in

CVD burden were observed in Georgia, where both ASDR and ASYR decreased by 39.1%, and in Mongolia, which recorded 33.4% declines in ASDR and 34.8% in ASYR.

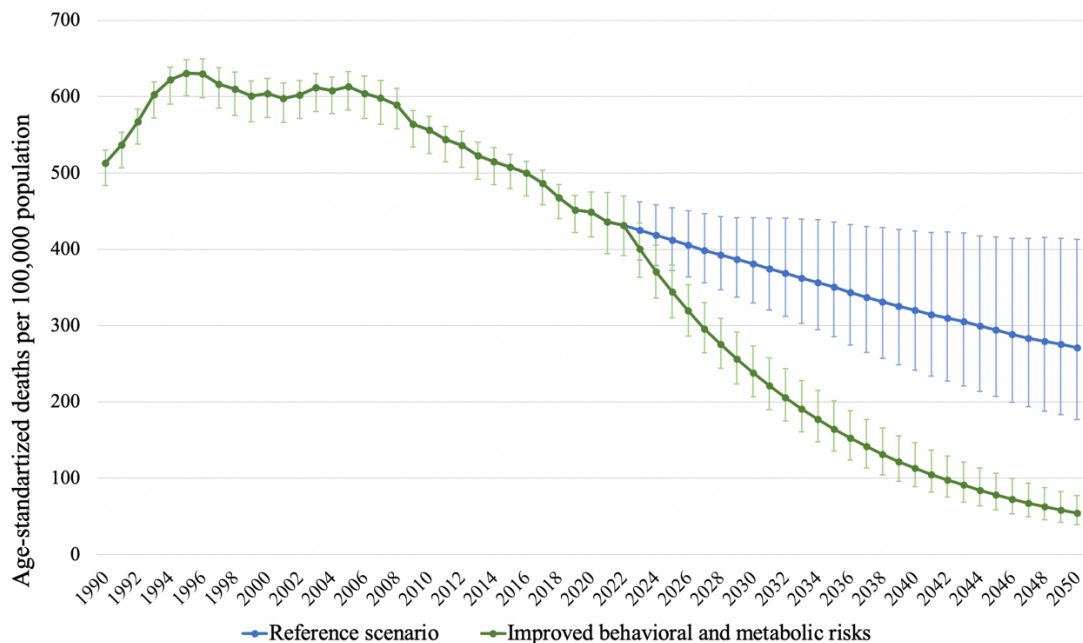


**Figure 4.** The relative change in ASDR of CVDs in Central Asian countries in 2021.

**CVD burden forecasting**

The GBD forecast of the CVD burden in Central Asia by 2050 is presented in Figure 5. Two scenarios are projected: the reference scenario and the improved behavioral and metabolic risks scenario. Although both predict a substantial reduction in the CVD burden across the region by 2050, the improved behavioral and

metabolic risks scenario indicates a more pronounced decline - from an ASDR of 436.10 (95% UI: 394.39-474.63) in 2021 to 51.11 (95% UI: 38.97-77.07) in 2050. In contrast, the reference scenario projects an ASDR of 270.90 (95% UI: 177.20-413.24) in 2050, with a considerably wider uncertainty interval spanning approximately 250 points.



**Figure 5.** Forecasted age-standardized death rates (ASDRs) for cardiovascular diseases in Central Asia from 2021 to 2050 under the GBD reference scenario and improved behavioral and metabolic risk scenario.

**Discussion**

Cardiovascular diseases continue to pose the greatest health burden in Central Asia, despite notable declines in age-standardized death rates and disability-adjusted life years between 1990 and 2021. In 2021, CVD accounted for an ASDR nearly double the rate for respiratory infections and tuberculosis, the second leading cause of death. Ischemic heart disease and

stroke were the leading causes of CVD burden in all the Central Asian countries. As for comparisons between countries, Turkmenistan has the highest burden of CVD, while Armenia had the lowest ASDR rate in 2021.

**CVD Subtypes: leading causes and patterns**

Ischemic heart disease and stroke remain the primary contributors to CVD-related deaths and

DALYs, accounting for approximately 89% of the total ASDR. According to the GBD Study from 2021, ischemic heart disease, ischemic stroke, and intracerebral hemorrhage were the leading causes of death globally (12). High systolic blood pressure (SBP) is a well-established and strongly harmful risk factor for ischemic heart disease (IHD) and stroke. Evidence from observational studies and clinical trials consistently demonstrates a clear dose-response relationship, indicating that the risk of IHD increases progressively with rising SBP levels (13). Even modest elevations in SBP above optimal levels are associated with a significantly increased likelihood of developing IHD, underscoring the critical importance of effective blood pressure control in cardiovascular disease prevention. According to the GBD 2021 Study, high systolic blood pressure is the modifiable risk factor with the highest burden for CVDs (14).

While the burden of most CVD subtypes declined, modest increases were observed in non-rheumatic valvular heart disease and cardiomyopathy. A similar trend is observed in China (15) and globally (16). This can be attributed to several interrelated factors. Firstly, population aging plays a central role, as non-rheumatic valvular heart disease (NRVHD) is an age-related condition with incidence rising substantially among older adults (16, 17). Secondly, improved health coverage and access to routine medical check-ups could lead to greater detection of both symptomatic and asymptomatic cases, contributing to higher reported incidence rates (18). Thirdly, increased life expectancy results in a larger elderly population at risk of developing NRVHD (19).

The ranking of CVD subtypes varies across countries. In Kazakhstan and Mongolia, for example, cardiomyopathy and myocarditis ranked third in disease burden, whereas hypertensive heart disease held this position in other Central Asian nations. This variability may reflect differences in national risk factor profiles, health care access, and quality of care, or to reporting or ICD coding biases in these countries. Additional epidemiologic research is needed to examine the distribution of these cardiac pathologies across these countries.

#### **Gender Disparities in CVD Burden**

Our findings revealed significant sex differences in CVD burden, with men experiencing nearly 1.5 times higher ASDR and ASYR than women. Physiologically, men tend to develop IHD at an earlier age than women, partly due to the protective effects of estrogen in premenopausal women, which delay the progression of atherosclerosis and reduce cardiovascular risk until menopause, after which risk rises sharply in women due to estrogen deficiency and

its impact on endothelial function, autonomic balance, and systemic inflammation (20). Behaviorally, men have a higher prevalence of modifiable risk factors such as smoking, which remains the most significant risk factor among males and contributes strongly to cardiovascular mortality (21). Additionally, men exhibit a more pronounced cardiovascular response to stress, characterized by elevated blood pressure and catecholamine surges, which may further increase their cardiovascular risk (22). Women, on the other hand, are more likely to present with non-obstructive coronary artery disease or microvascular dysfunction, which, although potentially underdiagnosed, often leads to lower mortality compared to the obstructive forms more commonly seen in men (23, 24). Furthermore, some studies suggest that women receive less aggressive referral to advanced testing and treatment for acute coronary events, but the overall lower burden of severe obstructive disease may partly mitigate this impact (25, 26). Lastly, differences in heart failure phenotypes, with men having higher rates of heart failure with reduced ejection fraction, associated with worse outcomes, also contribute to the disparity in ASDR and ASYR between sexes (27).

#### **Cross-Country Differences and Temporal Trends**

The analysis uncovered considerable heterogeneity in CVD burden among the nine Central Asian countries. Turkmenistan reported the highest ASDR and ASYR, while Armenia reported the lowest, indicating differing stages of epidemiological transition and differing capacities of public health systems. Turkmenistan's highest rates can be partially explained by the unfavorable trends in the prevalence of key NCD risk factors. According to a countrywide epidemiological study, alcohol consumption has significantly increased by 2020, including a 14% rise among women, and obesity rates have grown, particularly among men (28). The share of men with 1-2 risk factors rose by 4%, while the proportion of men without risk factors remains very low (below 17%) (28). These trends highlight persistent and emerging population-level health threats that contribute to Turkmenistan's substantial CVD burden, indicating the urgent need for targeted and locally adapted prevention strategies.

In the case of Armenia, according to WHO reports, the country has traditionally experienced lower mortality rates from CVDs than other Central Asian nations (29). In contrast, Kazakhstan had the highest stroke related ASDR, suggesting possible gaps in hypertension control and acute care services. The results may also reflect persistent disparities in community-based prevention and control of

hypertension, delays in ability to provide acute stroke care, and disparities in access to advanced cardiovascular specialty services. According to the nationwide study from Kazakhstan, based on admission and discharge reports, the all-cause mortality of stroke patients almost doubled between 2014 and 2019 (30), showing a concerning trend in stroke outcomes and highlighting potential deficiencies in early detection, timely intervention, and post-stroke management.

Between 1990 and 2021, all countries except Uzbekistan achieved reductions in ASDR and ASYR, with Georgia and Mongolia experiencing the most substantial improvements. The slight increase in Uzbekistan's ASDR may reflect limited progress in the country's healthcare response, particularly in the areas of disease prevention and effective treatment delivery. Despite broad health sector reforms since independence, Uzbekistan continues to face significant challenges such as underfunding, outdated infrastructure, shortages of trained personnel, and an overemphasis on hospital-based care (31, 32). Large differences in cardiovascular disease burden between Central Asian countries are likely to be explained not only by differences in risk factors but also by differences in health system capabilities and in levels of disease prevention and treatment facilities and access to specialized care for cardiovascular diseases.

### Projection of CVD Burden

Projections from the GBD forecasting model offer optimism. Under the improved behavioral and metabolic risk scenario, the ASDR for CVD in Central Asia is expected to decline by nearly 90% by 2050. Even the reference scenario predicts a substantial decrease. The wider uncertainty interval for the reference scenario reflects the total uncertainty of long-term projections of several critical assumptions such as population growth, socio-economic development, and major determinants of cardiovascular disease. The uncertainty regarding future outcomes of these health determinants allows for the design of flexible, adaptive disease prevention strategies. According to the GBD data for East Asia, South Asia, South-East Asia, Central Asia, and high-income Asia Pacific regions, the total number of deaths from cardiovascular diseases is projected to increase by 91.2% from 2025 to 2050, even though the age-standardized mortality rate is anticipated to decline by 23.0% (7). The improved-risk scenario projects a substantial decrease in the prevalence of major risk factors that contribute to CVD. However, the wide uncertainty intervals mean that actual future trends could be significantly affected by several factors including changes in policy and demographic trends not currently taken into account.

Reducing the burden of CVD may require a concerted effort to control hypertension, reduce tobacco use, and promote dietary improvements, in addition to other interventions.

Other studies use nationwide data to forecast the burden of CVDs worldwide. For example, Rehman and colleagues employed the non-homogeneous discrete grey model to forecast CVD mortality trends from 2020 to 2027 in six countries: Pakistan, India, China, Kenya, the USA, and Sweden, using mortality data from 2005 to 2019. Additionally, it introduced the Synthetic Relative Growth Rate and Doubling models to estimate the time required for CVD deaths to double or reduce. Findings suggest a continued rise in CVD-related deaths across all countries except Sweden, with the USA and China projected to experience the highest mortality (33). Despite China's anticipated death burden, it shows a relatively shorter doubling time, indicating potential for quicker mortality control (33). These insights highlight the urgent need for strengthened preventive strategies and health policy interventions to mitigate the global CVD burden. Findings support prioritization of blood pressure measurement, interventions to reduce tobacco consumption, and improvement of access to cardiovascular health care throughout the Central Asian region. The mortality rate for cardiovascular disease is declining on an age-standardized basis, but due to the population growth and aging, the absolute number of people dying from the disease will most likely continue to increase. Even though the age-standardized rate for the disease is decreasing, the challenge for the health care systems posed by the number of people suffering from the disease and by the number of people dying from it will not subside.

### Strengths and Limitations

Strengths of this study include the use of the comprehensive, systematically updated GBD dataset, which enables cross-country comparisons and long-term trend analysis. Including future projections across different scenarios provides valuable insight into the impact of policy choices on public health outcomes.

However, there are several limitations. First, GBD estimates rely on multiple data sources of varying quality, and some Central Asian countries may have underreported or incomplete mortality and morbidity data, especially in earlier years. Second, although age-standardized metrics allow comparison across time and countries, they may obscure within-country inequalities and subnational trends. Lastly, forecasting models are inherently uncertain and dependent on assumptions about future health policy, demographic changes, and data availability.

## Conclusion

This study confirms that cardiovascular disease remains the leading cause of mortality and disability in Central Asia, despite gradual progress since 1990. Wide variation exists between countries and between genders, with ischemic heart disease and stroke driving most of the burden. Projections suggest that significant reductions are possible by 2050 - particularly under scenarios that prioritize prevention and risk factor control. While age-standardized mortality is projected to decline, due to changes in the size and age structure of the population, the absolute number of cases and deaths from cardiovascular disease is likely to increase in the coming years. Health care requirements must therefore be planned on an on-going basis taking account of the anticipated increase in the number of

cases and deaths from cardiovascular disease. Targeted, evidence-based public health strategies tailored to regional needs are urgently required to realize these gains and reduce premature cardiovascular mortality in Central Asia.

### Abbreviations

ASDR - age-standardized death rates; ASYR - age-standardized DALY rates; CA - Central Asia; CVD - cardiovascular disease; DALY - disability-adjusted life year; DW - disability weight; GBD - Global Burden of Disease; IHD - ischemic heart disease; NCD - non-communicable disease; NRVHD - non-rheumatic valvular heart disease; SBP - systolic blood pressure; UI - uncertainty interval; YLD - years lived with disability; YLL - years of life lost due to premature death

## Acknowledgements

**Conflict of Interest:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**Data Availability Statement:** The datasets generated and/or analyzed during the current study are available in the GBD repository, <https://vizhub.healthdata.org/gb-results/>.

**Author Contributions:** Conceptualization, G.Z.; methodology, G.Z. and R.A.; validation, A.A., E. I., and Z.R.; formal analysis, G.Z.; investigation, N.G., A.O., and G.N.; resources, data curation, A.G.; writing - original draft preparation, G.Z. and R.A.; writing - review and editing, M.A. and A.O.; visualization, G.Z.; supervision, M.A. and A.G.; project administration, E.I. and A.R.; funding acquisition, A.G. All authors have read and agreed to the published version of the manuscript.

The preliminary results of this paper were presented at the Singapore Scientific Conference (December 8-11, 2025).

**Funding:** This study was supported by grants from the Ministry of Science and Higher Education of the Republic of Kazakhstan (Funder Project Reference: BR24992814, title: Development of innovative technologies and creation of modern infrastructure for sustainable development of South Kazakhstan region). The funder had no role in study design, data collection, and analysis, decision to publish, or preparation of the manuscript. A.G. is a PI of the project.

**Disclosure of AI Use:** No artificial intelligence (AI) tools or generative technologies were used in the preparation of this manuscript.

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