Preventive Medicine Reports 36 (2023) 102522

Contents lists available at ScienceDirect

Preventive Medicine Reports

journal homepage: www.elsevier.com/locate/pmedr

Analysis of the global burden of disease study highlights the global, regional, and national trends of idiopathic epilepsy epidemiology from 1990 to 2019

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ARTICLE INFO

Keywords:
Epilepsy
Global Burden of disease
Disability-adjusted life years
Incidence
Prevalence

ABSTRACT

Epilepsy is a profound disorder, accounting for roughly 1% of the global disease burden. It can result in premature death and significant disability. To comprehensively understand the current dynamics and trends of idiopathic epilepsy, a deep insight into its epidemiological attributes is vital. We evaluated the incidence, prevalence, mortality, and disability-adjusted life years associated with idiopathic epilepsy from 1990 to 2019 using data and methodologies from the Global Burden of Disease Study.

In 2019, there were approximately 2,898,222 individuals diagnosed with idiopathic epilepsy. Intriguingly, from 1990 to 2019, the age-standardized incidence rate of idiopathic epilepsy was consistently lower in women compared to men. Over these three decades, global mortality connected to idiopathic epilepsy increased by 13.95%. However, within the same period, age-standardized death rates for idiopathic epilepsy decreased from 1.94 per 100,000 population to 1.46 per 100,000 population. Predictions indicate an increase in the incidence of idiopathic epilepsy across all age brackets through 2035, especially among the elderly aged 80 and above. Mortality rates are projected to climb for those aged 80 and above while remaining relatively unchanged in other age demographics. Idiopathic epilepsy continues to be a significant contributor to both disability and death. The findings of our study underscore the critical importance of incorporating idiopathic epilepsy management into modern healthcare frameworks. Such strategic inclusion can enhance public awareness of relevant risk factors and the range of available therapeutic interventions.

1. Introduction

Epilepsy is one of the foremost neurological disorders, affecting nearly 1 % of the global population(Walton et al., 2021). It is characterized by recurrent unprovoked seizures stemming from various aetiologies(Paz and Huguenard, 2015). Despite the introduction of over 20 new antiseizure medications in recent decades, the proportion of patients achieving seizure freedom (a 100 % reduction in seizure frequency) remains unchanged(Hauser, 2018; Golyala and Kwan, 2017). Those with uncontrolled seizures suffer a reduced quality of life due to increased comorbidities, cognitive decline, and rising healthcare costs. They also face higher risks of injuries, premature death from status epilepticus, and sudden unexpected death in epilepsy(Laxer et al., 2014; Nevalainen et al., 2015; Amin and Benbadis, 2020; Lawn et al., 2004; Thurman et al., 2017; Zou et al., 2022; Klein et al., 2022).

While numerous underlying conditions can cause epilepsy, the

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https://doi.org/10.1016/j.pmedr.2023.102522
Received 28 August 2023; Received in revised form 20 November 2023; Accepted 21 November 2023
Available online 26 November 2023

Table 1
Incident Cases and ASIR of Idiopathic Epilepsy in 1990 and 2019 and Its Trends.

Characteristics	1990 Incident cases No. *10^2 (95 % UI)	ASIR per 100,000 No. (95 % UI)	2019 Incident cases No. *10^2 (95 % UI)	ASIR per 100,000 No.(95 % UI)	1990–2019 EAPC No. (95 % CI)
Overall	18595.17 [12817.83–25260.87]	33.22 [23.4–44.69]	28982.22 [20987.18–38233.76]	38.82 [27.99–51.28]	0.49 [0.46 to 0.52]
Sex					
Female	8492.56 [5863.01–11515.64]	30.71 [21.57–41.26]	13239.78 [9607.44–17468.04]	35.78 [25.63–47.63]	0.48 [0.45 to 0.51]
Male	10102.61 [6970.29–13710.58]	35.73 [25.32–48.09]	15742.44 [11412.71–20735.83]	41.83 [30.36–55.18]	0.49 [0.46 to 0.52]
Socio-demographic index					
High SDI	3102.41 [2112.76–4198.71]	40.55 [27.3–54.89]	4054.29 [2714.12–5463.15]	44.29 [29.01–60.92]	0.37 [0.31 to 0.42]
High-middle SDI	3488.34 [2443.24–4707.85]	30.94 [21.7–41.67]	4614.38 [3152.82–6116.32]	36.42 [24.7–50.24]	0.46 [0.41 to 0.51]
Middle SDI	5665.07 [3829.76–7831.89]	30.91 [21.29–42.27]	8553.16 [6053.42–11428.73]	38.21 [27.05–50.8]	0.63 [0.58 to 0.69]
Low-middle SDI	4000.23 [2367–5816.03]	31.49 [19.25–45.36]	6654.38 [4451.98–8998.64]	37.46 [25.47–50.67]	0.61 [0.54 to 0.68]
Low SDI	2327.87 [1292.59–3645.29]	37.6 [20.92–57.29]	5088.22 [3218.74–7342.12]	40 [26.46–55.65]	0.2 [0.15 to 0.25]
Region					
Andean Latin America	232.49 [98.84–364.38]	55.36 [24.01–86.19]	351.15 [159.7–532.54]	55.28 [25.08–83.69]	−0.03 [-0.12 to 0.07]
Australasia	82.46 [33.52–127.66]	42.69 [17.24–67.09]	112.26 [43.15–170.62]	42.48 [16.51–65.72]	−0.02 [-0.05 to 0.02]
Caribbean	151.81 [88.04–222.02]	41 [24.19–59.75]	191.55 [115.45–280.18]	42 [25.04–61.48]	0.05 [-0.02 to 0.11]
Central Asia	322.68 [190.51–470.02]	42.44 [25.16–61.35]	429.39 [250.93–626.88]	46 [27.06–66.9]	0.28 [0.22 to 0.35]
Central Europe	440.97 [298.92–605.09]	37.63 [25.36–51.52]	451.47 [301.77–609.78]	42.08 [27–57.95]	0.42 [0.39 to 0.45]
Central Latin America	1029.9 [666.62–1458.73]	56.84 [37.71–78.87]	1399.38 [935.62–1943.3]	57.1 [38.03–78.58]	−0.03 [-0.1 to 0.03]
Central Sub-Saharan Africa	285.26 [100.43–509.17]	43.16 [15.8–75.32]	699.79 [276.27–1208.78]	46.18 [18.5–77.28]	0.24 [0.07 to 0.42]
East Asia	2097.58 [1356.77–2947.99]	17.15 [11.26–24]	3163.58 [2177.38–4226.18]	24.59 [16.63–33.63]	0.69 [0.39 to 0.99]
Eastern Europe	704.19 [475.81–966.63]	33.12 [22.04–45.66]	628.46 [431.01–853.68]	33.34 [22.76–46.7]	−0.05 [-0.13 to 0.03]
Eastern Sub-Saharan Africa	959.4 [511.83–1518.97]	43.71 [23.71–66.94]	2116.25 [1283.55–3072.55]	46.53 [28.94–65.54]	0.17 [0.06 to 0.29]
High-income Asia Pacific	598.39 [374.72–829.15]	38.11 [23.52–53.49]	617.15 [389.05–840.79]	41.09 [24.77–58.18]	0.12 [0.05 to 0.2]
High-income North America	1045.47 [693.89–1450.92]	39.95 [26.21–56.13]	1310.09 [872.28–1766.97]	38.87 [25.59–53.3]	0.03 [-0.11 to 0.17]
North Africa and Middle East	1765.44 [1118.36–2524.23]	44.54 [28.38–63.02]	2954.53 [1950.44–4076.82]	48.24 [32.23–66.36]	0.46 [0.41 to 0.52]
Oceania	19.03 [8.36–32.96]	26.17 [11.9–44.42]	39.02 [15.71–68.15]	27.21 [11.29–46.92]	0.01 [-0.06 to 0.08]
South Asia	3708.53 [2172.17–5469.99]	30.31 [18.32–44.15]	6289.81 [4231.98–8541.18]	35.09 [23.88–47.28]	0.58 [0.47 to 0.69]
Southeast Asia	1482.4 [936.57–2121.57]	28.93 [18.71–40.72]	2307.89 [1590.5–3092.42]	36.21 [25.02–48.62]	0.75 [0.7 to 0.8]
Southern Latin America	197.77 [96.37–307.88]	39.13 [19.02–60.56]	270.18 [115.75–411.86]	43.48 [18.56–67.13]	0.34 [0.28 to 0.4]
Southern Sub-Saharan Africa	220.64 [137.38–321.93]	39.93 [25.7–56.82]	321.04 [208.11–451.93]	41.48 [27.07–57.53]	−0.32 [-0.58 to −0.07]
Tropical Latin America	760.44 [466.41–1109.61]	47.5 [29.78–68.48]	955.32 [619.61–1319.16]	44.56 [28.72–61.9]	−0.13 [-0.52 to 0.26]
Western Europe	1467.55 [937.12–1967.71]	41.43 [26.31–55.8]	1912.43 [1218.28–2587.08]	47.12 [29.21–66.21]	0.48 [0.41 to 0.55]
Western Sub-Saharan Africa	1022.78 [599.67–1530.44]	45.1 [27.4–64.96]	2461.46 [1561.94–3478.37]	47.55 [31.62–64.79]	0.12 [-0.03 to 0.28]

Table 2
Death Cases and ASDR of Idiopathic Epilepsy in 1990 and 2019 and Its Trends.

Characteristics	1990 Deaths cases No. *102 (95 % UI)	ASDR per 100,000 No. (95 % UI)	2019 Deaths cases No. *102 (95 % UI)	ASDR per 100,000 No.(95 % UI)	1990–2019 EAPC No. (95 % CI)
Overall	1000.54 [811.76–1122.26]	1.94 [1.61–2.15]	1140.11 [1001.78–1299.28]	1.46 [1.28–1.67]	−1.11 [-1.18 to −1.03]
Sex					
Female	434.48 [314.27–518.71]	1.66 [1.23–1.96]	485.65 [379.26–556.54]	1.21 [0.96–1.39]	−1.28 [-1.37 to −1.19]
Male	566.06 [452.99–626.43]	2.23 [1.85–2.45]	654.46 [586.93–757.67]	1.71 [1.53–1.98]	−0.99 [-1.06 to −0.92]
Socio-demographic index					
High SDI	86.22 [83.68–95.27]	0.96 [0.93–1.06]	133.59 [111.3–142.68]	0.92 [0.81–0.98]	−0.04 [-0.13 to 0.06]
High-middle SDI	156.03 [140.32–168.97]	1.38 [1.23–1.49]	148.41 [135.31–162.62]	0.91 [0.83–1]	−1.65 [-1.75 to −1.55]
Middle SDI	267.25 [228.76–291.41]	1.67 [1.45–1.81]	260.18 [232.17–304.39]	1.08 [0.96–1.27]	−1.62 [-1.69 to −1.55]
Low-middle SDI	332.82 [231.47–393.45]	3.35 [2.38–3.86]	366.95 [298.76–436.46]	2.32 [1.86–2.74]	−1.49 [-1.6 to −1.38]
Low SDI	157.71 [108.69–193.06]	3.5 [2.71–4.09]	230.29 [194.55–276.36]	2.66 [2.25–3.15]	−1 [-1.06 to −0.93]
Region					
Andean Latin America	8.77 [6.92–9.8]	2.54 [2.02–2.81]	8.21 [6.59–10.55]	1.32 [1.06–1.69]	−2.53 [-2.65 to −2.41]
Australasia	2.58 [2.46–2.71]	1.2 [1.14–1.26]	3.65 [3.34–3.89]	1.01 [0.94–1.08]	−0.73 [-0.93 to −0.54]
Caribbean	8.73 [6.3–10.61]	2.61 [1.96–3.11]	10.02 [7.91–12.22]	2.08 [1.63–2.54]	−0.79 [-1.02 to −0.56]
Central Asia	15.41 [14.82–16.58]	2.26 [2.18–2.43]	26.24 [22.53–30]	2.77 [2.38–3.16]	−0.08 [-0.61 to 0.45]
Central Europe	20.27 [19.65–21.35]	1.58 [1.53–1.66]	19.81 [17.12–22.5]	1.33 [1.15–1.5]	−0.63 [-0.69 to −0.57]
Central Latin America	33.53 [29.48–34.88]	2.33 [2.09–2.4]	42.96 [36.56–50.38]	1.73 [1.47–2.02]	−0.95 [-1.1 to −0.8]
Central Sub-Saharan Africa	14.83 [9.02–20.63]	3.19 [2.31–4.02]	22.8 [17.67–28.83]	2.32 [1.84–2.88]	−1.11 [-1.16 to −1.07]
East Asia	197.31 [166.08–225.68]	1.63 [1.39–1.87]	123.74 [106.17–146.41]	0.78 [0.67–0.92]	−2.89 [-3.06 to −2.71]
Eastern Europe	23.77 [22.08–25.1]	1 [0.93–1.06]	16.87 [15–19.39]	0.7 [0.62–0.82]	−2.37 [-2.78 to −1.97]
Eastern Sub-Saharan Africa	43.55 [30.04–52.69]	3.07 [2.36–3.59]	68.66 [58.11–84.97]	2.4 [2.1–2.86]	−0.92 [-0.96 to −0.87]
High-income Asia Pacific	12.08 [11.47–14.99]	0.68 [0.65–0.86]	14.28 [11.55–15.63]	0.49 [0.43–0.53]	−1.41 [-1.49 to −1.32]
High-income North America	19.64 [18.79–20.43]	0.63 [0.61–0.66]	26.27 [24.06–27.27]	0.57 [0.53–0.59]	−0.01 [-0.21 to 0.2]
North Africa and Middle East	62.39 [40.95–78.32]	1.78 [1.26–2.11]	65.7 [53.57–76.29]	1.18 [0.97–1.38]	−1.29 [-1.36 to −1.22]
Oceania	0.99 [0.56–1.33]	1.66 [1.02–2.15]	1.98 [1.2–2.74]	1.56 [0.99–2.13]	−0.12 [-0.2 to −0.04]
South Asia	365.59 [241.73–440.09]	3.97 [2.71–4.65]	394.54 [318.26–474.84]	2.51 [1.99–3.02]	−1.88 [-2.04 to −1.72]
Southeast Asia	32.79 [24.9–43.34]	0.81 [0.64–0.99]	41.45 [34.67–48.34]	0.64 [0.54–0.75]	−0.57 [-0.73 to −0.42]
Southern Latin America	5.09 [4.75–5.27]	1.06 [0.99–1.1]	6.94 [6.4–7.36]	0.95 [0.88–1.01]	−0.13 [-0.22 to −0.05]
Southern Sub-Saharan Africa	12.21 [10.89–13.49]	2.77 [2.51–3.01]	17.37 [15–19.93]	2.41 [2.1–2.75]	−0.5 [-0.92 to −0.08]
Tropical Latin America	20.17 [18.76–21.31]	1.46 [1.37–1.52]	30.22 [28.21–31.84]	1.29 [1.2–1.37]	−0.09 [-0.24 to 0.06]
Western Europe	49.63 [47.89–55.68]	1.09 [1.06–1.21]	92.34 [71.42–99.53]	1.26 [1.04–1.33]	0.66 [0.49 to 0.83]
Western Sub-Saharan Africa	51.2 [40.57–63.06]	3.21 [2.62–4.08]	106.06 [80.71–151.59]	3.08 [2.32–4.5]	−0.01 [-0.1 to 0.08]

Fig. 1. Distribution of DALYs,Deaths,Incidence and Prevalence by age group in different regions from 1990 to 2019.

etiology remains unknown in about half of the reported cases globally (Chouchi et al., 2019). Epilepsy accounts for 1 % of the global disease burden, with a staggering 80 % concentrated in developing countries with limited financial resources(de Boer et al., 2008). Idiopathic epilepsy, which may have genetic origins or an unclear etiology unrelated to structural, metabolic, infectious, or immunological factors, can be inherited (Olie et al., 2022; Hirose et al., 2005). It ranks as the fifth most common neurological condition globally, trailing behind stroke, migraine, dementia, and meningitis.

To gain a comprehensive understanding of idiopathic epilepsy's current state and trends, it's crucial to grasp its epidemiological characteristics. This knowledge can bolster public health responses and address disparities in the disease burden across regions. In our study, we evaluated the global, regional, and national impacts of idiopathic epilepsy by examining incidence, mortality rates, and disability-adjusted life years (DALYs) from the GBD Study 2019. We further categorized this data by country, region, gender, and the sociodemographic index (SDI) value. This approach allowed us to discern the effects of epilepsy on various populations. Our findings present a detailed view of the present-day burden of idiopathic epilepsy, making it a vital reference for clinical practices and policy formulation.

2. Methods

2.1. Data sources

Available data, standardized disease definitions, and prevalence information were gathered with idiopathic epilepsy using the Global Health Data Exchange query tool created by GBD collaborators on 2023–05-23. The GBD study data is publicly available and designed to enable researchers worldwide to address health challenges. We strictly adhere to Institute for Health Metrics and Evaluation (IHME)'s Terms of Use and Guidelines and have signed a free non-commercial user agreement with IHME (https://www.healthdata.org/Data-tools-practices/data-practices/ihme-free-charge-non-commercial-user-agreement). The GBD 2019 includes the most recent and extensive statistical analysis of descriptive epidemiological data related to 369 illnesses and injuries across 204 nations and territories, encompassing the time period from 1990 to 2019.([1]) In addition, a categorization method that is based on social and economic development was used to group these nations and territories into five different regions according to their SDI. The SDI is a multifaceted measure estimating the level of development based on per capita income, education level for those aged 15 and above, and total fertility rate for those under 25 years old. It ranges from 0 (least developed) to 1 (most developed)([1]). Further details of the general methodologies for GBD have been described elsewhere.(Charlson et al., 2016).

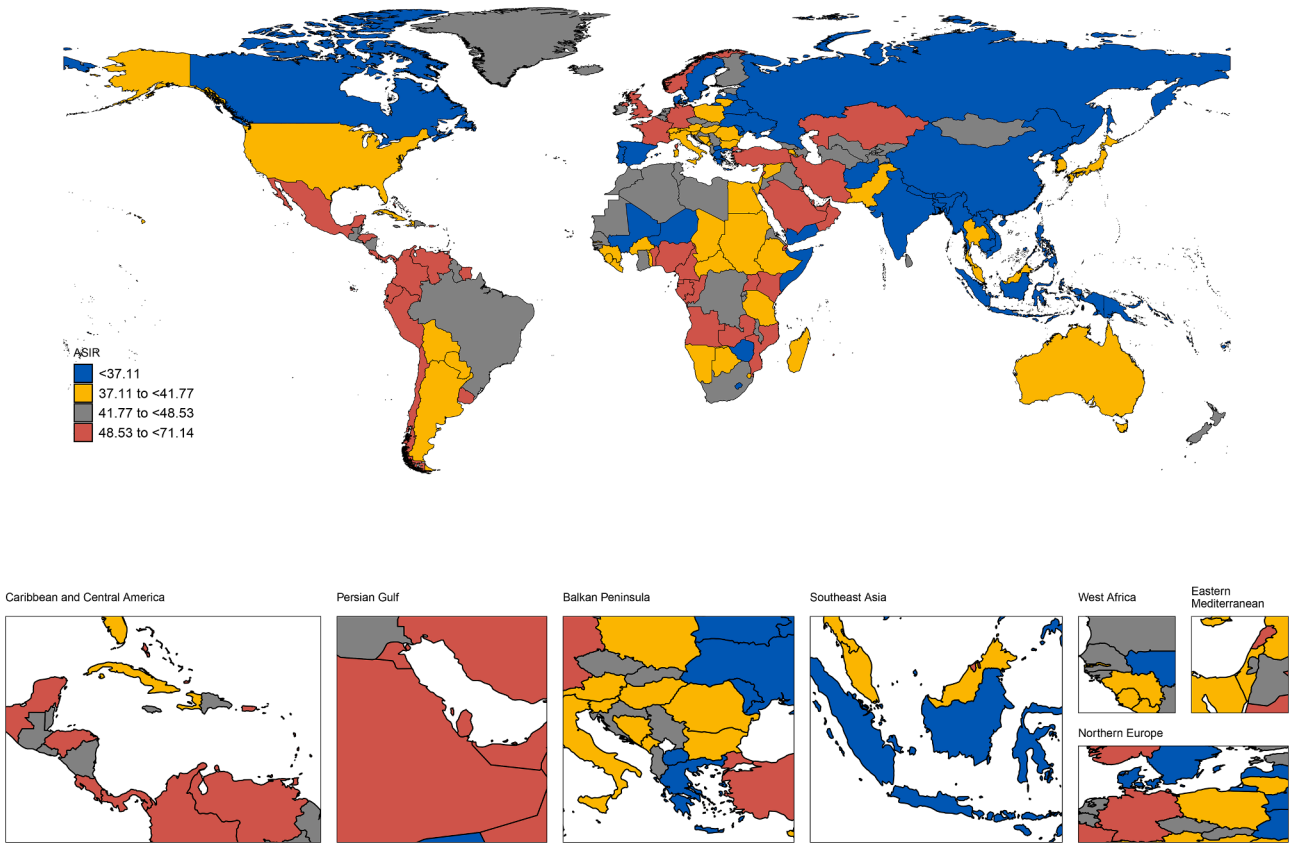

Fig. 2. Age-standardized incidence of idiopathic epilepsy per 100,000 men and women in 2019.

2.2. Measurements

Standard epidemiological metrics such as deaths, prevalence, incidence, and DALYs were applied in order to determine the disease burden of idiopathic epilepsy from 1990 to 2019. Idiopathic epilepsy mortality was calculated with the help of Cause of Death Ensemble modeling techniques, whereas the illness burden of non-fatal disorders was estimated with the use of DisMod-MR2.1 by the Global Burden of illness Study 2019(Global regional, 2016; Foreman et al., 2012). Calculating DALYs involves adding up the number of years of life lost (YLLs) and the number of years lived with disability (YLDs).(Charlson et al., 2016) We generated the estimated annual percentage change (EAPC) and the confidence interval (CI) that corresponds to it at 95 % in order to evaluate the direction in which the trend is moving. An age-standardized rate (ASR) is assumed to be increasing when both the age-standardized EAPC and the lower limit of the 95 % CI are positive; conversely, an age-standardized rate is thought to be decreasing when both the age-standardized EAPC and the upper limit of the 95 % CI are negative. Both of these conditions must be met for an ASR to be considered to be rising. We utilized the age structure provided by the World Health Organization's worldwide population standard in order to normalize the rates according to age.

2.3. Decomposition analysis

In order to comprehensively comprehend the determinants that influenced alterations in idiopathic epilepsy DALYs between 1990 and 2019, we performed decomposition analyses that accounted for two dimensions(Zhang et al., 2023): (i) population magnitude, age distribution, and epidemiological transformations, and (ii) the etiology of idiopathic epilepsy. For the specific method, refer to the previously published article(Zhang et al., 2023).

2.4. Cross-country social inequalities analysis

The slope of the inequality index and the health inequality concentration index were the two standard indicators that were utilized in order to quantify the uneven distribution of the burden of idiopathic epilepsy across nations(Gonçalves et al., 2019). These indicators are well-known for their capability of estimating absolute and relative slope inequality in a distinct manner(Gonçalves et al., 2019). The calculation of inequality slope indices involved the regression of national age-standardized DALYs associated with idiopathic epilepsy on relative social income indicators for all age groups. This was done in order to normalize the data for comparison across age groups. The location of the midpoint of the cumulative range of population groups ordered by GDP per capita is used to establish the scale bar(Ordunez et al., 2019). We utilized a weighted regression model to account for heteroscedasticity, and we logarithmically transformed the relative welfare values to solve the nonlinearity caused by marginal utility. This allowed us to get rid of the heteroscedasticity. Following the application of a Lorenz concentration curve to the cumulative relative distribution of the population (measured in DALYs) stratified by income and burden of disease, the health inequality concentration index was computed by numerically integrating the area under the curve(Ordunez et al., 2019).

2.5. Frontier analysis

In order to assess the correlation between the burden of idiopathic epilepsy and sociodemographic development, a quantitative methodology known as frontier analysis was employed to determine the minimum age-standardized DALY rate achievable based on the SDI's measurement of development status(Zhang et al., 2023). Supplementary Table S2 provides a detailed explanation of the frontier analysis methodology.

Table 3
DALY and Age-Standardized DALY Rate of Idiopathic Epilepsy in 1990 and 2019 and Its Trends.

Characteristics	1990		2019		1990–2019
	DALYs	Age-standardized DALY rate per 100,000	DALYs	Age-standardized DALY rate per 100,000	EAPC
	No. *102 (95 % UI)	No. (95 % UI)	No. *102 (95 % UI)	No.(95 % UI)	No. (95 % CI)
Overall	112856.23 [86140.48–141366.04]	204.32 [157.63–254.14]	130776.24 [99867.3–167340.86]	170.63 [130.42–218.26]	−0.78 [-0.82 to −0.73]
Sex					
Female	51407.24 [38271.64–65337.57]	187.35 [141.09–238.25]	58676.58 [44148.15–75281.6]	153.81 [115.82–197.91]	−0.88 [-0.94 to −0.81]
Male	61448.99 [47348.45–76253.05]	221.43 [172.81–273.4]	72099.66 [56208.9–91620.09]	187.41 [145.35–237.74]	−0.7 [-0.74 to −0.65]
Socio-demographic index					
High SDI	10761.17 [7603.36–14750.12]	129.84 [91.2–177.71]	12819.49 [8830.71–18871.28]	120.16 [81.78–176.38]	−0.11 [-0.19 to −0.03]
High-middle SDI	18758.48 [14751.71–23648.79]	163.61 [127.91–206.47]	17606.51 [12672.75–23602.02]	124.84 [89.53–168.73]	−1.21 [-1.3 to −1.12]
Middle SDI	32985.73 [25833.43–41885.36]	185.11 [145.82–235.24]	34779.14 [25569.03–45087.54]	147.56 [108.63–191.96]	−0.96 [-1.02 to −0.91]
Low-middle SDI	32828.08 [23295.93–41568.62]	276.07 [199.67–347.36]	37447.15 [29105.86–47994.3]	213.08 [166.07–271.6]	−1.08 [-1.14 to −1.02]
Low SDI	17461.34 [11577.78–23024.54]	309.33 [218.04–407.34]	28041.86 [21029.68–36911.3]	246.92 [188.89–321.76]	−0.87 [-0.91 to −0.83]
Region					
Andean Latin America	1259.77 [826.83–1771.59]	328.68 [214.9–464.85]	1371.91 [816.57–2112.08]	215.59 [127.52–333.1]	−1.73 [-1.83 to −1.62]
Australasia	282.72 [171.68–453.68]	137.55 [83.49–220.58]	344.07 [198.21–576.18]	115.85 [66.24–197.65]	−0.64 [-0.69 to −0.58]
Caribbean	966.85 [680.3–1307.28]	268.84 [191.29–361.06]	1072.54 [757.85–1455.25]	228.86 [160.15–310.29]	−0.56 [-0.74 to −0.38]
Central Asia	1962.72 [1469.9–2523.38]	274.74 [205.04–353.15]	2746.41 [2071.86–3651.43]	290.03 [217.82–387]	−0.26 [-0.6 to 0.08]
Central Europe	2455.83 [1832.23–3244.19]	199.23 [148.82–264.02]	2085.06 [1452.3–2881.08]	168.94 [117.78–239.45]	−0.63 [-0.68 to −0.58]
Central Latin America	5400.59 [3994.3–7305.35]	324.73 [239.33–433.43]	6252.64 [4479.98–8492.14]	249.54 [178.62–339.53]	−0.92 [-1.08 to −0.77]
Central Sub-Saharan Africa	2002.87 [1151.62–3011.2]	340.75 [204.41–517.09]	3669.67 [2108.91–5774.71]	279.63 [162.66–440.25]	−0.68 [-0.77 to −0.59]
East Asia	19264.48 [15434.53–23568.22]	153.19 [122.55–187.32]	14291.69 [10262.75–19207.47]	100.54 [72.44–134.1]	−1.93 [-2.14 to −1.73]
Eastern Europe	3056.68 [2265.94–4057.5]	134.85 [99.31–178.99]	2213.27 [1497.47–3132.26]	103.72 [70.41–146.79]	−1.52 [-1.73 to −1.3]
Eastern Sub-Saharan Africa	5549.79 [3636.7–7630.07]	286.55 [192.07–394.87]	9793.17 [7006.39–13602.4]	238.89 [172.6–324.02]	−0.79 [-0.85 to −0.72]
High-income Asia Pacific	1725.87 [1191.69–2449.03]	102.6 [70.27–146.32]	1489.29 [952.77–2299.08]	79.58 [50.57–124.72]	−1.13 [-1.22 to −1.04]
High-income North America	3093.93 [2090.52–4524.53]	109.26 [73.08–159.64]	3613.22 [2361.23–5309.59]	95.22 [62.13–139.2]	−0.03 [-0.18 to 0.11]
North Africa and Middle East	8390.94 [5756.56–10996.98]	214.46 [153.15–280.1]	9552.71 [6828.42–12931.69]	158.28 [112.61–213.23]	−0.95 [-0.98 to −0.91]
Oceania	123.74 [76.89–180.82]	185.88 [116.92–269.82]	246.08 [140.79–371.08]	180.25 [103.9–272.88]	−0.11 [-0.15 to −0.08]
South Asia	33697.29 [23336.93–42358.86]	293.38 [208.74–367.19]	36978.79 [28845.25–47121.77]	207.41 [162.1–263.76]	−1.41 [-1.49 to −1.34]
Southeast Asia	5896.48 [4048.88–8387.58]	123.86 [86.13–174.78]	8058.38 [5579.61–11192.11]	122.18 [84.27–170.83]	−0.04 [-0.09 to 0.01]
Southern Latin America	729.44 [455.99–1106.95]	146.75 [91.99–222.08]	880.19 [522.67–1399.97]	131.9 [77.71–211.46]	−0.31 [-0.37 to −0.24]
Southern Sub-Saharan Africa	1523.64 [1142.55–2021.25]	298.17 [225.39–385.59]	1985.22 [1463.33–2630.34]	256.42 [188.64–339.88]	−0.75 [-1.1 to −0.4]
Tropical Latin America	3749.05 [2617.11–5167.61]	247.47 [171.76–339.13]	4173.38 [2968.98–5675.18]	185.55 [132.01–251.82]	−0.79 [-1.15 to −0.44]
Western Europe	5427.84 [3734.75–7518.96]	137.59 [94.06–190.7]	6624.35 [4533.93–10187.21]	137.22 [91.39–212.5]	0.11 [0.02 to 0.19]
Western Sub-Saharan Africa	6295.7 [4544.43–8395.02]	316.41 [231.35–417.69]	13334.19 [9922.17–17883.45]	295.42 [222.14–397.74]	−0.25 [-0.37 to −0.13]

2.6. BAPC model

The Bayesian Age-Period-Cohort (BAPC) model has shown outstanding performance, achieving a 95 % confidence interval. It is optimally tailored for analyzing disease burden estimates categorized by age.(Wang et al., 2023) With age-specific population data from 1990 to 2019, estimated population data for 2020—2030, and the GBD world population age standard detailed in Appendix Table 13 of GBD 2019 (Charlson et al., 2016), we have used the BAPC model to project incidence and mortality rates for idiopathic epilepsy for the next decade. These numbers were used to paint a clear picture of the present state of affairs. The BAPC models were formulated with the aid of the R packages INLA (https://www.r-inla.org) and BAPC (https://r-forge.r-project.org/).

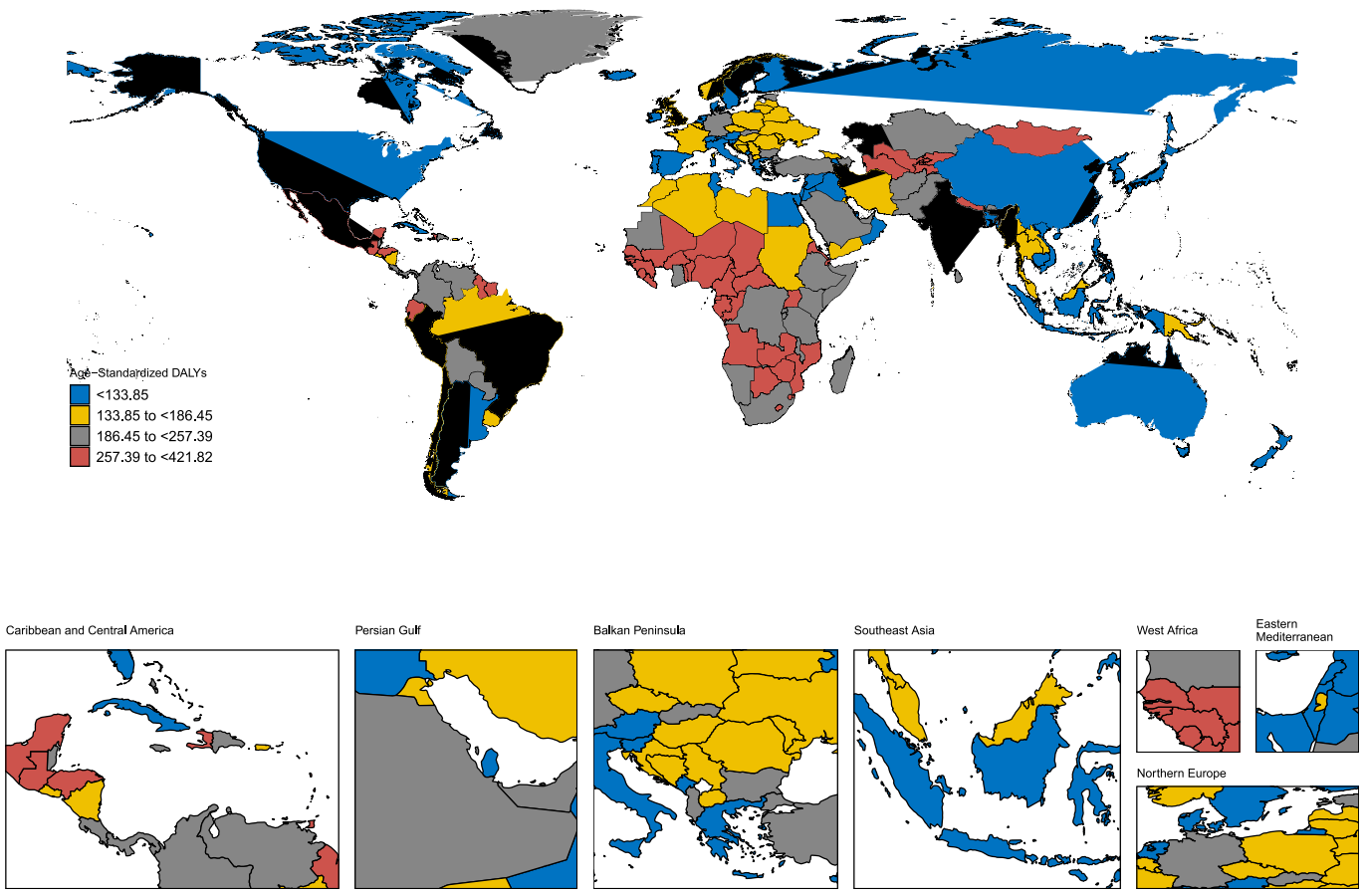

Fig. 3. Age-standardized DALYs of idiopathic epilepsy per 100,000 men and women in 2019.

2.7. Statistical analysis

In this study, a two-tailed *P* value of less than 0.05 was considered statistically significant. The R program (Version 4.2.1, R Foundation for Statistical Computing, Vienna, Austria) was used to perform all statistical tests and display all collected information graphically. The'maps' package was used to make the globe, and the'ggplot2' package was used to make the charts and graphs.

3. Results

3.1. Change in the incidence of idiopathic epilepsy

According to Table 1, the global incidence of idiopathic epilepsy in 2019 was 2,898,222 cases (95 % CI 2098718 to 3823376). In addition, the incidence of idiopathic epilepsy cases increased significantly between 1990 and 2019, resulting in a cumulative increase of 55.86 % (Table 1). In 1990, the age-standardized incidence rate (ASIR) for idiopathic epilepsy was recorded at 33.22 cases per 100,000 population (95 % UI, 23.4 to 44.69). By 2019, this rate had risen to 38.82 per 100,000 population (95 % UI, 27.99 to 51.28), reflecting an EAPC of 0.49 (95 % CI, 0.46 to 0.52). Over this 30-year period, a notable increase in the ASIR for idiopathic epilepsy was observed in both males (EAPC 0.49; 95 % CI, 0.46 to 0.52) and females (EAPC 0.48; 95 % CI, 0.45 to 0.51) (Table1, Supplemental Figure S1). From 1990 to 2019, the ASIR for idiopathic epilepsy in women was lower than in men.

Table 1 and Supplemental Figure S2 delineates that regions with either low or high SDI values exhibited a markedly elevated ASIR of idiopathic epilepsy compared to regions with intermediate SDI values. In 2019, high SDI regions recorded the most pronounced ASIR at 44.29 per 100,000 population (95 % UI, 29.01 to 60.92), closely followed by those with low SDI, which had an ASIR of 40 per 100,000 population (95 % UI, 26.46 to 55.92). Notably, the most substantial increase was observed in middle SDI regions, where the EAPC was the highest at 0.63 (95 % CI, 0.58 to 0.69). In contrast, regions with low SDI recorded the least increment in ASIR, with an EAPC of 0.2 (95 % CI, 0.15 to 0.25). Meanwhile, high SDI regions experienced an intermediate increase, showcasing an EAPC of 0.37 (95 % CI, 0.31 to 0.42).

As detailed in Table 1 and illustrated in Fig. 2, the 2019 ASIR of idiopathic epilepsy were most pronounced in Central Latin America, with 57.1 cases per 100,000 population (95 % UI, 38.03–78.58). This was closely followed by Andean Latin America at 55.28 cases, and North Africa and the Middle East at 48.24 cases per 100,000 population (95 % UI, 32.23–66.36). Conversely, the lowest incidence was observed in East Asia, registering at 24.59 cases per 100,000 population (95 % UI, 16.63–33.63). From 1990 to 2019, the most substantial rise in ASIR for idiopathic epilepsy was recorded in Southeast Asia (EAPC 0.75; 95 % CI, 0.7 to 0.8), whereas Southern Sub-Saharan Africa witnessed the most significant decline (EAPC −0.32; 95 % CI, −0.58 to −0.07).

3.2. Change in death due to idiopathic epilepsy

As can be seen in Table 2, the number of people throughout the world who have passed away as a result of idiopathic epilepsy has risen by 13.95 percent over the course of the past three decades, going from 100,054 (95 % UI 81176 to 112226) in 1990 to 114,011 (95 % UI 100178 to 129928) in 2019. On the other hand, the age-standardized death rates (ASDRs) of idiopathic epilepsy experienced a decline over the same duration. These rates went from 1.94 per 100,000 population (95 % UI 1.61 to 2.15) in 1990 to 1.46 per 100,000 population (95 % UI 1.28 to 1.67) in 2019, which corresponds to an EAPC of −1.11 (95 % CI −1.18 to −1.03). During this time period, the ASDR attributable to

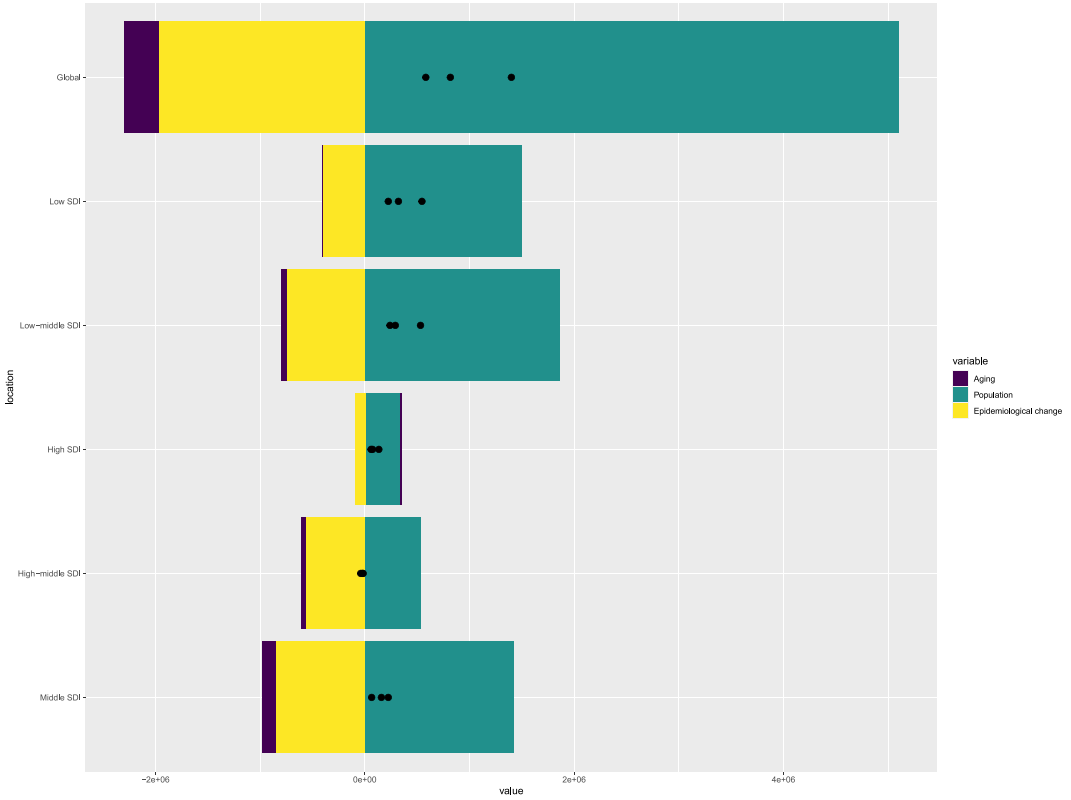

Fig. 4. Changes in idiopathic epilepsy DALYs according to population-level determinants of population growth, aging, and epidemiological change from 1990 to 2019 at the global level and by SDI quintile. The black dot represents the overall value of change contributed by all 3 components. For each component, the magnitude of a positive value indicates a corresponding increase in idiopathic epilepsy DALYs attributed to the component; the magnitude of a negative value indicates a corresponding decrease in idiopathic epilepsy DALYs attributed to the related component.

idiopathic epilepsy decreased for both genders (men: EAPC −0.99, 95 % CI −1.06 to −0.92; women: EAPC −1.28, 95 % CI −1.37 to −1.19), albeit with a slightly higher ASDR in men than in women (Table 2).

On a SDI scale, except for the high-middle and middle SDI quintiles, idiopathic epilepsy-related fatalities cases increased in the majority of SDI quintiles. However, ASDRs for idiopathic epilepsy decreased across all SDI quintiles (Table 2). In 2019, regions with low SDI (2.66 per 100,000 population, 95 % UI 2.25–3.15) and low-middle SDI (2.32 per 100,000 population, 95 % UI 1.86–2.74) had the highest ASDRs of idiopathic epilepsy, whereas regions with high-middle SDI had the lowest ASDR (0.91 per 100,000 population, 95 % UI 0.83–0.1) (Table 2). High-to-middle SDI regions also experienced the greatest decrease in idiopathic epilepsy ASDR (EAPC −1.65, 95 % CI −1.75 to −1.55) (Table 2). Notably, as shown in Fig. 1, a higher SDI was associated with a lower percentage of young individuals dying from idiopathic epilepsy. In contrast, between 1990 and 2019, the proportion of older individuals in each SDI who perished of idiopathic epilepsy increased. Supplemental Figure S3 depicts a progressive decline in mortality as the SDI rises.

On a regional scale, in 2019, the highest ASDR of idiopathic epilepsy were found in Western Sub-Saharan Africa (3.08 per 100,000 population, 95 % UI 2.32–4.50), Central Asia (2.77 per 100,000 population, 95 % UI 2.38–3.16), and South Asia (2.51 per 100,000 population, 95 % UI 1.99–3.02), whereas the lowest ASDR of idiopathic epilepsy in 2019 was observed in High-income Asia Pacific (0.49 per 100,000 population, 95 % UI 0.43–0.53) (Table 2). Over the period from 1990 to 2019, the age-standardized incidence rate (ASIR) of idiopathic epilepsy saw the most significant increase in Western Europe (EAPC 0.66, 95 % CI 0.49 to 0.83) and the most substantial decrease in East Asia (EAPC −2.89, 95 % CI −3.06 to −2.71).

3.3. Change in the DALYs due to idiopathic epilepsy

The total number of DALYs that may be attributable to idiopathic epilepsy in the world was 11,285,623 in 1990 (95 %UI 8,614,048 to 14,136,604) This number has since climbed to 13,077,624 (95 %UI 9,986,703 to 16,734,086) in 2019. In spite of this, the age-standardized DALY rate of idiopathic epilepsy declined throughout the course of this time with an EAPC of −0.78 (95 % CI −0.82 to −0.73) (Table3). Both men and women had a decline in the age-standardized DALY rate of idiopathic epilepsy from the year 1990 to 2019 (men: EAPC −0.7, 95 % CI −0.74 to −0.65; women: EAPC −0.88, 95 % CI −0.94 to −0.81).

In 2019, the highest age-standardized DALYs due to idiopathic epilepsy were found in the low SDI regions (246.92 per 100,000 population, 95 %UI 188.89–321.76), followed by the low-middle SDI regions (213.08 per 100,000 population, 95 % UI 166.07–271.6) (Table3). The number of age-standardized DALYs due to idiopathic epilepsy saw a decrease in all SDI regions, with the most substantial decrease occurring in high-middle SDI regions (-1.21, 95 % CI −1.3 to −1.12). Supplementary Figure S4 depicts a negative correlation between DALYs and increasing SDI.

In 2019, the regions that had the highest number of age-standardized DALYs caused by idiopathic epilepsy were Western Sub-Saharan Africa (295.42 per 100,000 population, 95 % UI 222.14–397.74), Central Asia (290.03 per 100,000 population, 95 % UI 217.82–387), and Central Sub-Saharan Africa (279.63 per 100,000 population, 95 % UI 162.66–440.25). Both high-income Asia Pacific and high-income North America were found to have the lowest age-standardized DALYs owing to idiopathic epilepsy (Fig. 3). High-income Asia Pacific had 79.58 per 100,000 population, while high-income North America had 95.22 per 100,000 population, with a 95 % confidence interval ranging from 62.13 to 139.2. Idiopathic epilepsy was responsible for a decline in the number

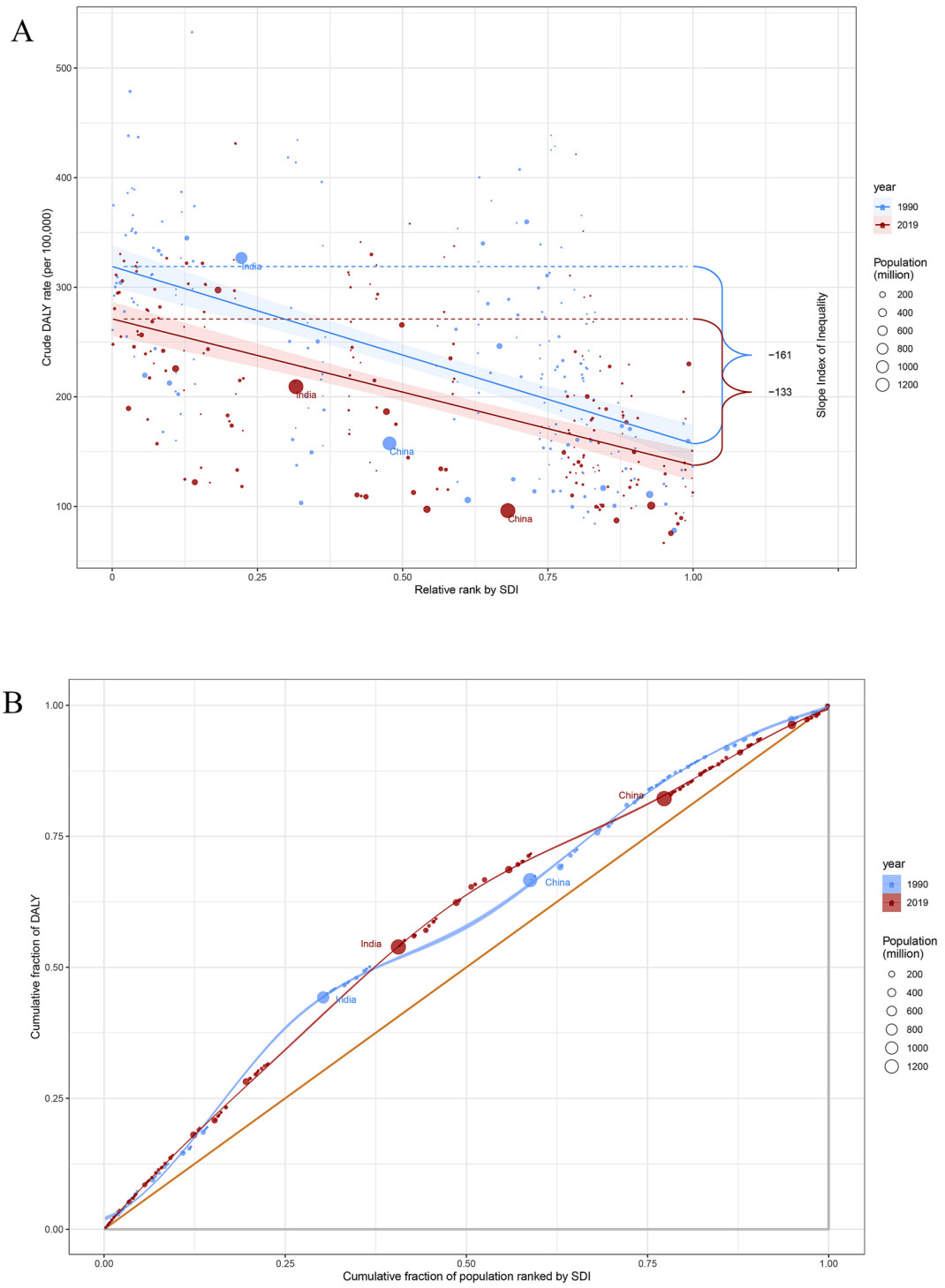

Fig. 5. Income-related health inequality regression and concentration curves for the burden of idiopathic epilepsy, 1990 and 2019; (A) Health inequality regression curves. (B) Health inequality concentration curves.

of age-standardized DALYs across the majority of areas, with the exception of Western Europe (EAPC 0.11, 95 % CI 0.02 to 0.19).

3.4. *Drivers of idiopathic epilepsy epidemiology: Population growth, aging, and epidemiologic changes*

Fig. 4 presents the decomposition analysis results across various SDI regions. It becomes evident that population factors are the primary contributors to the escalation of epilepsy-related DALYs, particularly in low-middle SDI regions. Further, the decomposition analysis from different regions reveals that population growth is the predominant reason for the increase in DALYs across most areas, with South Asia standing out as the most significant (refer to Supplementary Table S3 and Supplementary Figure S5).

3.5. *Cross-country social inequalities analysis*

According to the slope index of inequality, there was a difference of 161 DALYs per 100,000 between nations that had the lowest and greatest incomes in 1990, but that difference had dropped to 133 DALYs

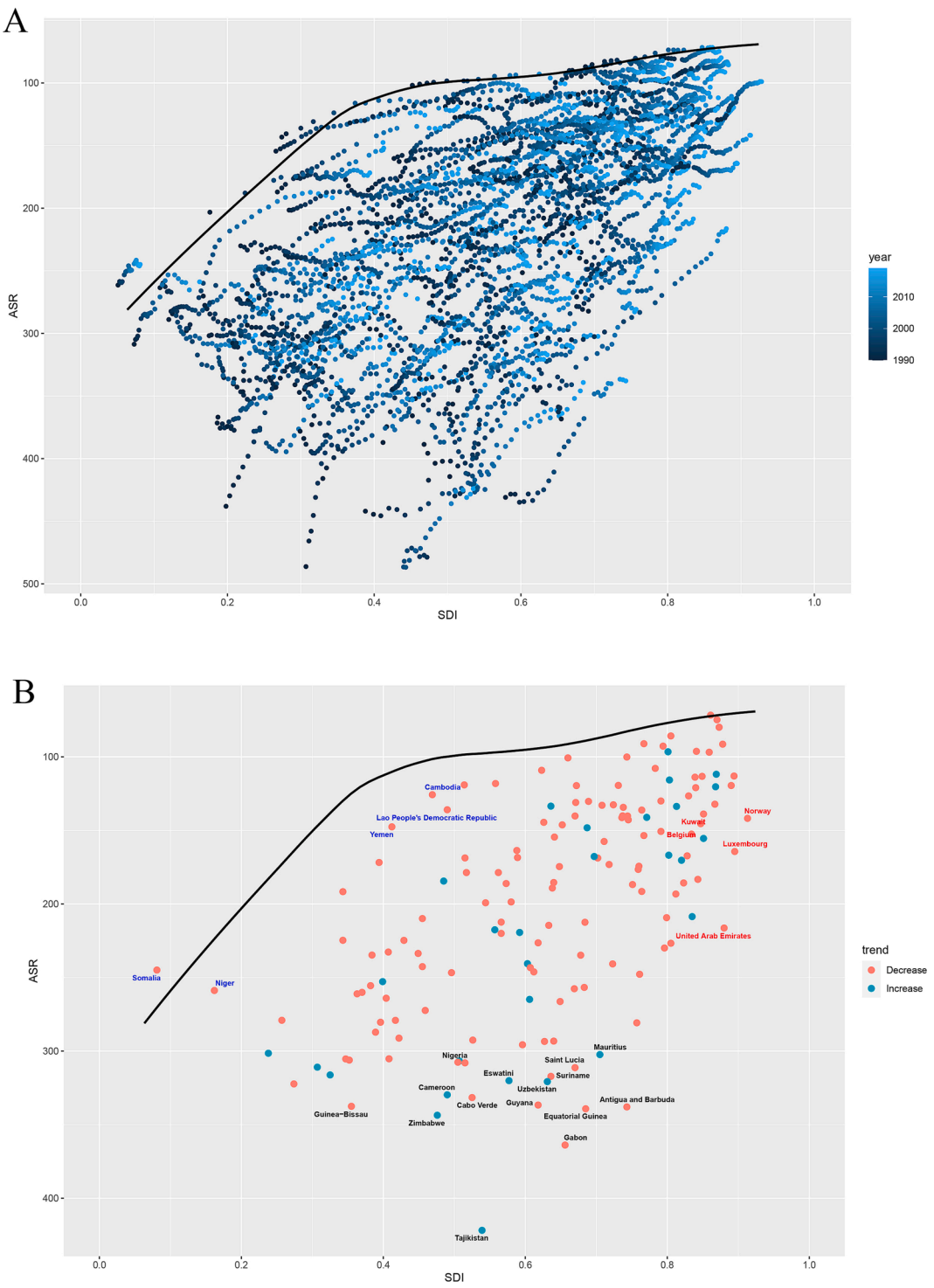

Fig. 6. Frontier Analysis. (A)Frontier analysis based on SDI and idiopathic epilepsy DALY rate from 1990 to 2019. The frontier is delineated in solid black color. (B) Frontier analysis based on SDI and age-standardized idiopathic epilepsy DALY rate in 2019.

per 100,000 in 2018 (Fig. 5A). As determined by the Health Inequality Concentration Index, the relative gradient inequality discovered that the concentration index curve was located above the absolute equity line in both the year 1990 and 2019. This suggests that the burden of DALYs caused by idiopathic epilepsy is disproportionately concentrated in persons that are at a lower socioeconomic status (Fig. 5B).

3.6. *Frontier analysis*

To enhance comprehension of the potential amelioration in idiopathic epilepsy DALY rates that can be feasibly attained based on a nation's developmental status, a frontier analysis was constructed utilizing age-standardized DALY rates and SDI data spanning from 1990 to 2019. The frontier line demarcates the nations and regions that exhibit the most favorable performance in terms of DALY rates, relative to their SDI. The effective difference, which is the distance from the frontier,

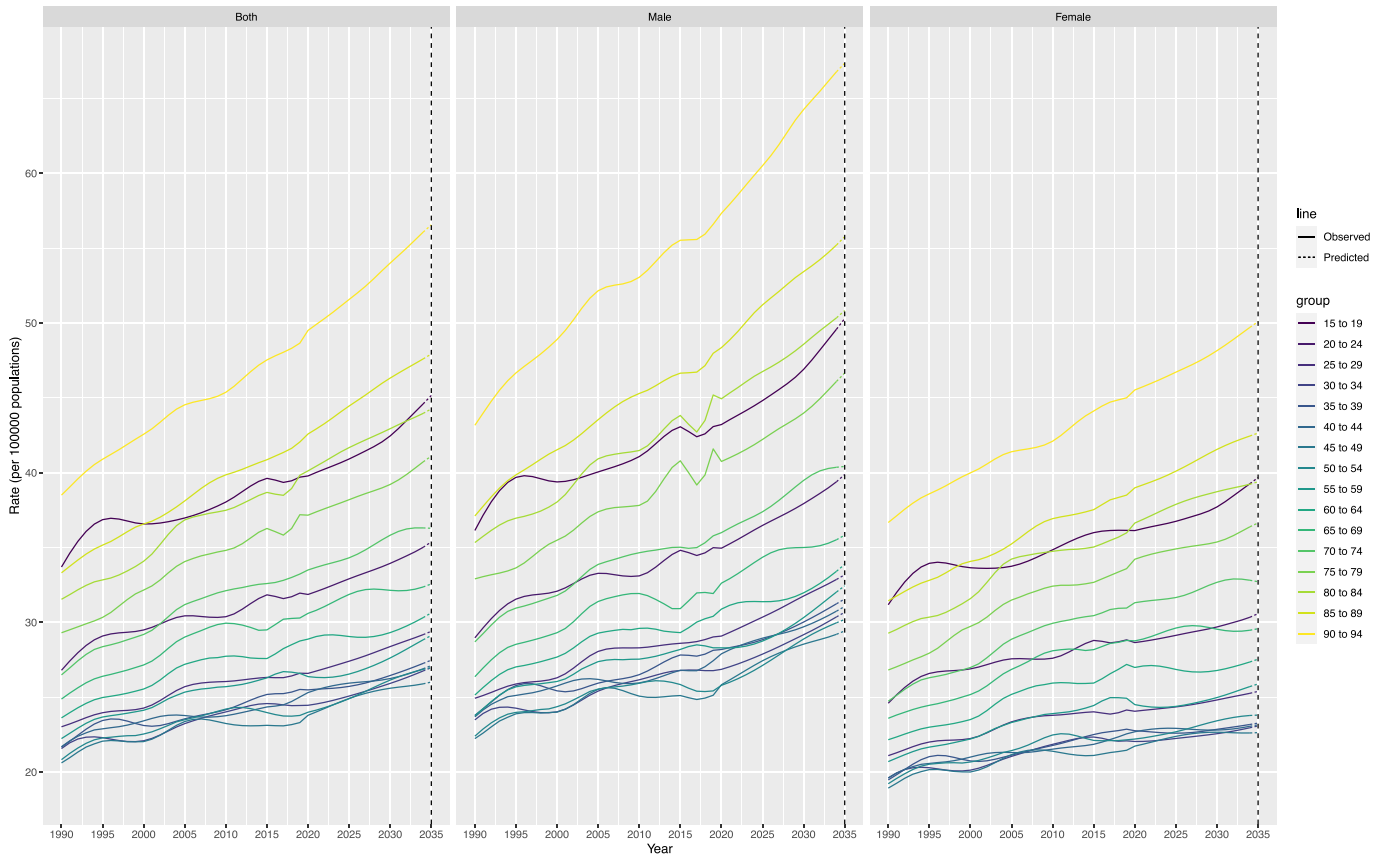

Fig. 7. Future forecasts of GBD in idiopathic epilepsy incidence rate.

denotes the disparity between a nation's observed and attainable DALYs. This disparity may be mitigated or eradicated by leveraging the sociodemographic resources of the country or territory. The disparity between each country and territory's development level and the frontier was determined by utilizing the 2019 DALYs and the SDI. In general, as the SDI increased, the effective difference demonstrated a tendency towards reduced magnitude and decreased variability. (Fig. 6A). On the other hand, in Fig. 6B, the frontier nations with low SDI (0.5) and low effective difference are indicated in blue. The 15 countries that have the most significant effective difference are shown in black. In addition, red indicates nations and territories that have a high SDI (more than 0.85), as well as a reasonably high effective difference given their level of development. The age-standardized idiopathic epilepsy DALYs rate increased between 1990 and 2019, as shown by the red dots, while the rate decreased, as shown by the blue dots, throughout the same time period.

3.7. The changes in idiopathic epilepsy disease burden from 2020 to 2030 in different sexes

To identify sex groups of concern in terms of epilepsy burden, we further analyzed sex differences in morbidity and mortality globally and by age group. Fig. 7 suggests that the incidence of idiopathic epilepsy will increase globally in the future, especially for those over 80 years of age, and even higher for those over 90 years of age, reaching 47 per 100,000 population and 52 per 100,000 population respectively by 2035. The incidence rate increases more rapidly in older men than in women. In terms of mortality, it will continue to rise for those over 80 years of age, while remaining relatively flat for the rest of the age group (Fig. 8). Mortality rates for men over 80 years of age will be higher than for women in 2035, but mortality rates for women over 80 years of age will increase at a faster rate than for men (Fig. 8).

4. Discussion

Our findings provide important insights into the global, regional, and national burden of idiopathic epilepsy from 1990 to 2019. We observed an overall rise in the incidence of idiopathic epilepsy cases, albeit the age-standardized incidence rate exhibited a modest increase. This aligns with prior research indicating a stable or slightly increasing incidence of epilepsy globally(Ngugi et al., 2010; Fiest et al., 2017). Intriguingly, the age-standardized incidence rate was higher in males than females over the 30-year period. This corroborates previous studies demonstrating a preponderance of idiopathic epilepsy in males(Hophing et al., 2022). The underlying reasons are unclear but may involve sex-based differences in genetic susceptibility and brain development(Hophing et al., 2022). Epilepsy is a widely recognized neurological disorder that can affect individuals across all age groups, with a higher incidence observed among the younger population(Boling et al., 2018). In our study, individuals younger than 20 years of age accounted for a major portion of the incidence, although there was a decline in the percentage of this cohort from 1990 to 2019. In addition, a significant increase in the proportion of people aged 80 years or older was observed. Consistent with our findings, prior research has demonstrated that the prevalence of idiopathic epilepsy is most prominent among both the pediatric and geriatric populations(Broekhuijsen-van Henten et al., 2010; Seo et al., 2020).The etiology of idiopathic epilepsy is multifaceted and encompasses genetic, metabolic, infectious, structural, immunological, and unidentified factors(Scheffer et al., 2017). Among the preventable causes of idiopathic epilepsy, prenatal or perinatal brain injury, central nervous system infections, traumatic brain injury, and stroke are the most significant, contributing to approximately 25 % of idiopathic epilepsy cases(Duncan et al., 2006; Liu et al., 1990). These causes are more prevalent in young children and older adults, which explains the higher incidence of idiopathic epilepsy in these two demographic groups.

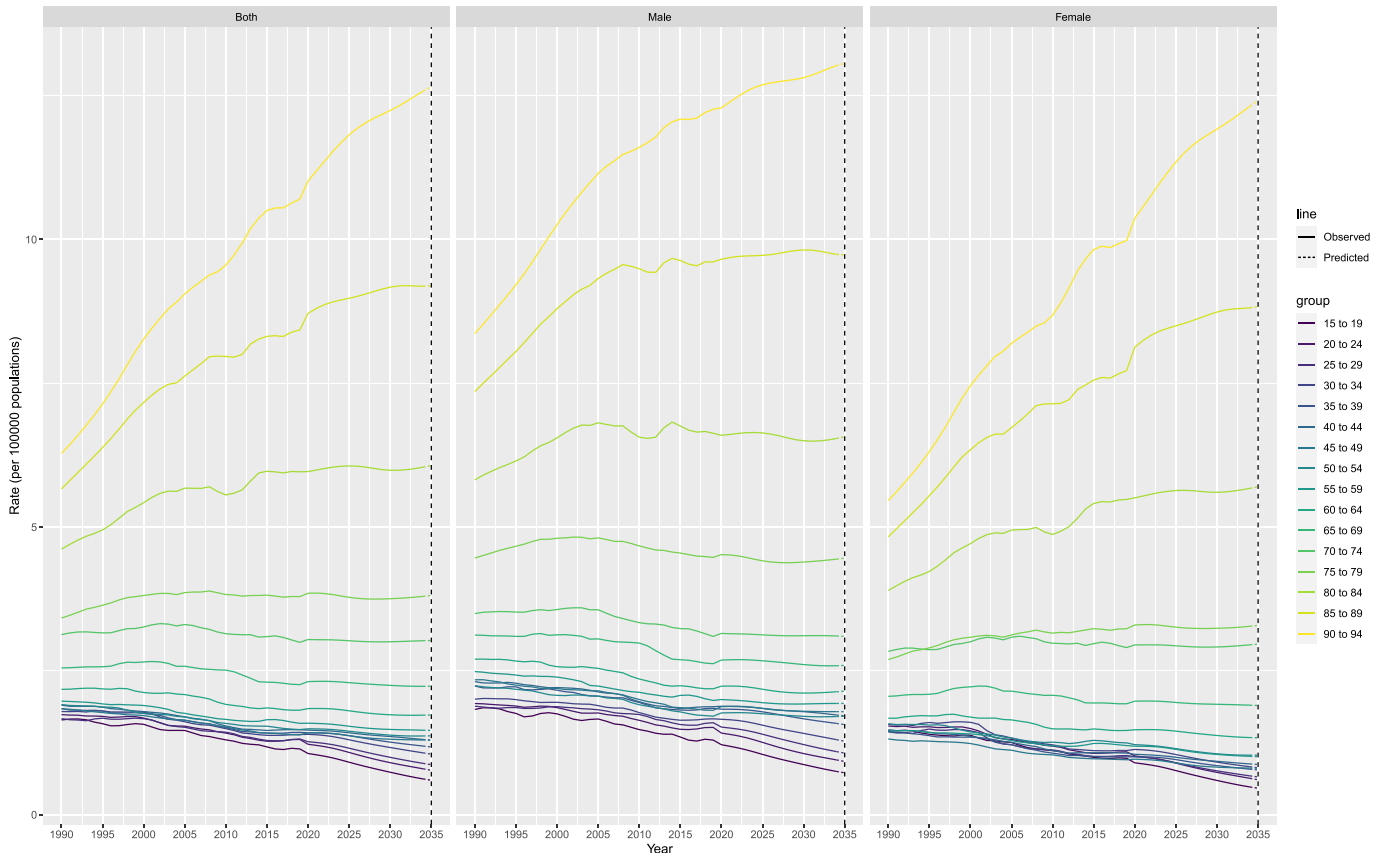

Fig. 8. Future forecasts of GBD in idiopathic epilepsy deaths rate.

Our results also highlight SDI regional variations in epilepsy incidence. Regions with low and high SDI had higher rates than intermediate SDI regions in 2019. Possible factors include differing availabilities of diagnostics, variable exposures to risk factors, and access to treatment (Meyer et al., 2010; Mbuba et al., 2008). The fastest rise occurred in middle SDI regions, reflecting improving detection amidst economic development. However, the lowest SDI regions saw the smallest increase, underscoring persistently limited diagnostics in deprived settings (Ba-Diop et al., 2014).

From 1990 to 2019, mortality linked to idiopathic epilepsy rose by 13.95 %. In all SDI regions, the ASDR due to idiopathic epilepsy displayed a decline over the same period. This downward trend in idiopathic epilepsy is, in part, credited to groundbreaking medical technological advancements and strides in prevention. Importantly, the diminishing ASDR signifies improved survival outcomes, more pronounced in regions with higher SDIs. This is consistent with research indicating a decrease in epilepsy-related mortality across several global regions(Thijs et al., 2019; Fine and Wirrell, 2020). However, low and low-middle SDI regions still experience the highest ASDR, reflecting healthcare gaps in poorer nations. Worryingly, the proportion of epilepsy deaths in the elderly rose over time across SDI regions. As populations age, epilepsy-related mortality may rise without bolstered prevention efforts.

Overall epilepsy DALYs escalated over the study period, predominantly driven by population growth. However, age-standardized DALY rates declined in all SDI regions, congruent with prior findings(Pacheco-Barrios et al., 1990; Kang et al., 2022,12(9):e59548.). The preponderance of DALYs in low and low-middle SDI regions mirrors the disproportionate burden shouldered by disadvantaged populations, pointing to the need for targeted interventions in poorer areas. The universal decline in age-standardized DALY rates suggests incremental improvements in managing epilepsy, which should be consolidated and accelerated moving forward. According to the findings of our research, the DALY rate in children under the age of five that was reported in 2019 due to idiopathic epilepsy was lower than the rate that was recorded in 1990. On the other hand, the DALY rate that was caused by idiopathic epilepsy in the senior population that was over 80 years old was greater than that which was seen in 1990. The former pattern may be explained by developments in medical and healthcare facilities, as well as by substantial breakthroughs in maternal and child health care systems ([3]). The latter trend, on the other hand, may be linked to the accelerated aging process and the rise in life expectancy(Pohlmann-Eden et al., 2016).

By 2035, projections indicate a significant rise in the incidence of idiopathic epilepsy across all age groups, but most markedly among the elderly, especially those aged 80 and above. While the rate of incidence is poised to climb more rapidly among elderly males, the anticipated surge in mortality rates is particularly notable for this demographic, with females expected to witness a steeper acceleration in mortality compared to males. Underpinning these trends are potential contributing factors, including neurodegenerative disorders, cerebrovascular complications, and adverse effects of antiseizure medications in the elderly. As a result, there's an imperative need to reinforce both pharmacological and non-pharmacological interventions tailored to this age bracket. Recommendations include meticulous dosing adjustments of antiseizure medications, the use of EEG monitoring for optimal therapeutic decisions, and lifestyle modifications to enhance seizure management.

According to the findings of frontier analysis, nations with economies that are not as developed have a bigger burden of idiopathic epilepsy than other countries do. This research sheds light on a substantial obstacle, but the frontier analysis we conducted gives a more positive outlook. There are a number of nations with idiopathic epilepsy DALYs that are located far from the boundary, which indicates that there are

chances that have not yet been taken advantage of to lessen the DALYs gap. Frontier nations exist at all SDI levels, with low SDI nations evidencing superior performance despite resource limitations. These nations could serve as models for optimizing health outcomes in contexts with limited resources. However, a number of countries with a high SDI, such as Luxembourg and Norway, performed poorly, indicating that other factors may impede advances in health outcomes enabled by sociodemographic prosperity. Future research should identify the determinants of success in exemplary nations as well as the obstacles to development in lagging nations. This information could contribute to efforts to reduce the burden of idiopathic epilepsy.

This study presented several significant limitations. Firstly, our analysis was predominantly dependent on the GBD database. The precision of this database is limited by the accessibility of national registry data, the vast number of undiagnosed idiopathic epilepsy cases, and the absence of data on other associated risk factors. Secondly, there isn't a system in place to categorize various types of epilepsy. It is imperative that future research on epilepsy incorporate data that can aid in such classification.

5. Conclusions

The global disease burden of idiopathic epilepsy remains significant, particularly in regions with low SDI. From 1990 to 2019, the incidence of idiopathic epilepsy has been increasing, and the burden of this condition in children and the elderly is progressively rising. This study serves as a foundation for the development of preventive and care measures for idiopathic epilepsy in diverse regions. The subsequent phase should entail sustaining the prioritization of idiopathic epilepsy as a public health concern and advocating for interventions to bridge the gaps in idiopathic epilepsy treatment, thereby mitigating the burden associated with this condition.

CRediT authorship contribution statement

Yuan-jie Zhang: Data curation, Formal analysis, Investigation, Methodology, Writing – original draft. **Xiang-meng Kong:** Conceptualization, Data curation, Formal analysis, Writing – original draft. **Jia-jie Lv:** Conceptualization, Formal analysis, Funding acquisition, Validation, Visualization, Writing – original draft. **Cheng-Hao Yang:** Supervision, Validation, Visualization, Writing – original draft. **Xin-yu Li:** Methodology, Resources, Software, Validation, Visualization, Writing – original draft. **Xi-tao Yang:** Investigation, Methodology, Resources, Software, Supervision, Visualization, Writing – original draft. **Zhi-lin Guo:** Validation, Visualization, Writing – original draft, Writing – review & editing. **Zhi-hua Cheng:** Investigation, Project administration, Resources, Visualization, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

GBD study 2019 data resources were available online from the Global Health Data Exchange (GHDx) query tool (https://ghdx.healthdata.org/gbd-results-tool).

Acknowledgments

No matter the old village doctors who are going to retire or the young who just set foot on the job, they have no regrets, no conditions and actively participated in the front-line work of epidemic prevention and control in China.

Author contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Consent for publication

We consent for publication

Ethics approval and consent to participate

An ethics approval and the consent to participate was not necessary.

Funding

There is no funding support in this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pmedr.2023.102522.

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