

Disease Control Priorities in Developing Countries, 3rd Edition Working Paper #14

Title:	The Health and Economic Benefits of Public Financing of Epilepsy Treatment in India
Author (1):	Itamar Megiddo <u>megiddo@cddep.org</u> Center for Disease Dynamics, Economics, and Policy
Author (2):	Abigail Colson Center for Disease Dynamics, Economics, and Policy
Author (3):	Daniel Chisholm World Health Organization
Author (4):	Tarun Dua World Health Organization
Author (5):	Ramanan Laxminarayan Center for Disease Dynamics, Economics, and Policy
Author (6):	Arindam Nandi Center for Disease Dynamics, Economics, and Policy
Keywords:	Epilepsy, India, cost-effectiveness, agent-based model

Abstract:

Objective: No national epilepsy program currently exists in India, where an estimated 6–10 million live with active epilepsy and only 47% of them are treated. The literature on epilepsy interventions in India and in South Asia focuses on cost-effectiveness analysis of 1st-line anti-epilepsy drugs (AEDs) and does not consider the economic effects of policies to increase treatment. We analyze the health and economic benefits (including from the health consumers' perspectives) of increasing effective coverage to 80% and publicly financing 1) 1st-line AEDs, 2) 1st- and 2nd-line AEDs, and 3) and 1st- and 2nd-line AEDs and surgery.

Methods: We use IndiaSim, an agent-based model, and incorporate an epilepsy disease model. Agents are in one of four states: disease free, untreated with seizures, treated with seizures, and treated without seizures. We analyze the benefits from policy intervention over a 35-year period, until the model population reaches a new equilibrium state. To evaluate the health benefits and cost-effectiveness we calculate the percent of the population that is epileptic and untreated, the disability-adjusted life years (DALYs) averted, direct medical costs paid by the government and dollars per DALY averted. To analyze the economic benefits we estimate the out-of-pocket (OOP) expenditure averted, and money-metric value of insurance.

Results: Over 35 years the sequential incremental (to the baseline) DALYs averted and dollars per DALY averted are: 788 (774–802) DALYs per 100,000 persons and \$9.22 (\$9.05–\$9.39) per DALY averted in intervention 1; 107 (94–120) DALYs per 100,000 and \$982 (\$568–\$1,397) per DALY in intervention 2; and 66 (53–80) per 100,000 and \$2,221 (-\$4,530–8,973) per DALY in intervention 3. The population averts \$19,627 (\$18,315–\$20,940) OOP expenditure per 100,000 in intervention 1, an additional \$88,325 (\$86,619–\$90,031) per 100,000 in intervention 2, and \$31,394 (\$29,399–\$33,390) in intervention 3. The money-metric value of insurance follows a similar trend between interventions and typically decreases with wealth. Poorer states that avert a high OOP have the highest money-metric value of insurance. Protection is above \$25,000 per 100,000 persons in Bihar, West Bengal, Jammu and Kashmir, and the eastern states of Minpur and Tripura.

Significance: Expanding and publicly financing epilepsy treatment in India averts substantial disease and financial burden across wealth quintiles and in all states in India. All three interventions considered are cost-effective in India.

Introduction

An estimated 50 million people globally suffer from epilepsy, 80% of whom live in the developing world (1). Epilepsy can be effectively treated in the majority of cases (2), and first-line drugs are cost-effective in the developing world (3), but the high treatment gap in low- and mid-income countries means that people with the disease often do not receive and benefit from the available treatments (4). This under-treatment leads to a high disease burden associated with epilepsy; the disease caused approximately 17.4 million disability-adjusted life years (DALYs) in 2010. This comprises approximately 0.7% of the total disease burden in 2010 (5); epilepsy was the 20th leading cause of years lived with disability (6).

An estimated 6–10 million individuals live with active epilepsy in India (7–9), but less than half receive any epilepsy treatment (4). To overcome the treatment gap and improve care for people with epilepsy, the Ministry of Health has hosted meetings to discuss the creation of a national epilepsy program that would potentially increase public awareness about epilepsy, train healthcare workers to better identify the disease, and provide first-and second-line anti-epilepsy drugs (AEDs) (7), but no national epilepsy program currently exists. Other experts have noted the need for an expanded epilepsy surgery program in India (10–12). Increasing access to and financing epilepsy treatment in India has a potentially great impact: in addition to the high disease burden, epilepsy also causes a high financial burden in India. Analysis by Thomas et al. found that in 1998 epilepsy treatment in India cost patients 88.2% of the country's per capita GNP, and total epilepsy spending in India amounted to over \$1.7 billion (1998 USD) (13). Working papers are in draft form. This working paper is distributed for purposes of comment and discussion only. It may not be reproduced without permission from the author. Copies of working papers are available from the author or at <u>www.dcp-3.org</u>

This paper evaluates both the cost-effectiveness and financial benefits of a national program that publicly finances and expands coverage of epilepsy treatment in India. Using IndiaSim (14), an agent-based model (ABM) that simulates India's population and health system, we examine the impact, relative to the current baseline, of incrementally implementing three policy intervention scenarios. In Intervention 1 the government provides first-line AEDs and coverage of the first-line therapy increases to 80%. In Intervention 2 the government provides both first- and second-line AEDs, and coverage of both first- and second-line therapy is 80%. Finally, in Intervention 3, first-line AEDs, second-line AEDs, and epilepsy surgery are all publicly financed and coverage of all three treatments is 80%. For each scenario we estimate the policy intervention's impact on five measures: DALYs averted, incremental direct government expenditure, dollars per DALY averted, out-of-pocket (OOP) expenditure averted, and the money-metric value of insurance.

Methods

Population data

India's third District Level Household Survey (DLHS-3), conducted 2007–2008, forms the basis of IndiaSim. DLHS-3 includes data from 720,000 Indian households, covering 3.4 million individuals from 601 districts (15). The survey contains information on household demographics, socioeconomic status, and health-seeking behavior. IndiaSim's

population is based on a randomly selected subset of DLHS-3 that includes approximately 1 million individuals who compose 135,000 households.

Disease data

Incidence, spontaneous remission, and excess mortality rates used in our epilepsy model (Table 1) are by age and gender, obtained from the World Health Organization's (WHO) DISMOD II and data from the Global Burden of Disease 2010 for the South Asian region (16,17). Table 2 lists the treatment-related input data used in the model. In the baseline scenario we assume a treatment gap of 53% (4), indicating that 47% of individuals with epilepsy receive treatment. Although the treatment gap includes both individuals who do not seek treatment (the treatment demand gap) and individuals who seek treatment but do not receive it (the treatment supply gap), we assume that this gap comes solely from individuals not seeking treatment. In the model, everyone who seeks epilepsy treatment receives it, meaning we do not include treatment seeking and consultation costs for those who are not being treated.

The model includes three treatment options for patients with epilepsy: first-line antiepileptic drugs (AEDs), lamotrigine, and surgery. Unlike some analyses of epilepsy treatment in low- and mid-income countries (18,19), we do not limit first-line AEDs to phenobarbital, but instead assume first-line drugs are prescribed according to the frequency distribution in Table 2, reflecting the clinician's choice of treatment (2). We assume patient adherence to a given treatment regimen is 70%, the median value used in a past cost-effectiveness analysis of epilepsy drugs in the developing world (3). We

assume seventy percent of patients respond to first-line AEDs, based on the efficacy of the older first-line drugs (20). Our model includes two options for second-line treatment for individuals who do not respond to first-line AEDs: a second-line AED (lamotrigine) or surgery. We assume one-third of patients are eligible for surgery, and use Engel et al.'s finding that 64% of patients who receive surgery will be seizure-free following the procedure (21), as India-based studies have similar results (10). The remaining two-thirds of patients who do not respond to first-line AEDs will be treated with a second-line AED, assumed to be lamotrigine, and 42% of patients taking lamotrigine will become seizure-free follow.

We calculated median retail prices for AEDs from CIMS India data (23). The government prices were reduced based on available price information from the National Pharmaceutical Pricing Authority (24). The average annual medical and travel costs related to epilepsy were taken from an India-specific analysis of epilepsy patient costs from 2001 (13). The medical cost of surgery was taken from a 2000 study of patient costs at an epilepsy facility in India (10), adjusted for costs included elsewhere in our model. We assume patient travel costs for surgery are twice those for regular epilepsy treatment, as the procedure is only available in tertiary care facilities.

Income data

We use in our analysis data on the gross domestic product (GDP) per capita from the World Bank (25). The wealth quintile GDP per capita distribution is from expenditure data in the National Sample Survey (NSS) 60th round schedule 25 (26), and the state

GDP per-capita distribution is from the Indian government Press Information Bureau (27).

Model

The ABM is a patch model representative of the population at the state level. A patch represents 1 of 34 states (data on Nagaland is unavailable in DLHS-3). In each patch sets of individuals are grouped into households representing families.

The model is iterative (timestep of one day), with stochastic disease events and household reactions to them occurring each day. The disease model is presented in Figure 1. Each day healthy individuals acquire epilepsy at the rate $\Lambda_{i,j}$, for age group *i* of gender *j*, and move into the "epileptic without treatment" state. Individuals naturally clear the disease at the remission rate $\sigma_{N,i,j}$. Those who seek and receive treatment (at the rate c_I) move into the "epileptic with 1st-line therapy" category. Patients adhere to the treatment at the rate α . Those taking 1st-line therapy that continue to experience epileptic seizures after two months switch to 2nd-line treatment — one third are eligible for surgery and the rest take lamotragine — if they are covered (c_2) and move into "epileptic with 2nd-line therapy" state. We assume that wealth quintiles I-III only choose to undergo surgery if it is provided for free; otherwise they too take lamotragine. Patients who adhere to treatment and stop experiencing seizures naturally or due to treatment at rates σ_{tI} (1st-line therapy) and σ_{t2} (2nd-line therapy) continue taking AEDs for five years. They move into the "seizure-free with 1st/2nd line therapy" state.

Newborns enter the "healthy seizure-free" state according to a household child birth function (see Megiddo et al. (14) for more detail) tied to the state specific birth rates. Individuals die naturally at rates from WHO life tables (28). Those in epileptic states also die at the rate of excess mortality (Table 1).

The model was programmed in C++.

Analysis

We run a 50-year burn period, at our baseline assumptions, until the model reaches an equilibrium state. Following the burn period we run each scenario 100 times for 35 years, until we reach a new equilibrium state (in the policy intervention scenarios). Analysis was done in R.

We analyze the effects of the policy interventions on health outcomes and on economics outcomes. Specifically, we estimate the health burden alleviated by calculating the DALYs averted and present the dollars per DALY averted to measure the cost-effectiveness of interventions. We apply 3 disability weights to calculate DALYs: 0.072 for seizure-free patients; 0.319 for patients with seizures; and 0.42 for untreated epileptic individuals (29). The DALYs and the policy intervention costs are discounted at 3% and summed up over the 35-year period. We measure the dollars per DALY from the government's perspective, and do not include the OOP expenditure. We compare interventions to the baseline status quo (not to a null case).

We estimate the economic impact of the interventions by calculating the (epilepsy specific) out-of-pocket expenditure averted and the money-metric value of insurance — the price individuals are willing to pay to avoid expenditure due to a shock events — following Vergeut et al. (30,31). The outcomes are presented in present day US\$. OOP expenditure, and expected income (given spending on treatment) are discounted at 3%.

Results

The prevalence across the 35 simulation years three groups (treated and seizure-free, treated with seizures, and untreated epileptics) is presented in Figure 2. In the baseline scenario prevalence remains relatively constant, although fluctuations persist as our population demographics change with time. Approximately 0.091% of the population is treated and seizure-free, 0.030% is treated with seizures, and 0.456% is untreated with epilepsy in the baseline.

Health benefits

In the intervention scenarios the treated and seizure-free portion of the population increases significantly in the first 5 years of simulation and then show a small increasing trend over the remaining 30 years. After 5 (35) years 0.0125% (0.0128%) of the population is treated and seizure-free in intervention 1, 0.0133% (0.0153%) in intervention 2, and 0.0135% (0.0157%) in intervention 3. The prevalence of treated with seizures in intervention 1 mimics the baseline scenario prevalence but is slightly higher (approximately 0.031% of the population). The group's prevalence in interventions 2 and

3 rises up to 0.056% and 0.074% respectively, after 35 years. The portion of untreated individuals with epilepsy in the population decreases significantly over the duration of simulation. After 35 years 0.350% of the population is epileptic and untreated in intervention 1, 0.313% in intervention 2, and 0.286% in intervention 3.

Table 3 includes the incremental present day DALYs averted (across wealth quintiles). The results represent the present day value for 35 years of policy implementation. Intervention 1 averts 788 (774–802) DALYs per 100,000 persons. Intervention 2 averts an additional 107 (94–120) DALYs per 100,000 and intervention 3 averts 66 (53–80) DALYs incremental to intervention 2. The DALYs averted in intervention 1 are similar across wealth quintiles, but slightly lower in quintile V. Intervention 2 averts the most DALYs in wealth quintiles IV and V and intervention 3 only averts DALYs in quintiles I-III.

Row 1 of figure 3 shows maps of DALYs averted incremental to the baseline per 100,000 in each state. In intervention 1 Delhi and the east coast states stretching from West Bengal to Tamil Nadu avert the most DALYs; they all avert over 850 DALYs per 100,000 persons over a 35-year period. Punjab, Arunachal Pradesh, Uttarakhand, and Gujarat gain the most from intervention 2 (relative to intervention 1), each averting over 150 additional DALYs per 100,000. In a few states we cannot discern a significant difference between interventions 1 and 2; these include states that benefited the most from intervention 1 (except Tamil Nadu) and Assam, and Jammu and Kashmir. Intervention 3 does not have a significant impact on DALYs averted in most states. A few exceptions are Uttar Pradesh (an additional 76 DALYs averted per 100,00 persons; Working papers are in draft form. This working paper is distributed for purposes of comment and discussion only. It may not be reproduced without permission from the author. Copies of working papers are available from the author or at <u>www.dcp-3.org</u> CI 51–101), Bihar (90 CI 45–135), Assam (107 CI 41–172), and Karnataka (89 CI 16– 163).

Costs and cost-effectiveness

The sequential incremental present day government expenditure on interventions over 35 years (Table 3) is: \$7,219 (\$7,175–\$7,242) per 100,000 persons in intervention 1; \$82,907 (\$81,599–82,595) per 100,000 in intervention 2; and \$70,433 (\$69,619–\$71,247) in intervention 3. Government expenditure is highest on quintiles I-III in intervention 2 and on quintiles IV and V in intervention 3. Government expenditure in intervention one is lowest in Puducherry (\$3,342 per 100,000; CI \$2,702–\$3,981) and Goa (\$4,416 per 100,000; CI \$3,209–\$5,624) and is highest in West Bengal and Tripura, which spend over \$11,000 per 100,000 persons (Figure 3; row 2). Both latter states increase expenditure the most from intervention 1 to intervention 2 (over \$120,000 increase on average). Though they continue to spend the most in intervention 3, their increase in spending from intervention 2 to intervention 3 is low.

The sequential incremental dollars-per-DALY are presented in Figure 4: \$9.22 (\$9.05– \$9.39) per DALY averted in intervention 1; \$982 (\$568–\$1,397) in intervention 2; and \$2,221 (-\$4,530–8,973) in intervention 3. The dollars per DALY averted with respect to the baseline for interventions 2 and 3 are \$101 (\$99–\$103) and \$167 (\$164–\$170) respectively. All three policy interventions are "very cost-effective" under current conditions according to WHO guideline definitions (32).

Economic benefits

The population averts \$19,627 (\$18,315–\$20,940) OOP expenditure per 100,000 over 35 years in intervention 1 (Table 3). The OOP expenditure averted seems to decrease with wealth, but the trend is not significant. Intervention 2 averts an additional \$88,325 (\$86,619–\$90,031) per 100,000, and intervention 3 averts \$31,394 (\$29,399–\$33,390) on top of that. Intervention 2 averts significantly more OOP expenditure for wealth quintiles I-III than quintiles IV and V. Quintiles I-III do not avert any additional OOP expenditure in intervention 3, while quintiles IV and V each avert over \$13,500 per 100,000 over the 35-year period. The OOP expenditure averted distribution across states (Figure 3; row 3) is distributed similarly to the government expenditure.

The sequential incremental money-metric value of insurance of intervention over the 35 year period, presented in Table 3, is \$4,792 (\$4,624–\$4,961) per 100,000 in intervention 1, \$6,214 (\$5,992–\$6,436) per 100,000 in intervention 2, and \$616 (\$351–\$881) in intervention 3. The sequential incremental insurance value decreases with wealth in the first 2 interventions, but does not provide any additional insurance coverage for wealth quintiles I-III in intervention 3.

Poorer states and states with high OOP expenditure averted tend to value intervention the most. In intervention 1, the money metric value of insurance is higher than \$9,000 per 100,00 persons in 7 states (Figure 3; row 4). These include the eastern states of Bihar and West Bengal, northeastern states of Tripura, Manipur, and Meghalaya, Uttar Pradesh, and Jammu and Kashmir.. In richer states in which OOP expenditure averted is relatively low

the money-metric is similarly low; the money-metric value of insurance in Tamil Nadu and Maharashtra is below \$3,000 per 100,000. In interventions 2 and 3 the money-metric value of insurance is above \$4,500 and \$6,500 respectively, but the trend across states is similar to intervention 1.

Discussion

In this paper we analyze 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 low- and mid-income countries (3,18,33), severe under-treatment of epilepsy persists. We evaluate a hypothetical national epilepsy program that increases coverage from the current level of 47% of people with epilepsy receiving treatment to 80%. We demonstrate the incremental benefits to various Indian subpopulations achieved through government financing of first-line AEDs (intervention 1), first- and second-line AEDs (intervention 2), and first-line AEDs, second-line AEDs, and surgery (intervention 3).

We find the health benefits accrued under intervention 1 to be relatively equal across wealth quintiles because we assume an equal treatment gap across wealth quintiles. Variations in DALYs averted across states in intervention 1 primarily reflect the underlying demographic differences of the states. Intervention 2, however, provides greater incremental health benefits to the higher income quintiles and the generally wealthier western states, such as Gujarat, because surgery has a higher efficacy than lamotrigine, and we assume that income quintiles I–III will not seek surgery when it is Working papers are in draft form. This working paper is distributed for purposes of comment and discussion only. It may not be reproduced without permission from the author. Copies of working papers are available from the author or at <u>www.dcp-3.org</u>

financed out-of-pocket. Quintiles IV and V do pay out-of-pocket for surgery in intervention 2, and thus they benefit from its higher efficacy. Intervention 3, in contrast, only provides health benefits incremental to intervention 2 to individuals in income quintiles I–III, as they are the only people who receive surgery in intervention 3 who were not receiving it previously.

Government costs and OOP averted typically reflect each other in our analysis; as government costs increase for a given subpopulation, so does the OOP averted for that group. The exception is the incremental OOP averted for income quintiles Q1–Q3 when moving from Intervention 2 to Intervention 3. Again, because of the assumption that individuals in Q1–Q3 do not seek surgery when required to pay for it out-of-pocket, transitioning to publicly financed surgery increases the government's costs for the policy intervention but has an insignificant impact on OOP averted.

Financial risk protection (money-metric value of insurance) is typically highest in poor subpopulations that avert the most OOP expenditure. In the interventions in our analysis, that includes the eastern states of Bihar and West Bengal, northeastern states of Tripura, Manipur, and Meghalaya, Uttar Pradesh, and Jammu and Kashmir. 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 policy interventions.

Our intervention 2 (increasing coverage of first- and second-line treatments to 80% and government financing of first- and second-line AEDs but not surgery) is very similar to

the program described by Tripathi et al. as the national epilepsy program currently under consideration in India (7). Our analysis shows that such a program would be cost saving for India, though we do not include the program costs necessary to increase coverage, such as healthcare worker training or public outreach campaigns to increase knowledge about epilepsy. Higher income quintiles would gain slightly more health benefits than lower income quintiles under a program that increases the coverage of treatment (including surgery) and provides AEDs but does not finance surgery.

Although this paper adds to the discussion on expanding coverage of epilepsy treatment in India, it does suffer from several limitations. We assume that both income and treatment costs will be constant over the 35-year period of analysis. Further, the costs included in the analysis are not an exhaustive list of costs associated with the policy interventions described. We do not include the costs to the government to distribute AEDs or the program and infrastructure costs needed to achieve 80% coverage of epilepsy treatment. As recently as 2009 less than 200 epilepsy surgeries were conducted in India annually (12). In intervention 3 of the model, however, approximately 45,000 patients receive epilepsy surgery in a given year. We do not include the costs needed to achieve this increase in capacity. Including these costs would increase the government expenditure required to implement the intervention scenarios.

We find epilepsy treatment in India to be more cost-effective than previous analyses found for India (18), South Asia (19), and the developing world at large (3). All three studies use disability weights of 0.15 based on past Global Burden of Disease (GBD) studies, despite belief that the weight was too low. GBD 2010 updated the disability Working papers are in draft form. This working paper is distributed for purposes of comment and discussion only. It may not be reproduced without permission from the author. Copies of working papers are available from the author or at <u>www.dcp-3.org</u>

weights for epilepsy to 0.42 for untreated epilepsy, 0.319 for treated epilepsy with seizures, and 0.072 for treated epilepsy without seizures. Using higher disability weights increases the cost-effectiveness of a given intervention, as it results in the interventions averting a higher number of DALYs than if a lower disability weight were used. Our cost-effectiveness results for intervention 1, which covers first-line AEDs, are also not directly comparable to Chisholm's results for first-line drugs because we look at the impact of increasing from 47% to 80% coverage and he studies a scenario of going from 0% coverage to 50% and then increasing from 50% to 80%.

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 output.

We find that increasing coverage of epilepsy treatment and providing publicly financed first- and second-line epilepsy therapy is cost-effective in India. These results enable policy makers to consider the health and financial benefits potential programs accrue to different Indian subpopulations and can help guide future decision-making about a national epilepsy program in India.

References

- World Health Organization. Atlas: Epilepsy Care in the World [Internet]. Geneva; 2005. Available from: http://books.google.com/books?hl=en&lr=&id=ZJfku__6BKMC&oi=fnd&pg=PA 6&dq=Atlas:+Epilepsy+Care+in+the+World&ots=TnCCRBMfwU&sig=VnPZ9F 1HTC2VYn8gcgR2QwIgrHA
- Schmidt D, Schachter SC. Drug treatment of epilepsy in adults. Bmj [Internet]. 2014 Feb 28 [cited 2014 Feb 28];348(feb28 2):g254–g254. Available from: http://www.bmj.com/cgi/doi/10.1136/bmj.g254
- Chisholm D. Cost-effectiveness of first-line antiepileptic drug treatments in the developing world: a population-level analysis. Epilepsia [Internet]. 2005 May;46(5):751–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15857443
- Meyer A-C, Dua T, Ma J, Saxena S, Birbeck G. Global disparities in the epilepsy treatment gap: a systematic review. Bull World Health Organ [Internet]. 2010 Apr [cited 2013 Jul 1];88(4):260–6. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2855595&tool=pmcen trez&rendertype=abstract
- Murray CJL, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet [Internet]. 2012 Dec [cited 2012 Dec 14];380(9859):2197–223. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0140673612616894
- Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati 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 [Internet]. 2012 Dec [cited 2012 Dec 14];380(9859):2163–96. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0140673612617292
- 7. Tripathi M, Jain D, Devi M. Need for a national epilepsy control program. Ann Indian Neurol [Internet]. 2012 [cited 2014 Mar 7];(2):2012–5. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3345606/
- 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 [Internet]. 1999 [cited 2012 Jul 12];2:29–30. Available from: http://www.annalsofian.org/article.asp?issn=0972-

2327;year=1999;volume=2;issue=1;spage=43;epage=48;aulast=Gourie;type=0 Working papers are in draft form. This working paper is distributed for purposes of comment and discussion only. It may not be reproduced without permission from the author. Copies of working papers are available from the author or at <u>www.dcp-3.org</u>

- 9. Sridharan R, Murthy BN. Prevalence and pattern of epilepsy in India. Epilepsia [Internet]. 1999 May;40(5):631–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10386533
- 10. Rao MB, Radhakrishnan K. Is epilepsy surgery possible in countries with limited resources? Epilepsia [Internet]. 2000 Jan;41 Suppl 4(1):S31–4. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10963475
- 11. Chandra Ps. The need for developing comprehensive epilepsy surgery units in India. Indian J Neurosurg [Internet]. 2012 [cited 2012 Jul 6];1(1):1. Available from: http://www.ijns.in/text.asp?2012/1/1/1/94361
- Radhakrishnan K. Epilepsy surgery in India. Neurol India [Internet]. 2009 Oct;57(1):4–6. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3208913&tool=pmcen trez&rendertype=abstract
- Thomas S V, Sarma PS, Alexander M, Pandit L, Shekhar L, Trivedi C, et al. Economic burden of epilepsy in India. Epilepsia [Internet]. 2001 Aug;42(8):1052– 60. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11554893
- 14. Megiddo I, Nandi A, Ashok A, Laxminarayan R. IndiaSim: An Agent-based Model for Estimating the Health and Economic Benefits of Secondary Prevention of Coronary Heart Diseases in India. 2014.
- 15. IIPS. DLHS-3 District Level Household and Facility Survey. International Institute of Population Sciences, Mumbai, India; 2010.
- 16. World Health Organization. DISMOD II [Internet]. 2001. Available from: http://www.who.int/healthinfo/global_burden_disease/tools_software/en/
- 17. Institute for Health Metrics and Evaluation. Global Burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010) [Internet]. 2013 [cited 2014 Mar 24]. Available from: http://www.healthmetricsandevaluation.org/gbd/research/project/global-burden-diseases-injuries-and-risk-factors-study-2010
- 18. Chow J, Darley S, Laxminarayan R. Cost-effectiveness of disease interventions in India. Washingt DC Resour Futur [Internet]. 2007 [cited 2012 Feb 14]; Available from: http://www.rff.org/Publications/Documents/RFF-DP-07-53.pdf
- 19. Chandra V, Pandav R, Laxminarayan R, Tanner C, Manyam B, Rajkumar S, et al. Neurological Disorders. In: Jamison DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB, et al., editors. Disease Control Priorities in Developing

Countries [Internet]. Second Edi. Washington, DC: Oxford University Press; 2006. p. 627–44. Available from: http://www.dcp2.org/pubs/DCP/32/

- 20. Annegers JF, Hauser W a, Elveback LR. Remission of seizures and relapse in patients with epilepsy. Epilepsia [Internet]. 1979 Dec;20(6):729–37. Available from: http://www.ncbi.nlm.nih.gov/pubmed/499118
- Engel Jr J, Wiebe S, French J, Sperling M, Williamson P, Spencer D, et al. Practice parameter: Temporal lobe and localized neocortical resections for epilepsy. Epilepsia [Internet]. Wiley Online Library; 2003 [cited 2012 Feb 14];44(6):741–51. Available from: http://onlinelibrary.wiley.com/doi/10.1046/j.1528-1157.2003.48202.x/full
- 22. Schiller Y, Najjar Y. Quantifying the response to antiepileptic drugs: Effect of past treatment history. Neurology [Internet]. 2008 [cited 2014 Mar 10];70(54-65). Available from: https://www.neurology.org/content/70/1/54.full
- 23. CIMS India [Internet]. 2014. Available from: http://www.cimsasia.com/
- 24. National Pharmaceutical Pricing Authority. Statement showing the details of Drugs, Rate, and MRP/CP of Medicines purchased by Government Organization in Bulk during 2006-07 [Internet]. Available from: http://www.nppaindia.nic.in/bulkpuchaseofmadicines.pdf
- 25. The World Bank. GDP per capita (current US\$). 2012.
- National Sample Survey Organisation. National Sample Survey 2004 (60th Round)
 Schedule 25 Morbidity and Healthcare. Ministry of Statistics and Programme Implementation (MOSPI); 2004.
- 27. Bureau PI. Statewise Per Capita a Income and Gross Domestic Product at current prices. 2013.
- 28. World Health Organization. Life expectancy: Life tables India [Internet]. [cited 2014 Feb 26]. Available from: http://apps.who.int/gho/data/view.main.60740
- 29. Institute for Health Metrics and Evaluation. Global Burden of Disease Study 2010 (GBD 2010) Disability Weights [Internet]. 2014 [cited 2014 Mar 24]. Available from: http://ghdx.healthmetricsandevaluation.org/record/global-burden-disease-study-2010-gbd-2010-disability-weights
- Verguet S, Laxminarayan R, Jamison D. Universal Public Finance of Tuberculosis Treatment in India: An Extended Cost-Effectiveness Analysis. Health Econ. Disease Control Priorities in Developing Countries, 3rd Edition; 2014;

- 31. Verguet S, Murphy S, Anderson B, Johansson KA, Glass R, Rheingans R. Public finance of rotavirus vaccination in India and Ethiopia: an extended costeffectiveness analysis. Vaccine [Internet]. Elsevier Ltd; 2013 Oct 1 [cited 2013 Dec 12];31(42):4902–10. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23871824
- World Health Organization (WHO). WHO Guide To Cost-Effectiveness Analysis [Internet]. Edejer TT-T, Baltussen R, Adam T, Hutubessy R, Acharya A, Evans DB, et al., editors. Geneva; 2003. Available from: http://www.who.int/choice/publications/p_2003_generalised_cea.pdf
- 33. Laxminarayan R, Chow J, Shahid-Salles SA. Intervention Cost-Effectiveness: Overview of Main Messages. In: Jamison DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB, et al., editors. Disease Control Priorities in Developing Countries [Internet]. Second Edi. Washington, DC: Oxford University Press; 2006. p. 35–86. Available from: http://www.dcp2.org/pubs/DCP/2/

Tables

Table 1. Disease input parameters

		Male		Female		
Age Group (years)	Incidence	Remission	Excess mortality	Incidence	Remission	Excess mortality
<1	0.0014	0.2111	0.0067	0.0013	0.0013	0.0054
1-4	0.0012	0.1714	0.0053	0.0011	0.0011	0.0043
5-9	0.0009	0.1023	0.0028	0.0009	0.0009	0.0022
10-14	0.0007	0.0606	0.0021	0.0007	0.0007	0.0016
15-19	0.0007	0.0686	0.0042	0.0006	0.0006	0.0032
20-24	0.0006	0.0691	0.0058	0.0006	0.0006	0.0045
25-34	0.0004	0.0544	0.0072	0.0004	0.0004	0.0055
35-44	0.0004	0.0459	0.0089	0.0004	0.0004	0.0068
45-54	0.0005	0.0545	0.0084	0.0004	0.0004	0.0064
55-64	0.0006	0.0683	0.0078	0.0005	0.0005	0.0059
65-74	0.0009	0.1022	0.0104	0.0008	0.0008	0.0079
75-84	0.0012	0.1398	0.0139	0.0012	0.0012	0.0106
85+	0.0014	0.1711	0.0189	0.0014	0.0014	0.0145

Variable	Value	Source
Treatment parameters		
Treatment gap	53%	Meyer et al. 2010
Adherence	70%	Chisholm (2005)
1st-line AED distribution		
Phenobarbital (30mg)	50%	Authors' assumption
Carbemazepine (200mg)	30%	
Phenytoin (100mg)	10%	
Valproate (200mg)	10%	
2nd-line treatment distribution		
2nd-line AED (lamotrigine)	67%	Authors' assumption
Surgery	33%	
% respond to treatment		
1st-line AED	70%	Annegers et al. (1979)
2nd-line AED	42%	Schiller & Najjar (2008)
Surgery	64%	Engel et al. (2003)
Cost paramters		
Drugs: retail price		http://www.cimsasia.com/India/
		Median of brands in India; weighted
1st-line AED	\$34.19	by 1st-line distribution
2nd-line AED	\$211.37	Median of brands in India
Drugs: government purchase price		
		Calculated from retail prices and
		government purchase prices India
1st-line AED	\$11.91	and Tamil Nadu
2nd-line AED	\$102.81	
Average annual costs		
Non-surgical medical costs*	\$22.90	Thomas et al. (2001)
Travel cost	\$16.46	Thomas et al. (2001)
Surgery costs (one-time)		
		Calculated from Rao &
		Radhakrishnan (2000), excluding
Surgery-related medical costs	\$1,093.53	AEDs and non-surgical medical costs
		Authors' assumption, based on
Travel cost	\$32.92	Thomas et al. (2001)

Table 2. Treatment input parameters

* Includes outpatient consultation, diagnostic investigation, and hospitalization.

Quintile	I – poorest	II	III	IV	V – richest	Total			
Policy intervention 1 (incremental to baseline)									
DALYs averted	156	161	159	160	151	788			
	(150–162)	(155–166)	(152–166)	(155–166)	(144–158)	(774–802)			
Government expenditure	\$1,499	\$1,394	\$1,544	\$1,414	\$1,369	\$7,219			
	(\$1,478–\$1,520)	(\$1,373–\$1,415)	(\$1,525–\$1,563)	(\$1,395–\$1,432)	(\$1,348–\$1,389)	(\$7,175–\$7,242)			
OOP expenditure averted	\$4,507	\$4,064	\$3,947	\$3,326	\$3 <i>,</i> 783	\$19,627			
	(\$3 <i>,</i> 824–\$5,190)	(\$3,516–\$4,613)	(\$3,421–\$4,473)	(\$2,755–\$3,897)	(\$3,155–\$4,412)	(\$18,315–\$20,940)			
Money-metric value of insurance	\$1,926	\$1,024	\$886	\$657	\$299	\$4,792			
	(\$1,785–\$2,067)	(\$959–\$1,089)	(\$834–\$938)	(\$614–\$700)	(\$278–\$319)	(\$4,624–\$4,961)			
Policy intervention 2 (incremental to policy intervention 1)									
DALVS guartad	20	15 y IIILEI VEIILIOII 2 (IIILI	16	25	21	107			
DALIS UVERLEU	(14, 26)	(0, 20)	10 (10, 22)	(20, 20)	(JE JO)	(04, 120)			
Covernment evnenditure	(14-20) \$19.295	(9-20) \$17.451	(10-22)	(20-50) \$14 E40	(20-00) ¢10.050	(94-120) \$22.007			
Government experiature	ې۲۵,۷۵۵ (خ19,040, خ19, ۲۵۵)	ې۲۲,451 (خ17,210, خ17,622)	ې10,400 (خ10,221, خ10,700)	ې14,54U (خ14 کړی د 4 م	۶۲۵,۵۵۵ (خ12 ۲۵۵ خ12 ۲۶۶)				
OOD and and the second and	(\$18,049-\$18,520)	(\$17,219-\$17,083)	(\$18,231-\$18,700)	(\$14,343-\$14,737)	(\$13,130-\$13,577)	(\$81,599-\$82,595)			
OOP expenditure avertea	\$22,996	\$21,080	\$23,857	\$12,333 (\$44,502,\$42,074)	\$8,054 (67.402.60.04.6)	\$88,325			
	(\$22,167-\$23,825)	(\$20,415-\$21,756)	(\$23,161-\$24,552)	(\$11,593-\$13,074)	(\$7,192-\$8,916)	(\$86,619-\$90,031)			
Money-metric value of insurance	\$2,495	\$1,361	\$1,320	\$778 (t-c-c-c-c)	\$259	\$6,214			
	(\$2,312–\$2,679)	(\$1,278–\$1,445)	(\$1,250–\$1,390)	(\$722–\$834)	(\$231–\$288)	(\$5,992–\$6,436)			
Policy intervention 3 (incremental to policy intervention 2)									
DALYs averted	20	23	22	1	0	66			
	(14–26)	(18–29)	(16–28)	(-4–7)	(-7–6)	(53–80)			
Government expenditure	\$12,690	\$12,941	\$12,867	\$15,949	\$15,986	\$70,433			
	(\$12,274-\$13,106)	(\$12,603-\$13,279)	(\$12,491-\$13,243)	(\$15,607-\$16,292)	(\$15,621-\$16,350)	(\$69,619-\$71,247)			
OOP expenditure averted	\$125.75	\$62.65	\$4.73	\$13,748.08	\$17,453.15	\$31,394			
	(-\$839–\$1,090)	(-\$718–\$843)	(-\$827–\$836)	(\$12,883–\$14,613)	(\$16,452-\$18,454)	(\$29,399–\$33,390)			
Money-metric value of insurance	\$7.45	\$4.42	\$2.62	\$360.23	\$241.52	\$616			
-	(-\$211–\$226)	(-\$95–\$104)	(-\$81–\$87)	(\$293–\$427)	(\$208–\$275)	(\$351–\$881)			

Table 3. Incremental health and economic outcomes per 100,000 persons (20,000 in each wealth quintile)

Results are over 100 simulations and 35 years; they are presented in present day values. Baseline effective coverage for 1st-line and 2nd-line therapy is 47% and treatment is paid out-of-pocket; intervention 1 effective coverage for 1st-line therapy is 80% and for 2ndline therapy 47% and treatment for the latter is paid out-of-pocket; intervention 2 effective coverage for 1st-line and 2nd-line therapy is 80% and treatment is paid out-ofpocket only for surgery; and intervention 3 effective coverage for 1st-line and 2nd-line therapy is 80% and neither is paid for out-of-pocket. Wealth quintiles I-III only choose to undergo surgery when there is no out-of-pocket charge. OOP – out of pocket; DALYs – disability-adjusted life years

Figures

Figure 1. 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 1st-(1st-line AEDs) and 2nd-line (Lamotragine or surgery along with 1st-line AED) therapy; 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. Individuals are born into the healthy and seizure-free category, and individuals die (exogenous deaths or epilepsy deaths in the epileptic states) and leave the model from all states.



Figure 2. Epileptic prevalence groups over time

Policy scenarios — Baseline — Intervention 1 — Intervention 2 — Intervention 3

Results are over 100 simulations. Baseline effective coverage for 1st-line and 2nd-line therapy is 47% and treatment is paid out-of-pocket; intervention 1 effective coverage for 1st-line therapy is 80% and for 2nd-line therapy 47% and treatment for the latter is paid out-of-pocket; intervention 2 effective coverage for 1st-line and 2nd-line therapy is 80% and treatment is paid out-of-pocket only for surgery; and intervention 3 effective coverage for 1st-line and 2nd-line therapy is 80% and neither is paid for out-of-pocket. Wealth quintiles I-III only choose to undergo surgery when there are no out-of-pocket charges.

Figure 3. Health and economic outcomes per 100,000 persons in each state



Results are over 100 simulations and 35 years; they are presented in present day values. Baseline effective coverage for 1st-line and 2nd-line therapy is 47% and treatment is paid out-of-pocket; intervention 1 effective coverage for 1st-line therapy is 80% and for 2nd-

line therapy 47% and treatment for the latter is paid out-of-pocket; intervention 2 effective coverage for 1st-line and 2nd-line therapy is 80% and treatment is paid out-of-pocket only for surgery; and intervention 3 effective coverage for 1st-line and 2nd-line therapy is 80% and neither is paid for out-of-pocket. Wealth quintiles I-III only choose to undergo surgery when there are no out-of-pocket charges. States in which the standard error is large and we cannot differentiate the results from no effect are greyed out. OOP – out of pocket; DALYs – disability-adjusted life years.



Figure 4. Sequential incremental dollars per disability-adjust life year (DALY)

averted

Results are over 100 simulations. Costs and health benefits are discounted at 3% and aggregated over 35 years. Baseline effective coverage for 1st-line and 2nd-line therapy is 47% and treatment is paid out-of-pocket; intervention 1 effective coverage for 1st-line therapy is 80% and for 2nd-line therapy 47% and treatment for the latter is paid out-of-pocket; intervention 2 effective coverage for 1st-line and 2nd-line therapy is 80% and treatment is paid out-of-pocket only for surgery; and intervention 3 effective coverage for 1st-line and 2nd-line therapy is 80% and neither is paid for out-of-pocket. Wealth quintiles I-III do not choose to undergo surgery unless it is free of charge.