The Global Cost of Epilepsy: A Systematic Review and Extrapolation

ILAE Task Force on the Global Cost of Epilepsy

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Key Points: Based on review and extrapolations of cost data from the existing epilepsy cost-of-illness literature, this study estimates the direct and indirect cost of epilepsy worldwide and shows the distribution by region and income. The average cost per person with epilepsy is estimated to be $4,467 per year in 2019, ranging from $204 in low-income countries to $11,432 in high-income countries. Applying average costs to the estimated prevalence of 52.5 million cases, and adjusting for the treatment gap, total epilepsy costs were $119.27 billion. Most of the costs are in the wealthiest countries where a small portion of the world's epilepsy population reside.

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Summary

Objective: Global action for epilepsy requires information on the cost of epilepsy, which is currently unknown for most countries and regions of the world. To address this knowledge gap, the International League Against Epilepsy, Commission on Epidemiology formed the Global Cost of Epilepsy Task Force.

Methods: We completed a systematic search of the epilepsy cost-of-illness literature and identified studies that provided a comprehensive set of direct healthcare and/or indirect costs, followed standard methods of case identification and cost estimation, and used data on a representative population or sub-population of people with epilepsy. Country-specific costs per person with epilepsy were extracted and adjusted to generate an average cost per person in 2019 US Dollars. For countries with no cost data, estimates were imputed based on average costs per person of similar income countries with data. Per person costs for each country were then applied to data on the prevalence of epilepsy from the Global Burden of Disease Collaborative adjusted for the treatment gap.

Results: One-hundred-and-one COI studies were included in the direct healthcare cost database, 74 from North America or Western Europe. Thirteen studies were used in the indirect cost database, eight from North America or Western European. The average annual cost per person with epilepsy in 2019 ranged from $204 in low-income countries to $11,432 in high-income countries based on this highly skewed database. The total cost of epilepsy, applying per person costs to the estimated 52.51 million people in the world with epilepsy and adjusting for the treatment gap was $119.27 billion.

Significance: Based on a summary and extrapolations of this limited database, the global cost of epilepsy is substantial and highly concentrated in countries with well-developed healthcare systems, higher wages and income, limited treatment gaps, and a relatively small percentage of the epilepsy population.

Key words: Epilepsy, Cost, Prevalence, Global, Total, Per Person, Distribution

Introduction

The 73rd Session of the World Health Assembly's resolution calling for the development of a global action plan for epilepsy requires global, regional, and country-specific knowledge of the cost of epilepsy[1]. Cost-of-illness (COI) studies may be used to help policy makers set priorities by showing the economic value in reducing the burden of a specific disease and providing important information for cost-effectiveness and cost-benefit analysis of prevention and treatment strategies. Prior efforts to compile this information for epilepsy have been limited to systematic reviews of individual country studies (most recently Allers, et al. and Strzelczyk, et al.) [2,3], extrapolation of cost estimates from multiple studies for the United States [4], and extrapolation of cost estimates for all countries in Western Europe based on studies from some of the countries. [5,6] To address this gap in information, the International League Against Epilepsy (ILAE), Commission on Epidemiology formed the Global Cost of Epilepsy Task Force (TF) to estimate the total cost of epilepsy worldwide, including direct healthcare costs – payments by individuals, governments, insurers, and fiduciary organizations for epilepsy-specific treatment and indirect costs – lost earnings of people with epilepsy and their caregivers related to absence from work, excess unemployment, reduced productivity at work, and excess mortality.

The project had to address numerous challenges to develop the global cost estimates. Existing COI studies in epilepsy are still largely limited to direct healthcare cost studies from high-income countries with very few from middle-income, and less than a handful from low-income countries. Existing studies are difficult to compare due to the substantial variation in methods used, such as differences in study perspective (incidence versus prevalence, societal

versus government), cost items included and identification procedures used, sources of data, population sampled, and time frame.[7] In addition, differences in the relative prices and availability of treatments must also be addressed. Finally, while the epidemiologic literature focuses on determining the number of people with active epilepsy in a population, the COI literature includes people with inactive epilepsy (previously diagnosed but in remission) and active epilepsy who receive treatment and incur costs.

Methods

Employing an approach similar to that used for global studies in dementia[8] and regionally for epilepsy [5,6] we conducted a systematic search of epilepsy COI studies throughout the world, extracted costs presented in these studies, and made several adjustments to generate a single estimate of per person and total epilepsy-attributable direct healthcare and indirect cost for people with epilepsy by country in 2019 U.S. Dollars (USD). We then estimated per person and total costs for countries with no data based on the median cost per person in countries in the same income category with data adjusted to reflect health care expenditures and income in each country. We then applied the estimates to the latest available data on epilepsy prevalence in each country from the Global Burden of Disease (GBD) Collaboration, adjusted healthcare costs for the treatment gap, and aggregated to arrive at regional and global costs.[9]

Literature Search

To search the COI literature, pre-specified criteria were applied to electronic databases including MEDLINE (via PubMed), EMBASE, EBSCOhost, Web of Science and Scopus. Search

strategies were developed for each database, combining one or more disease-related search term with one or more cost-related search term. The specific search protocol, following PRISMA guidelines,[10] is available as online supporting information. The protocol was registered with PROSEPRO (CRD42020178600).

Articles identified from each search were uploaded to the Covidence systematic review online software (Covidence Systematic Review Software, Veritas Health Innovation, Melbourne, Australia, www.covidence.org), where duplicates were automatically excluded, and a four-stage review process was conducted. In Stage 1, two TF members independently reviewed the titles, abstracts and/or summaries, to exclude studies based on the following criteria:

1. Studies published prior to 1 January 2000.
2. Purely modeling studies.
3. Letters to the editor or commentaries.
4. Lack of per person cost estimates.
5. Lack of definitions of epilepsy used to identify cases.
6. Focus on an incomplete set of therapies, interventions, or cost items.
7. Not population-based (i.e., data from single-site or provider}.

Studies were limited to those published after 2000 due to the introduction of newer anti-seizure medications around this time, which likely result in lower cost estimates (and hence, outdated costs) in earlier studies.

In Stage 2, articles not excluded in Stage 1 were then reviewed independently in their entirety by two members of the TF to ensure studies met the following inclusion criteria:

1. Empirical estimates of total or per person direct healthcare and/or indirect costs for people with epilepsy.
2. Estimates based on the general epilepsy population or a representative sample of subpopulations (e.g., adult or pediatric patients, controlled or drug-resistant epilepsy, with or without comorbidity, on different types of medication, etc.) that can be generalized.
3. Discernible case identification criteria and procedures.
4. Clear description of the design, data sources, and procedures for identifying epilepsy-attributable costs.

Selected articles then underwent a quality assessment in Stage 3**.** The process involved two members of the TF independently assessing each manuscript based on four criteria: 1) accuracy of case identification; 2) representativeness of cases; 3) accuracy of cost identification and attribution; and 4) comprehensiveness of costs. Each reviewer scored the article on each criterion as 1 – low, 2 – moderate, and 3 - high, based on specific definitions used for each that are available in the Figure 1. Only articles with moderate or high-quality scores across all four criteria were selected.

In Stage 4 selected articles were randomly assigned to one member of the TF who extracted the per person cost estimates from the article using a pre-designed RedCAP questionnaire. [11] The extracted data were then independently confirmed by a second member of the TF. The resultant database was exported from RedCAP as an Excel Spreadsheet (Microsoft Corporation, Redmond, Washington, USA) and used in the analysis.

Calculation of Country-Specific Per Person Cost Estimates

The focus of the cost data extracted from selected studies varied in terms of perspective, coverage time frame, population, types of epilepsy, severity, types of therapy, and age group. A number of adjustments were made to these data to develop estimates of the average direct healthcare cost per person for the general population of people with epilepsy in a given country.

Costs for brand versus generic drug users
The weighted average of cost estimates was derived with weights based on the distribution of cases on each type of drug.

Costs for drug-resistant versus stable patients
The weighted average of the cost estimates was used based on the distribution of cases by type, if available from the study, or 20/80 weights for drug-resistant/stable, based on the distribution of cases typically found in the cost literature. [12–15]

Costs for individuals in different parts of a country or treatment settings
The weighted average was used based on the distribution of cases by setting from the study, if available, or a simple average was used.

Costs reported for different age groups
Weighted average used based on distribution of cases by age group when available. If not, the simple average costs for all ages was used.

Costs for multiple years
The mid-point year or simple average of all years was used.

Costs for year of onset and follow-up years
The weighted average of the cost estimates was used based on the distribution of cases, if available, or 15/85 incidence/prevalence weights from the cost literature. [12,13]

Costs for patients on different number of anti-seizure medications (ASM) or different ASM brands
The weighted average was used based on the distribution of cases in the study.

Costs for patients with different severity of epilepsy (i.e., based on seizure frequency, emergency room visit or hospitalization, number of changes in drug use, etc.)
The weighted average was used based on the distribution of cases in the study.

Costs for patients with drug-resistant epilepsy only
The costs could not be used for the general epilepsy population.

Costs for patients with "active/inactive" epilepsy
The selected studies defined inactive cases as in remission one or more years. Weights were used based on distribution of cases by type, if available, or 15/85 inactive/active weights based on the distribution of cases found in the cost literature. [12,13]

A number of studies of direct healthcare costs also included estimates of indirect costs and a few studies were found that estimated indirect costs only. The indirect cost estimates from these studies ranged from lost earnings associated with epilepsy-related absence from work, excess unemployment, reduced productivity at work, and premature mortality for people with epilepsy and their caregivers. Some used wages and others GDP per capita to value lost earnings and the groups for which indirect costs were presented (patients only, patients' and caregivers, employed patients only, employable age patients only, etc.) varied. Like direct healthcare costs, we adjusted the data from the 13 selected studies of indirect costs to generate a comparable indirect cost per person estimate for all people with epilepsy at the country level. All the studies had to include costs based on absence from work plus either excess unemployment or reduced productivity or both. A few studies also included earnings losses associated with premature mortality. When the study reported total indirect costs for selected sub-groups (workers, working age, adults, etc.) in a given country we divided the costs by the total epilepsy population (including those with no indirect costs) to derive indirect cost per person.

Both the direct healthcare and indirect cost data were for various years and reported in various currencies. To adjust the costs to 2019 USD, we followed standard methods[16] using the World Bank GDP inflation deflator [17] for the relevant country to adjust for inflation from the

study year to 2019 and the World Bank 2019 Purchasing Power Parity (PPP) exchange rate[18] to convert to USD.

When cost data for a given country were available from multiple studies, the un-weighted mean of all available estimates was used for the country. The median was considered but not used due to the relatively small number of countries with three or more studies. In some cases where one study estimate was an outlier from the others, and there was a discernable methodological rationale for the difference, it was excluded.

Extrapolations for Countries with No Cost Data

The direct healthcare cost database included estimates from multiple countries within each World Bank income category (low-income, lower-middle-income, upper-middle- income, and high-income). Either the average or median (depending on the number and range) among countries with data in each category was used to estimate costs for similar income countries with no data. To reflect the variation among countries within income category, the cost for a given country was adjusted by an index of the relative health expenditure per capita[19] within the country compared to other countries in the same income category. Health spending per capita was selected for the adjustment index because it had the strongest correlation with epilepsy costs across the countries with data (Pearson correlation coefficient of 0.75) compared to Gross Domestic Product (GDP) per capita (0.64), and the GBD Socio-demographic Index (a compound measure of income per capita, education, and fertility) (0.47).

The median indirect cost per person of countries in similar income categories was adjusted by an index of the relative GDP per capita[20] of the country compared to the income group average to estimate indirect cost per person for countries without data. GDP per capita

was selected for the indirect cost adjustment because it had the strongest correlation with indirect cost of epilepsy across countries with data (Pearson correlation coefficient of 0.74) compared to Health Spending per capita (0.57), and the GBD Socio-demographic Index (0.52).

Developing Global Costs

The inflation and currency adjusted epilepsy-specific per person costs were then multiplied by the latest estimates of the number of people with epilepsy in 195 individual countries available from the GBD study and aggregated at GBD super region, World Bank income category grouping[21], and global levels. The GBD Collaboration is the most comprehensive initiative to measure levels and geographic and temporal trends of diseases and injuries worldwide (http://www.healthdata.org/gbd/about/protocol). The Collaboration provides estimates of prevalence, incidence, premature mortality, and disability for more than 300 diseases and injuries in 195 countries, by sex and age from 1990 to the present, with comparisons over time, within populations and countries. The 2019 estimates of epilepsy prevalence, which are the latest available, refer to idiopathic epilepsy and other epilepsies caused by infectious agents (i.e., meningitis, tetanus, malaria, cysticercosis, cystic echinococcosis) preterm birth complications, neonatal encephalopathy, neonatal sepsis, neonatal hemolytic disease, brain cancer, traumatic brain injury, congenital anomalies, and stroke. GBD estimates include people having seizures (active epilepsy) and those in remission (inactive epilepsy). Although these figures may underestimate the entire burden of idiopathic and symptomatic epilepsy as defined by the ILAE,[22] they represent the most comprehensive estimate of the number of people with epilepsy in whom epilepsy-specific direct healthcare and indirect costs can be attributed.

Sensitivity Analysis

The healthcare cost per person data from the COI literature overestimate the actual healthcare cost of epilepsy per person in countries due to the epilepsy treatment gap (e.g., people who are not diagnosed or receiving treatment for their epilepsy).[23] To adjust our estimates accordingly, data from the most comprehensive treatment gap literature survey available to date[24] were applied to each country's epilepsy prevalence based on their income category - 65% for low-income countries, 52% lower-middle, 55% upper-middle, and 10% high income – before multiplying by per person healthcare costs to calculate total healthcare costs.

In the global COI literature, GDP per capita has also been shown to be correlated with disease-specific cost data and used to adjust regional cost estimates in imputing costs for countries without data.[7] To determine the sensitivity of the results to using GDP per capita to adjust median values of cost rather than healthcare spending, we generated estimates with both and compared the difference.

Results

Literature Search

Using the search criteria and procedures outlined above, 17,067 references were identified in the initial electronic search (Figure 2), of which 9,649 were duplicates, 7,075 were excluded based on review of titles and abstracts and 54 review articles identified. One-hundred fifty-five of the remaining 343 were excluded after full text review: 80 only provided total or partial cost estimates for people with epilepsy; 20 were found to be from the same study; and 55 did not present original empirical data or new analysis. One-hundred eighty-eight articles

remained and underwent a quality assessment. One hundred one studies met the quality requirements for the direct healthcare cost database: 46 North America, 32 Western Europe, 4 Eastern Europe, 1 Latin America, 8 East Asia, 5 Central Asia, 5 Africa. Thirteen indirect cost studies were selected: 4 Western Europe, 4 East Asia, 3 North America, 1 Africa, 1 Eastern Europe.

Cost Estimates

Table 1 shows the 2019 costs per person estimates from the 101 selected studies for 22 countries with direct healthcare cost data and from the 13 studies for eight countries with indirect cost data by income category. Direct healthcare costs range from less than $1 per person per year in Burundi to $10,659 in Canada. The mean for low-income countries was $55. The mean for high-income countries $4,476. Indirect costs ranged from $150 in Nigeria to $14,206 in Denmark.

Based on the per person costs for countries with cost data and extrapolations for the remaining countries (173 without direct healthcare cost data and 187 without indirect cost data), the worldwide average annual cost of epilepsy per person in 2019 is estimated at $4,467 (the sum of direct healthcare cost per person - $1,687 – and indirect cost per person - $2,780 – Table 2, row 5, columns 4 and 8, respectively). Direct healthcare spending ranged from $54 in low-income to $3,160 in high-income countries and indirect costs ranged from $150 in low-income to $8,272 in high-income countries. The total cost of epilepsy, assuming average direct healthcare and indirect costs apply to all 52.51 million people in the world with epilepsy (GBD estimate for 2019), is $145.91 billion - 54% direct and 46% indirect. Adjusting direct healthcare costs for existing estimates of the treatment gap, total epilepsy costs fall to $119.27 billion -

44% direct and 56% indirect. Using GDP per capita rather than health care spending per capita to extrapolate direct healthcare costs for countries with no data increased per person average direct healthcare costs slightly to $1,775 and lowered total costs to $143.75 billion (not included in the table). Individual country estimates are available as online supplementary information.

The distribution of costs does not reflect the distribution of cases. As shown in the table, most of the costs are in 62 high-income countries (71% of total costs not considering the treatment gap, 83% including the treatment gap) with only 15% of the world's epilepsy population. Only about 6% of the costs of epilepsy are in the 78 low- and lower-middle-income countries where 50% of the population with epilepsy reside. The cost figure in these countries accounts for only 4% of global costs when the treatment gap is considered.

The concentration of costs is also reflected at the regional level (Table 3) with 64% of total costs (75% considering the treatment gap) found in 31 countries located in Australia/New Zealand, South Asia, North America, and Western Europe where only 12% of the population with epilepsy live.

Discussion

The global cost of epilepsy is substantial but varies significantly across countries depending on the prevalence of epilepsy, costs per person, and the epilepsy treatment gap. The latter two are highly correlated with income resulting in the concentration of costs in high-income countries and regions of the world while most of the population living with epilepsy resides in low- and middle-income countries and regions. The cost of epilepsy includes

substantial indirect as well as direct healthcare costs given its chronic nature and effects over the life course. The latter varies with the development of the healthcare system and access to healthcare. The former is associated with employment opportunity and wage levels in each country.

Epilepsy direct healthcare costs are relatively low compared to other more common disease conditions, based on limited comparisons available. For example, our estimate of the 2019 direct healthcare cost of epilepsy worldwide ($78.95 billion) was 50% of the 2015 estimate of the healthcare cost of dementia.[25] Healthcare costs for epilepsy in the United Kingdom in 2019 were $955.86 million in our study compared to dementia – $1.57 billion, cancer – $3.96 billion, coronary heart disease – $2.16 billion, and stroke – $1.65 billion.[25] Estimates of the indirect cost of these conditions are not available for comparison but given that epilepsy affects young as well as older ages, the work-related indirect healthcare costs over a person's lifetime may be relatively more important.

These findings provide support for policy and program advocacy that target direct healthcare as well as indirect costs of epilepsy and reflect the conditions in different regions of the world. In high income countries, the high cost of healthcare and indirect costs suggests a focus on improving efficiency in healthcare delivery, ensuring equity in access, and reducing costs of care while also addressing barriers to employment and work productivity of people living with epilepsy. In lower income regions of the world the relatively low cost of the disease reflects the lack of available healthcare services and employment opportunities. Additional investments are needed to expand access to services for the general population and educate the population on the benefits of treatment.

As the first study to generate country, regional, and global estimates of the cost of epilepsy, the TF was able to follow a general approach that has been used in cross-country cost studies for epilepsy. Where choices had to be made, we chose methods that were as objective and transparent as possible. The results are conservative but reasonable when compared to previous research from 13 review articles published since 2000[26-46]. Thirty-nine direct healthcare cost per person estimates for 12 countries were adjusted to 2019 USDs and compared to ours. Differences ranged from 86% below to 49% above with an overall average difference of 10% below. The average direct healthcare cost per person quoted in the review articles for all studies was $2,839 per year compared to our average of $2,454 for the same studies we compared.

Our estimates for Western European countries are comparable to those from the European Brain Study (EBS),[6] the only other multi-country regional cost study to date. Substantial differences were found between for prevalence and costs after updating the EBS cost estimates to 2019 USD (Table 4). The TF prevalence figures are 21% higher than the EBS prevalence estimates, only a part of which can be explained by population growth (1.5% in 2010-2019). The direct healthcare and indirect cost per person are 53% lower and 27% higher, respectively, compared to the EBS. The TF total cost estimate for the region is 8% lower than the EBS estimate when not including the treatment gap and 12% lower when including the treatment gap.

Most cost estimates from the COI literature are based on sub-populations of people with the disease that must be adjusted to the general population. The best method In aggregating to the general population would be to multiply the cost for people in different sub-

populations by the prevalence estimates of each sub-population.[7] This approach is impractical for multi-country cost studies given the lack of detailed epidemiological and cost data. The TF developed a systematic approach for generating general population estimates from sub-population data without detailed data that involved: 1) deriving weighted averages of sub-population estimates for treatment groups based on the distribution of people in different treatment categories either available from the study or COI literature, and 2) applying the estimated treatment gap percentage from the growing treatment gap literature to population prevalence to account for the lower direct cost of the untreated.

The major limitation of the TF estimates is the limited number and skewed nature of direct healthcare and indirect cost data at the country level leading to the large number of extrapolations required in the analysis. The lack of indirect cost information from most countries in the world (not only concerning the patient but also the caregiver, especially in low and middle-income countries) is even more pronounced, with only one study from a lower-middle income country deemed to be of high enough quality to be included in the indirect cost database. Even when the information is available, it is difficult to aggregate and compare due to differing measures, sources, sub-populations, designs, and periods of time. For example, some cost studies reflect healthcare prices or tariffs set by the government or insurance companies that do not represent actual costs, thereby influencing the reported total cost. Acknowledging these limitations highlights the urgent need for undertaking high quality, COI studies particularly in low- and lower-middle income countries around the world. More standardized studies of more representative samples of people with epilepsy from different parts of the world are needed to provide evidence on the distributional impact of epilepsy

worldwide. It is the hope of this TF that these results can stimulate future research to better understand the nature and distribution of the economic burden of this often treatable, chronic condition.

Figure Legend

Figure 1 Quality Assessment Scoring Criteria

The figure describes the criteria and scoring for assessing the quality of the cost studies that were reviewed.

Figure 2 PRISMA Diagram of Systematic Review of COI Studies

The figure describes the resulting number of cost studies after each stage of the literature search.

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Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines

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Table 1. Direct Healthcare and Indirect Cost Data Extracted from the COI Literature

Country	Direct Healthcare Cost Per Person (2019 USD)	Indirect Cost Per Person (2019 USD)	World Bank Income Category (1-Low-income, 2 Lower middle-income, 3-Upper middle income, 4-High income
Burundi	$ 0.57		1
Congo	$ 108.44		1
Mean	**$ 54.50**		
India	$ 53.82		2
Nigeria	$ 654.59	$ 149.56	2
Mean	**$ 354.20**		
Bulgaria	$ 3,062.26		3
Mexico	$ 1,666.00		3
China	$ 449.23	$ 321.23	3
Russia	$ 2,470.20		3
Mean	**$ 2,048.20**		
Australia	$ 2,525.00		4
Hungary	$ 553.81		4
Poland	$ 657.23	$ 1,520.80	4
Korea	$ 1,166.39	$ 2,123.31	4
Netherlands	$ 2,191.77		4
UK	$ 2,320.76		4
Sweden	$ 2,403.25	$ 13,632.37	4
Denmark	$ 4,157.36	$ 14,205.64	4
Italy	$ 4,498.33		4
Spain	$ 6,988.86	$ 11,058.91	4
Germany	$ 7,095.51		4
France	$ 7,464.71		4
US	$ 9,984.04	$ 5,924.50	4
Canada	$ 10,659.16		4
Mean	**$ 4,476.16**	**$ 6,117.04**	

Table 2. Prevalence (GBD 2019) and Cost (2019 USD) by World Bank Income Category

Countries	Prevalence 2019 (GBD)	%	Healthcare Cost Per Person	Total Healthcare Cost (thousands)	%	Total Healthcare Cost Considering Treatment Gap (thousands)	Indirect Cost Per Person	%	Total Indirect Cost (thousands)	%	Total Healthcare and Indirect Cost (thousands)	%	Total Healthcare and Indirect Cost Considering Treatment Gap (thousands)	%
Low Income - 29	4,527,579	8.6	$54	$219,693	0.3	$29,419	$150	0.1	$647,622	1.0	$867,314	0.6	$677,040	0.6
Lower Middle Income - 49	21,665,389	41.3	$359	$4,305,968	5.5	$1,278,872	$150	2.4	$2,843,243	4.3	$7,149,210	4.9	$4,122,115	3.5
Upper Middle Income - 55	18,262,503	34.8	$1,986	$28,540,300	36.1	$9,618,081	$319	18.4	$6,184,054	9.2	$34,724,854	23.8	$15,802,135	13.2
High Income - 62	8,056,182	15.3	$3,160	$45,883,792	58.1	$41,387,180	$8,272	79.1	$57,279,162	85.5	$103,162,954	70.7	$98,666,342	82.7
Total Countries - 195	52,511,653	100.0	$1,687	$78,954,207	100.0	$52,314,137	$2,780	100.0	$66,954,079	100.0	$145,908,287	100.0	$119,268,216	100.0

Table 3. Prevalence (GBD 2019) and Cost (2019 USD) by GBD Super Region

GBD Super Regions	Prevalence 2019	%	Direct Healthcare Cost Per Person	Total Direct Healthcare Cost (thousands)	%	Total Direct Healthcare Cost Considering Treatment Gap (thousands)	%	Indirect Cost Per Person	Total Indirect Cost (thousands)	%	Total Direct Healthcare and Indirect Cost (thousands)	%	Total Direct Healthcare and Indirect Cost Considering Treatment Gap (thousands)	%
Central Europe, Eastern Europe, and Central Asia 29 Countries	2,968,537	5.7	$1,323	$4,141,508	5.2	$1,797,853	3.4	$1,583	$3,184,214	4.8	$7,325,722	5.0	$4,982,067	4.2
Australasia, South Asia, North America (High Income) 8 Countries	3,491,634	6.6	$4,666	$28,034,204	35.5	$25,286,852	48.3	$8,879	$22,450,054	33.5	$50,484,258	34.6	$47,736,906	40.0
Southern Latin America 3 Countries	418,764	0.8	$3,313	$1,868,413	2.4	$791,336	1.5	$2,488	$707,886	1.1	$2,576,299	1.8	$1,499,222	1.3
Western Europe 23 Countries	2,828,374	5.4	$4,851	$15,491,532	19.6	$13,973,362	26.7	$11,505	$27,424,819	41.0	$42,916,351	29.4	$41,398,181	34.7
Latin America and Caribbean 32 Countries	5,909,182	11.3	$1,826	$14,570,657	18.5	$5,024,127	9.6	$2,060	$2,860,007	4.2	$17,430,664	11.9	$7,884,134	6.6
North Africa and Middle East 21 Countries	3,928,880	7.5	$1,146	$4,521,966	5.7	$1,829,492	3.5	$2,343	$3,728,808	5.6	$8,250,774	5.7	$5,558,300	4.7
South Asia 5 Countries	12,993,217	24.7	$146	$909,810	1.2	$270,213	0.5	$104	$1,386,313	2.1	$2,296,124	1.6	$1,656,528	1.4
Sub-Saharan Africa 46 Countries	5,157,409	9.8	$465	$1,983,659	2.5	$635,737	1.2	$153	$720,023	1.0	$2,703,681	1.9	$1,355,759	1.1
Southeast Asia, East Asia, and Oceania 28 Countries	14,815,656	28.2	$764	$7,432,459	9.4	$2,705,165	5.2	$709	$4,491,955	6.7	$11,924,414	8.2	$7,197,119	6.0
Totals 195 Countries	52,511,653	100.0	$1,687	$78,954,207	100.0	$52,314,137	100.0	$2,780	$66,954,079	100.0	$145,908,287	100.0	$119,268,216	100.0

Table 4. Comparison: European Brain Study (2010 Prevalence, Cost Literature Extractions, Extrapolations) versus ILAE TF Study (2019 Prevalence, Cost Literature Extractions, Extrapolations)

2010 EU24, Iceland, Norway, Switzerland	Prevalence	Total Cost Per Person (weighted average across countries)	Total Cost (billion)	Total Cost Considering TG (billion)	Direct Healthcare Cost Per Person (weighted average)	Total Direct Healthcare Cost (billion)	Indirect Costs Per Person (weighted average across countries)	Total Indirect Costs (billion)
European Brain Study	2,643,001	$14,923	$ 47.86	$ 47.86	$8,531	$22.55	$7,404	$ 19.57
ILAE Task Force Study	3,185,238	$13,479	$ 43.94	$ 42.32	$4,042	$15.74	$9,437	$ 28.20
Percent Difference	20.52	-9.68	-8.18	-11.57	-$53	-30.19	$27	44.11