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Global, regional and national burden of epilepsy in children and adolescents, 1990–2021: A systematic analysis for the Global Burden of Disease Study 2021

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Abstract

Background: Epilepsy is a common neurological disease that heavily impacts children and adolescents and carries serious physical, cognitive, psychological, social and economic consequences for patients and their caregivers.

Methods: Data was obtained via the Global Burden of Disease Study 2021. We reported numbers, rates and percentage changes of prevalence, mortality and disability-adjusted life years (DALYs).

Results: In 2021, there were 18.15 million [95% UI: 14.61–21.85] prevalent cases of epilepsy in children and adolescents worldwide, 8.24 million [5.77–11.13] of which were idiopathic epilepsy and 9.91 million [8.72–11.06] of which were secondary epilepsy. While mortality and DALY rates of idiopathic epilepsy declined between 1990 and 2021, the burden of secondary epilepsy remained substantial and, in some cases, increased—particularly in low-SDI regions. The prevalence rate of secondary epilepsy increased by 16.14% [4.28–29.24], driven by increases in epilepsy attributable to neonatal encephalopathy (82.02%), neonatal jaundice (18.45%) and malaria (77.03%). There were notable geographic variations in the burden of epilepsy, with the burden generally concentrated in Sub-Saharan Africa, Latin America and the Caribbean and Southeast Asia.

Conclusions: While efforts to reduce premature mortality of epilepsy have been successful, the burden on children and adolescents living with epilepsy is still significant. A healthcare gap remains for vulnerable populations with increased risk of infectious diseases, perinatal insults, poor sanitation and limited access to healthcare. Global and national action is needed to improve access to specialist

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care and medication, manage comorbidities, address stigma and discrimination and strengthen primary prevention initiatives.

KEYWORDS
children and adolescents, epidemiology, epilepsy, global, pediatrics

1 | INTRODUCTION

Epilepsy is a brain condition characterized by recurrent, unprovoked seizures and is one of the most common neurological diseases.[1,2] Epilepsy heavily impacts children and adolescents, with the prevalence in those aged 0–19 estimated at 702.5 per 100,000.[3] It carries long-standing physical, cognitive and socioeconomic consequences for patients and their caregivers.[4,5] Psychiatric/behavioural comorbidities such as autism spectrum disorders (ASDs) and attention-deficit/hyperactivity disorder (ADHD) are common in children with epilepsy, occurring in up to 60% of patients as opposed to 23% in children without epilepsy.[4,6] Stigma and discrimination further complicate diagnosis, treatment and education.[7]

Approximately 70% of children and adolescents with epilepsy achieve seizure freedom with appropriate antiseizure medications (ASMs).[1,8,9] However, despite ASMs costing as little as $5 USD per person annually,[1] access to healthcare varies by location. Approximately 70% of all epilepsy patients reside in low- and middle-income countries, where up to 75% of patients do not receive appropriate treatment.[1,2] A lack of prioritization on health agendas, issues with financing, poor drug supply and cultural stigma contribute to the healthcare gap in these regions.[10] Modifiable risk factors, including perinatal risk factors and central nervous system infections, account for approximately 25% of epilepsy cases and are key targets for prevention.[1,2]

The Global Burden of Diseases, Injuries and Risk Factors Study (GBD) 2021 provides systematic and comprehensive estimates of prevalence, incidence, deaths, disability-adjusted life years (DALYs), years lived with disability (YLDs) and years of life lost (YLLs) for 371 causes from 1990 to 2021 and supersedes all previous GBD cycles. This study presents the burden of epilepsy in children and adolescents (<20 years) by age, sex, geographic location, the Socio-demographic Index (SDI) and attributable cause from 1990 to 2021.

2 | METHODS

2.1 | Overview

The GBD 2021 produced global, regional and national epidemiological estimates across 204 countries and territories. Detailed methodologies are detailed in prior publications[11,12] and in Figures S1 and S2, Table S1. This study adheres to the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) guidelines (Table S2).

2.2 | Case definition

Epilepsy was defined as a condition with: (1) recurrent (two or more) epileptic seizures, unprovoked by any immediate identified cause and (2) at least one epileptic seizure in the previous 5 years, regardless of treatment. Following the 1985 ILAE Proposal,[13] epilepsy includes idiopathic epilepsy (where there is no identifiable cause other than genetic predisposition) and secondary epilepsy (where there is a known cause). As the majority of data sources used the 1985 ILAE definitions, this study does as well. The GBD identified all etiologies for which there is published evidence of an association with epilepsy, including: neglected tropical diseases (malaria, cysticercosis, cystic echinococcosis, food–borne trematodiases, zika virus), other infectious diseases (meningitis, encephalitis, tetanus) and neonatal disorders. The latter include neonatal preterm birth, neonatal encephalopathy due to birth asphyxia and trauma (henceforth neonatal encephalopathy), neonatal sepsis and other neonatal infections (henceforth neonatal infection), hemolytic disease and other neonatal jaundice (henceforth neonatal jaundice). This study focuses on the burden of epilepsy in patients under the age of 20 years.

2.3 | Mortality estimates

The input data sources for idiopathic epilepsy included vital registration, verbal autopsy and mortality surveillance data. Mortality estimates were computed using a Cause of Death Ensemble modelling (CODEm) approach, which employs out-of-sample predictive validity testing of statistical models and their combinations. YLLs, which represent the burden of disease caused by premature mortality, were calculated by multiplying the number of deaths by the predicted life expectancy.

2.4 | Non-fatal outcome estimates

Data sources for epilepsy included population-based surveys and clinical data sources. A systematic review covering the period from Jan 10, 2016 to Jan 28, 2020, added 23 studies to the 438 from GBD 2019. Datapoints with non-optimal diagnostic methods or alternate definitions of epilepsy were adjusted. DisMod-MR 2.1, a Bayesian meta-regression tool, was used to model the combined epilepsy impairment envelope. The envelope was split into primary and secondary epilepsy, then further stratified by severity level. For secondary epilepsy, the sequela prevalence values for each cause were modelled separately, then adjusted so that their sums fit the envelope. YLDs, representing the years of healthy life lost due to disability, were calculated by multiplying the prevalence of each severity level by its respective disability weight. DALYs were calculated as the sum of YLLs and YLDs.

2.5 | Statistical analysis

Estimates were presented as the mean estimate across 500 draws, followed by the 95% uncertainty interval (95% UI) in square brackets. Uncertainty was propagated through all computations and calculated as the 2.5th and 97.5th percentile values of draws. Percentage changes were deemed significant when the 95% UI did not include zero.

SDI is a composite measure of socioeconomic development and consolidates information about a location's economy, education and fertility.[14] Correlations between estimates and SDI (categorized by quintile and country) were analyzed. All secondary statistical analyses and visualizations were performed using R software (version 4.4.1).

3 | RESULTS

3.1 | The Global Burden of Epilepsy in Children and Adolescents in 2021

In 2021, there were 18.15 million [95% UI: 14.61–21.85] prevalent cases of epilepsy in children and adolescents (0–19 years), corresponding to a global prevalence rate of 688.43 [554.43–829.14] per 100,000 population (Table 1, Table S3a). Of all epilepsy cases, 8.24 million [5.77–11.13] were idiopathic epilepsy and 9.91 million [8.72–11.06] were secondary epilepsy. YLDs associated with epilepsy in children and adolescents totaled 6.01 million [3.87–8.74] (idiopathic: 2.81 million [1.70–4.54], secondary: 3.20 million [2.14–4.41]).

Neonatal disorders were the leading global causes of secondary epilepsy in children and adolescents. Among these, neonatal preterm birth caused the highest burden, with a prevalence rate of 217.82 [184.03–254.66] and a YLD rate of 70.14 [45.43–99.38], followed by neonatal encephalopathy, neonatal infection and neonatal jaundice (Figure S3). Additional contributors to secondary epilepsy included malaria and meningitis, as well as other infectious diseases. Idiopathic epilepsy accounted for 28.10 thousand [22.33–32.86] deaths and 4.98 million [3.81–6.63] DALYs in children and adolescents in 2021 (Table S3b).

3.2 | Trends in the Burden of Epilepsy from 1990 to 2021

Between 1990 and 2021, the absolute number of prevalent cases in children and adolescents increased by 27.75% [95% UI: 15.72–41.69] (14.20 million [11.76–16.80] in 1990 to 18.15 million [14.61–21.85] in 2021), while the prevalence rate increased only marginally (9.46% [−.84 to 21.41]; 628.91 [520.66–743.86] in 1990 to 688.43 [554.43–829.14] in 2021). This rise was largely driven by secondary epilepsy, which saw significant rises in both number (35.53% [21.69–50.82]) and rate (16.14% [4.28–29.24]), whereas idiopathic epilepsy remained stable.

Temporal trends in prevalence and YLD rates of secondary epilepsy differed by attributable cause. The burden attributable to neonatal preterm birth and neonatal infections remained stable, while epilepsy caused by neonatal encephalopathy, neonatal jaundice and malaria increased significantly (Figure 1). Conversely, the burden of epilepsy attributable to cysticercosis, cystic echinococcosis and other infectious diseases decreased significantly.

Mortality due to idiopathic epilepsy in children and adolescents decreased substantially from 1990 to 2021, in both number (−20.46% [−33.45 to −.97]) and rate (−31.85% [−42.97 to −15.15]). While the number of DALYs was stable (−8.93% [−21.31 to 6.80]), the DALY rate decreased by 21.96% [−32.57 to −8.49].

3.3 | Burden of Epilepsy by Sex and Age Group

In 2021, the global epilepsy prevalence rate in patients under 20 years was 725.27 [95% UI: 585.72–873.31] in males and 649.24 [524.37–778.85] in females (Table 2).

TABLE 1 Global prevalence and YLDs rates of epilepsy, idiopathic epilepsy, secondary epilepsy and underlying causes of secondary epilepsy in children and adolescents (<20 years) in 2021 and percentage change from 1990 to 2021.

	Prevalence		YLDs	
	Rate, per 100,000, 2021 [95% UI]	**Percentage change, 1990–2021 [95% UI]**	**Rate, per 100,000, 2021 [95% UI]**	**Percentage change, 1990–2021 [95% UI]**
Epilepsy	688.43 [554.43 to 829.14]	9.46 [−.84% to 21.41%]	227.92 [146.81 to 331.39]	−3.70 [−18.02% to 12.61%]
Idiopathic epilepsy	312.55 [218.86 to 422.37]	2.39 [−14.41% to 23.60%]	106.42 [64.43 to 172.37]	−9.86 [−27.80% to 12.01%]
Secondary epilepsy	375.87 [330.67 to 419.68]	16.14 [4.28% to 29.24%]	121.50 [81.15 to 167.43]	2.43 [−12.53% to 20.22%]
Neglected tropical diseases and malaria				
Malaria	9.61 [8.54 to 10.77]	77.03 [70.20% to 83.77%]	3.56 [2.34 to 4.98]	59.68 [41.57% to 84.59%]
Cysticercosis	1.80 [.64 to 3.73]	−30.66 [−35.42% to −26.02%]	.60 [.19 to 1.31]	−39.39 [−49.88% to −26.84%]
Cystic echinococcosis	.10 [.06 to .14]	−26.53 [−45.31% to −11.98%]	.03 [.02 to .05]	−37.85 [−55.01% to −19.54%]
Food-borne trematodiases	.26 [.05 to .61]	−80.86 [−84.33% to −77.30%]	.07 [.01 to .19]	−85.79 [−91.04% to −78.75%]
Zika virus	.00 [.00 to .01]	.00 [.00% to .00%]	.00 [.00 to .00]	.00 [.00% to .00%]
Other infectious diseases				
Meningitis	4.88 [4.06 to 5.71]	−62.24 [−63.73% to −60.74%]	1.78 [1.18 to 2.52]	−65.46 [−68.90% to −61.05%]
Encephalitis	1.47 [1.16 to 1.76]	−61.23 [−63.82% to −58.72%]	.48 [.31 to .69]	−67.29 [−72.54% to −60.25%]
Tetanus	.04 [.03 to .04]	−39.24 [−42.80% to −36.46%]	.01 [.01 to .02]	−45.76 [−51.73% to −38.52%]
Neonatal disorders				
Neonatal preterm birth	217.82 [184.03 to 254.66]	3.78 [−5.99% to 14.55%]	70.14 [45.43 to 99.38]	−9.82 [−24.05% to 6.21%]
Neonatal encephalopathy	79.15 [65.08 to 95.92]	82.02 [3.76% to 268.88%]	25.01 [16.08 to 36.60]	68.15 [−7.03% to 253.56%]
Neonatal infections	46.91 [31.03 to 66.61]	45.18 [−17.62% to 254.42%]	15.19 [8.45 to 23.79]	36.95 [−21.96% to 249.93%]
Neonatal jaundice	13.84 [11.81 to 16.02]	18.45 [11.89% to 25.28%]	4.61 [3.09 to 6.36]	3.93 [−7.94% to 19.13%]

The YLD rate was 239.74 [154.12–346.94] in males and 215.36 [138.52–313.10] in females. The rates for epilepsy and its subtypes were also comparable between sexes. From 1990 to 2021, the prevalence rate of secondary epilepsy increased by 12.96% [1.41–25.91] in males and 20.10% [7.64–34.14] in females, while other changes were generally not significant (Table S4a).

The idiopathic epilepsy mortality rate in 2021 was 1.22 [.92–1.44] in males and .90 [.65–1.10] in females, and DALY rates were 205.81 [157.81–268.56] in males and 171.31 [126.77–236.19] in females (Table S4b). Both sexes experienced comparable decreases in mortality and DALY rates over time.

Burden of epilepsy varied by age, with prevalence and YLDs lowest at <28 days and highest at 15–19 years for both sexes (Figure 2A). For both males and females, the burden of epilepsy attributable to malaria, cysticercosis, cystic echinococcosis, food–borne trematodiases and tetanus increased progressively with age, while zika virus primarily impacted children under 12 months (Figure 2B–D, Figure S4a). Epilepsies attributable to meningitis and encephalitis showed bell-shaped distributions peaking at 2–4 years and 10–14 years, respectively. Neonatal disorders had a bell-shaped trend as well, although the differences between age groups were less. Notably, the peaks of meningitis and encephalitis were the same between sexes, while the peaks for all four neonatal disorders occurred at younger age groups for females.

Idiopathic epilepsy exhibited a bimodal pattern for mortality and DALYs, peaking at >12 months and 15–19 years for both sexes. Incidence declined with age for both sexes, with rates highest at <28 days (Figure S4b).

The burden associated with secondary epilepsy generally decreased across all age groups between 1990 and 2021; Malaria was an exception with increases in all age groups (Table S5a). The burden of combined epilepsy, idiopathic epilepsy and epilepsy due to neonatal disorders generally declined in younger age groups while older age groups underwent insignificant or positive changes (Table S5a,b).

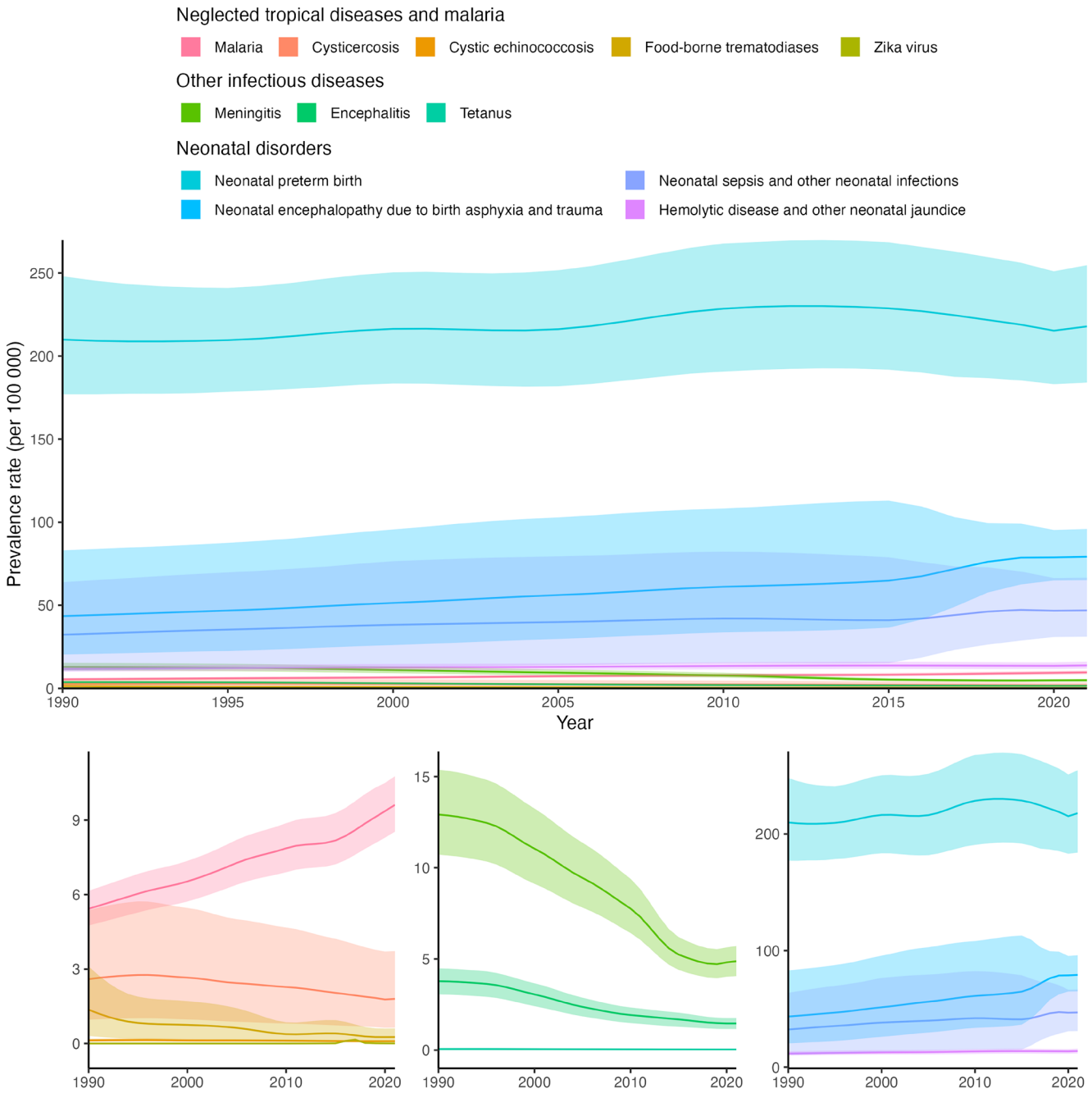

FIGURE 1 Rate of prevalence for underlying causes of secondary epilepsy, <20 years, both sexes, global, 1990–2021. Ribbons indicate 95% uncertainty intervals. The top panel of this figure shows trends of all causes of secondary epilepsy; bottom panels show more detailed trends grouped by cause type (right: Neglected tropical diseases and malaria, center: Other infectious diseases, left: Neonatal disorders).

3.4 | Burden of Epilepsy by Geographic Location

In 2021, highest national prevalence rates of epilepsy in those below 20 years were reported in Trinidad and Tobago (1224.26 [95% UI: 824.75–1639.92]; Figure 3A). Regionally, the burden of epilepsy was highest in Sub-Saharan African (SSA) and Latin America and the Caribbean (LAC) nations (Figure 3B). In contrast, prevalence rates were lowest in nations in East Asia (China: 451.11 [363.82–542.03]) and Western Europe. Similarly, YLD rates were highest in SSA nations (Gabon: 411.58 [190.38–702.77]) and lowest in Western European nations (Spain: 113.64 [40.54–261.56]).

From 1990 to 2021, the prevalence and YLDs of combined and idiopathic epilepsy remained constant globally and in most countries. Conversely, secondary epilepsy prevalence rose globally and especially in SSA, where 42 out of 46 nations saw increases. The YLD rate of secondary epilepsy also rose in SSA and parts

TABLE 2 Global prevalence and YLDs rates (per 100,000) of epilepsy, idiopathic epilepsy, secondary epilepsy and underlying causes of secondary epilepsy in children and adolescents (<20 years), male and female, in 2021 and percentage change from 1990 and 2021.

	Prevalence				YLDs			
	Male		Female		Male		Female	
	Rate, 2021 [95% UI]	Percentage change, 1990–2021 [95% UI]	Rate, 2021 [95% UI]	Percentage change, 1990–2021 [95% UI]	Rate, 2021 [95% UI]	Percentage change, 1990–2021 [95% UI]	Rate, 2021 [95% UI]	Percentage change, 1990–2021 [95% UI]
Epilepsy	725.27 (585.72 to 873.31)	7.54 (−2.45% to 19.10%)	649.24 (524.37 to 778.85)	11.73 (.81% to 24.28%)	239.74 (154.12 to 346.94)	−5.63 (−19.73% to 10.82%)	215.36 (138.52 to 313.10)	−1.41 (−15.65% to 15.07%)
Idiopathic epilepsy	324.02 (228.44 to 436.85)	1.50 (−15.36% to 23.47%)	300.36 (207.57 to 408.08)	3.37 (−13.36% to 23.91%)	110.36 (67.45 to 177.92)	−10.79 (−28.88% to 11.36%)	102.24 (61.41 to 166.37)	−8.84 (−26.82% to 12.02%)
Secondary epilepsy	401.26 (349.74 to 448.19)	12.96 (1.41% to 25.91%)	348.88 (310.38 to 387.64)	20.10 (7.64% to 34.14%)	129.38 (85.07 to 179.10)	−.73 (−15.49% to 17.15%)	113.12 (76.06 to 155.00)	6.42 (−8.71% to 23.47%)
Neglected tropical diseases and malaria								
Malaria	9.16 (8.10 to 10.29)	77.99 (70.57% to 85.01%)	10.10 (8.97 to 11.27)	76.21 (69.46% to 83.02%)	3.40 (2.26 to 4.80)	60.41 (41.30% to 88.74%)	3.73 (2.42 to 5.22)	59.08 (40.38% to 82.80%)
Cysticercosis	1.40 (.46 to 3.01)	−29.98 (−35.03% to −25.28%)	2.23 (.82 to 4.56)	−30.94 (−36.11% to −25.90%)	.47 (.14 to 1.05)	−39.04 (−51.17% to −24.45%)	.75 (.24 to 1.61)	−39.49 (−50.79% to −25.00%)
Cystic echinococcosis	.09 (.05 to .14)	−23.63 (−43.02% to −7.84%)	.10 (.06 to .15)	−29.04 (−46.73% to −15.08%)	.03 (.02 to .05)	−35.04 (−53.27% to −15.97%)	.03 (.02 to .06)	−40.26 (−56.28% to −22.58%)
Food–borne trematodiases	.31 (.06 to .71)	−80.28 (−83.74% to −76.57%)	.21 (.04 to .49)	−81.70 (−85.01% to −78.08%)	.08 (.02 to .23)	−85.35 (−91.16% to −77.21%)	.06 (.01 to .16)	−86.44 (−91.45% to −80.94%)
Zika virus	.00 (.00 to .01)	.00 (.00% to .00%)	.00 (.00 to .01)	.00 (.00% to .00%)	.00 (.00 to .00)	.00 (.00% to .00%)	.00 (.00 to .00)	.00 (.00% to .00%)
Other infectious diseases								
Meningitis	5.08 (4.25 to 5.95)	−62.39 (−63.97% to −60.73%)	4.67 (3.88 to 5.46)	−62.08 (−63.67% to −60.52%)	1.85 (1.21 to 2.63)	−65.54 (−69.39% to −60.75%)	1.70 (1.13 to 2.40)	−65.39 (−69.27% to −60.23%)
Encephalitis	1.50 (1.17 to 1.81)	−59.56 (−62.39% to −57.06%)	1.43 (1.13 to 1.71)	−62.92 (−65.33% to −60.38%)	.49 (.31 to .71)	−66.03 (−71.97% to −58.90%)	.47 (.30 to .67)	−68.56 (−73.81% to −61.39%)
Tetanus	.04 (.03 to .04)	−39.05 (−43.31% to −35.72%)	.04 (.03 to .04)	−39.43 (−42.23% to −36.90%)	.01 (.01 to .02)	−45.64 (−51.82% to −38.37%)	.01 (.01 to .02)	−45.87 (−51.29% to −38.76%)
Neonatal disorders								
Neonatal preterm birth	225.72 (189.54 to 266.40)	−1.72 (−10.54% to 7.91%)	209.41 (177.98 to 242.50)	10.74 (−.60% to 23.03%)	72.71 (46.97 to 102.65)	−14.94 (−28.48% to .60%)	67.41 (43.76 to 95.32)	−3.27 (−18.52% to 14.24%)
Neonatal encephalopathy	91.33 (75.33 to 109.98)	76.21 (.70% to 251.48%)	66.20 (54.07 to 81.59)	90.69 (7.77% to 292.92%)	28.63 (18.30 to 41.38)	62.17 (−8.88% to 231.69%)	21.16 (13.63 to 30.92)	77.06 (−2.51% to 288.54%)
Neonatal infections	53.02 (35.29 to 75.21)	47.29 (−17.65% to 279.83%)	40.41 (26.50 to 57.16)	42.09 (−16.16% to 232.15%)	17.18 (9.55 to 26.92)	38.08 (−22.97% to 266.27%)	13.08 (7.26 to 20.02)	35.16 (−21.94% to 221.28%)
Neonatal jaundice	13.62 (11.56 to 15.80)	17.04 (10.18% to 23.82%)	14.08 (12.08 to 16.25)	19.94 (13.28% to 26.88%)	4.52 (3.02 to 6.24)	2.53 (−9.97% to 17.89%)	4.71 (3.15 to 6.51)	5.41 (−6.56% to 20.70%)

of South and Southeast Asia (India, Indonesia and the Philippines).

The burden of epilepsy due to infectious diseases was generally concentrated in equatorial regions like SSA, LAC and Southeast Asia (Figure 3C–J, Figure S5a,b). There was cause-specific geographical variation; for example, malaria and meningitis-attributable epilepsy were concentrated in Central and Western SSA, while tetanus primarily impacted Southeast Asia. Food-borne trematodiases attributable epilepsy was mostly confined to Ecuador, China and Laos, which together accounted for 99.56% of the global burden. In contrast, epilepsy from neonatal disorders showed a more widespread distribution (Figure 3K–N).

In 2021, the burden of idiopathic epilepsy was prominent in SSA, Central Asia and LAC. Although mortality decreased or remained unchanged in most countries from 1990 to 2021, some, such as Japan, the USA and Italy, experienced increases (Figure S5c).

3.5 | Trends between the Burden of Epilepsy and SDI

A clear inverse relationship was observed between epilepsy DALYs burden and SDI. In 2021, the DALY rate for idiopathic epilepsy was highest in the lowest SDI quintile and decreased progressively with increasing SDI quintiles (Figure 4A). Since 1990, the high SDI quintile has stagnated while the other quintiles underwent significant decreases, leading to the high and high-middle SDI quintiles having approximately equal rates from 2019 onward. The YLDs for both idiopathic and secondary epilepsy followed a similar trend (Figure 4B,C). In contrast, prevalence rates showed no consistent SDI gradient (Figure S6).

4 | DISCUSSION

This study highlights the substantial and persistent global burden of epilepsy in children and adolescents, with prominent variation by cause, age, geography and socioeconomic development. While the overall burden of idiopathic epilepsy has declined over the past three decades, the burden of secondary epilepsy—which is often preventable or treatable—has persisted and, in some cases, even increased. These patterns suggest that epilepsy in youths reflects both biological vulnerability and broader inequities in health systems and socioeconomic conditions.

A key finding is the shifting burden from idiopathic toward secondary epilepsy. Approximately half of all epilepsy-related prevalence and YLDs were attributed to secondary causes, and over 95% of that was linked to neonatal disorders and modifiable risk factors.[15] Notably, epilepsy attributable to neonatal encephalopathy, neonatal jaundice and malaria increased over time. This may reflect both improved neonatal survival and persistent gaps in early intervention and perinatal care.[1]

The burden of epilepsy was more substantive in lower SDI quintiles and countries, especially in Sub-Saharan Africa and Latin America. This pattern likely reflects an increased risk of infectious diseases and perinatal insults,[15,16] as well as poor sanitation and limited access to healthcare (health worker/specialist density and distribution, available diagnostic tools and medications, total health-related costs).[17,18] Parasite-associated epilepsies (including those caused by malaria, cysticercosis and cystic echinococcosis) were particularly common in these regions.[17] As more children survive these conditions, the burden of parasite-associated epilepsy is evolving; for instance, in Central and Western SSA, the primary presentation of malaria is expected to shift from severe anaemia in younger children (<5 years) to cerebral malaria in school-age children and adolescents.[19]

Beyond medical infrastructure, the broader psychosocial impact of epilepsy—including social stigma—contributes to the considerable burden of epilepsy. Negative perceptions derived from cultural and religious beliefs, which may lead to rejection from the community, physical/verbal/sexual abuse and discrimination for patients and their caregivers, may reduce healthcare-seeking behaviours and lead to underreporting, further compounding disparities.[20–23] Children and adolescents with epilepsy also face increased risks of comorbid conditions, including ADHD, depression, anxiety, ASD, sleep disorders, migraines and cognitive impairment.[6,24] These comorbidities are underdiagnosed and undertreated, especially in underdeveloped regions, despite their strong association with reduced quality of life.[6,18,25]

Despite global efforts, the overall burden of epilepsy in children and adolescents has remained unchanged since 1990. While prevalence and YLDs of idiopathic epilepsy have remained stable, sustained declines in mortality—likely reflecting improved availability and effectiveness of treatments—have driven reductions in DALY rates. However, underreporting and misclassification of epilepsy-related deaths remain barriers to accurately capturing trends.[26–28] Recent reviews suggest that the risk of premature mortality is disproportionately high in children and adolescents with epilepsy, with standardized mortality ratios ranging from 3.1 to 22.4 times that of the general population.[26,29] Although this study found that mortality rates have improved, sustained management and surveillance are necessary to maintain and further advancements in this vulnerable population.

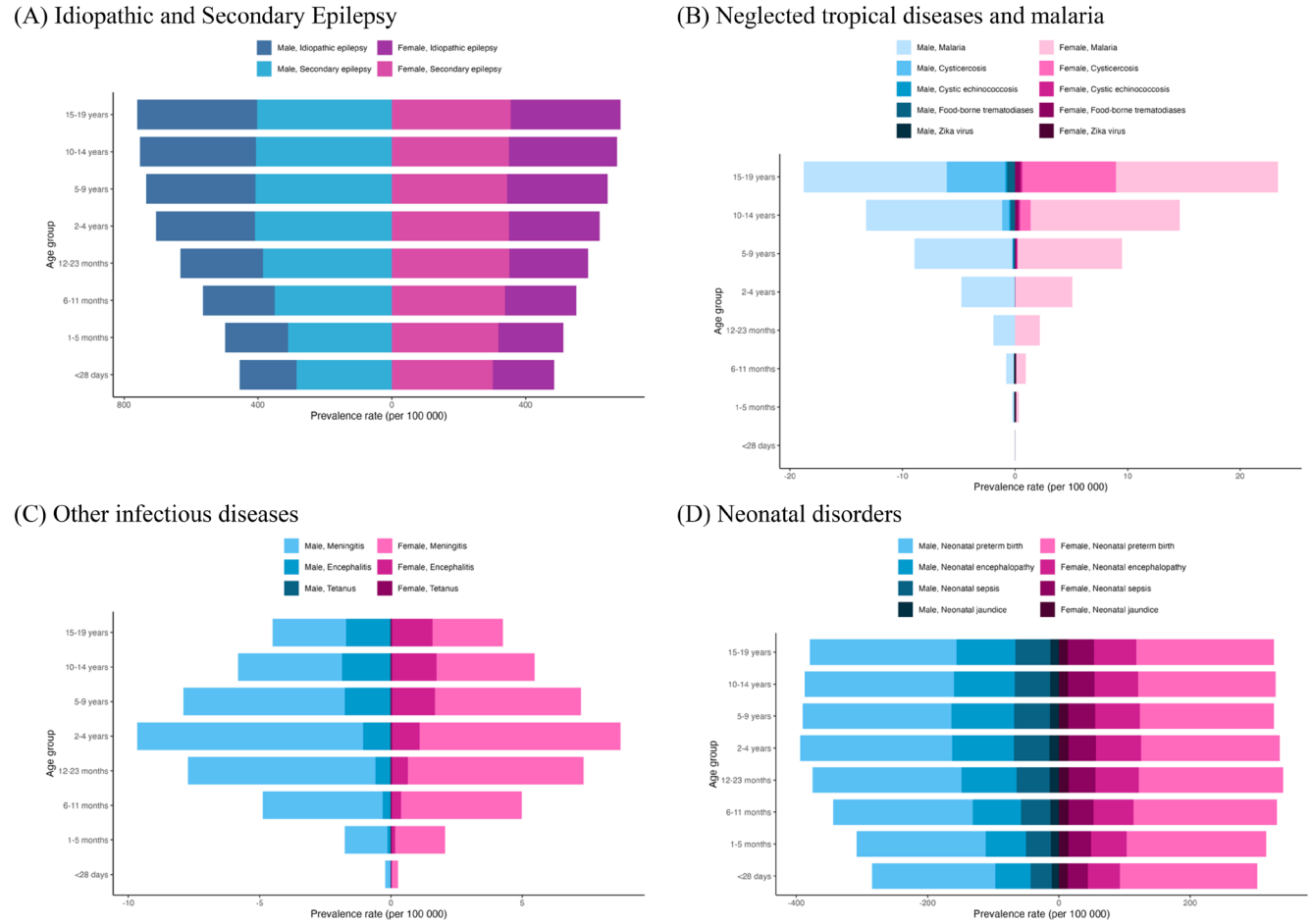

FIGURE 2 Prevalence rates of epilepsy by cause and age group, male and female, Global, 2021.

Sex- and age-specific findings were largely consistent with prior literature,[3,27,30,31] showing near-equal burden between sexes and the highest incidence in the first year of life. There are established disparities by seizure type and epilepsy syndrome, showing male predominance (infantile spasms), female predominance (juvenile absence epilepsy) or no significant gap (temporal lobe epilepsy).[30,32] These variations are likely linked to sex hormones, neurosteroids, biological differences in neuronal networks and genetic predispositions.[32,33] Sex disparities can also be seen in response to medication and sexual/reproductive development.[30,34] This study confirmed that the incidence of idiopathic epilepsy was indeed highest in the youngest age group (<28 days), even when further disaggregated by age, emphasizing the importance of early-life interventions. However, biologically driven sex disparities may not have been captured in this study's aggregate analysis.

The specific impact of the COVID-19 pandemic on children and adolescents with epilepsy is unclear and requires further investigation. Recent studies found that SARS-CoV-2 infections could directly induce or exacerbate seizures, and people with epilepsy were at higher risk of COVID-19 incidence and mortality.[35,36] Patients also experienced difficulties in epilepsy management, including restricted access to care (lower availability of diagnostic tools and medication, postponed consultations and surgeries), difficulties maintaining/initiating dietary therapies, interactions between ASMs and COVID-19 therapies and mental health complications.[37–40] These secondary effects highlight the vulnerability of this population during global health emergencies.

Given the substantial burden of epilepsy, an interdisciplinary approach from all levels of health and social services is required. Initiatives such as the WHO Mental Health Gap Action Programme[41] (targeting the treatment gap and mental health gap of mental, neurological and substance use disorders in low- and middle-income countries) and the 'Intersectoral Global Action Plan on Epilepsy and Other Neurological Disorders'[2] have provided guidelines for and improved public health responses to epilepsy. However, further investments are needed to improve specialist density and distribution, improve essential medicine availability and affordability,

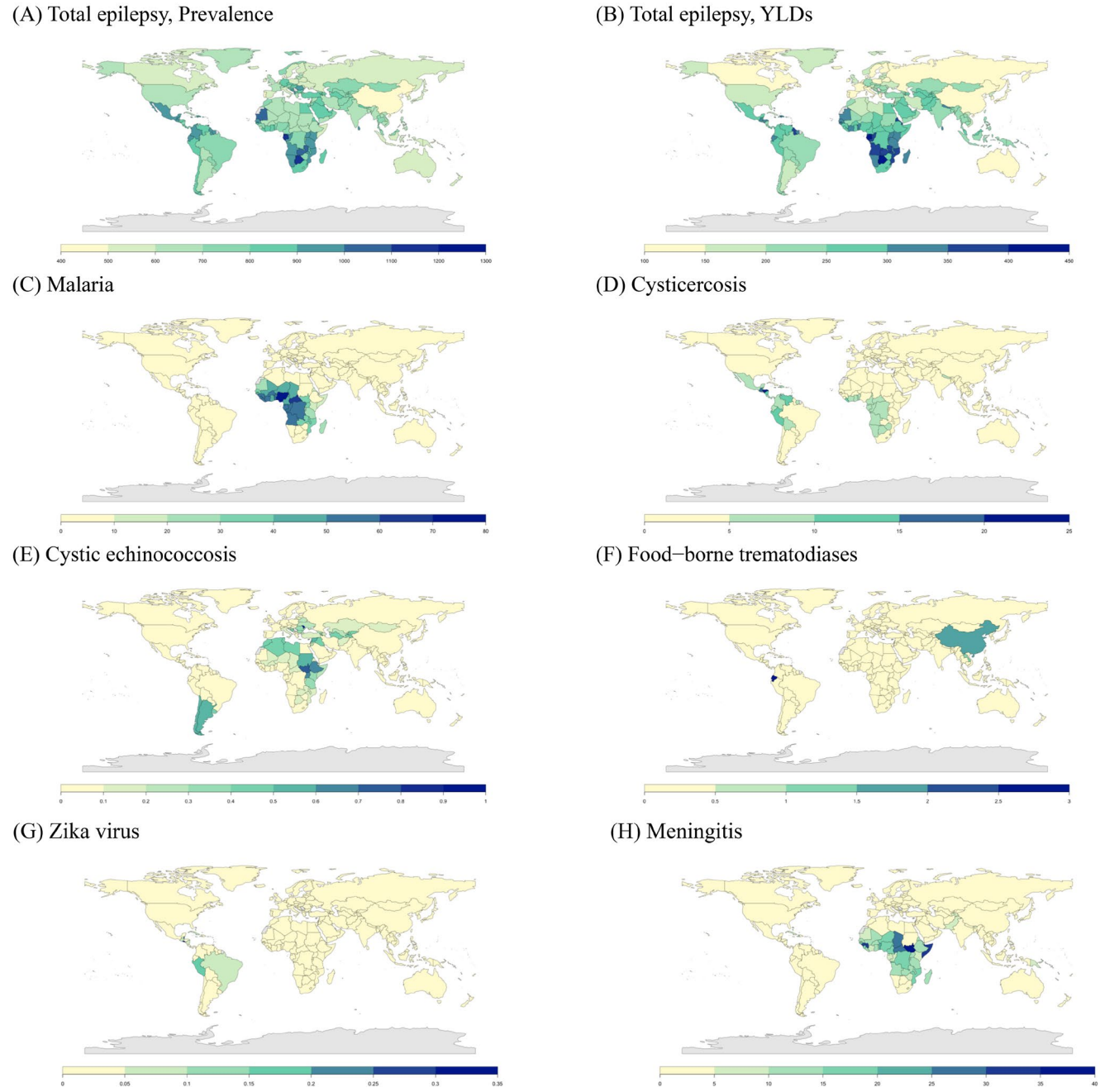

FIGURE 3 Rate of (A) prevalence, (B) YLDs for Total epilepsy, <20 years, both sexes, countries and territories, 2021; and Rate of prevalence for causes of Secondary epilepsy: (C) Malaria, (D) Cysticercosis, (E) Cystic echinococcosis, (F) Food−borne trematodiases, (G) Zika virus, (H) Meningitis, (I) Encephalitis, (J) Tetanus, (K) Neonatal preterm birth, (L) Neonatal encephalopathy, (M) Neonatal infections, (N) Neonatal jaundice, <20 years, both sexes, countries and territories, 2021. YLDs, Years Lived with Disability. Countries with missing data were marked in grey.

manage mental health and comorbidities and increase awareness and education to combat stigma. Primary prevention in maternal, obstetric, paediatric, communicable disease control and environmental health could have a meaningful impact on the trajectory of secondary epilepsy. Improved funding and research infrastructure are essential, particularly for ASM use in children, the development of epilepsy from brain infections and targeted surveillance.

This study is the first systematic analysis to provide global, regional and national estimates for epilepsy and its subtypes in patients under 20 years. While previous studies have provided broader estimates, this study presents updated detailed estimates by age (disaggregating

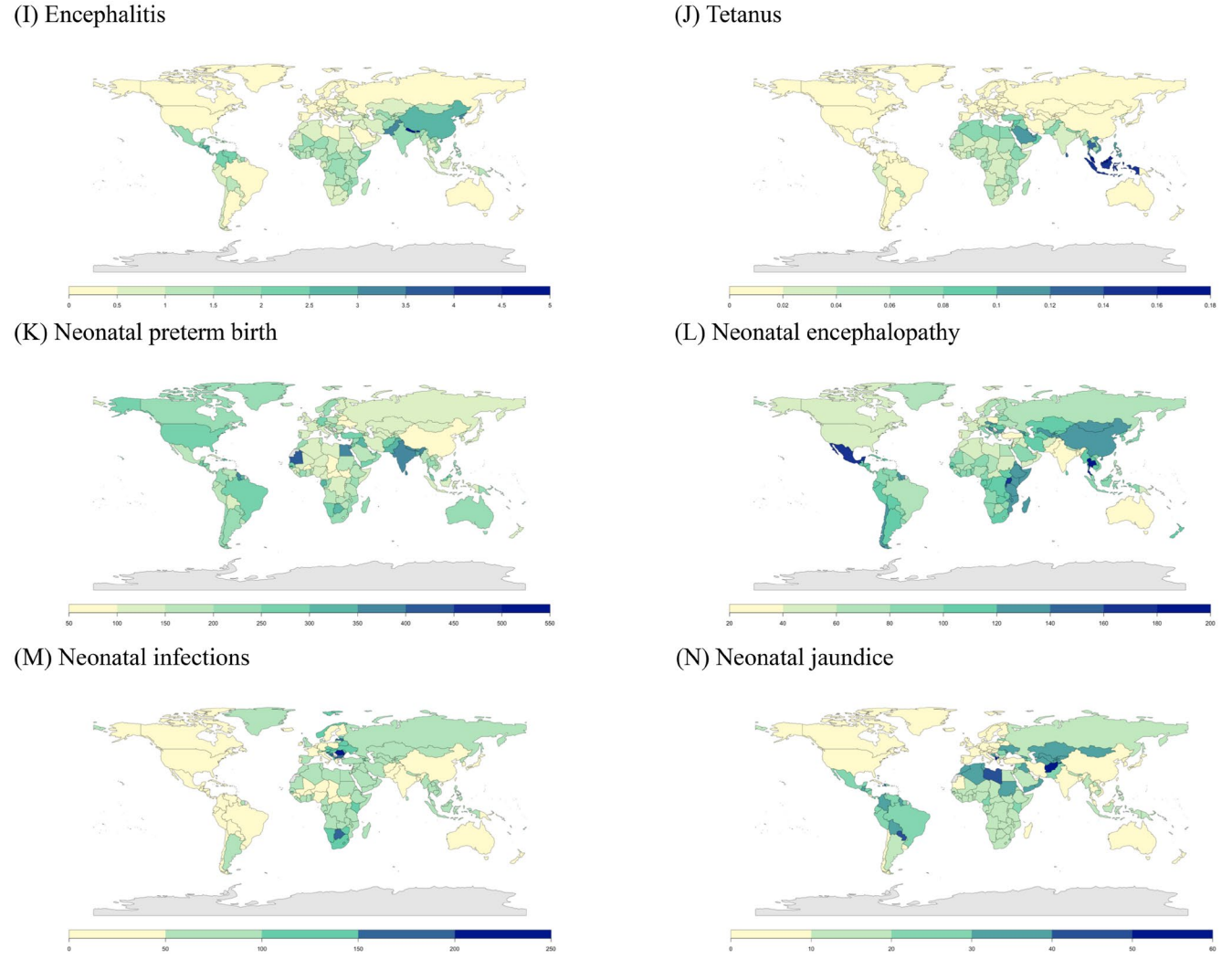

FIGURE 3 (Continued)

the <5 years age group further into <28 days, 1–5 months, 6–11 months, 12–23 months, 2–4 years) and attributable cause. This level of detail is enabled by the GBD modelling framework, which incorporates a broad range of etiologies—including rare and geographically restricted causes such as congenital Zika virus infection in LAC. Although such diseases contribute only minimally to the global totals, they can have a significant impact in affected regions. These comprehensive estimates are important for regional monitoring and planning, thereby providing essential evidence for policymaking and resource allocation of health and social services. However, there are several limitations to this study. First, the accuracy of data is limited by the sources available. Only 93 of the 204 countries and territories recognized by this study had reliable data sources. Second, this study does not provide an analysis of many causes of secondary epilepsy, including stroke, brain tumours and developmental brain abnormalities. As estimates for cause-specific epilepsy were adjusted so that their sums fit the secondary epilepsy envelope, other secondary causes may be overestimated. Third, analysis by seizure type and epilepsy syndrome was not available due to limitations in data granularity. Fourth, premature mortality due to secondary epilepsy was not available. Mortality due to secondary epilepsy is considered higher than that of idiopathic epilepsy,[26,27] and the unmeasured burden (deaths, YLLs, DALYs) of secondary epilepsy is likely substantial.

In conclusion, this study highlights the shifting trends of epilepsy in children and adolescents and the urgent need for expanded epilepsy prevention and care strategies. While mortality due to idiopathic epilepsy has decreased, the prevalence of secondary epilepsies has increased. In particular, neonatal encephalopathy, neonatal jaundice and malaria-attributable epilepsy prevalence rates increased significantly. Lower SDI regions were

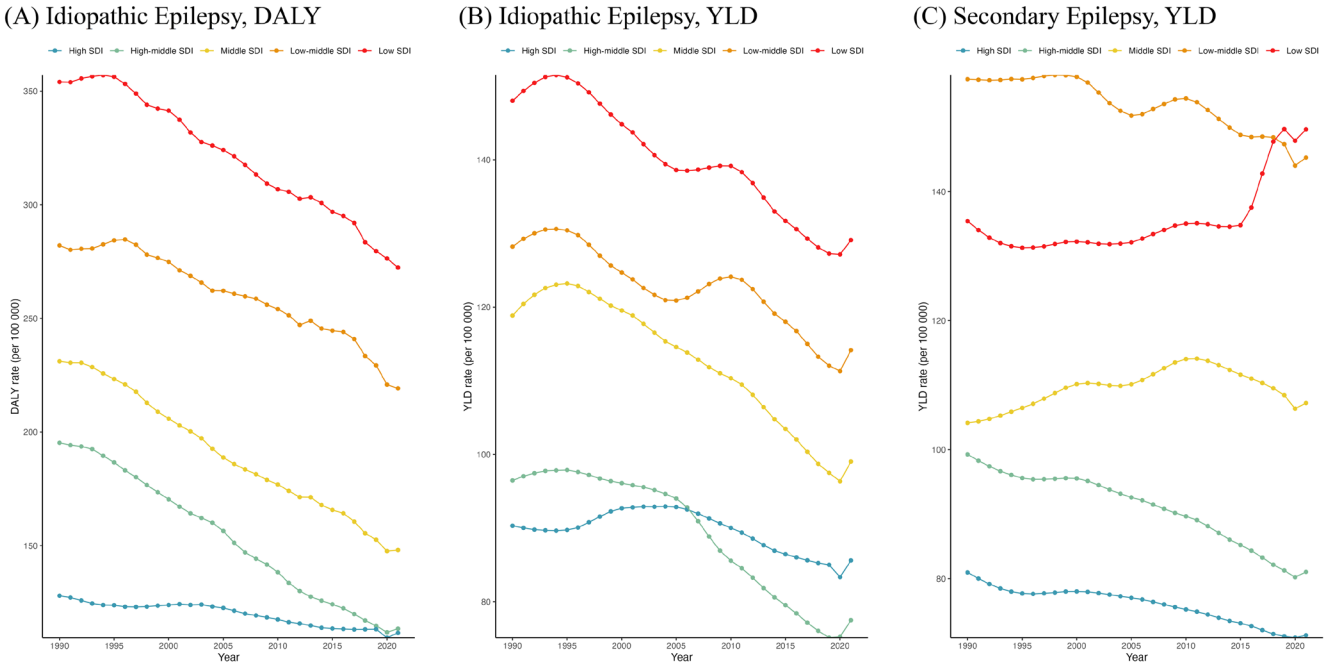

FIGURE 4 (A) DALY, (B) YLD rate of Idiopathic Epilepsy, (C) YLD rate of Secondary Epilepsy, <20 years, both sexes, GBD quintiles, 2021. DALYs, Disability-Adjusted Life Years. YLDs, Years Lived with Disability.

disproportionately burdened, reflecting systemic inequities in maternal and pediatric healthcare and social determinants of health. Targeted efforts in these areas, along with improved investment in psychiatric comorbidities and development of epilepsy due to brain infections, as well as continued surveillance, are essential to reducing global disparities and improving outcomes for youths with epilepsy.

AUTHOR CONTRIBUTIONS

Yun Seo Kim collected data, carried out the initial analyses, drafted the initial manuscript and critically reviewed and revised the manuscript. Min Seo Kim and Seoyeon Park conceptualized and designed the study, carried out the initial analyses and critically reviewed and revised the manuscript. Lee Smith, Joaquim Radua, Sarah Soyeon Oh, Stefania I Papatheodorou, Hoon Chul Kang, Ara Ko and Dong Keon Yon critically reviewed and revised the manuscript. Jae Il Shin conceptualized and designed the study and critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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CONFLICT OF INTEREST STATEMENT

None of the authors have any conflicts of interest to disclose. There are no conflicts of interest related to the study design or its results.

DATA AVAILABILITY STATEMENT

To download the data used in these analyses, please visit the Global Health Data Exchange GBD2021 website at https://ghdx.healthdata.org/gbd-2021.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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