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LETTER

Global disparities in childhood neuroblastoma: trends, burden, and inequities from 1990 to 2021

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Childhood neuroblastoma, a leading cause of cancer-related mortality in young children, accounts for approximately 8%–10% of pediatric cancers[1]. Originating from neural crest cells of the sympathetic nervous system, these tumors affect primarily children younger than 5 years of age and are often diagnosed in advanced stages, because of their aggressive nature and vague early symptoms[2-4]. Although advances in diagnostics and multimodal treatment have increased survival in high-income regions, stark disparities in outcomes persist globally. Particularly in low- and middle-income countries, limited access to early detection, specialized care, and essential therapies has contributed to persistent mortality[5-8]. Using data from the Global Burden of Disease (GBD) Study 2021, we analyzed trends in the incidence, mortality, and disability-adjusted life years (DALYs) attributable to neuroblastoma in children aged 0-14 years across 204 countries from 1990 to 2021, and identified key demographic, regional, and socio-economic factors contributing to the global burden of childhood neuroblastoma.

Global disease burden and temporal trends

In 2021, neuroblastoma was responsible for an estimated 174,186.3 DALYs [95% uncertainty interval (UI): 127,104.64–223,265.92, **Table 1**]. From 1990 to 2021, global DALYs increased by 20.08%, rising from 145,057.4 (95% UI: 120,924.8–173,294.3), with an estimated annual percentage change (EAPC) of 0.46 [95% confidence interval (CI): 0.36–0.56]. Whereas age-standardized DALY rates globally rose modestly, from 8.24 (95% UI: 6.84–9.91) to 9.02 (95% UI: 6.44–11.68) per 100,000, pronounced heterogeneity was observed among regions. High-socio-demographic index (SDI) regions experienced notable declines (EAPC: −1.15; 95% CI: −1.35 to −0.96), whereas low-middle SDI regions showed the largest increases (EAPC: 1.54; 95% CI: 1.35–1.73). South Asia had the steepest rise (EAPC: 1.73; 95% CI: 1.38–2.08), and sub-Saharan Africa showed similar increasing trends. Although years of life lost (YLLs) dominated DALYs globally, the EAPC for years lived with disability (YLDs) surpassed that of YLLs in several regions, particularly in low-middle SDI settings (YLD EAPC: 2.01 *vs.* YLL EAPC: 1.53), thus suggesting that more children are surviving but experiencing lasting morbidity.

Regional and national disparities in disease burden

Marked regional differences were observed (**Figure 1**). In 2021, Malawi reported the highest age-standardized DALY rate, at 38.78 per 100,000, and was followed by Trinidad and Tobago

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Table 1 Global burden of childhood neuroblastoma and other peripheral nervous system tumors from 1990 to 2021

Location	1990		2021		1990–2021
	Numbers	ASR	Numbers	ASR	EAPC
DALYs					
Global	145,057.36 (120,924.76–173,294.3)	8.24 (6.84–9.91)	174,186.3 (127,104.64–223,265.92)	9.02 (6.44–11.68)	0.46 (0.36 to 0.56)
Low-middle SDI	32,911.41 (24,850–43,611.56)	6.71 (5.02–9.08)	54,242.65 (38,164.86–72,461.29)	9.75 (6.74–13.43)	1.54 (1.35 to 1.73)
Middle SDI	39,660.93 (32,221.61–46,615.78)	6.91 (5.54–8.31)	42,712.62 (31,748.88–53,985.24)	7.99 (5.89–10.3)	0.69 (0.46 to 0.92)
Low SDI	16,054.22 (10,755.5–24,982.99)	6.31 (4.14–9.86)	38,449.7 (20,758.04–61,655.36)	8.17 (4.36–13.2)	1.1 (0.68 to 1.52)
High SDI	30,823.93 (29,178.43–32,348.24)	17.04 (15.94–18.15)	19,471.08 (17,170.44–21,760.02)	11.78 (10.27–13.27)	−1.15 (−1.35 to −0.96)
High-middle SDI	25,479.35 (21,510.78–29,833.77)	9.5 (7.93–11.38)	19,178.88 (14,878.35–23,223.51)	8.77 (6.69–10.92)	−0.02 (−0.31 to 0.26)
GBD super regions					
South Asia	31,073.6 (20,840.55–42,991.32)	6.97 (4.56–9.69)	50,618.87 (34,477.6–71,561.32)	10.87 (7.23–15.79)	1.73 (1.38 to 2.08)
Sub-Saharan Africa	18,474.94 (12,374.9–27,765.87)	7.37 (4.86–11.12)	46,946.49 (23,144.95–76,329.4)	9.59 (4.69–15.64)	1.2 (0.85 to 1.56)
Southeast Asia, East Asia, and Oceania	26,046.53 (19,386.44–34,334.12)	5.21 (3.81–7.04)	24,828.13 (18,692.86–30,506.92)	5.85 (4.31–7.39)	0.63 (0.41 to 0.85)
High-income	34,841.53 (33,230.73–36,355.63)	19.25 (18.2–20.39)	22,675.59 (19,866.84–25,516.33)	13.51 (11.65–15.38)	−1.06 (−1.24 to −0.89)
Latin America and Caribbean	18,014.48 (16,250.63–19,778.78)	12.65 (11.27–14.17)	15,413.84 (12,473.12–19,035.78)	11.06 (8.71–13.77)	−0.13 (−0.6 to 0.35)
North Africa and Middle East	8,735.94 (6,124.25–12,544.18)	6.05 (4–8.98)	9,986.29 (7,196.85–13,356.37)	5.55 (3.84–7.86)	0.09 (−0.16 to 0.34)
Central Europe, Eastern Europe, and Central Asia	7,870.35 (6,851.08–9,532.92)	7.57 (6.53–9.18)	3,717.09 (2,969.4–4,400.12)	4.81 (3.78–5.81)	−1.7 (−1.98 to −1.43)
YLL					
Global	141,840.07 (118,398.48–169,250.1)	8.06 (6.67–9.69)	169,981.65 (123,925.12–217,945.87)	8.8 (6.28–11.44)	0.46 (0.35 to 0.56)
Low-middle SDI	32,298.92 (24,462.2–42,971.4)	6.59 (4.95–8.92)	53,082.84 (37,396.37–71,046.14)	9.54 (6.61–13.13)	1.53 (1.34 to 1.72)
Middle SDI	38,841.49 (31,568.29–45,666.25)	6.77 (5.42–8.13)	41,620.09 (30,992.42–52,622.83)	7.79 (5.77–10.04)	0.67 (0.44 to 0.9)
Low SDI	15,769.88 (10,546.04–24,639.25)	6.19 (4.06–9.72)	37,712.55 (20,377.48–60,738.31)	8.02 (4.28–12.99)	1.1 (0.68 to 1.52)
High SDI	29,938.89 (28,362.95–31,432.26)	16.55 (15.51–17.65)	18,831.35 (16,545.26–21,075.19)	11.4 (9.95–12.82)	−1.16 (−1.36 to −0.97)
High-middle SDI	24,866.3 (21,047.29–29,053.29)	9.28 (7.74–11.13)	18,606.64 (14,423.43–22,541.62)	8.51 (6.49–10.63)	−0.05 (−0.33 to 0.24)
GBD super regions					
South Asia	30,510.59 (20,559.63–42,093.91)	6.84 (4.49–9.49)	49,553.69 (33,736.07–69,991.79)	10.64 (7.05–15.45)	1.72 (1.37 to 2.07)

Table 1 Continued

Location	1990		2021		1990–2021
	Numbers	ASR	Numbers	ASR	EAPC
Sub-Saharan Africa	18,137.67 (12,171.46–27,310.18)	7.24 (4.77–10.94)	46,000.58 (22,597.09–74,896.44)	9.4 (4.57–15.37)	1.19 (0.84 to 1.55)
Southeast Asia, East Asia, and Oceania	25,491.29 (18,927.73–33,546.19)	5.1 (3.73–6.86)	24,135.39 (18,212.09–29,658.63)	5.68 (4.2–7.19)	0.6 (0.38 to 0.83)
High-income	33,834.91 (32,351.27–35,347.88)	18.7 (17.66–19.81)	21,933.73 (19,192.95–24,809.7)	13.07 (11.27–14.89)	−1.07 (−1.25 to −0.9)
Latin America and Caribbean	17,634.88 (15,899.54–19,360.95)	12.38 (11.03–13.87)	15,029.07 (12,165.35–18,554.19)	10.78 (8.49–13.46)	−0.14 (−0.61 to 0.33)
North Africa and Middle East	8,549.55 (5,989.46–12,287.65)	5.92 (3.92–8.77)	9,714.25 (7,018.89–12,984.87)	5.4 (3.74–7.65)	0.07 (−0.18 to 0.32)
Central Europe, Eastern Europe, and Central Asia	7,681.18 (6,688.04–9,267.46)	7.38 (6.36–8.94)	3,614.94 (2,891.91–4,262.55)	4.68 (3.67–5.65)	−1.72 (−1.99 to −1.44)
YLD					
Global	3,217.3 (1,998.41–4,852.01)	0.18 (0.11–0.28)	4,204.65 (2,551.19–6,643.59)	0.22 (0.13–0.35)	0.7 (0.59 to 0.81)
Low-middle SDI	612.49 (326.8–1,018.64)	0.13 (0.07–0.21)	1,159.81 (660.62–1,917.02)	0.21 (0.12–0.35)	2.01 (1.81 to 2.22)
Middle SDI	819.44 (478.35–1,310.49)	0.14 (0.08–0.23)	1,092.53 (676.19–1,694.09)	0.2 (0.12–0.32)	1.35 (1.1 to 1.6)
Low SDI	284.34 (139.16–532.25)	0.11 (0.05–0.21)	737.14 (329.95–1,420.7)	0.16 (0.07–0.3)	1.33 (0.86 to 1.81)
High SDI	885.05 (600.39–1,249.47)	0.49 (0.33–0.68)	639.73 (443.24–907.36)	0.39 (0.26–0.54)	−0.79 (−1.05 to −0.53)
High-middle SDI	613.05 (394.89–934.23)	0.23 (0.15–0.35)	572.24 (372.25–842.86)	0.26 (0.17–0.39)	0.74 (0.43 to 1.04)
GBD super regions					
South Asia	563.01 (282.29–982.47)	0.13 (0.06–0.22)	1,065.18 (576.41–1,807.46)	0.23 (0.12–0.4)	2.26 (1.86 to 2.67)
Sub-Saharan Africa	337.27 (172.88–615.67)	0.13 (0.07–0.24)	945.91 (394.53–1,779)	0.19 (0.08–0.36)	1.5 (1.1 to 1.9)
Southeast Asia, East Asia, and Oceania	555.24 (315.08–906.24)	0.11 (0.06–0.19)	692.74 (432.97–1,043.75)	0.16 (0.1–0.24)	1.54 (1.3 to 1.78)
High-income	1,006.62 (684.1–1,417.38)	0.56 (0.37–0.78)	741.86 (514.99–1,050.93)	0.44 (0.3–0.63)	−0.75 (−0.97 to −0.52)
Latin America and Caribbean	379.59 (234.3–575.3)	0.27 (0.16–0.4)	384.78 (246.93–600.16)	0.28 (0.17–0.43)	0.38 (−0.16 to 0.91)
North Africa and Middle East	1,86.4 (101.51–321.31)	0.13 (0.07–0.23)	272.04 (164.12–430.98)	0.15 (0.09–0.25)	0.91 (0.62 to 1.19)
Central Europe, Eastern Europe, and Central Asia	189.16 (122.22–287.49)	0.18 (0.12–0.28)	102.15 (66.89–152.53)	0.13 (0.08–0.2)	−1.28 (−1.56 to −0.99)

This table summarizes key metrics, including age-standardized rates (ASR), estimated annual percentage changes (EAPC), and disability-adjusted life years (DALYs), further divided into years lived with disability (YLDs) and years of life lost (YLLs). The socio-demographic index (SDI) is included to contextualize findings across levels of development. Uncertainty intervals (UI) are presented for precision.

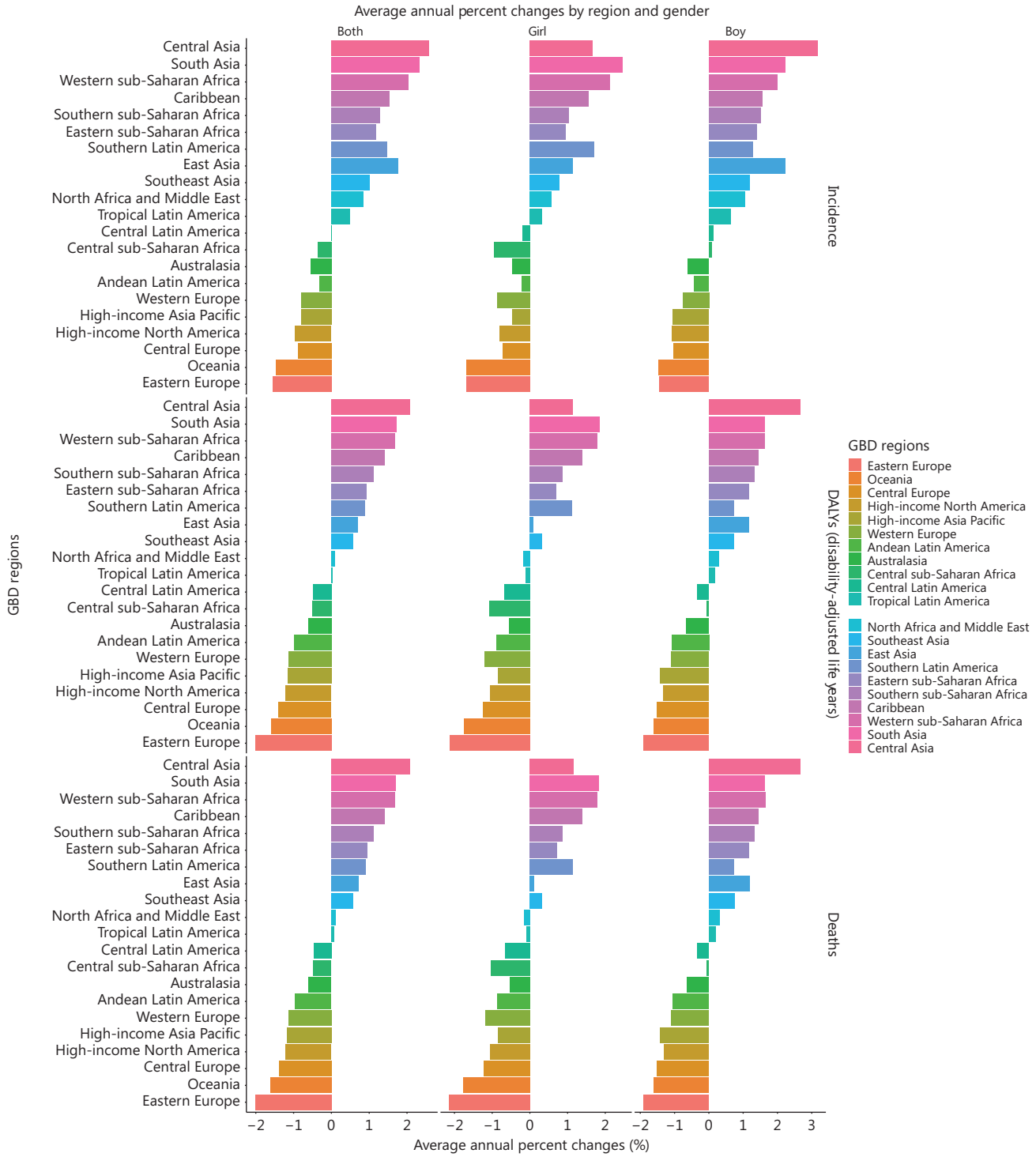


Figure 1 Trends in the burden of childhood neuroblastoma from 1990 to 2021, stratified by gender and GBD region. The figure illustrates changes in incidence rates, DALYs, and death rates, and highlights disparities across regions and genders. DALYs refer to disability-adjusted life years.

(36.59) and Malta (32.42). The sharpest national increases since 1990 were seen in Saint Vincent and the Grenadines, Guyana, and Tokelau. In contrast, Europe and Latin America showed major declines, and Greenland led the decrease in DALYs. High-SDI countries, such as those in North America and Oceania, maintained low burden levels, because of

widespread access to early diagnosis and comprehensive care (**Figure S1**). Across the 21 GBD super-regions, South Asia and sub-Saharan Africa recorded the most substantial increases in DALYs, whereas Western Europe and North America continued to experience consistent declines. The growth in DALY burden in lower-income regions reflects both an expanding child population and limited access to effective therapies, thereby highlighting a widening inequity in pediatric oncology outcomes[9,10].

Gender-based differences and socioeconomic inequities

Neuroblastoma continues to exhibit gender-based disparities. In 2021, the global age-standardized incidence rate (ASIR) was 0.34 per 100,000 in boys and 0.24 in girls. DALY rates followed the same trend: 10.25 per 100,000 in boys versus 7.89 in girls. This gap was particularly evident in East Asia, where the EAPC for incidence reached 2.23 and the DALYs reached 1.17 in boys, whereas those in girls were 1.14 and 0.09, respectively. These patterns suggest a biological predisposition or gender-specific access issues, possibly exacerbated by gender norms in healthcare utilization. The global burden was also stratified by SDI. High-SDI regions experienced decreasing trends in DALYs (EAPC: −1.15), whereas low-SDI (EAPC: 1.2; 95% CI: 0.85–1.56) and low-middle SDI countries experienced steep increases. In 2021, the DALY rates in sub-Saharan Africa surpassed 9.59 per 100,000, a value more than three times higher than observed in high-SDI regions. This disparity is attributable to inadequate diagnostic infrastructure, late-stage presentations, and unaffordable treatments. Countries with under-resourced healthcare systems consistently ranked highest in neuroblastoma burden, thus exemplifying how structural inequities perpetuate poor outcomes.

Epidemiological shifts and health inequality metrics

Epidemiological trends reflect a redistribution of disease burden. Central and South Asia recorded among the fastest-growing incidence rates (EAPC: 2.58 and 2.34) and DALY rates (EAPC: 2.07 and 1.73), whereas high-income regions, such as Eastern Europe and Oceania, saw declines (e.g., Eastern Europe DALY EAPC: −2.01). Correlation analyses revealed a shift (**Figure S2**): in 1990, the low baseline DALY regions had lower EAPCs ($r = -0.156$), whereas by 2021, these regions showed significantly higher EAPCs ($r = 0.315$, $P < 0.05$). Health inequality indices further captured global transitions. Between 1990 and 2021, the slope index of inequality for DALYs decreased from 7 to 5, thereby indicating a modest narrowing of absolute disparities (**Figure S3**). The concentration index shifted from 0.18 to −0.02, thereby suggesting that the burden moved from wealthier to poorer regions. Countries with large populations, such as India and China, had a substantial impact on these metrics; however, the overall trend reflected a global distribution of the neuroblastoma burden. Gender inequality also persisted: the slope index of the inequality values was consistently higher for boys than girls, a finding indicating unresolved gender-based barriers in care delivery.

Demographic drivers and projections to 2045

Demographic factors had dominant roles in shaping the neuroblastoma burden. In low-SDI countries, population growth explained nearly 80% of the increase in incidence, deaths, and DALYs (**Figure S4**). High birth rates in sub-Saharan Africa and South Asia contributed to a substantial increase in the population at risk. In contrast, in high-SDI countries, favorable epidemiological changes, including early diagnosis, risk stratification, and use of therapies such as anti-GD2 immunotherapy, accounted for more than 70% of the observed decline in disease burden. Despite temporary declines from 2019 to 2021 (probably because of the effects of the COVID-19 pandemic on diagnosis and reporting), projections indicated continued growth in absolute burden, particularly in low-SDI countries (**Figure S5**). By 2045, the global neuroblastoma incidence is expected to reach 0.32 per 100,000, with higher rates in boys (0.37) than in girls (0.27). Mortality is projected to reach 0.11 per 100,000, and the DALYs may increase to 8.57 per 100,000. These estimates suggest that global health inequities will further widen unless substantial investments are made in pediatric oncology infrastructure and equitable healthcare access.

Neuroblastoma remains a major pediatric health challenge disproportionately affecting children in low- and middle-SDI regions. Whereas high-SDI countries have decreased disease burden through advances in early detection, risk-adapted therapy, and healthcare infrastructure, children in resource-limited settings continue to face high mortality and

long-term disability. This study leveraged data from the GBD Study 2021 release, which included the first neuroblastoma-specific estimates, thereby enabling comprehensive global and regional analyses. Although descriptive in nature, the study provides valuable insights into geographic, temporal, and socioeconomic disparities in neuroblastoma burden. Key limitations include reliance on modeled estimates in regions with limited primary data and the absence of clinical variables such as disease stage or molecular subtype. These findings underscore the urgent need for a coordinated and equitable global health strategy that addresses systemic barriers to care, through capacity building in pediatric oncology, implementation of early detection programs, international collaboration for affordable therapies, and enhanced data systems to track outcomes.

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Conflict of interest statement

No potential conflicts of interest are disclosed.

Author contributions

Conceived and designed the analysis: Zhigang Liu, Daqing Ma, Qiang Shu.
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Performed the analysis: Rui Zhang, Zhigang Liu.
Wrote the paper: Zhigang Liu, Rui Zhang.

Data availability statement

Data are available from the GBD official website: https://ghdx.healthdata.org/gbd-2021.

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