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Health and economic benefits of public financing of epilepsy treatment in India: An agent-based simulation model

Itamar Megiddo, Abigail Colson, Dan Chisholm, Tarun Dua, Arindam Nandi, Ramanan Laxminarayan

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Summary

Objective

An estimated 6–10 million people in India live with active epilepsy, and less than half are treated. We analyze the health and economic benefits of three scenarios of publicly financed national epilepsy programs that provide: (1) first-line antiepilepsy drugs (AEDs), (2) first- and second-line AEDs, and (3) first- and second-line AEDs and surgery.

Methods

We model the prevalence and distribution of epilepsy in India using IndiaSim, an agent-based, simulation model of the Indian population. Agents in the model are disease-free or in one of three disease states: untreated with seizures, treated with seizures, and treated without seizures. Outcome measures include the proportion of the population that has epilepsy and is untreated, disability-adjusted life years (DALYs) averted, and cost per DALY averted. Economic benefit measures estimated include out-of-pocket (OOP) expenditure averted and money-metric value of insurance.

Results

All three scenarios represent a cost-effective use of resources and would avert 800,000–1 million DALYs per year in India relative to the current scenario. However, especially in poor regions and populations, scenario 1 (which publicly finances only first-line therapy) does not decrease the OOP expenditure or provide financial risk protection if we include care-seeking costs. The OOP expenditure averted increases from scenarios 1 through 3, and the money-metric value of insurance follows a similar trend between scenarios and typically decreases with wealth. In the first 10 years of scenarios 2 and 3, households avert on average over US$80 million per year in medical expenditure.

Significance

Expanding and publicly financing epilepsy treatment in India averts substantial disease burden. A universal public finance policy that covers only first-line AEDs may not provide significant financial risk protection. Covering costs for both first- and second-line therapy and other medical costs

alleviates the financial burden from epilepsy and is cost-effective across wealth quintiles and in all Indian states.

Key Points

- The high burden of epilepsy in India impacts households financially in addition to disease-related burdens
- Provision of first-line antiepileptic drugs (AEDs) can significantly reduce the disease burden and is cost-effective
- Cost-effectiveness analyses of mental health disorders are a useful tool for policy decisions, but they do not capture the financial burden on households
- Public finance of first-line AEDs does not necessarily protect households from financial shock if we consider care-seeking costs
- A program that publically finances second-line AEDs provides better financial risk protection for the Indian population

Roughly 80% of the 50 million people globally who have epilepsy live in low- and middle-income countries (LMICs).[1] Most cases of epilepsy can be effectively treated using first-line drugs,[2] which are cost-effective,[3-5] but poor knowledge and stigma, low prioritization within the health system, high out of pocket costs, and lack of human resources, diagnostic facilities, and drug supply have led to a large number of untreated epilepsy cases,[1, 6-14] and consequently a high disease burden in these countries. In 2010, epilepsy caused approximately 17.4 million disability-adjusted life years (DALYs) globally. Globally, epilepsy ranks 20th as a cause of years lived with disability.[15]

An estimated 6–10 million individuals live with active epilepsy in India,[11, 16, 17] but less than half receive appropriate and sufficient epilepsy treatment.[6] To overcome the treatment gap and improve quality of care for people with epilepsy, India's Ministry of Health and Family Welfare has proposed the creation of a national epilepsy program to increase public awareness about epilepsy, train healthcare workers to better identify the disease, and provide first- and second-line antiepileptic drugs (AEDs).[11] Experts have also noted the need for an epilepsy surgery program in India.[14, 18-20] In 1998, the per patient cost of epilepsy treatment was as high as 88.2% of the country's per capita gross national product (GNP), and epilepsy-related costs, which includes medical costs, travel, and lost work time, exceeded $2.6 billion (2013 USD).[21]

We evaluate the health and economic benefits of a national program that finances and expands coverage of epilepsy treatment in India. Using IndiaSim,[22-24] an agent-based simulation model (ABM) of India's population and health system, we examine the incremental impact of implementing three universal public finance (UPF) policy scenarios. In scenario 1, the program provides first-line AEDs. In scenario 2, the program provides both first- and second-line AEDs. In scenario 3, first-line AEDs, second-line AEDs, and epilepsy surgery are publicly financed. In each scenario the program increases coverage of the specified interventions to 80% through public and private provision, and it covers related medical expenditures—diagnostics, outpatient consultation, and inpatient costs. For each scenario we conduct an extended cost-effectiveness analysis (ECEA)[25] by estimating the policies' impacts on five measures: DALYs averted, incremental government expenditure, incremental dollars per DALY averted or the incremental cost-effectiveness ratio (ICER), out-of-pocket (OOP) expenditure averted, and the money-metric value of insurance.

Methods

Model

IndiaSim is representative of the Indian population and health system at the district level. Details about IndiaSim are in Appendix S1 and in earlier publications.[22, 23] We use it to model a baseline scenario with a treatment gap of 64.3%[26] and intervention scenarios with 80% effective coverage for patients with epilepsy.

The disease model is presented in Figure 1. Healthy individuals acquire epilepsy at a daily rate $\Lambda_{i,j}$, for age group i of gender j, and move into the "epilepsy without treatment" state. They clear the disease without treatment at the remission rate $\sigma_{N,i,j}$. Those in epilepsy states die at the rate of excess mortality (Table S1).

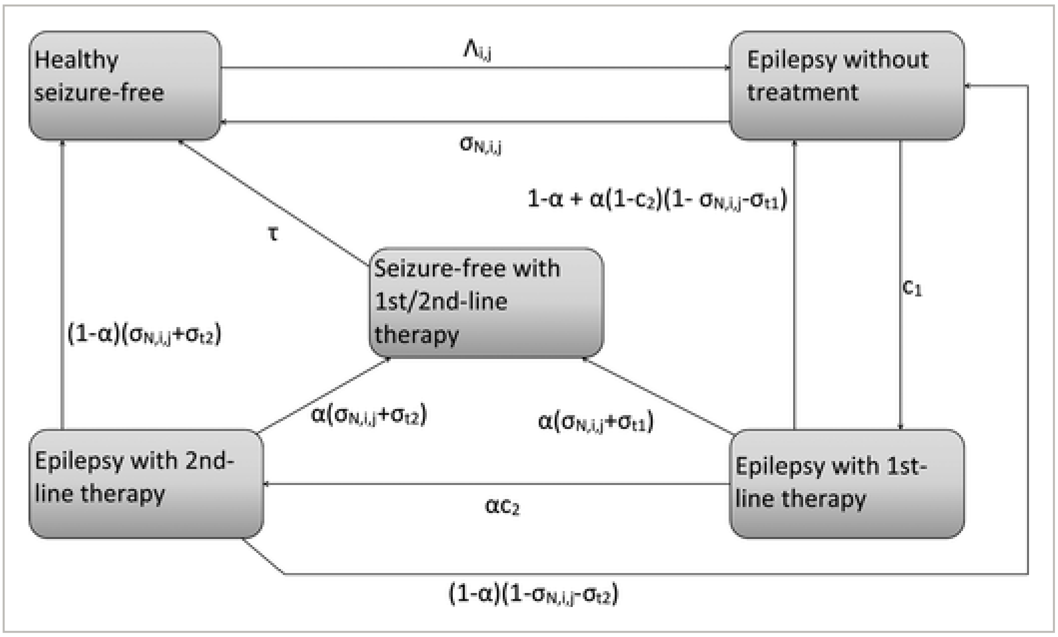

Figure 1

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Epilepsy model $\Lambda_{i,j}$ is the incidence rate for age group i of sex j; c_1 and c_2 are the effective coverage of first- (first-line AEDs) and second-line (lamotrigine or surgery along with first-line AED) therapy; 1-α is the treatment dropout rate due to adherence; $\sigma_{N,i,j}$ is the natural clearance rate for age group i of gender j, and σ_{t1} and σ_{t2} are the clearance rates with therapy; and τ is the rate of stopping treatment when not having seizures. Those in the seizure-free with therapy state are still medically considered to have active epilepsy. Individuals are born into the healthy and seizure-free category. They die from exogenous causes (in any state) or epilepsy-related causes (in states with active epilepsy) and are removed from the model.

The model includes three treatment options for patients with epilepsy: first-line AEDs, lamotrigine, and surgery. Lamotrigine is an example of a new-generation AED as the second-line treatment. First-line drugs are prescribed according to the frequency distribution in Table 1.[2] Those who seek and receive treatment (at the rate c_1) move into the "epilepsy with first-line therapy" category. A proportion of patients, α, adhere to the treatment. Patients treated with first-line therapy who continue to experience epileptic seizures after 2 months are switched to second-line treatment if they are covered (c_2) and move into "epilepsy with second-line therapy" state. A third of these patients are eligible for surgery (randomly selected in the model) and the rest are treated with lamotrigine. Because epilepsy surgery is expensive and available data indicate that <500 surgeries are performed each year in India,**14**, **20** we assume that at baseline, only the top 1% of the population income distribution is able to pay for surgery. Patients who are eligible for surgery but cannot afford it are treated with lamotrigine. Patients who adhere to treatment and stop experiencing seizures naturally or due to treatment at rates σ_{t1} (first-line therapy) and σ_{t2} (second-line therapy) continue being treated with AEDs for 5 years, at which point they move into the "seizure-free with first/second line therapy" state. They continue to be defined to have active epilepsy for a mean period $1/\tau$, set to 5 years in our model.

Table 1. Treatment input parameters

Variable	Value	Sensitivity range	Source
Treatment parameters			
Treatment gap	64.3%	45–84%	Mbuba et al. 2008**26** and distributed according to NSS 60th round schedule 25**31**
Adherence	70%	49–91%	Chisholm 2005**3**
1st-line AED distribution		Range shown in costs	
Phenobarbital (30 mg)	50%		Authors' assumption
Carbamazepine (200 mg)	30%		
Phenytoin (100 mg)	10%		
Valproate (200 mg)	10%		
Second-line treatment distribution			
Second-line AED (lamotrigine)	67%		Authors' assumption
Surgery	33%		

[a] Includes outpatient consultation, diagnostic investigation, and hospitalization; costs have been inflated to 2013 prices using GDP deflators.

We consider the costs for implementing the program, calculated with the World Health Organization (WHO) Mental Health Gap Action Programme (mhGAP) tool, in addition to patients' medical and care-seeking costs. See Tables 1 and S1 for model parameters and costs.

Analysis

We conduct analysis of IndiaSim output using R (version 3.1.2) and report health and economic outcomes at state and national levels for the first 10 years of intervention. Health burden is measured in DALYs. Economic impact is measured using ICERs and epilepsy-specific OOP expenditure averted. Financial risk protection is measured by the money-metric value of insurance—the price individuals are willing to pay to avoid the risk of financial shock.**25**, **27** We report the mean present value for the 10 years, discounted at 3% annually. Costs and expenditures are in 2013 US dollars. We conduct a Latin Hypercube Sampling (LHS) sensitivity analysis and construct 95% uncertainty ranges (URs). Further details on these calculations are in Appendix S1.

Results

The outcomes for the UPF policies are in Table 2 and in Figures 2-4.

Table 2. Incremental health and economic outcomes per 100,000 persons (20,000 in each wealth quintile)

Quintile	I – poorest	II	III	IV	V – richest	Total
Baseline						
DALYs	510 (500–520)	495 (485–505)	500 (490–515)	490 (480–505)	495 (480–505)	2,490 (2,455–2,535)
DALYs averted from null case	100 (90–110)	110 (100–120)	115 (100–125)	130 (120–140)	125 (110–135)	580 (545–595)
Policy scenario 1 (incremental to baseline)						
DALYs averted	175 (165–185)	165 (155–175)	170 (160–180)	165 (155–175)	160 (150–170)	835 (805–870)
Incremental government expenditure	$28,950 ($28,300–$29,610)	$28,890 ($28,240–$29,540)	$29,130 ($28,490–$29,770)	$29,060 ($28,400–$29,710)	$29,060 ($28,400–$29,72O)	$145,090 ($141,860–$148,230)
OOP expenditure averted	−$4,550 (−$5,860–$3,240)	−$3,710 (−$4,800–$2,630)	−$4,010 (−$5,130–$2,890)	−$2,200 (−$3,460–$940)	−$2,760 (−$4,030–$1,500)	−$17,230 (−$23,010–$12,740)
Money-metric value of insurance	−$6,870 (−$7,830–	−$3,490 (−$4,070–	−$2,500 (−$2,900–	−$1,390 (−$1,660–	−$960 (−$1,360–	−$15,210 (−$16,480–

Results are over 100 simulations and 10 years. They are presented in present day values. Baseline effective coverage for first-line and second-line therapy is 36% and treatment is paid out of pocket. All policy scenarios cover the annual medical costs (consultation, diagnostics, and inpatient). In scenario 1, effective coverage for first-line therapy is 80%, and effective coverage for second-line therapy is 36%. Second-line treatment and surgery are paid out of pocket. In scenario 2, effective coverage for first-line and second-line therapy is 80%, and only surgery is paid out of pocket. In scenario 3, effective coverage for first-line and second-line therapy is 80%, and no treatment is paid out of pocket. Only the top 1% of the population chooses to undergo surgery when it is covered out of pocket; 95% uncertainty range in parentheses. DALYs, disability-adjusted life years; OOP, out of pocket. Costs are rounded to the nearest 10 and DALYs in the baseline and scenario 1 are rounded to the nearest 5.

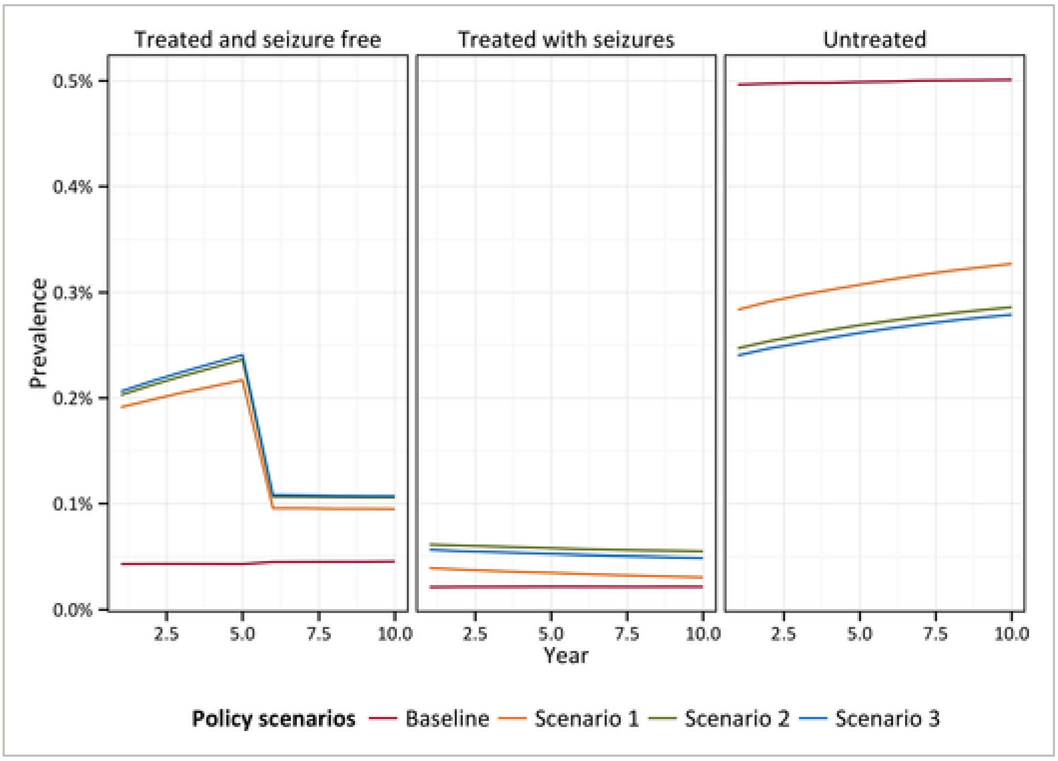

Figure 2

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Prevalence of active epilepsy over time. Results are over100 simulations. The plot includes only individuals with active epilepsy-seizure in the last 5 years. The treated and seizure-free group includes those that have not had recent seizures, but have had seizures in the last 5 years. Baseline effective coverage for first-line and second-line therapy is 36% and treatment is paid out of pocket. All policy scenarios cover the annual medical costs (consultation, diagnostics, and inpatient). In scenario 1, effective coverage for first-line therapy is 80%, and effective coverage for second-line therapy is 36%. Second-line treatment and surgery are paid out of pocket. In scenario 2, effective coverage for first-line and second-line therapy is 80%, and only surgery is paid out of pocket. In scenario 3, effective coverage for first-line and second-line therapy is 80%, and no treatment is paid out of pocket. Only the top 1% of the population chooses to undergo surgery when it is covered out of pocket.

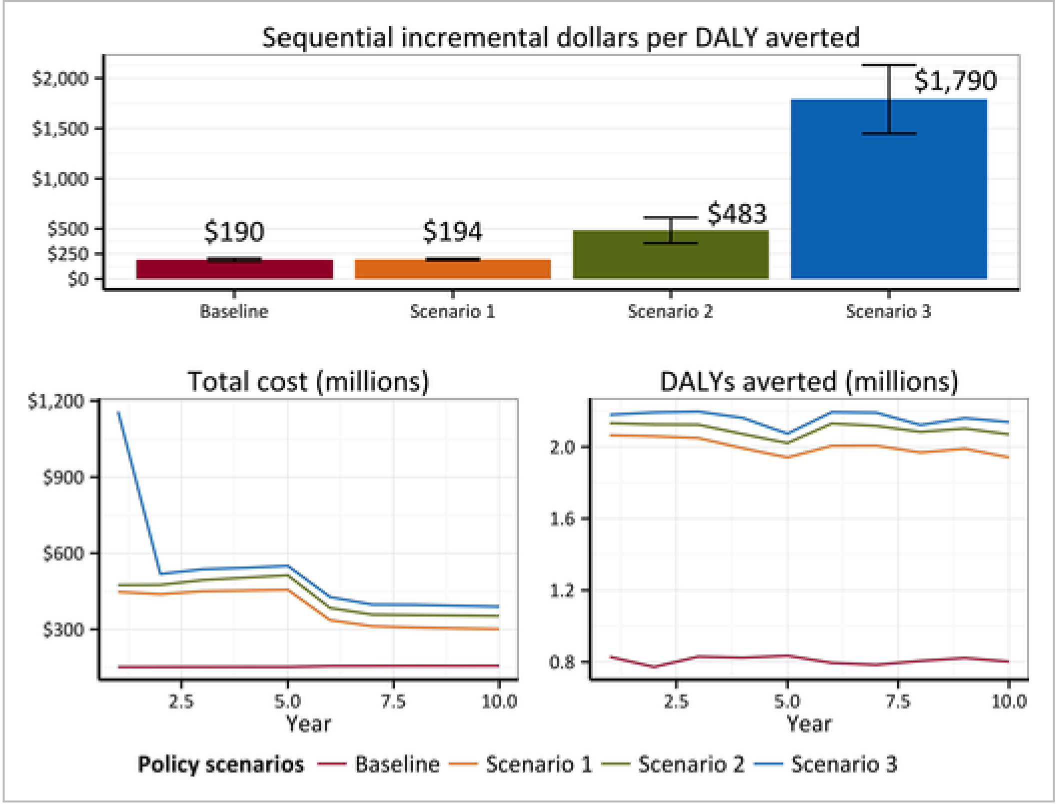

Figure 3

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Cost-effectiveness. Results are over 100 simulations. DALYs, disability-adjusted life years. In row 1 the costs and health benefits are discounted at 3% and aggregated over the 10 years. The costs include both government expenditure and out-of-pocket (OOP) expenditure for diagnostics, treatments, inpatient costs, and first- and second-line therapies. Row 2 represents the mean nondiscounted total costs and DALYs averted for the entire Indian population each year. All policy scenarios cover the annual medical costs (consultation, diagnostics, and inpatient). In scenario 1, effective coverage for first-line therapy is 80%, and effective coverage for second-line therapy is 36%. Second-line treatment and surgery are paid out of pocket. In scenario 2, effective coverage for first-line and second-line therapy is 80%, and only surgery is paid out of pocket. In scenario 3, effective coverage for first-line and second-line therapy is 80%, and no treatment is paid out of pocket. Only the top 1% of the population chooses to undergo surgery when it is covered out of pocket. Error bars are the 95% uncertainty range.

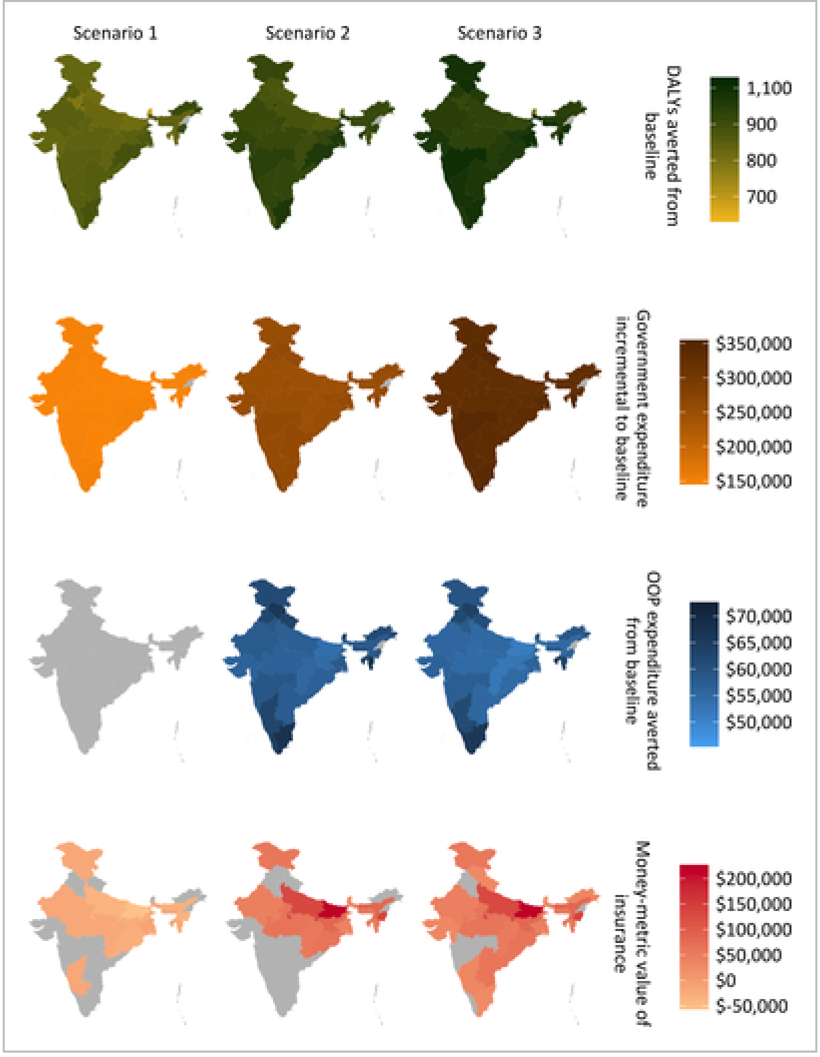

Figure 4

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Health and economic outcomes per 100,000 persons in each state. Results are over 100 simulations and 10 years; they are presented in present day values. OOP, out of pocket; DALYs, disability-adjusted life years. States in which the standard error is large and we cannot differentiate the results from no effect are grayed out. In the OOP expenditure averted plot (row 3), two states—Assam and Odisha—have significant negative results; they were grayed out for clarity in the color scale of the maps. All policy scenarios cover the annual medical costs (consultation, diagnostics, and inpatient). In scenario 1, effective coverage for first-line therapy is 80%, and effective coverage for second-line therapy is 36%. Second-line treatment and surgery are paid out of pocket. In scenario 2, effective coverage for first-line and second-line therapy is 80%, and only surgery is paid out of pocket. In scenario 3, effective coverage for first-line and second-line therapy is 80%, and no treatment is paid out of pocket. Only the top 1% of the population chooses to undergo surgery when it is covered out of pocket.

Health benefits

The model predicts roughly 7 million total active epilepsy cases—individuals with epileptic seizures in the last 5 years—in India at baseline. By the sixth year, the UPF policies relieve the burden of active epilepsy cases by approximately 1.5–2 million across India and significantly increase the number of treated patients among those with active epilepsy.

Figure 2 presents prevalence rates for the key health states of the model (treated and seizure-free, treated with seizures, and untreated with seizures) over 10 years for each scenario. Prevalence of treated and seizure-free patients is highest in the first 5 years in UPF scenarios 1 through 3 (close to five times the baseline prevalence). Prevalence drops significantly when patients who stopped experiencing seizures in year 1 are no longer medically considered to have active epilepsy in year 6 (approximately 2.1–2.3 times the baseline prevalence in scenarios 1 through 3).

The burden of untreated individuals with epilepsy declines by roughly 43% (UR 40–45%), 50% (UR 48–52%), and 52% (UR 50–54%) in scenarios 1 through 3, relative to baseline. It increases with nonadherence to treatment. In year 10 of scenario 3, there is approximately 44% (UR 42–46%) fewer untreated individuals with epilepsy than at baseline.

Total DALYs averted in UPF scenarios are presented in Table 2. Over 10 years, treatment in the baseline scenario averts 580 (UR 545–595) DALYs per 100,000 individuals compared to no treatment. Over the same period, in scenario 1, 835 (UR 805–870) DALYs per 100,000 persons are averted incremental to the baseline. In scenario 2 an additional 65 (UR 56–76) DALYs per 100,000 are averted, and in scenario 3 an additional 44 (UR 35–53) DALYs incremental to scenario 2. That amounts to approximately 800,000 DALYs averted each year in the baseline, and 1.8–2.3 million DALYs averted in scenarios 1 through 3 (Fig. 3 row 2 column 2).

At baseline, treatment averts more DALYs in rich populations (e.g., 125 UR 110–135/20,000 in the richest quintile over the 10 years) than in poor ones (e.g., 100 UR 90–110/20,000 in the poorest quintile) compared to the no treatment scenario. The UPF policies flatten the distribution of DALYs averted by the treatment interventions across wealth quintiles (Table 2). In scenario 1, treatment averts 160 (UR 150–170) DALYs per 20,000 (incremental to the baseline) in the richest 20% and 175 (UR 165–185) DALYs in the poorest 20%.

Goa and Maharashtra have the highest rates of averted DALYs (e.g., 1,350 UR 1,010–1,690 and 1,010 UR 950–1,065 DALYs averted per 100,000 in scenario 3 in Goa and Maharashtra), although the differences between states are not large (Fig. 4 row 1 and Figs. S1–S4 in the Appendix S1). In absolute numbers the differences are far greater. The most DALYs are averted in Uttar Pradesh (298,950 UR 289,440–308,470 DALYs averted in the mean year in scenario 3), and combined with Bihar, Madhya Pradesh, and Rajasthan it accounts for >50% of the DALYs averted in India in each UPF scenario. Those states also have the greatest burden in the baseline.

Government expenditures

The sequential, incremental present day government expenditure (including diagnostics, AEDs, surgeries, and medical consultation) in the first 10 years of the scenarios (Table 2) is: $145,090 (UR $141,860–$148,230)/100,000 persons in scenario 1; $107,590 (UR $97,360–$117,430)/100,000 in scenario 2; and $77,720 (UR $68,770–$86,650) in scenario 3. The government spends the most money in the first 5 years of the UPF scenarios (Fig. 3 row 2 column 1). After 5 years, many new patients will no longer have active epilepsy and will stop treatment, so government costs will drop. The costs are especially high at the initial stages of scenario 3 when surgery is available to many new patients. Only 50–500 surgeries are performed each year in the status quo and in UPF scenarios 1 and 2. Approximately 400,000 surgeries need to be performed in the initial stages of scenario 3 to cover 80% of eligible existing epilepsy cases (who do not respond to first-line therapy), and following the initial stage, 40,000–50,000 surgeries need to be performed each year. See Figure 4 row 2 and Figures S5–S7 for state-wise values.

Private, out-of-pocket expenditures

There is no significant OOP expenditure averted in UPF scenario 1. Mean OOP expenditure increases by $17,230 (UR $12,740–$23,010)/100,000 in the first 10 years (Table 2). The policies in the scenario save $19,740 (UR $18,780–$20,690) out of pocket per 100,000 on first-line therapy and $20,150 (UR $19,170–$21,130) on other medical costs, but those savings are countered by new patients' care-seeking costs (approximately $27,000/100,000) and increase in second-line drug purchases (approximately $30,000/100,000 not covered in scenario 1) if patients do not respond to first-line therapy and choose to continue treatment. Similarly to government expenditure, OOP expenditure drops when new patients experience remission and stop treatment. In year 7, the scenario's policies avert $750 (UR $190–$1,310) OOP expenditure per 100,000 relative to the baseline, and in year 10 they avert $1,510 (UR $980–$2,040).

Policies in scenarios 2 and 3 avert OOP expenditure as a result of the increased public financing. In the first 10 years of scenario 2, OOP expenditure averted is $75,760 (UR $68,000–$83,160)/100,000 incremental to scenario 1, and the OOP expenditure averted in scenario 3 is similar. The range of the rates of OOP expenditure averted per 100,000 across states is relatively small—from approximately $45,000 to $72,000 averted in the first 10 years of scenario 2 and slightly more in scenario 3 (Fig. 3 row 3 and Figs. S8–S10 in Appendix S1). On average over $80 million OOP expenditure is averted in India per year in both scenarios 2 and 3, although the value is approximately $40–$60 million in the first few years. Only the top 1% of the population has more OOP expenditure averted in scenario 3 than in scenario 2 (Table 2) because others do not pay for surgeries in the baseline.

Cost-effectiveness

The sequential ICERs relative to no treatment are presented in Figure 3: $190 (UR $175–$205) in the baseline, $194 (UR $185–$204) per DALY averted in scenario 1, $483 (UR $355–$611) in scenario 2, and $1,790 (UR $1,448–$2,131) in scenario 3. The dollars per DALY averted with respect to no treatment—that is, the average cost-effective ratios—are $158 (UR $149–$167), $173 (UR $163–$183) and $220 (UR $206–$234) in scenarios 1, 2, and 3, respectively. All three policy scenario are “very cost-effective” under WHO guidelines.[28]

Financial risk protection

The sequential, incremental money-metric value of insurance sum of the first 10 years of the policies is −$15,210 (−$16,470 to −$13,940)/100,000 in scenario 1, $65,360 ($60,180–$70,530)/100,000 in scenario 2, and $2,600 ($2,050–$3,150) in scenario 3 (Table 2). The UPF in scenario 1 does not offer financial risk protection. This affects the poor the most because they increase their effective coverage and their travel frequency the most (Table 2). Poor states such as Bihar, which has a money-metric value of insurance of $53,010 (UR −$62,360 to −$43,660)/100,000 summed over the 10 years, also suffer financially.

In scenarios 2 and 3, the trend of financial risk protection across the wealth distribution flips from the distribution in scenario 1. In scenario 2 the poor have the highest financial risk protection ($30,770 UR $26,200–$35,340/20,000 in quintile I in the 20 years), and the rich have the least protection ($1,270 UR $730–$1,810 in quintile V). In this scenario the money-metric value of insurance is extremely high in Bihar at $223,890 (UR $184,680–$263,100)/100,000, and it is also above $100,000 in Manipur and Uttar Pradesh (Fig. 3 row 4 and Fig. S12; for scenarios 1 and 3 also see figures S11 and S13, respectively). The rich and rich states have higher protection in scenario 3 than in scenario 2 (e.g., financial risk protection in Delhi is approximately $13,000 higher, whereas it is $1,000 lower in Bihar).

Discussion

In this article, we compute the health and financial benefits of expanding coverage and publicly financing epilepsy treatment in India. Although past analyses find epilepsy treatment is cost-effective in LMICs,[3-5, 29, 30] severe undertreatment of epilepsy persists. We evaluate a hypothetical national epilepsy program and demonstrate the incremental benefits to various Indian subpopulations achieved through government financing of first-line AEDs (scenario 1), first- and second-line AEDs (scenario 2), and first-line AEDs, second-line AEDs, and surgery (scenario 3). The key findings are presented qualitatively in Table 3.

Table 3. Key findings

	Epilepsy treatment provided in UPF	Cost	Cost-effectiveness (WHO guidelines)	Disease burden averted	Financial risk protection
Scenario 1	First-line AEDs	High (approximately $220–$255 million per year through year 5,then $160–$185 million per year)	Very cost-effective	High and somewhat progressive	Low or none
Scenario 2	First- and second-line AEDs	High (slightly higher than in scenario 1)	Very cost-effective	High (slightly higher than in scenario 1 and similarly progressive)	High and very progressive
Scenario 3	First- and second-line AEDs and surgery	Extremely high (extremely high through year 5, then slightly higher than in scenario 2)	Very cost-effective	High (slightly higher than in scenario 2 and similarly progressive)	High (slightly higher than in scenario 3, but less progressive)

Increasing coverage requires substantial government investment, especially in the initial stages of the UPF scenarios. In our analysis we assume an immediate increase of coverage, and therefore the costs are extremely high in the first few years. In the first 5 years of scenario 1, the government would spend $220–$255 million ($365–$440 million in scenario 2) per year, and in the next 5 years it would spend $160–$185 million ($285–$325 million in scenario 2) per year. In scenario 3 the government would spend approximately $1 billion dollars in year one, $410–$480 million in the next 4 years, and $320–$390 million each year following that. The immediate increase in coverage is likely infeasible, and in reality the higher costs in the initial stages can be spread out over a longer period. Despite that, this analysis points to the substantial initial investment needed, especially in a scenario with surgery public financing (scenario 3).

We find that the scenario 1 health benefits are high but the UPF policy offers minimal financial risk protection and can increase financial risk. The health benefits accrued in scenario 1 are higher for the lower income quintiles because their care-seeking increases the most from the baseline scenario, where coverage in this population is the lowest. Our baseline data on the distribution of health-seeking behavior by wealth (NSS 60th round, schedule 25)[31] may even underestimate the slope, and therefore the relative health benefits to the poor in scenario 1. Variations in DALYs averted across states in scenario 1 primarily reflect the underlying demographic differences of the states. Approximately 1 million DALYs per year would be averted in India in the scenario 1 UPF relative to the baseline. Over half of the averted DALYs would be in the states Uttar Pradesh, Bihar, Madhya Pradesh, and Rajasthan.

When we consider OOP expenditures that the government may not cover in a UPF (e.g., travel costs), the results of the ECEA are more informative than a standard cost-effectiveness analysis (CEA). The increased supply of treatment may not be fully utilized by subpopulations that cannot afford the associated care-seeking costs. The lack of financial risk protection may mean that the health benefits we estimate are exaggerated. Moreover, even if the health benefits in scenario 1 seem progressive, the opposite may be true when a full accounting of costs is undertaken.

In contrast with scenario 1, scenarios 2 and 3 provide significant financial risk protection, although their health benefits incremental to those of scenario 1 are small (if scenario 1's benefits are realized). Indians would spend a mean of $84 million and $81 million per year less out of pocket in scenarios 2 and 3, respectively. The UPF in scenario 2 is progressive and provides the most protection for the poor and poor states. In our analysis, >50% of the OOP expenditure averted (and DALYs averted) and approximately 70% of the financial risk protection come from Uttar Pradesh, Bihar, Madhya Pradesh, and Rajasthan. If financial limitations prevent the government from fully implementing an epilepsy program, identifying these states—and potentially others—where the intervention has a high impact can improve the focus of policies.

Because we assume only the richest 1% of the population seeks surgery in the baseline, scenario 3 contributes more to the health of the bottom 99% relative to scenario 2, but it provides additional financial protection only for the top 1%. The poor actually spend more out of pocket in scenario 3 than in scenario 2 because of additional care-seeking costs. Per case travel and lodging (care-seeking) costs would likely drop in a UPF policy that increases surgery coverage because new facilities in communities would need to be built. However, additional expenses would shift toward building the facilities.

Scenario 2 (increasing coverage of first- and second-line treatments to 80% and public financing of those therapies) is similar to the program described by Tripathi et al.[11] as the national epilepsy program currently under consideration in India. We find that such a program would be cost-effective for India. Demand-side interventions (e.g., public education) to increase care-seeking in a UPF similar to scenario 2 may be needed alongside the supply-side ones (e.g., increasing availability of AEDs and training on AED principles),[13] but in the short term this scenario is likely more feasible than scenario 3, a UPF that also covers surgery. A recent survey identified 18 centers that conducted presurgical evaluation and surgery for epilepsy in India.[32] The number of surgeries performed in the leading centers has increased over threefold since 1995–2000. However, the facilities are unevenly dispersed across the country—50% of the facilities are in southern India and several are located around Delhi, leaving the center, east, and west uncovered—and two thirds are nongovernmental. To increase the number of surgeries performed each year, existing facilities need to expand their epilepsy programs at a more rapid pace and new facilities need to be built, especially in poorly covered areas. Clearly, this process will take time, but scenario 3 is incrementally cost-effective to scenario 2, and progress toward increasing epilepsy surgery in India can be made while implementing policies in line with scenario 2.

Evaluating prospective national epilepsy policies with an agent-based model allows for exploring the distribution of impact across different population subgroups, but the accuracy and level of detail possible in such an analysis is restricted by the quality of the input parameters. Here we extrapolate impact across states and income quintiles based on the underlying population distribution of those groups, but we do not capture all potentially relevant covariates. Improving the model parameters would improve the model's estimates. Many psychiatric and somatic disorders, not considered in the model, are more common among people with epilepsy than the general population.[33] These comorbidities impact physician decisions, patient behavior, and health outcomes. Adverse drug interactions need to be taken into account by physicians, and comorbidities can increase readmission,[34] increase households' OOP expenditure, and affect patients' decisions. The designing of health services for epilepsy patients in UPF can further benefit from taking comorbidities into consideration.

In addition, although this article adds to the discussion on expanding coverage of epilepsy treatment in India, it does have several limitations. We assume that both income and treatment costs will be constant over the 10-year period of analysis. Furthermore, the costs included in the analysis are not an exhaustive list of costs associated with the policy scenarios described. We do not include the costs of the program to build new facilities or alter the travel costs paid out of pocket, presuming they would be lower with higher coverage and more facilities.

Our findings highlight the importance of considering the financial impacts of interventions and moving beyond CEA and disease burden analyses. Previous analyses have already shown that increasing first-line epilepsy therapy reduces the disease burden and is cost-effective,[3-5, 29, 30] and we confirm that result in our model. However, our results show that a UPF policy on first-line therapy alone fails to protect from financial shock, and that affects poor populations the most adversely. Moreover, the lack of financial risk protection may mean the health benefits of the policy are not fully realized. A policy that increases the distribution of second-line therapy further reduces the disease burden (although only by a small amount), while also providing substantial financial risk protection. Accordingly, this analysis provides economic evidence in support of the proposed national epilepsy program in India.

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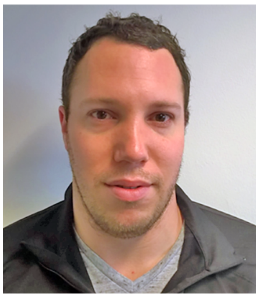
Disclosure

None of the authors has any conflict of interest to disclose. DC and TD are staff members of the World Health Organization (WHO). The authors alone are responsible for the views expressed in this publication and they do not necessarily represent the decisions, policy, or views of WHO. 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.

Biography



Itamar Megiddo is a health economics researcher and disease modeler at CDDEP.

Supporting Information

Filename	Description
epi13294-sup-0001-SupInfo.docx Word document, 6.8 MB	**Appendix S1.** Modeling details. **Table S1.** Disease input parameters. **Figure S1.** Significance of state-wise DALYs per 100,000 in the baseline scenario. **Figure S2.** Significance of state-wise DALYs averted per 100,000 in UPF scenario 1 (from the baseline scenario). **Figure S3.** Significance of state-wise DALYs averted per 100,000 in UPF scenario 2 (from the baseline scenario). **Figure S4.** Significance of state-wise DALYs averted per 100,000 in UPF scenario 3 (from the baseline scenario). **Figure S5.** Significance of state-wise government expenditure per 100,000 in UPF scenario 1. **Figure S6.** Significance of state-wise government expenditure per 100,000 in UPF scenario 2. **Figure S7.** Significance of state-wise government expenditure per 100,000 in UPF scenario 3. **Figure S8.** Significance of state-wise out-of-pocket expenditure averted per 100,000 in UPF scenario 1. **Figure S9.** Significance of state-wise out-of-pocket expenditure averted per 100,000 in UPF scenario 2. **Figure S10.** Significance of state-wise out-of-pocket expenditure averted per 100,000 in UPF scenario 3. **Figure S11.** Significance of state-wise money-metric value of

References

1 World Health Organization. *Atlas: epilepsy care in the world*. Geneva: World Health Organization; 2005.

Google Scholar

2 Schmidt D, Schachter SC. Drug treatment of epilepsy in adults. *BMJ* 2014; **348**: g254.

PubMed | Web of Science® | Google Scholar

3 Chisholm D. Cost-effectiveness of first-line antiepileptic drug treatments in the developing world: a population-level analysis. *Epilepsia* 2005; **46**: 751–759.

PubMed | Web of Science® | Google Scholar

4 Gureje O, Chisholm D, Kola L. Cost-effectiveness of an essential mental health intervention package in Nigeria. *World Psychiatry* 2007; **6**: 42–48.

PubMed | Web of Science® | Google Scholar

5 Chisholm D, Saxena S. Cost effectiveness of strategies to combat neuropsychiatric conditions in sub-Saharan Africa and South East Asia: mathematical modelling study. *BMJ* 2012; **344**: e609.

PubMed | Web of Science® | Google Scholar

6 Meyer A-C, Dua T, Ma J, et al. Global disparities in the epilepsy treatment gap: a systematic review. *Bull World Health Organ* 2010; **88**: 260–266.

PubMed | Web of Science® | Google Scholar

7 Radhakrishnan K, Pandian JD, Santhoshkumar T, et al. Prevalence, Knowledge, Attitude, and Practice of Epilepsy in Kerala, South India. *Epilepsia* 2000; **41**: 1027–1035.

CAS | PubMed | Web of Science® | Google Scholar

8 Neni SW, Latif AZA, Wong SY, et al. Awareness, knowledge and attitudes towards epilepsy among rural populations in East Coast Peninsular Malaysia: a preliminary exploration. *Seizure* 2010; **19**: 280–290.

PubMed | Web of Science® | Google Scholar

9 Mbuba CK, Ngugi AK, Fegan G, et al. Risk factors associated with the epilepsy treatment gap in Kilifi, Kenya: a cross-sectional study. *Lancet Neurol* 2012; **11**: 688–696.

PubMed | Web of Science® | Google Scholar

10 Maiga Y, Albakaye M, Diallo LL, et al. Current beliefs and attitudes regarding epilepsy in Mali. *Epilepsy Behav* 2014; **33**: 115–121.

PubMed | Web of Science® | Google Scholar

11 Tripathi M, Jain D, Devi M. Need for a national epilepsy control program. *Ann Indian Acad Neurol* 2012; **15**: 89–93.

CAS | PubMed | Web of Science® | Google Scholar

12 Dua T, de Boer HM, Prilipko LL, et al. Epilepsy care in the world: results of an ILAE/IBE/WHO Global Campaign Against Epilepsy survey. *Epilepsia* 2006; **47**: 1225–1231.

CAS | PubMed | Web of Science® | Google Scholar

13 Mbuba CK, Newton CR. Packages of care for epilepsy in low- and middle-income countries. *PLoS Med* 2009; **6**: e1000162.

PubMed | Web of Science® | Google Scholar

14 Rathore C, Rao MB, Radhakrishnan K. National epilepsy surgery program: realistic goals and pragmatic solutions. *Neurol India* 2014; **62**: 124–129.

PubMed | Web of Science® | Google Scholar

15 Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; **380**: 2163–2196.

PubMed | Web of Science® | Google Scholar

16 Devi G, Satishchandra P, Gururaj G. National workshop on public health aspects of epilepsy for senior personnel of state health departments in India. *Ann Indian Acad Neurol* 1999; **2**: 29–30.

Google Scholar

17 Sridharan R, Murthy BN. Prevalence and pattern of epilepsy in India. *Epilepsia* 1999; **40**: 631–636.

CAS | PubMed | Web of Science® | Google Scholar

18 Rao MB, Radhakrishnan K. Is epilepsy surgery possible in countries with limited resources? *Epilepsia* 2000; **41**(Suppl. 4): S31–S34.

PubMed | Web of Science® | Google Scholar

19 Ps C. The need for developing comprehensive epilepsy surgery units in India. *Indian J Neurosurg* 2012; **1**: 1.

Google Scholar

20 Radhakrishnan K. Epilepsy surgery in India. *Neurol India* 2009; **57**: 4–6.

PubMed | Web of Science® | Google Scholar

21 Thomas SV, Sarma PS, Alexander M, et al. Economic burden of epilepsy in India. *Epilepsia* 2001; **42**: 1052–1060.

CAS | PubMed | Web of Science® | Google Scholar

22 Megiddo I, Colson AR, Nandi A, et al. Analysis of the Universal Immunization Programme and introduction of a rotavirus vaccine in India with IndiaSim. *Vaccine* 2014; **32**(S1): A151–161.

PubMed | Web of Science® | Google Scholar

23 Nandi A, Megiddo I, Prabhakaran D, et al. Meeting Abstracts: an agent-based simulation modelling approach to extended cost-effectiveness analysis of health interventions. *Lancet* 2013; **381**(Suppl.): S96.

PubMed | Google Scholar

24 Nandi A, Colson AR, Verma A, et al. The health and economic benefits of scaling up a home-based neonatal care package in rural India: a modeling analysis. *Health Policy Plan* 2015 Nov 11 [Epub ahead of print].

PubMed | Web of Science® | Google Scholar

25 Verguet S, Laxminarayan R, Jamison DT. Universal public finance of tuberculosis treatment in India: an extended cost-effectiveness analysis. *Health Econ* 2014; **24**: 318–332.

PubMed | Web of Science® | Google Scholar

26 Mbuba CK, Ngugi AK, Newton CR, et al. The epilepsy treatment gap in developing countries: a systematic review of the magnitude, causes, and intervention strategies. *Epilepsia* 2008; **49**: 1491–1503.

PubMed | Web of Science® | Google Scholar

27 Verguet S, Murphy S, Anderson B, et al. Public finance of rotavirus vaccination in India and Ethiopia: an extended cost-effectiveness analysis. *Vaccine* 2013; **31**: 4902–4910.

PubMed | Web of Science® | Google Scholar

28 WHO. *Making choices in health: WHO guide to cost-effectiveness analysis*. Geneva: World Health Organization; 2003.

Google Scholar

29 Chow J, Darley S, Laxminarayan R. *Cost-effectiveness of disease interventions in India*. Washington DC: Resour Futur; 2007.

Google Scholar

30 Laxminarayan R, Chow J, Shahid-Salles SA. Intervention cost-effectiveness: overview of main messages. In DT Jamison, JG Breman, AR Measham, G Alleyne, M Claeson, DB Evans, et al., (Eds) *Disease control priorities in developing countries*, Washington, DC: Oxford University Press; 2006: 35–86.

Web of Science® | Google Scholar

31 National Sample Survey Organisation. *National Sample Survey 2004 (60th Round) – Schedule 25 – Morbidity and Healthcare*. New Delhi: Ministry of Statistics and Programme Implementation (MOSPI); 2004.

Google Scholar

32 Menon RN, Radhakrishnan K. A survey of epilepsy surgery in India. *Seizure* 2015; **26**: 1–4.

PubMed | Web of Science® | Google Scholar

33 Gaitatzis A, Carroll K, Majeed A, et al. The epidemiology of the comorbidity of epilepsy in the general population. *Epilepsia* 2004; **45**: 1613–1622.

PubMed | Web of Science® | Google Scholar

34 Hasan O, Meltzer DO, Shaykevich SA, et al. Hospital readmission in general medicine patients: a prediction model. *J Gen Intern Med* 2010; **25**: 211–219.

PubMed | Web of Science® | Google Scholar

35 Annegers JF, Hauser WA, Elveback LR. Remission of seizures and relapse in patients with epilepsy. *Epilepsia* 1979; **20**: 729–737.

CAS | PubMed | Web of Science® | Google Scholar

36 Schiller Y, Najjar Y. Quantifying the response to antiepileptic drugs: effect of past treatment history. *Neurology* 2008; **70**: 54–65.

PubMed | Web of Science® | Google Scholar

37 Engel J Jr, Wiebe S, French J, et al. Practice parameter: temporal lobe and localized neocortical resections for epilepsy. *Epilepsia* 2003; **44**: 741–751.

PubMed | Web of Science® | Google Scholar

38 Current Index of Medical Specialities India (CIMS). Available at: http://www.cimsasia.com/. Accessed October 10, 2014.

Google Scholar

39 Management Sciences for Health. International Drug Price Indicator Guide. Available at: http://erc.msh.org/mainpage.cfm?file=1.0.htm&module=DMP&language=English. Accessed October 29, 2014.

Google Scholar

40 World Health Organization. WHO | Price multiplier for different coverage levels. Available at: http://www.who.int/choice/cost-effectiveness/inputs/price_multiplier/en/. Accessed December 19, 2014.

Google Scholar

Citing Literature