Postprint: Global Burden of Congenital Heart Defects, 1990-2021, and Future Trends Prediction

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Abstract

Background Congenital heart defects represent a common form of congenital malformation and constitute the leading cause of mortality among children under five years of age with birth defects in both developed and developing countries. Presently, congenital heart defects remain a substantial global health challenge, characterized by pronounced regional disparities and health inequities, with considerable scope for improvement in life-cycle disease management. Consequently, comprehensive evaluation of the disease burden attributable to congenital heart defects is imperative for formulating targeted prevention and treatment strategies.

Objective To examine the temporal evolution of the disease burden of congenital heart defects from 1990 to 2021 and project developmental trends through 2050, thereby providing an evidence base for policy formulation and offering insights toward achieving the 2030 Sustainable Development Goals.

Methods Utilizing the 2021 Global Burden of Disease database (GBD 2021), we quantified and analyzed the absolute numbers and age-standardized rates of prevalence, mortality, disability-adjusted life years (DALYs), and years lived with disability (YLDs) for congenital heart defects globally, across 21 regions, and in 204 countries. Correlation analysis, health inequality analysis, and frontier analysis were integrated to comprehensively characterize the disease burden and temporal trends. A Bayesian age-period-cohort model was employed to forecast the disease burden from 2022 to 2050.

Results In 2021, the global age-standardized rates of prevalence, mortality, DALYs, and YLDs for congenital heart defects were 210.70/100,000, 3.86/100,000, 345.24/100,000, and 14.25/100,000, respectively. The estimated average annual percentage change (AAPC) from 1990 to 2021 was

0.02%, -2.53%, -2.48%, and 0.11%, respectively. During 1990–2021, low Socio-demographic Index (SDI) regions exhibited the highest age-standardized mortality and DALYs rates, whereas high SDI regions demonstrated the highest age-standardized prevalence and YLDs rates. SDI demonstrated positive correlations with age-standardized prevalence rate (=0.45, P<0.001) and age-standardized YLDs rate (=0.71, P<0.001) of congenital heart defects. Conversely, SDI showed negative correlations with age-standardized mortality rate and DALYs rate (both =-0.54, both P<0.001). Absolute health inequality in congenital heart defects decreased from 1990 to 2021, while relative health inequality increased. Projections indicate that by 2050, the global age-standardized rates of prevalence, mortality, DALYs, and YLDs will reach 218.24/100,000, 0.91/100,000, 118.48/100,000, and 14.73/100,000, respectively.

Conclusion From 1990 to 2021, the global disease burden of congenital heart defects exhibited a declining trend, with regional burden decreasing as SDI increased.

Full Text

Changes and Trend Prediction in the Global Burden of Congenital Heart Defects, 1990-2021

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Abstract

Background: Congenital heart defects represent a common form of congenital malformation and constitute the leading cause of death among children under five years of age with birth defects in both developed and developing countries. Currently, congenital heart defects remain a major global health challenge, characterized by pronounced regional disparities and health inequities, with considerable room for improvement in lifecycle disease management. Comprehensive assessment of the disease burden is therefore essential for developing targeted prevention and treatment strategies.

Objective: To examine changes in the burden of congenital heart defects from 1990 to 2021 and project trends through 2050, providing evidence for policy formulation and contributing to the achievement of the 2030 Sustainable Development Goals.

Methods: Using the 2021 Global Burden of Disease Database (GBD 2021), we analyzed the number and age-standardized rates of prevalence, mortality, disability-adjusted life years (DALYs), and years lived with disability (YLDs) for congenital heart defects across 204 countries and 21 regions. We employed correlation analysis, health inequality analysis, and frontier analysis to comprehensively characterize disease burden and trends, and utilized a Bayesian age-period-cohort model to forecast burden from 2022 to 2050.

Results: In 2021, the global age-standardized rates of prevalence, mortality, DALYs, and YLDs for congenital heart defects were 210.70/100,000, 3.86/100,000, 345.24/100,000, and 14.25/100,000, respectively. The corresponding estimated average annual percentage changes (AAPC) from 1990 to 2021 were 0.02%, -2.53%, -2.48%, and 0.11%. During 1990-2021, low socio-demographic index (SDI) regions exhibited the highest age-standardized mortality and DALYs rates, while high SDI regions showed the highest prevalence and YLDs rates. SDI correlated positively with age-standardized prevalence (=0.45, P<0.001) and YLDs rates (=0.71, P<0.001), but negatively with mortality (=-0.54, P<0.001) and DALYs rates (=-0.54, P<0.001). Absolute health inequality decreased while relative inequality increased. Projections to 2050 indicate that global age-standardized rates will reach 218.24/100,000 for prevalence, 0.91/100,000 for mortality, 118.48/100,000 for DALYs, and 14.73/100,000 for YLDs.

Conclusion: From 1990 to 2021, the global burden of congenital heart defects declined, with regional burden decreasing as SDI increased.

Keywords: Cardiovascular diseases; Congenital heart defects; Global burden of disease; Trend analysis; Health inequalities analysis; Prediction model

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Congenital heart defects refer to structural developmental abnormalities of the heart or great vessels. Advances in medical technology have substantially improved survival rates, with over 90% of affected children now surviving to adulthood. A systematic analysis of 260 studies from 1970-2017 found that global prevalence has been increasing by approximately 10% every five years. The economic burden is substantial: a 2017 U.S. cross-sectional study revealed that nearly 50% of families with affected children experienced financial hardship due to medical costs, with 17% unable to pay medical bills in full.

Congenital birth defects account for 9.4% of deaths among children under five globally, making congenital heart defects a critical barrier to achieving Sustainable Development Goal 3.2, which aims to reduce under-five mortality to fewer than 25 deaths per 1,000 live births by 2030. Research using GBD 2017 data demonstrated that congenital heart defect mortality decreases with rising socio-demographic index (SDI), while prevalence increases with SDI, though without detailed analysis of individual countries and regions. A GBD 2019 analysis showed that despite overall declining mortality, congenital heart defects remain the leading cause of non-communicable disease death among individuals under 20, with widening international disparities. However, no studies have reported on disease burden using the latest GBD 2021 data. This study aims to comprehensively examine the relationship between congenital heart defects burden and SDI by analyzing prevalence, mortality, DALYs, and YLDs, assessing variations across countries and regions, and providing scientific evidence for optimal health outcomes and prevention strategies.

1.1 Data Sources

This study utilized GBD 2021 (https://vizhub.healthdata.org), which includes health loss data for 371 diseases and injuries across 204 countries and 811 subnational locations. We extracted data on congenital heart defect prevalence, mortality, DALYs, and YLDs from 1990-2021. GBD classifies causes into four levels, with congenital heart defects categorized as a Level 4 disease. DALYs measure disease burden in years lost due to ill health, disability, or early death. SDI is a composite indicator of development status, with GBD 2021 dividing 204 countries and 21 regions into five categories: low, low-middle, middle, high-middle, and high SDI.

1.2 Statistical Methods

To eliminate the influence of age distribution differences, we first applied direct age standardization using the world standard population age structure from GBD 2021. The standardized rate was calculated as: standardized rate = Σ(age-specific rate × proportion of standard population in corresponding age group).

We then conducted trend analysis using Joinpoint regression, which calculates the average annual percentage change (AAPC) and 95% confidence intervals (95%CI) through optimal model fitting with logarithmic transformation of rates. AAPC = (e^β - 1) × 100%, where β is the regression coefficient from the log-linear model lny = βx. Trends were interpreted as increasing when 95%CI > 0, decreasing when 95%CI < 0, and stable when 95%CI included 0.

To explore the relationship between development level and disease burden, we employed a dual-dimensional analytical framework. Spearman rank correlation analysis quantified the association strength between SDI and standardized rates (values). Frontier analysis assessed optimization potential by calculating the "effective difference" between observed and theoretically achievable minimum burden based on SDI-defined best-practice frontiers. This distance represents the gap between observed burden and potential minimum burden achievable through optimized resource allocation.

For health equity assessment, we integrated two complementary indicators: (1) the inequality slope index, which measures absolute burden differences between

SDI extremes (positive values indicating burden concentration in high-SDI countries, negative values in low-SDI countries, with absolute magnitude reflecting inequality severity); and (2) the concentration index, calculated through integration of Lorenz concentration curves (range -1 to 1), where negative values indicate burden concentration in low-SDI countries. These metrics provide comprehensive evaluation from both absolute difference and relative distribution perspectives.

We constructed a Bayesian age-period-cohort model to forecast prevalence, mortality, DALYs, and YLDs from 2022-2050. This model generates posterior distributions by integrating prior information with sample data, providing estimates with 95% uncertainty intervals (UI) and effectively handling time-dependent and demographic variation data. All analyses were performed using R version 4.3.3, with P<0.05 considered statistically significant.

2.1 Disease Burden of Congenital Heart Defects at Global, National, and Regional Levels, 1990-2021

From 1990-2021, the global burden of congenital heart defects showed a declining trend. In 2021, the number of prevalent cases was 15.77 million (95%UI=14.04-17.39 million), deaths 250,000 (95%UI=207,800-304,100), DALYs 22.31 million person-years (95%UI=18.70-27.21 million), and YLDs 1.04 million person-years (95%UI=598,100-1,608,700), representing changes of +33.83%, -52.58%, -52.35%, and +31.02% from 1990, respectively.

The 2021 age-standardized rates were 210.70/100,000 (95%UI=187.92-232.48) for prevalence, 3.86/100,000 (95%UI=3.19-4.70) for mortality, 345.24/100,000 (95%UI=288.34-422.16) for DALYs, and 14.25/100,000 (95%UI=8.27-21.88) for YLDs. Corresponding AAPCs from 1990-2021 were 0.02% (95%CI=0.01-0.02), -2.53% (95%CI=-2.56 to -2.50), -2.48% (95%CI=-2.51 to -2.46), and 0.11% (95%CI=0.09-0.12). In 2021, males had higher numbers of deaths, DALYs, and YLDs than females (male:female ratios of 1.26:1, 1.26:1, and 1.05:1, respectively), while female prevalence was approximately 1.06 times that of males.

Across the five SDI regions, standardized mortality and DALYs rates declined from 1990-2021. Low-SDI regions consistently showed the highest rates, while high-SDI regions showed the highest prevalence and YLDs rates. The high-middle SDI region experienced the largest declines in mortality and DALYs rates (AAPC=-4.33%, 95%CI=-4.51 to -4.14; and AAPC=-4.25%, 95%CI=-4.42 to -4.08, respectively). For prevalence and YLDs rates, all regions except high-SDI showed increasing trends .

Among the 21 GBD regions in 2021, the highest standardized prevalence, mortality, DALYs, and YLDs rates were observed in high-income Asia Pacific, Oceania, Oceania, and Western Europe, respectively, while the lowest rates were in Southern Latin America, high-income Asia Pacific, Australasia, and Eastern Sub-Saharan Africa. Despite overall global decline, most regions showed increasing prevalence and YLDs rates, with Eastern Asia showing the largest increase in YLDs rate (AAPC=0.46%, 95%CI=0.44-0.48) and Southern Latin America showing the largest increase in prevalence (AAPC=0.20%, 95%CI=0.17-0.22). High-income Asia Pacific had the largest declines in mortality and DALYs rates (AAPC=-4.98%, 95%CI=-5.35 to -4.62; and AAPC=-4.50%, 95%CI=-4.81 to -4.19), while Central Asia was the only region with increasing mortality and DALYs rates .

Among 204 countries in 2021, Austria, Afghanistan, Afghanistan, and Armenia had the highest standardized prevalence, mortality, DALYs, and YLDs rates, respectively, while Greenland, San Marino, San Marino, and Ethiopia had the lowest. From 1990-2021, 93.63% of countries showed declining mortality and DALYs rates, with Estonia and Belarus experiencing the largest declines. Meanwhile, 72.55% of countries showed increasing prevalence, and 80.00% showed increasing YLDs rates.

2.2 Correlation Between SDI and Congenital Heart Defects

SDI correlated positively with standardized prevalence (=0.45, P<0.001) and YLDs rates (=0.71, P<0.001), but negatively with mortality (=-0.54, P<0.001) and DALYs rates (=-0.54, P<0.001). Notably, standardized mortality and DALYs rates initially increased with SDI before peaking and then declining [Figure 1: see original paper].

2.3 Health Inequality Analysis of Congenital Heart Defects, 1990-2021

Health inequality analysis revealed that disease burden disproportionately concentrated in low-SDI countries and regions, with inequality increasing over time. The concentration index for mortality and DALYs rose from -0.27 in 1990 to -0.39 in 2021. The inequality slope index for mortality and DALYs decreased from -16 to -6 and from -1,431 to -535, respectively. Thus, while absolute health inequality decreased, relative inequality increased [Figure 2: see original paper].

2.4 Optimization Space Analysis for Congenital Heart Defects, 1990-2021

Frontier analysis identified Afghanistan, Tokelau, Haiti, Niue, and Yemen as having the largest effective differences from theoretical boundaries. For DALYs rates, high-SDI countries such as Monaco, Lithuania, and Switzerland showed relatively high effective differences, indicating substantial gaps between observed and potentially achievable minimum burden. This suggests considerable room for improvement even in well-resourced settings [Figure 3: see original paper].

2.5 Projected Global Burden of Congenital Heart Defects, 2022-2050

Projections indicate that by 2050, global congenital heart defects will reach 19.16 million prevalent cases (95%UI=8.10-30.22 million), 90,800 deaths (95%UI=1,500-406,500), 8.36 million DALYs (95%UI=0.26-17.55 million), and 1.21 million YLDs (95%UI=0.44-1.98 million). Age-standardized rates are projected to reach 218.24/100,000 (95%UI=88.31-348.17) for prevalence, 0.91/100,000 (95%UI=0.01-4.33) for mortality, 118.48/100,000 (95%UI=2.67-250.43) for DALYs, and 14.73/100,000 (95%UI=5.17-24.30) for YLDs. The decline in burden will be greater among males than females, with persistent gender and regional disparities [Figure 4: see original paper].

Discussion

From 1990-2021, the global burden of congenital heart defects declined, with higher burden observed in males and in low-SDI regions. Significant variation exists across countries and regions, with children and adolescents bearing a substantial burden. These findings underscore the need for lifecycle management, improved transition from pediatric to adult care, and prevention of late complications to reduce overall burden.

The increasing prevalence reflects multiple factors. Changing fertility patterns have led to delayed childbearing and increased maternal age, while improved diagnostic capabilities enable better detection during pregnancy and after birth. Additionally, evolving legal and religious contexts have facilitated prenatal screening and voluntary termination of pregnancies with severe defects. The observed prevalence increase likely represents improved detection rather than true increase in incidence. The heavier burden among males may relate to biological, hormonal, and fetal stress differences, though evidence remains limited. Systemic inequalities, structural barriers, and socioeconomic determinants of health contribute to the observed SDI correlations and widening health inequities, yet substantial improvement potential exists.

Congenital heart defects remain the leading cause of death from birth defects among children under five globally. Policymakers should consider gender, age, SDI, and regional factors to develop targeted, individualized care strategies. Access to care is a critical predictor of survival, necessitating rational resource allocation, enhanced telehealth capacity, increased medical infrastructure and specialists in low-SDI regions, and strengthened prenatal and postnatal diagnosis. Timely surgical intervention, quality improvement, and multidisciplinary collaboration are essential to reduce regional disparities.

This study has several limitations. First, underdeveloped regions may have limited epidemiological surveillance capacity, leading to underreporting. Second, diagnostic standard variations may affect comparability. Third, GBD limitations preclude analysis of specific defect types or risk factors, and limited primary data from low-income countries may lead to overestimation of burden in these settings. Finally, GBD' s single-cause mortality framework may exclude deaths from late complications like pulmonary hypertension or heart failure in older populations.

In conclusion, the global burden of congenital heart defects decreased from 1990-2021, with higher burden in low-SDI regions and among males. Despite overall decline, significant regional disparities persist, particularly affecting children and adolescents. These findings highlight the need for comprehensive lifecycle management and targeted interventions to reduce the burden of congenital heart defects.

Author Contributions: ZHANG Bingqing, WANG Zhongkai, and PENG Yunzhu designed the study, wrote, and revised the manuscript. WU Changyong performed data analysis and figure preparation. SUN Huang and LI Ruijie conducted data verification and study design. LIU Wenjie performed data validation. LUO Yihua and ZHENG Lihui collected and organized data. PENG Yunzhu provided quality control and final approval. All authors confirmed the final manuscript.

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