

Evolving global patterns of congenital heart anomalies from 1990 to 2021

Enhui Yang¹, Hao Lin², Yuansi Zhang³, Yu Zhang^{1*}, Feng Chen^{1,4,5*}

¹Department of Child Healthcare, Wenzhou People's Hospital, Zhejiang Province, China

²Department of Gastroenterology, Pingyang Hospital of Wenzhou Medical University, Zhejiang Province, China

³Department of Traditional Chinese Medicine, Wenzhou Yebo Proctology Hospital, Zhejiang Province, China

⁴Children's Heart Center, Institute of Cardiovascular Development and Translational Medicine, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Zhejiang Province, China

⁵Zhejiang Provincial Clinical Research Center for Pediatric Disease, Zhejiang Province, China

*Corresponding authors:

Feng Chen

Yu Zhang

Department of

Child Healthcare

Wenzhou People's Hospital

Zhejiang Province

325000, China

E-mail:

chenfeng19920410@126.com,

25457057@qq.com

Submitted: 26 February 2025; **Accepted:** 18 May 2025

Online publication: 23 June 2025

Arch Med Sci

DOI: <https://doi.org/10.5114/aoms/205265>

Copyright © 2025 Termedia & Banach

Abstract

Introduction: Congenital heart anomalies (CHAs) remain a significant global health issue for children, evidenced by persistent disparities in healthcare access across different socio-demographic index (SDI) regions and genders, despite slight decreases in prevalence.

Material and methods: This cross-sectional study used the Global Burden of Disease 2021 dataset to analyze CHAs in children aged 0–14 from 204 countries. Data analysis was performed using R software, incorporating global mapping, Joinpoint regression, and estimation of annual percent changes and rates, stratified by age, sex, and SDI.

Results: A total of 218,909,652 children, including 113,892,505 (52.03%) males and 105,017,147 (47.97%) females, were included in the analysis. From 1990 to 2021, the global prevalence of CHAs in children decreased by 4.294% (95% uncertainty interval [UI], –5.696–2.695%). Over three decades, CHA-associated deaths decreased from 497,979 (95% UI: 282,166–642,052) to 222,415 (95% UI: 181,359–275,182). The global mortality rate decreased from 28.633 (95% UI: 16.224–36.918) to 11.055 (95% UI: 9.014–13.678) per 100,000 population, while the prevalence rate changed from 377.257 cases per 100,000 in 1990 to 361.060 cases per 100,000 in 2021. Among the five SDI regions, the low SDI region had the highest CHA-associated mortality rate in 2021.

Conclusions: The study highlights the persistent global challenge of CHAs, particularly in low-SDI regions. It underscores the need for targeted public health interventions to reduce disparities and improve health outcomes globally.

Key words: congenital heart defects, child health, global health, health disparities, epidemiological monitoring.

Introduction

Congenital heart anomalies (CHAs) represent a major burden to global child health, particularly in regions with a low Socio-demo-

graphic Index (SDI) [1]. Although global data from 1990 to 2021 show a modest decline in the overall prevalence of CHAs, mortality rates remain disproportionately high in low-SDI areas, reflecting persistent gaps in public health infrastructure and access to medical care. This disparity underscores that while prevalence has only slightly decreased, the associated mortality has declined more markedly, likely due to advancements in diagnosis and treatment in high-SDI settings [2, 3].

Recent advancements in CHA diagnosis and treatment, such as routine use of fetal echocardiography and pulse oximetry for early screening, and the critical roles of 3D printing and virtual reality in surgical planning, have been significant [4–8]. Additionally, the advancement of interventional catheter techniques and minimally invasive surgical approaches has expanded treatment options, reduced surgical risks, and improved long-term outcomes. However, data from 204 countries reveal significant regional variations in CHA incidence and mortality rates, with the highest mortality rates in low-SDI regions. These findings underscore the impact of disparities in public health strategies and healthcare services across regions on the survival and quality of life of CHA patients.

In the Global Burden of Disease (GBD) framework, CHAs are classified into five sub-categories based on anatomical features and treatment requirements: 1) single ventricle and single ventricle pathway defects; 2) complex congenital heart defects excluding single ventricle cases; 3) malformations of great vessels, congenital valvular heart disease, and patent ductus arteriosus; 4) ventricular septal defects (VSD) and atrial septal defects (ASD); and 5) other congenital cardiovascular anomalies. A proportion of VSD/ASD cases with favorable outcomes and no clinical symptoms are modeled as asymptomatic. These classifications enable more accurate modeling and burden estimation of CHA worldwide [9].

This study used the Global Burden of Disease (GBD) database to analyze CHA trends and outcomes in children across socioeconomic backgrounds, aiming to provide insights for healthcare professionals to refine prevention and management strategies and ultimately reduce CHAs' global impact on children.

By leveraging the most up-to-date GBD 2021 data, the study further examined disparities across SDI levels and between sexes, addressing gaps in current literature. These findings are intended to inform equitable resource allocation and guide public health planning toward improving cardiovascular outcomes among children worldwide.

Material and methods

Data collection and approval

This cross-sectional study was approved by the Ethical Board of Wenzhou People's Hospital, with a waiver of informed consent granted due to the use of de-identified data analysis. Data concerning children aged 0 to 14 years with CHAs were collected using the Global Health Data Exchange tool developed by the GBD study collaborators, covering prevalence, mortality, and disability-adjusted life years (DALYs). DALYs are a summary measure used to quantify the overall burden of disease. They represent the total number of healthy years lost due to illness, disability, or premature death. DALYs are the sum of two components: years of life lost (YLLs) due to premature mortality and years lived with disability (YLDs) due to time spent in less than full health. These metrics were assessed for the period 1990–2021 across 204 countries and territories (10).

Global and regional burden analysis

We generated global maps and regional comparative analyses to explore the burden of CHAs, using R (version 4.4.1) with ggplot2 and sf packages for visualization.

Temporal trend analysis

Trends in CHA metrics from 1990 to 2021 were assessed using Joinpoint regression analysis with the Joinpoint R package, calculating both annual percent change (APC – the yearly percentage change of a specific health indicator over a given time period; it reflects the direction and magnitude of the trend, typically calculated using a log-linear regression model, and represents the relative change per year compared to the previous year) and estimated annual percentage change (EAPC – a summary measure derived from fitting a regression model to time-series data, estimating the average annual percent change over time; it includes a 95% confidence interval and is widely used in epidemiological studies to assess whether the trend of a health outcome is increasing, decreasing, or stable over a specific period) with 95% CIs to identify significant changes over time.

Population and SDI analysis

Population-level data were stratified by age, sex, and SDI categories, analyzing the relationship between socioeconomic development and CHA burden. Descriptive statistics and SDI-specific disease rates were computed, with data manipulation and visualization conducted using dplyr and ggplot2 packages in R.

Statistical analysis

All statistical procedures were performed in R Studio, with results presented as means along with 95% uncertainty intervals. Significance was determined using two-sided tests with p -values < 0.05.

Results

CHAs in children: global trends

Prevalence

A total of 218,909,652 children – 113,892,505 (52.03%) males; 105,017,147 (47.97%) females – were included in the analysis. From 1990 to 2021, the global prevalence of CHAs decreased by 4.294% (95% UI: –5.696–2.695%). The cor-

responding prevalence rate decreased accordingly from 377.257 cases per 100,000 people (95% UI: 333.461–424.687) in 1990 to 361.060 cases per 100,000 people (95% UI: 320.042–406.507) in 2021; the EAPC was 0.007 (95% CI: –0.041 to –0.055) (Table I).

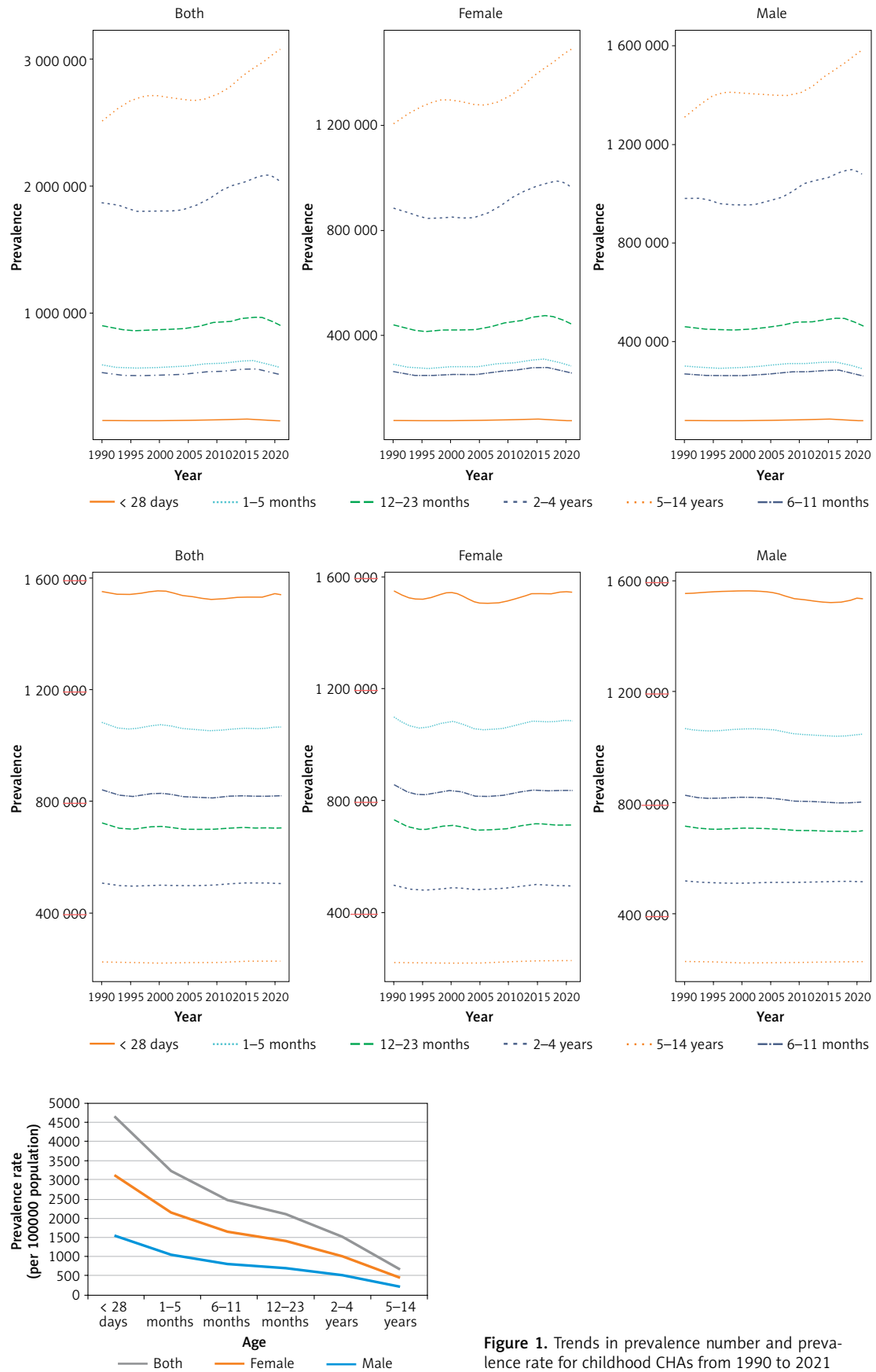
From 1990 to 2021, the prevalence among children under one year of age showed a declining trend, with the most significant decrease observed in neonates within the first 28 days of life (3.661%). Conversely, the prevalence among children over 1 year of age increased, with the most pronounced increase observed in children aged 5 to 14 years (22.423%). In 1990 and 2021, the prevalence rates of CHAs in neonates within the first 28 days of life were 1.551% and 1.539%, re-

Table I. Prevalence of CHA in children from 1990 to 2021 globally, in five SDI regions, and 21 areas

Location	Rate per 100 000 (95% UI)					
	1990		2021		1990-2021	
	Prevalence number	Prevalence rate	Prevalence number	Prevalence rate	Percent change	EAPC
Global	6561075.196 (5799385.971–7385953.323)	377.257 (333.461–424.687)	7264017.670 (6438791.054–8178361.477)	361.060 (320.042–406.507)	–4.294 (–5.696–2.695)	0.007 (–0.041–0.055)
SDI						
High	756338.687 (674838.315–846643.680)	407.054 (363.192–455.656)	677421.951 (602130.069–764377.151)	392.625 (348.987–443.023)	–3.545 (–5.247–1.927)	–0.041 (–0.067–0.014)
High-middle	1054061.147 (934616.498–1193535.294)	385.224 (341.571–436.197)	842046.563 (747054.029–949359.032)	364.695 (323.554–411.173)	–5.329 (–7.983–2.519)	0.162 (0.033–0.292)
Middle	2073587.244 (1834609.215–2333774.909)	359.241 (317.839–404.317)	1950145.474 (1735293.441–2196938.987)	344.025 (306.123–387.562)	–4.235 (–6.961–1.162)	0.056 (–0.021–0.132)
Low-middle	1761024.506 (1534004.409–2000880.191)	373.010 (324.924–423.815)	2068011.022 (1819242.446–2328074.302)	356.651 (313.748–401.502)	–4.386 (–6.527–1.958)	–0.032 (–0.067–0.003)
Low	910463.580 (794505.006–1043123.907)	397.733 (347.077–455.685)	1720886.063 (1502752.478–1968948.507)	373.922 (326.525–427.822)	–5.987 (–7.802–3.900)	–0.177 (–0.205–0.149)
Region						
Andean Latin America	580863.723 (518784.724–650666.635)	328.986 (292.353–371.310)	59736.814 (52609.045–67566.720)	330.133 (290.741–373.404)	0.348 (–2.801–3.711)	0.024 (–0.040–0.088)
Australasia	15563.430 (13554.943–17826.952)	339.371 (295.575–388.729)	19705.507 (17077.271–22656.820)	343.832 (297.973–395.328)	1.314 (–2.864–5.665)	0.051 (–0.005–0.107)
Caribbean	39062.180 (34635.883–43907.510)	342.278 (303.493–384.734)	37694.106 (33462.278–42280.413)	327.630 (290.847–367.493)	–4.280 (–6.893–1.473)	–0.143 (–0.170–0.115)
Central Asia	143931.245 (125917.168–164817.490)	575.927 (503.846–659.502)	164093.817 (143263.149–187731.043)	592.915 (517.648–678.322)	2.950 (–0.123–5.961)	0.316 (0.146–0.486)
Central Europe	129496.924 (113119.099–148653.545)	439.217 (383.668–504.190)	81427.131 (71052.107–93517.904)	460.009 (401.397–528.313)	4.734 (2.112–7.373)	0.270 (0.183–0.358)

Table I. Cont.

Location	Rate per 100 000 (95% UI)					
	1990		2021		1990-2021	
	Prevalence number	Prevalence rate	Prevalence number	Prevalence rate	Percent change	EAPC
Central Latin America	242038.775 (216161.668–271995.643)	375.946 (335.753–422.477)	242666.153 (215804.444–273317.688)	382.242 (339.930–430.524)	1.675 (–0.996–4.762)	0.077 (0.060–0.093)
Central Sub-Saharan Africa	108524.062 (93709.398–126240.365)	428.972 (370.413–499.001)	225413.558 (196011.198–260846.310)	384.130 (334.025–444.511)	–10.453 (–15.203–5.293)	–0.304 (–0.360–0.248)
East Asia	1183969.606 (1035172.409–1350105.265)	358.959 (313.847–409.329)	868331.289 (768970.942–985422.838)	324.789 (287.625–368.586)	–9.519 (–14.135–4.616)	0.099 (–0.069–0.267)
Eastern Europe	233063.599 (202388.332–267448.175)	452.885 (393.277–519.701)	149291.310 (129500.974–171810.392)	421.203 (365.367–484.737)	–6.996 (–9.278–4.677)	0.330 (0.125–0.536)
Eastern Sub-Saharan Africa	327266.583 (286693.632–372453.772)	361.338 (316.541–411.230)	588697.751 (517030.881–665777.841)	329.929 (289.764–373.128)	–8.692 (–10.929–6.520)	–0.305 (–0.333–0.277)
High-income Asia Pacific	157127.020 (140786.085–175982.599)	446.389 (399.966–499.957)	98720.535 (88247.662–110436.529)	440.215 (393.514–492.459)	–1.383 (–3.686–1.082)	–0.039 (–0.067–0.010)
High-income North America	225228.901 (198567.580–254606.953)	365.171 (321.944–412.803)	223601.653 (195008.810–254350.991)	340.758 (297.184–387.618)	–6.685 (–10.084–3.197)	–0.215 (–0.259–0.171)
North Africa and Middle East	580863.723 (518784.724–650666.635)	413.469 (369.280–463.156)	755278.647 (673064.252–847038.987)	411.996 (367.149–462.050)	–0.356 (–2.063–1.434)	0.125 (0.072–0.177)
Oceania	9179.169 (8051.932–10451.682)	342.524 (300.460–390.008)	17728.692 (15514.732–20228.459)	348.930 (305.356–398.130)	1.870 (–1.871–6.322)	0.077 (0.045–0.109)
South Asia	1578563.096 (1374375.380–1808753.921)	364.260 (317.143–417.377)	1739986.599 (1531917.779–1978758.563)	343.178 (302.141–390.271)	–5.788 (–8.078–3.110)	–0.043 (–0.094–0.007)
Southeast Asia	550689.516 (485755.221–624092.387)	322.517 (284.487–365.506)	541644.584 (477983.560–614801.768)	313.718 (276.845–356.090)	–2.728 (–4.359–1.185)	–0.073 (–0.089–0.057)
Southern Latin America	45729.017 (39807.231–52189.978)	306.363 (266.689–349.648)	45050.680 (38999.990–51535.761)	310.790 (269.048–355.529)	1.445 (–4.223–7.565)	0.130 (0.094–0.166)
Southern Sub-Saharan Africa	81754.747 (72474.642–92532.816)	395.154 (350.300–447.249)	93772.052 (83404.382–106070.146)	389.648 (346.567–440.750)	–1.394 (–4.080–1.925)	0.080 (0.024–0.136)
Tropical Latin America	178942.019 (160965.020–199995.341)	333.760 (300.230–373.028)	164218.704 (146205.026–183555.033)	327.174 (291.285–365.698)	–1.973 (–5.867–1.824)	–0.030 (–0.122–0.062)
Western Europe	307742.034 (278412.732–341655.115)	433.328 (392.030–481.081)	296961.140 (265579.107–333060.249)	435.949 (389.879–488.944)	0.605 (–2.383–3.114)	0.099 (0.064–0.134)
Western Sub-Saharan Africa	373478.414 (326146.358–430759.268)	424.988 (371.128–490.169)	849996.949 (739636.826–971008.929)	395.782 (344.396–452.129)	–6.872 (–8.666–4.687)	–0.211 (–0.248–0.175)



spectively (Figure 1 and Supplementary Table SIII ~~Please SEND the supplementary tables!!!! We haven't got in Editorial System!!!!!!!!!!!!!!~~).

In 2021, the prevalence of CHAs was higher in girls than in boys. The male–female ratio of CHA prevalence among children in different age groups followed a unimodal distribution, peaking in neonates within the first 28 days of life (Supplementary Table SIII and Figure 1).

Death

Over the past 30 years, the global number of child deaths related to CHAs decreased by 55.336% (from 497,979 deaths with a 95% UI of 282,166–642,052 in 1990 to 222,415 deaths with a 95% UI of 181,359–275,182 in 2021). Similarly, the mortality rate associated with CHAs decreased from 28.633 deaths per 100,000 people (95% UI: 16.224–36.918) in 1990 to 11.055 deaths per 100,000 people (95% UI: 9.014–13.678) in 2021; the EAPC was –2.574 (95% CI: –2.737 to –2.410) (Supplementary Table SI).

A decrease in the mortality rate associated with CHAs was observed across all age groups of children. The largest decrease in the mortality rate (49.515%) occurred in newborns within the first 28 days of life. In 2021, among children under 1 year of age and those aged 2–4 years, the mortality rate associated with CHAs was higher in boys than in girls (rate per 100 000 children under 28 days of age: boys, 914.500 deaths; girls, 595.260 deaths; 1–5 months: boys, 117.663 deaths; girls, 106.471 deaths; 6–11 months: boys, 53.867 deaths; girls, 52.275 deaths; 2–4 years: boys, 4.487 deaths; girls, 4.125 deaths). In children aged 12–23 months and 5–14 years, the rate was higher among girls than among boys (12–23 months: boys, 14.568 deaths; girls, 14.813 deaths; 5–14 years: boys, 1.337 deaths; girls, 1.351 deaths). In boys, the lowest CHA-associated mortality rate was observed among those aged 5 to 14 years (1.337); in girls, the lowest rate was observed among those aged 2 to 4 years (1.351) (Supplementary Table SIV and Supplementary Figure S1).

DALYs

From 1990 to 2021, the global number of DALYs associated with CHAs in children decreased by 54.588%, from 44,749,235 (95% UI: 25,585,020–575,955,340) in 1990 to 20,321,186 (95% UI: 16,692,532–25,028,860) in 2021. The EAPC was –2.527 (95% CI: –2.687 to –2.366) (Supplementary Table SII).

Over the same period, there was a decline in the DALY rate associated with CHAs for children in all age groups. The greatest reduction (62.977%)

occurred among children aged 12–23 months. In both 1990 and 2021, the highest number of DALYs associated with CHAs was observed in children under 28 days of age, with 13,611,565 DALYs in 1990 and 6,674,473 DALYs in 2021. In 2021, the DALY rate for CHAs in children aged 12–23 months was higher among girls (1,367.344 ~~?????~~ 1,367.344 per 100,000 ~~????~~) than boys (1,349.648 ~~????????????~~). For all the other age groups, boys had a higher DALY rate than girls did (Supplementary Table SV and Supplementary Figure S2).

CHAs in children: SDI regional trends

Prevalence

In 2021, the low-middle-SDI group had the highest number of cases of CHAs in children (2,068,011 cases; 95% UI: 1,819,242–2,328,074). The greatest decrease in the prevalence of CHAs among children was observed in the low-SDI group (EAPC = –0.177; 95% CI: –0.205 to –0.149) (Table I, Figure 2).

Death

Across the five SDI groups, a significant decrease in mortality rates linked to CHAs in children was observed. Notably, the low-SDI regions presented the highest number of deaths related to CHAs (86447; 95% UI: 59760–117370, $p < 0.001$), whereas the high-middle-SDI regions presented the greatest reduction in CHA-related mortality rates (81.362%). In 2021, the highest mortality rate for CHAs in children was observed in low-SDI regions (18.784; 95% UI: 12.985–25.503), and the lowest mortality rate was observed in high-SDI regions (2.366; 95% UI: 1.926–2.874). Among these regions, the high-middle-SDI regions had the lowest EAPC in CHAs-related mortality (–4.867; 95% UI: –5.148 to –4.585) (Supplementary Table SI, Supplementary Figure S3).

DALYs

In 1990, the global rate of DALYs for CHAs in children aged 0–14 years was 2,573.050 (95% UI: 1,471.121–3,311.704) per 100,000 people. By 2021, this figure had decreased to 1,010.069 (95% UI: 829.706–1,244.065), indicating a long-term downward trend ($p < 0.001$). Among the regions, the low-SDI regions had the highest DALY rate in 1990, at 3,525.146 (95% UI: 1,266.476–5,155.793) per 100,000 people ($p < 0.001$). By 2021, this rate had dropped to 1,692.466 (95% UI: 1,175.580–2,285.878), approximately halving the burden. Regarding sex differences, the charts indicated that, globally, male children usually had a higher rate of DALYs than females did, a trend that was consistent across different SDI regions and especially

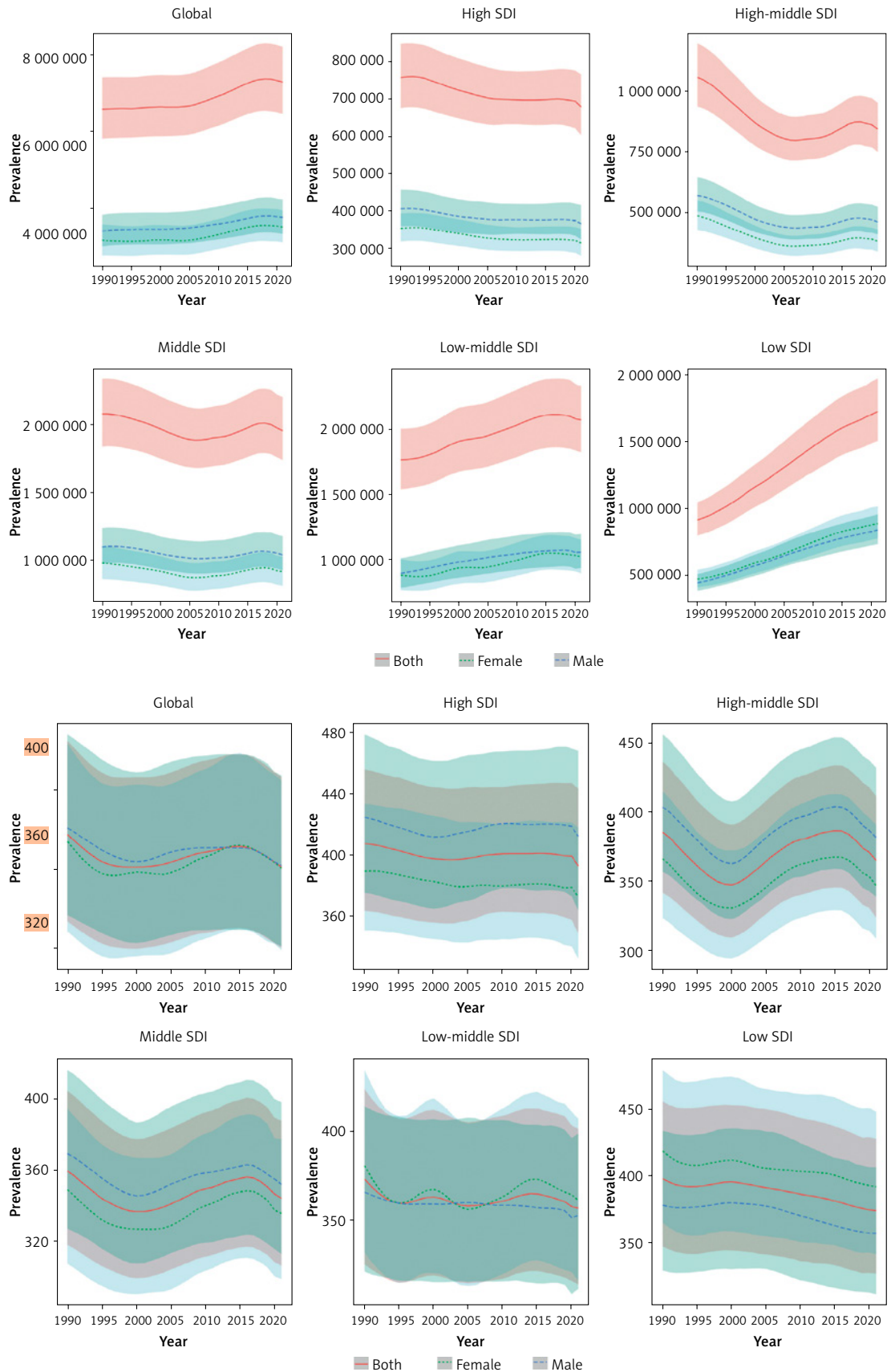


Figure 2. Epidemiological trends in prevalence number and prevalence rate of childhood CHAs from 1990 to 2021 in five sociodemographic index (SDI) regions

pronounced in the low-SDI regions (Supplementary Table SII, Supplementary Figure S4).

CHA in children: geographic regional trends

Prevalence

Among 21 geographic regions globally, South Asia had the highest number of CHA cases in children in 1990, totaling 1,578,563 (95% UI: 1,374,375 to 1,808,754), whereas Oceania had the fewest, with only 9,179 cases (95% UI: 8,052 to 10,452). By 2021, South Asia still had the highest number of cases, at 1,739,987 (95% UI: 1,531,918 to 1,978,759); the number of cases in Oceania slightly increased to 9,179 (95% UI: 15,515 to 20,228). Additionally, in 1990, the lowest prevalence of CHAs in children was in Tropical Latin America, at 333.760 cases per 100,000 people (95% UI: 269.048 to 355.529), with Central Asia having the highest prevalence, at 575.927 cases per 100,000 (95% UI: 503.846 to 659.502). By 2021, Southern Latin America had the lowest prevalence, at 310.790 cases per 100,000 people (95% UI: 300.230 to 373.028), Central Asia had the highest rate, at 592.915 cases per 100,000 people (95% UI: 517.648 to 678.322). From 1990 to 2021, the greatest increase in the prevalence of CHAs in children was observed in Eastern Europe, with an average annual percentage change of 0.330 (95% CI: 0.125 to 0.536), whereas Eastern Sub-Saharan Africa experienced a decline, with an average annual percentage change of -0.305 (95% CI: -0.333 to -0.277). At the global and continental levels, the prevalence of birth defects showed a slight in-

crease with rising socio-demographic index (SDI) levels ($r = 0.2135$, $p < 0.001$), indicating a weak but positive correlation between prevalence and SDI (Table I, Figure 3).

Death

In 1990, South Asia had the highest number of deaths from CHAs in children, totaling 116,856 deaths (95% UI: 72,956 to 162,097), whereas Australasia had the fewest, at 247 deaths (95% UI: 225 to 276). By 2021, South Asia still had the highest number of deaths at 51,312 (95% UI: 36,235 to 72,898), with an SDI of 0.558; Australasia had the fewest deaths at 95% UI, 68 to 119, with an SDI of 0.846. From 1990 to 2021, the high-income Asia-Pacific region experienced the largest decrease in the mortality rate, with an EAPC of -5.352 (95% CI: -5.5168 to -5.1872); however, Central Asia experienced a slight increase in the mortality rate, with an EAPC of 0.920 (95% CI: 0.608 to 1.232). In 2021, the mortality rates in 13 regions were above the global average (11.055 deaths per 100,000 people), whereas those in 14 regions were below the global average. The correlation analysis between DALYs and SDI revealed that with increasing SDI levels, DALYs decreased significantly, indicating a strong negative correlation between DALYs and SDI ($r = -0.8307$, $p < 0.001$) (Supplementary Table SI and Supplementary Figure S5).

DALYs

In 1990, East Asia had the highest number of DALYs associated with CHAs in children, totaling

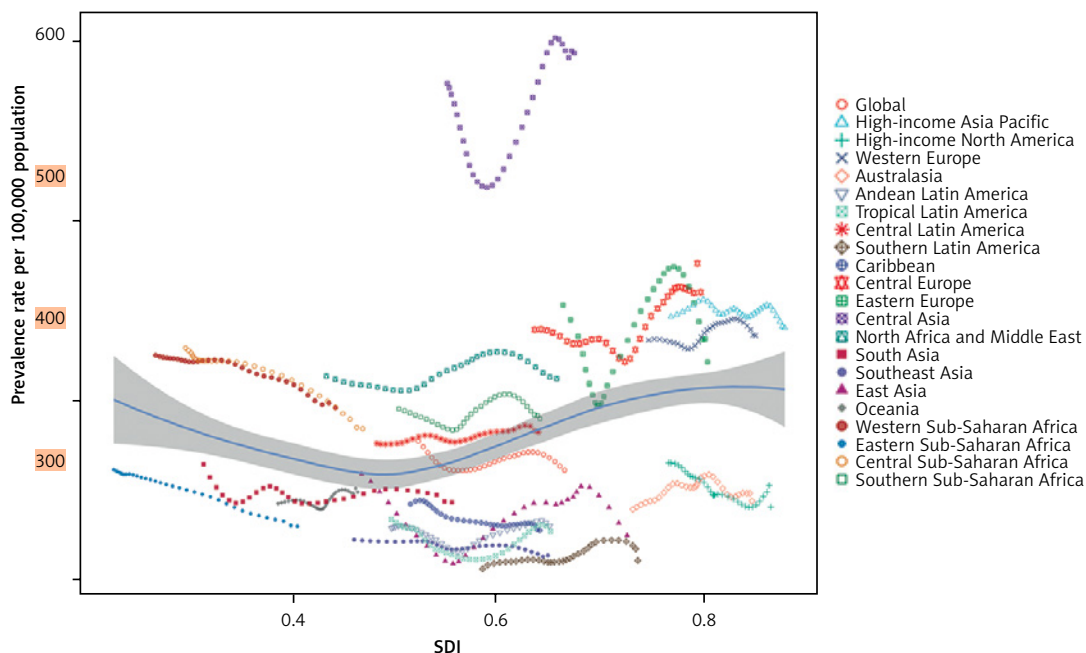


Figure 3. Correlation analysis of childhood CHA prevalence rate with socio-demographic index (SDI) across 21 regions from 1990 to 2021

10,443,910 (95% UI: 6,546,745 to 14,441,534). By 2021, Southeast Asia had the highest number, with 4,697,324 DALYs (95% UI: 3,334,571 to 6,610,005), whereas Australasia had the lowest number, at only 10,356 (95% UI: 7,848 to 12,726). During this period, Oceania had the highest DALY rate, at 2,911.336 per 100,000 people (95% UI: 1,203.550 to 4,414.854); Australasia had the lowest rate, at 180.695 per 100,000 people (95% UI: 136.939 to 222.045). From 1990 to 2021, Central Asia experienced an increase in the DALY rate (EAPC = 0.916; 95% CI: 0.610 to 1.223), whereas East Asia experienced the most significant decrease (EAPC = -5.197; 95% CI: -5.48–-4.913, $p < 0.001$). In 2021, 9 regions had DALY rates above the global average (1010.069) and 12 regions had rates below it. The analysis showed a strong negative correlation between mortality rate and SDI, with mortality rate decreasing significantly as SDI increased ($r = -0.8325$, $p < 0.001$) (Supplementary Table SII, Supplementary Figure S6).

CHAs in children: national trends

Prevalence

In 2021, among 204 countries, India had the highest number of CHA cases in children, with 1,249,145 cases (95% UI: 1,101,670–1,412,452). Armenia had the highest prevalence of CHAs in children, at 649.051 cases per 100,000 people (95% UI: 566.055–741.582). Georgia experienced the largest increase in the prevalence of CHAs in children (EAPC = 0.759; 95% CI: 0.523–0.995), whereas Equatorial Guinea experienced the largest decrease (EAPC = -0.700; 95% CI: -0.710 to -0.689). In 2021, India had the highest prevalence of CHAs among children, while Dominica had the

lowest value. The global prevalence of CHAs in children in 2021 was 361.060 (95% UI: 320.042–406.507); 97 countries had a prevalence rate higher than the global average, and 107 countries had a prevalence rate lower than the global average (Supplementary Table SVI, Figure 4).

Death

In 2021, India had the highest number of deaths related to CHAs among children, totaling 35,232 (95% UI: 25,272–50,611). Afghanistan had the highest mortality rate for CHAs among children, at 59.127 (95% UI: 28.978–84.462), whereas San Marino had the lowest, at 0.446 (95% UI: 0.246–0.796). Guatemala experienced the largest increase in the mortality rate, with an EAPC of 3.234 (95% CI: 2.428–4.046); conversely, Saudi Arabia experienced the most significant decrease, with an EAPC of -7.888 (95% CI: -8.028 to -7.749). In 2021, Afghanistan had the highest mortality rate related to CHAs among children, whereas San Marino had the lowest rate. The global mortality rate for CHAs in children in 2021 was 11.055 (95% UI: 9.014–13.678), with 58 countries having rates above the global average and 146 countries having rates below it (Supplementary Table SVII, Supplementary Figure S7).

DALYs

In 2021, India had the highest number of DALYs related to CHAs among children, totaling 3,239,958 (95% UI: 2,351,581–4,603,448). Afghanistan had the highest rate of CHAs-related DALYs among children, at 5,306.324 (95% UI: 2,618.402–7,558.485). Guatemala experienced the largest increase in DALY rates for CHAs, with

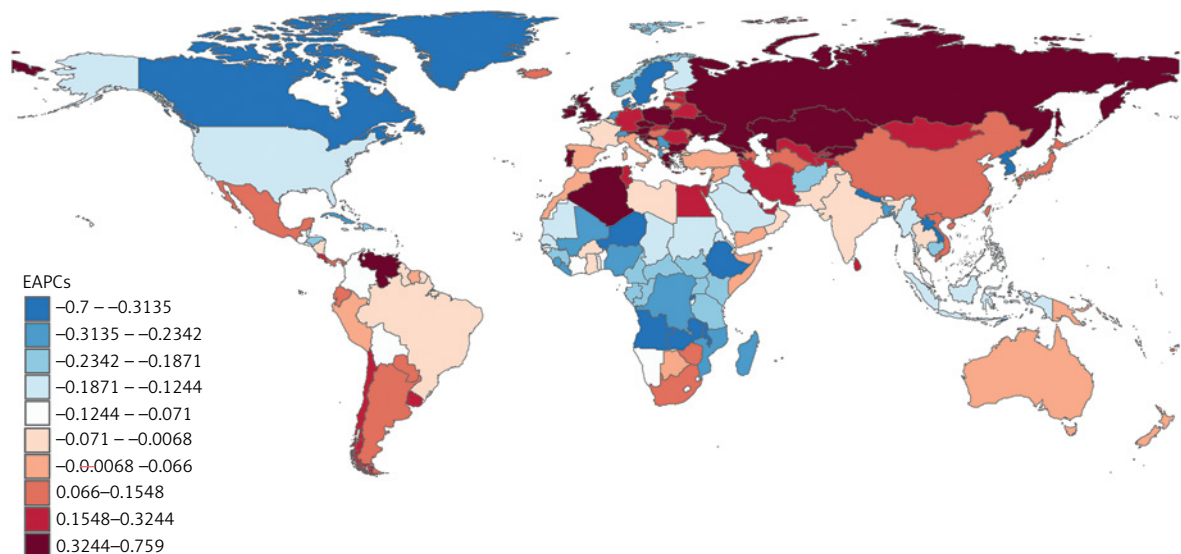


Figure 4. Changes in EAPC (estimated annual percentage change) for prevalence of CHA in children across 204 countries and territories

an EAPC of 3.151 (95% CI: 2.372 to 3.936). Conversely, Saudi Arabia and Turkey experienced the most significant decreases, with EAPCs of -7.605 (95% CI: -7.754 to -7.455) and -5.17 (95% CI: -5.50 to -4.84), respectively. Afghanistan had the highest DALY rate related to CHAs among children, whereas San Marino had the lowest rate. In 2021, the global DALY rate for CHAs among children was 1,010.069 (95% UI: 829.706–1,244.065), with 59 countries having rates above the global average and 145 countries having rates below it (Supplementary Table SVIII, Supplementary Figure S8).

Discussion

Data from the last thirty years reveal significant regional disparities in the impact of CHAs on children aged 0 to 14 years across different economic areas worldwide. With increasing medical and societal costs, CHA has emerged as a significant concern within the global public health sphere. This study, which used GBD data from 1990–2021, examined the prevalence, mortality and DALY rates of CHAs among children in regions with varying SDIs [11–13]. The findings highlight that despite overall advancements in medical technology, the burden of CHAs remains pronounced in lower-middle-SDI regions. This underscores the persistent challenges in addressing CHAs faced globally and highlights areas where urgent interventions are needed. This study underscores the importance of developing targeted prevention and management strategies to address the specific needs of these populations, aiming to foster the development and refinement of global public health policies.

From 1990 to 2021, there was a significant decrease in the number of deaths and DALYs associated with CHAs in children aged 0 to 14 years worldwide. This trend is likely due to advancements in medical technology, more effective early intervention measures, and increased attention to pediatric cardiac health within global health systems. Research indicates that improved neonatal cardiac screening and treatment techniques have significantly reduced mortality and health burdens in these age groups [14–17]. However, despite a slight decrease in the global prevalence of CHAs in children, the total number of cases has increased, primarily due to population growth, lifestyle changes, and environmental changes driven by globalization [18, 19]. In particular, the notable increase in prevalence among children aged 5 to 14 years may reflect the accumulation and manifestation of potential cardiac risk factors as children age.

Moreover, our study revealed sex differences in the distribution of CHAs, with higher incidence rates among girls than boys. These differences might be related to genetic factors, hormonal

levels, and their impacts on cardiac development [20–22]. SDI analysis revealed that regions with higher SDIs experienced more pronounced decreases in CHA prevalence, likely due to greater investment in healthcare resources, broader coverage of health services, and better living conditions in these areas [23].

With the acceleration of globalization, the risk factors for CHAs have also shown certain trends. Advances in genetic technology have enabled more accurate identification of genetic and chromosomal abnormalities related to CHAs [24], whereas global changes in environmental pollution and lifestyles have led to new triggers for the development of CHAs. Additionally, as the prevalence of CHAs and other chronic diseases increases among pregnant women, these conditions become significant factors affecting fetal cardiac development [25].

In terms of global disease surveillance and health strategies for CHAs, some progress has been made, especially in high-SDI regions, where improved prenatal and antenatal health screenings have reduced the incidence and mortality associated with CHAs.

Beyond postnatal treatment improvements, the widespread adoption of prenatal screening – including fetal echocardiography – has allowed for earlier detection of severe cases, enabling informed decisions such as selective termination of pregnancies with fatal or uncorrectable anomalies. In certain cases, in utero interventions have also been implemented to address specific defects prior to birth. These strategies have collectively contributed to the observed decline in CHA-related mortality in high- and middle-SDI regions. Their integration into public health policy in lower-SDI regions could offer significant benefits in mitigating the burden of CHAs. However, due to the limited resources and inadequate health education, low-SDI regions still face challenges in prevention and early intervention for CHAs [11, 26].

Future policy directions should focus more on the equitable distribution of global health resources, particularly in terms of enhancing medical facilities and public health education levels in low-SDI regions. Furthermore, strengthening international cooperation and sharing effective genetic screening and environmental intervention technologies may be key to reducing the global burden of CHAs.

This study has several limitations. First, the analysis relied heavily on the GBD database, meaning that data accuracy may be constrained by the completeness of national registry data and the number of undiagnosed cases. Additionally, due to the lack of detailed classification of congenital heart anomalies (CHAs) into anatomical and functional types, this study could not provide

in-depth insights into specific epidemiological characteristics. Moreover, the study did not include a systematic analysis of risk factors associated with CHAs, limiting our understanding of how these factors influence CHA development. Furthermore, low- and middle-income countries (LMICs) often lack comprehensive CHA registries, with many regions relying solely on limited hospital records or localized data, which may not be representative, potentially underestimating the burden of CHAs in certain areas. For instance, in resource-limited countries such as Myanmar, the absence of key data on CHAs further exacerbates errors in global burden estimates. Additionally, the underdeveloped public health infrastructure in LMICs, coupled with inadequate screening and diagnostic capabilities, may result in many CHA cases being undiagnosed or misdiagnosed, further affecting the accuracy of burden estimation. Biases in sample selection may also impact data representativeness, compromising the reliability of global burden estimates. While this study employed data weighting and multi-source calibration methods to mitigate these biases and validated its findings by comparing them with data from high-income countries, the impact of missing or low-quality data cannot be fully eliminated. Future research should focus on refining data categorization methods to incorporate more detailed CHA classification and explore new methodologies, such as predictive models, to more accurately assess and manage the global CHA burden. Additionally, strengthening CHA screening systems in LMICs, enhancing diagnostic capabilities, and improving data collection and long-term monitoring mechanisms will help reduce data bias and provide a more scientific and accurate foundation for developing public health policies and interventions.

In conclusion, this study demonstrated that despite significant advancements in the treatment and diagnosis of CHAs in children over the past three decades – reflected in the decline in the associated mortality rates and DALYs – the prevalence of CHAs has remained relatively unchanged. Research has also highlighted significant disparities in CHA incidence across different sexes and SDI regions, highlighting global inequalities in the distribution of public health resources and health education. Future policies need to address these disparities with targeted strategies to alleviate the global burden of CHAs, especially by enhancing resource allocation and international cooperation among low-SDI regions.

Acknowledgments

Enhui Yang, Hao Lin, and Yuansi Zhang contributed equally as co-first authors.

Data availability

The data for this study are available through the Global Health Data Exchange query tool (<https://vizhub.healthdata.org/gbd-results/>).

Funding

No external funding.

Ethical approval

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

References

1. Liu Y, Chen S, Zühlke L, et al. Global birth prevalence of congenital heart defects 1970-2017: updated systematic review and meta-analysis of 260 studies. *Int J Epidemiol* 2019; 48: 455-63.
2. Kang L, Cao G, Jing W, Liu J, Liu M. Global, regional, and national incidence and mortality of congenital birth defects from 1990 to 2019. *Eur J Pediatr* 2023; 182: 1781-92.
3. Umapathi KK, Sparks K, Dhanpalreddy H, et al. Burden of mental health disorders among older children and teenagers with congenital heart disease: a population-based analysis. *J Am Coll Cardiol* 2021; 77: 501.
4. Hu XJ, Ma XJ, Zhao QM, et al. Pulse oximetry and auscultation for congenital heart disease detection. *Pediatrics* 2017; 140: e20171154.
5. Bishop KC, Kuller JA, Boyd BK, Rhee EH, Miller S, Barker P. Ultrasound examination of the fetal heart. *Obstet Gynecol Survey* 2017; 72: 54-61.
6. Ladak LA, Hasan BS, Gullick J, Gallagher R. Health-related quality of life in congenital heart disease surgery in children and young adults: a systematic review and meta-analysis. *Arch Dis Childhood* 2019; 104: 340-7.
7. Piskarev Y, Sun Y, Righi M, et al. Fast-response variable-stiffness magnetic catheters for minimally invasive surgery. *Adv Sci* 2024; 11: e2305537.
8. Strzelecka I, Stodki M, Chrzanowski J, Rizzo G, Respondek-Liberska M. An investigation of the optimal inter-pregnancy interval following pregnancy with a fetus with congenital heart disease. *Arch Med Sci* 2022; 18: 388-94.
9. GBD 2021 Diseases and Injuries Collaborators. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet* 2024; 403: 2133-61.
10. Murray CJL. Findings from the Global Burden of Disease Study 2021. *Lancet* 2024; 403: 2259-62.
11. Li Y, Cao GY, Jing WZ, Liu J, Liu M. Global trends and regional differences in incidence and mortality of cardiovascular disease, 1990-2019: findings from 2019 global burden of disease study. *Eur J Prev Cardiol* 2023; 30: 276-86.
12. Curry C, Zühlke L, Mocumbi A, Kennedy N. Acquired heart disease in low-income and middle-income countries. *Arch Dis Childhood* 2018; 103: 73-7.

13. Chowdhury D, Elliott PA, Asaki SY, et al. Addressing disparities in pediatric congenital heart disease: a call for equitable health care. *J Am Heart Assoc* 2024; 13: e032415.
14. Sachdeva R, Valente AM, Armstrong AK, et al. ACC/AHA/ASE/HRS/ISACHD/SCAI/SCCT/SCMR/SOPE 2020 appropriate use criteria for multimodality imaging during the follow-up care of patients with congenital heart disease: a report of the American College of Cardiology Solution Set Oversight Committee and Appropriate Use Criteria Task Force, American Heart Association, American Society of Echocardiography, Heart Rhythm Society, International Society for Adult Congenital Heart Disease, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and Society of Pediatric Echocardiography. *J Am Coll Cardiol* 2020; 75: 657-703.
15. Spence C, Khoo N, Mackie A, et al. Exploring the promise of telemedicine exercise interventions in children and adolescents with congenital heart disease. *Canadian J Cardiol* 2023; 39: S346-58.
16. Liu Y, Chen S, Zühlke L, et al. Global prevalence of congenital heart disease in school-age children: a meta-analysis and systematic review. *BMC Cardiovasc Disord* 2020; 20: 488.
17. Welke KF, Pasquali SK, Lin P, et al. Regionalization of congenital heart surgery in the United States. *Semin Thorac Cardiovasc Surg* 2020; 32: 128-37.
18. Steurer MA, Baer RJ, Chambers CD, et al. Mortality and major neonatal morbidity in preterm infants with serious congenital heart disease. *J Pediatr* 2021; 239: 110-6.e3.
19. Su Z, Zou Z, Hay SI, et al. Global, regional, and national time trends in mortality for congenital heart disease, 1990-2019: an age-period-cohort analysis for the Global Burden of Disease 2019 study. *EClinicalMedicine* 2022; 43: 101249.
20. van Weerd JH, Koshiha-Takeuchi K, Kwon C, Takeuchi JK. Epigenetic factors and cardiac development. *Cardiovasc Res* 2011; 91: 203-11.
21. Chapman K. Cardiac gluco- and mineralocorticoid receptors: from development to pathology. *Ann d'Endocrinol* 2021; 82: 173.
22. Luo Y, Safabakhsh S, Palumbo A, et al. Sex-based mechanisms of cardiac development and function: applications for induced-pluripotent stem cell derived-cardiomyocytes. *Int J Mol Sci* 2024; 25: 5964.
23. Kemper AR, Lam WKK, Bocchini JA Jr. The success of state newborn screening policies for critical congenital heart disease. *JAMA* 2017; 318: 2087-8.
24. Wang H, Lin X, Lyu G, He S, Dong B, Yang Y. Chromosomal abnormalities in fetuses with congenital heart disease: a meta-analysis. *Arch Gynecol Obstet* 2023; 308: 797-811.
25. Liu Y, Yue L, Chang L. Maternal gestational diabetes mellitus and congenital heart disease in offspring: a meta-analysis. *Hormone Metab Res* 2024; 56: 574-84.
26. Cao G, Liu J, Liu M. Global, regional, and national incidence and mortality of neonatal preterm birth, 1990-2019. *JAMA Pediatr* 2022; 176: 787-96.