Global disparities in the epilepsy treatment gap: a systematic review

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Objective To describe the magnitude and variation of the epilepsy treatment gap worldwide.
Methods We conducted a systematic review of the peer-reviewed literature published from 1 January 1987 to 1 September 2007 in all languages using PubMed and EMBASE. The purpose was to identify population-based studies of epilepsy prevalence that reported the epilepsy treatment gap, defined as the proportion of people with epilepsy who require but do not receive treatment. Negative binomial regression models were used to assess trends and associations.
Findings The treatment gap was over 75% in low-income countries and over 50% in most lower middle- and upper middle-income countries, while many high-income countries had gaps of less than 10%. However, treatment gaps varied widely both between and within countries. They were significantly higher in rural areas (rate ratio, RR: 2.01; 95% confidence interval, CI: 1.40–2.89) and countries with lower World Bank income classification (RR: 1.55; 95% CI: 1.32–1.82). There was no significant trend in treatment gap over time (RR: 0.92; 95% CI: 0.79–1.07).
Conclusion There is dramatic global disparity in the care for epilepsy between high- and low- income countries, and between rural and urban settings. Our understanding of the factors affecting the treatment gap is limited; future investigations should explore other potential explanations of the gap.

Une traduction en français de ce résumé figure à la fin de l'article. *Al final del artículo se facilita una traducción al español.* الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Introduction

Epilepsy affects 50 million people worldwide, and 80% of them live in the developing world.[1] An individual with epilepsy suffers recurrent seizures unprovoked by acute brain insults or metabolic derangements. Seizures are characterized by a brief period of uncontrolled involuntary shaking. They may be partial, involving only one part of the body, or generalized, involving the entire body, and they may be accompanied by loss of consciousness and of control of bowel or bladder function. Some individuals continue to have frequent seizures despite optimal treatment with anti-epileptic drugs. However, more than 70% of patients who are treated achieve long-term remission or freedom from seizures, usually within 5 years of diagnosis.[2]

Cost-effective epilepsy treatments are available and an accurate diagnosis can be made without technological equipment. Nonetheless, a vast majority of individuals with epilepsy in many resource-poor regions do not receive treatment.[3–5] Untreated epilepsy is a critical public health issue, as people with untreated epilepsy face potentially devastating social consequences and poor health outcomes. Due to stigma, many persons with epilepsy have lower employment and education levels and lower socioeconomic status. For example, children with epilepsy who have a seizure at school may be dismissed, while adults may be barred from marriage or employment.[2,6] In addition, persons with epilepsy have poor health outcomes, including greater psychological distress, more physical injuries such as fractures and burns, and increased mortality.[7–12]

The epilepsy treatment gap, defined as the proportion of people with epilepsy who require treatment but do not receive it, has been proposed as a useful parameter to compare access to and quality of care for epilepsy patients across populations.[13,14] Prior anecdotal and descriptive estimates suggest a treatment gap of more than 80% in many low-income countries,[13,15] yet one recent systematic review and meta-analysis suggests that the treatment gap in developing countries is as low as 56%.[16] This intriguing discrepancy may be due to the methodological limitations of the prior systematic review, which had an excessively narrow search strategy, included only English-language articles, and used meta-analytic techniques to generate a population estimate of the treatment gap. First, the search strategy focused on "treatment gap" and "treatment status". Many epilepsy prevalence studies report treatment data, but as the term "treatment gap" only recently came into usage in the research literature,[13] many studies with treatment gap data may have been missed using this search strategy. Second, many studies, particularly from low-income countries, are published in local rather than international journals. By not including languages other than English, many studies with treatment gap data may have been missed. Finally, the use of meta-analytic techniques to generate a unitary estimate of the treatment gap may have biased the estimates for two reasons: first, there was considerable unexplained heterogeneity among treatment gap estimates, and second, included studies were conducted in populations that were not representative of developing countries as a whole.

In this systematic review and analysis of the variation in the epilepsy treatment gap, we have greatly expanded the scope of the systematic review by searching for population-based epilepsy prevalence studies in all languages. We have also described the

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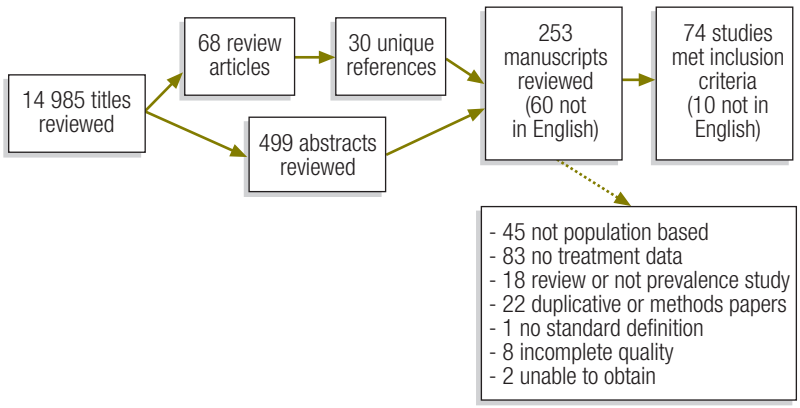
(*Submitted: 19 March 2009 – Revised version received: 19 August 2009 – Accepted: 20 August 2009 – Published online: 25 September 2009*)

Fig. 1. **Flowchart of study selection for systematic review of population-based studies of epilepsy prevalence and treatment gap**



magnitude of the treatment gap worldwide and conducted some preliminary assessments of its variation.

Methods

We conducted a systematic review of the peer-reviewed literature published in all languages from 1 January 1987 to 1 September 2007 using PubMed and EMBASE. Search terms included PubMed MeSH terms and keywords "epilepsy" AND "morbidity," OR "epilepsy" AND "delivery of health care," OR "treatment gap" AND "epilepsy". This generated 14 985 titles. Hand searching of 68 reviews of epilepsy prevalence generated an additional 30 unique titles. All titles were reviewed to identify potential epilepsy prevalence studies, then 499 abstracts and 253 full manuscripts were reviewed to identify population-based epilepsy prevalence studies (Fig. 1). Data were extracted and reviewed independently by two authors.

To be included in the analysis, epilepsy prevalence studies had to be based on a population-based sample and apply a standard definition of epilepsy. A population-based sample was defined as a door-to-door or other probability sample of a regional or national population. Studies in which the sample was drawn from a medical care setting were excluded to avoid underestimating the treatment gap. School-based populations in countries where school attendance was low were also excluded. Finally, studies based on methods shown to produce unreliable community-based samples in epilepsy prevalence studies, such as the key informant method, were excluded as well.[17,18]

The standard definition of epilepsy had to be internally consistent and to differentiate epilepsy from provoked seizures, febrile seizures and isolated seizures. For lifetime epilepsy, acceptable definitions included a history of more than one unprovoked seizure. For active epilepsy, acceptable definitions included a history of more than one unprovoked seizure and either recent seizures (within the previous 5 years) or current use of anti-epilepsy medication. If the treatment gap or other information was missing from the manuscript, we tried to contact the authors to obtain the information before excluding the study.

Further analysis of the variation in epilepsy treatment gap estimates was limited to studies of active epilepsy, as studies using lifetime epilepsy could overestimate the treatment gap. For example, some individuals captured when considering the lifetime prevalence of epilepsy may be in terminal remission and off treatment.[19] Including them in the estimates would overestimate the treatment gap because by not being on anti-epileptic drugs, these individuals are receiving the recommended standard of care.

We analysed the variation in the epilepsy treatment gap by study area (urban versus rural), country income category and year. We used negative binomial regression models to examine associations and trends and used separate models to examine the association between treatment gap and study area, country income category and year. Treatment gaps were expressed as the number of untreated persons with active epilepsy, with the number of persons having active epilepsy used as the exposure variable. Studies were classified as rural or not rural based on the site description in the methods section of the manuscripts. Countries were classified as low, lower middle, upper middle or high-income economies using World Bank criteria.[20] Prevalence year was extracted from the manuscripts; if no prevalence year was provided, the year of publication was used instead. World Bank income category and prevalence year, arranged in 5-year intervals, were treated as ordered categorical variables. Stata 10 (StataCorp LP, College Station, TX, United States of America) was used for the analysis. Significance level was set at $P \leq 0.05$.

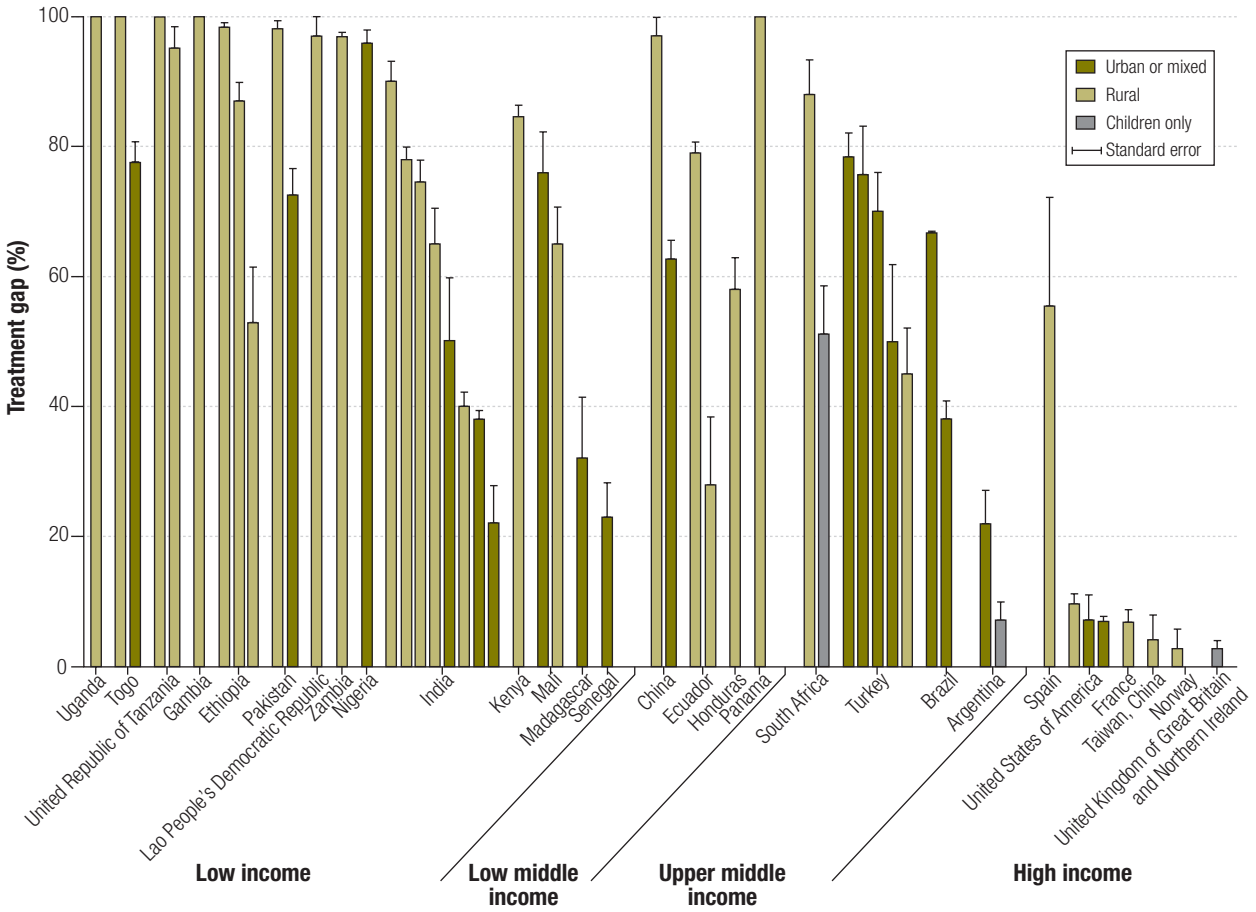
Results

Our search yielded 157 epilepsy prevalence studies that met our stated inclusion criteria, but 83 (nearly 53%) of them did not collect treatment gap data. Therefore, our final sample consisted of 74 studies representing 38 countries (Table 1 and Table 2, available at: http://www.who.int/bulletin/volumes/88/4/09-064147/en/index.html). Of note, we reviewed 60 articles in languages other than English (Chinese, English, French, German, Italian, Japanese, Portuguese, Russian, Spanish and Turkish) and 10 of them were included in the study. Manuscripts included in our final sample were published in English, French, Spanish and Turkish.

Active epilepsy was used to estimate the treatment gap in 54 populations from 28 countries (Table 1) and lifetime epilepsy was used to estimate the treatment gap in 18 populations from 16 countries (10 of which were not among the countries for which the active epilepsy gap was estimated). (Table 2). Studies spanned nearly 30 years, from 1978 to 2006, and originated across the globe, including Africa, Asia, Europe and North and South America. Study populations differed markedly in terms of type of study area (urban versus rural), sample size and degree to which they represented the entire country. Nearly 47% (34/72) of the included studies were drawn from rural populations. Treatment gaps were calculated from samples ranging from 5 to 1175 epilepsy cases. Samples were drawn from many different populations; some were nationally representative, while others represented small ethnic groups, indigenous groups, schoolchildren or military recruits.

Treatment gaps estimated from active epilepsy prevalence ranged widely between countries. Gaps were 10% or less in China (Province of Taiwan), Norway, Singapore, the United Kingdom of Great

Fig. 2. **Epilepsy treatment gap (%) and standard errors, by country and World Bank income category**



Britain and Northern Ireland, the United States of America, and select populations in Argentina, Brazil and France. In sharp contrast, treatment gaps were greater than 95% in China, Ethiopia, the Gambia, the Lao People's Democratic Republic, Nigeria, Pakistan, Panama, Togo, Uganda, the United Republic of Tanzania and Zambia (Fig. 2). A wide range of treatment gaps was observed within countries as well. For example, treatment gaps in India ranged from 22% in an urban middle- income population to 90% in a sample of rural villages.[18,21]

Like treatment gaps estimated from active epilepsy prevalence, the gaps estimated from lifetime prevalence also ranged widely, from 6% in Singapore to 100% in Bolivia (Fig. 3).[22,23] In most cases, gaps estimated from lifetime prevalence were larger than those estimated from active epilepsy prevalence. However, paradoxically, in a few low-income countries such as Pakistan and India, the treatment gap estimated from lifetime prevalence was smaller than some or all of the gap estimates based on active epilepsy prevalence.

For the analysis of the variation in the treatment gap, only studies estimating the gap from individuals with active epilepsy were used. In these studies, rural populations had treatment gaps nearly twice as high as populations from towns or from suburban, semi-urban or urban locations (rate ratio, RR: 2.01; 95% confidence

Fig. 3. **Epilepsy treatment gap (%) and standard errors calculated from lifetime prevalence estimates**

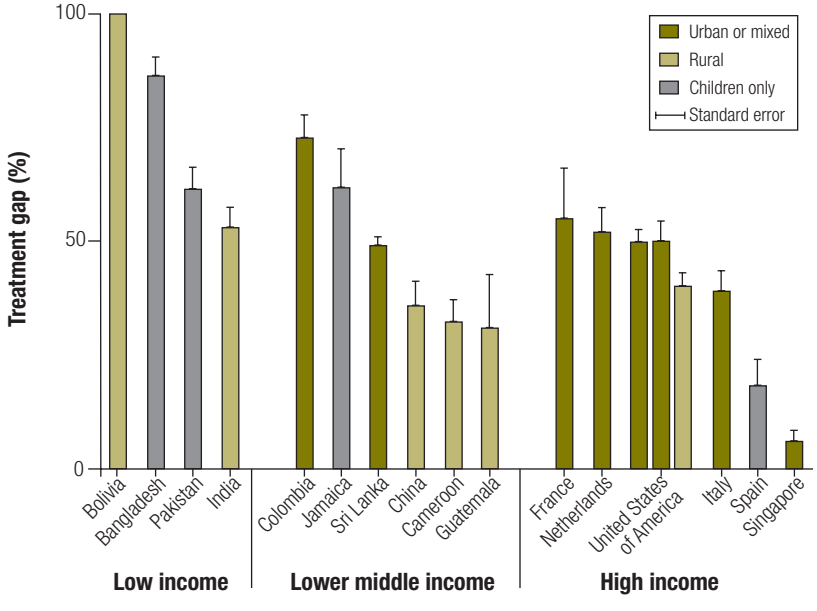
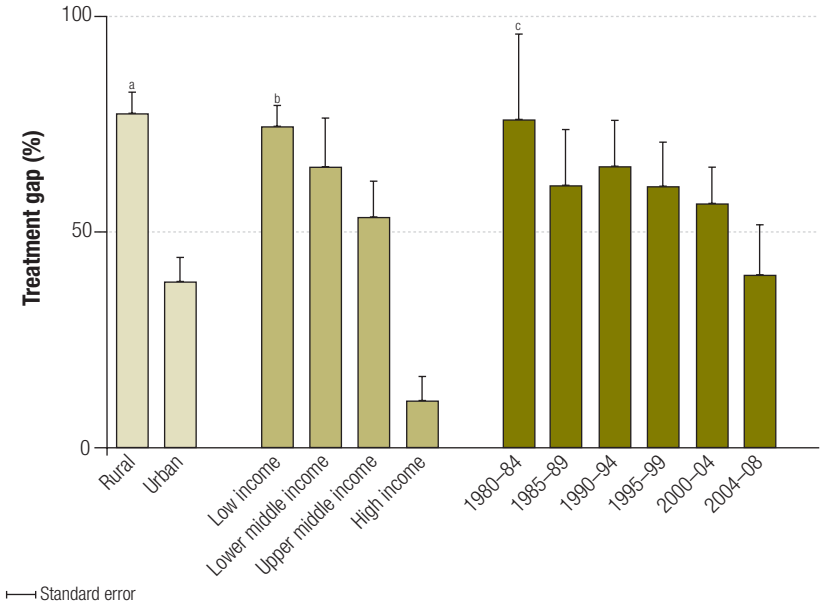


Fig. 4. **Mean epilepsy treatment gap (%) and standard errors by rural/urban status, World Bank income category and year data collected**



[a] RR = 2.01; 95% CI: 1.40–2.89, $P < 0.001$[a]
[b] RR = 1.55; 95% CI: 1.32–1.82, $P < 0.001$[b]
[c] RR = 0.92; 95% CI: 0.79–1.07, $P = 0.28$[c]

interval, CI: 1.40–2.89; Z: 3.77; $P < 0.001$) (Fig. 4). For example, in India the treatment gap ranged from 40 to 90% in rural areas and from 22 to 50% in mixed, suburban and urban populations.[18,21,24,25] Similar trends were observed in Brazil, China, Pakistan and Togo. However, there were a few exceptions: in a rural population from Rajasthan, India, the treatment gap was 40% (the third lowest in India),[25] while in a rural population of Mali it was 65% (versus 76% in an urban population).[26,27]

There was a significant trend towards larger epilepsy treatment gaps in countries with lower incomes; for every one-level decrease in World Bank income category, the treatment gap increased by a factor of 1.55 (95% CI: 1.32–1.82; Z: 5.34; $P < 0.001$) (Fig. 4). However, within high-income countries, larger gaps were found in select populations. In a small sample from Spain, the treatment gap was greater than 50%, while among the Guaymi Indians in Panama the gap was 100%.[28,29] Similarly, select populations in low-income countries had surprisingly small gaps; suburban and urban populations in India, Madagascar and Senegal had treatment gaps of less than 30%.[21,30–32]

Direct comparisons of treatment gaps over time were difficult to carry out because of differences in study methods and populations. In Ethiopia, two studies in the same population in which the same methods were used showed a gap of 98% in 1986–1988 and a gap of 87% among new cases identified during a repeat survey in 1990.[33,34] Overall, treatment gaps decreased from 1980 to the present, but no significant trend over time was detected (RR: 0.92; 95% CI: 0.79–1.07; Z: −1.08; $P = 0.28$).

Discussion

The results of this systematic review of the literature suggest that there are dramatic global disparities in the care and treatment of epilepsy patients. Treatment gaps for active epilepsy exceeded 75% in most low-income countries and 50% in most lower middle- and upper middle-income countries. In stark contrast, many high-income countries had gaps of less than 10%. However, treatment gaps varied widely, both between and within countries.

Our search methods resulted in more comprehensive estimates of the epilepsy treatment gap than those employed in previous studies. First, our systematic and thorough search strategy and rigorous inclusion criteria ensured the quality of included studies. Second, our wider search strategy, which focused on epilepsy prevalence rather than on the treatment gap, captured 26 more studies than did a recent systematic review,[16] even when we applied the same inclusion criteria. Third, our search of the non-English-language literature led to an additional 10 studies.

The subsequent analysis of the variation in the treatment gap showed significantly higher gaps in rural areas and lower-income countries. These findings are consistent with those for other health indicators, such as the rates of vaccination coverage and of maternal, infant and under-five mortality, which suggest wide disparities in care between rural and urban areas and between high- and low-income countries.[35–40] On the other hand, epilepsy treatment gaps have decreased from 1980 to the present, though the trend is not statistically significant.

While intriguing, these preliminary analyses do not fully explain the variation in the treatment gap, which may additionally reflect local or regional differences in access to and quality of epilepsy care or in the availability of individual or regional economic resources.[13,16] In addition, cultural differences in the stigma associated with epilepsy may determine whether an individual seeks care for epilepsy or not.[2,6]

In our analysis, we found that the treatment gap varied widely both within and between countries and that it was significantly associated with country income classification and a population's status as urban or rural. Similarly, prior studies of the gap demonstrated significant heterogeneity in treatment gap estimates.[16] The wide variation among estimates as well as the systematic variation as a function of selected covariates suggests that meta-analytic techniques may not be appropriate for obtaining overall population estimates of the epilepsy treatment gap. Further study into the influence of macroeconomic and microeconomic factors and of resources for the care of people with epilepsy and other neurologic disorders will be critical to understanding the reasons for this heterogeneity. Accounting for the systematic variation in the gap is essential to creating summary estimates of the gap. Combining demographic approaches with multiple imputation techniques could generate more representative gap estimates.

Our data set had several limitations. First, our sample was limited because we excluded epilepsy prevalence studies that did not collect treatment information (nearly half of those identified) or that calculated the gap from a potentially biased sample, such as clinic or hospital

patients. Using lifetime prevalence to calculate the gap could have resulted in an overestimate, so we only included data on lifetime prevalence for descriptive purposes.

Furthermore, our ability to generate national treatment gap estimates was limited. Most treatment gap estimates were based on data from selected populations that were not representative of the nation as a whole. A sample not representative of the population was not a criterion for exclusion because it was a limitation of nearly all the studies reviewed. Among the studies we included were several performed in a rural or urban area only,[34,41] among the elderly or children exclusively,[27,42,43] in areas with a high prevalence of epilepsy,[44] in military[22,45] or school populations,[46] or in regions populated by only one or a few ethnic groups.[7,47] Likewise, several included studies had been conducted in ethnic or social groups that differed from the population of the country as a whole. Examples include the Parsi community in India,[21] the Bakairi indians from Brazil,[44] the Zay society in Ethiopia[48] or the Guaymi indians of Panama.[28] Therefore, caution should be exercised in extrapolating treatment gap estimates from such select populations to the country as a whole without proper adjustment.

Although we tried to minimize variation by means of our inclusion criteria, study methods – case ascertainment, sampling technique, the definitions of active epilepsy and of adequate treatment, etc. – differed widely among studies. The quality and comparability of treatment gap data could be improved by applying standard definitions for adequate treatment and active epilepsy and by using more nationally representative population-based samples to generate active epilepsy prevalence and estimate the treatment gap. Better insight into the causes of this gap would be obtained if epilepsy prevalence studies routinely collected information on other sociodemographic characteristics, the availability and accessibility of local or regional health services and treatment, and the stigma associated with seeking care.

Conclusion

In summary, our systematic review of the epilepsy treatment gap worldwide shows a dramatic global disparity in the care of epilepsy patients between high- and low-income countries and between rural and urban settings. Epilepsy is a common and potentially serious neurological disorder that can be diagnosed and treated inexpensively. Historically, epilepsy has received little public health attention despite poor health outcomes and potentially devastating social consequences from untreated disease. In recent years, many countries have undertaken initiatives to decrease the epilepsy treatment gap, notably the demonstration projects such as the Global Campaign Against Epilepsy, conducted jointly by the International League against Epilepsy, the International Bureau for Epilepsy and the World Health Organization. Large community based trials in Brazil and China have demonstrated that epilepsy can be treated with inexpensive and effective drugs at the community level by primary health professionals with basic training.[5,49] Increased commitment by the global health community is needed to reduce the treatment gap and thereby reduce the potentially devastating social consequences and poor health outcomes resulting from untreated epilepsy. ■

Acknowledgements

We thank John Boscardin, Associate Professor of Medicine and Biostatistics, for his help with the statistical analysis.

Funding: Ana-Claire Meyer: Veterans Affairs/Robert Wood Johnson Clinical Scholars Program, American Academy of Neurology Practice Research Training Fellowship. Gretchen Birbeck: The Global Burden of Diseases, Injuries, and Risk Factors Study.

Competing interests: None declared.

ملخص

التباين العالمي في فجوة معالجة الصرع: مراجعة منهجية

الغرض: وصف المقدار والتباين العالمي في فجوة معالجة الصرع.

الطريقة: أجرى الباحثون مراجعة منهجية للمنشورات التي خضعت لمراجعة الزملاء ونشرت خلال الفترة من أول كانون الثاني/يناير 1987 حتى أول أيلول/سبتمبر 2007 بجميع اللغات المستخدمة في موقعي النشريات الطبية على الإنترنت PubMed و EMBASE. وكان الهدف وراء ذلك تحديد الدراسات السكانية لانتشار الصرع التي أبلغت عن وجود فجوة في معالجة الصرع، ويمكن تعريف الفجوة على أنها نسبة المصابين بالصرع الذين يحتاجون إلى العلاج ولكن لا يحصلون عليه. استخدمت نماذج توزيع التحوف ثنائي الحد لتقييم الاتجاهات والارتباطات.

الموجودات: بلغت فجوة المعالجة أكثر من 75% في البلدان المنخفضة الدخل، وأكثر من 50% في أغلب البلدان الواقعة في المرتبة السفلى والمرتبة العليا من البلدان المتوسطة الدخل، في حين بلغت أقل من 10% في أغلب البلدان المرتفعة الدخل، إلا أن فجوة المعالجة تباينت على نحو واسع سواء بين البلدان بعضها البعض أو في داخل البلدان نفسها. وكانت الفجوة أعلى بدرجة يعتد بها في المناطق الريفية (نسبة المعدل rate ratio: 2.01؛ وفاصلة الثقة confidence interval 95%: 1.40 - 2.89) وفي البلدان منخفضة الدخل حسب تصنيف البنك الدولي (نسبة المعدل: 1.55؛ وفاصلة الثقة 95%: 1.32 - 1.82). ولم يكن هنا اتجاه يعتد به في الفجوة العلاجية مع مرور الوقت (نسبة المعدل: 0.92؛ فاصلة الثقة 95%: 0.79 - 1.07).

الاستنتاج: هناك تباين ملحوظ في رعاية الصرع بين البلدان المرتفعة الدخل والبلدان المنخفضة الدخل، وبين المناطق الريفية والمناطق الحضرية. ومازال الإلمام بالعوامل التي تؤثر في الفجوة العلاجية محدوداً؛ وينبغي أن تستكشف الاستقصاءات مستقبلاً سائر التفسيرات المحتملة لهذه الفجوة.

Résumé

Disparités mondiales dans l'insuffisance de traitement de l'épilepsie : revue systématique

Objectif Décrire l'ampleur et les variations de l'insuffisance du traitement de l'épilepsie dans le monde.

Méthodes A l'aide de PubMed et d'EMBASE, nous avons réalisé une revue systématique de la littérature examinée par des pairs et publiée entre le 1er janvier 1987 et le 1er septembre 2007 dans toutes les langues. L'objectif était d'identifier des études en population de la prévalence de l'épilepsie indiquant l'insuffisance du traitement de cette maladie, définie comme la proportion des personnes épileptiques ayant besoin d'être traitées, mais ne recevant pas de traitement. Des modèles par régression binomiale négative ont été utilisés pour évaluer les tendances et les associations.

Résultats L'insuffisance du traitement de l'épilepsie dépassait 75 % dans les pays à faible revenu et 50 % dans la plupart des pays à revenu moyen inférieur et moyen supérieur, alors que dans de nombreux pays à revenu élevé, cette insuffisance était inférieure à 10 %. Néanmoins, l'insuffisance du traitement variait fortement d'un pays à l'autre et au sein d'un même pays. Elle était significativement plus importante dans les zones rurales (risque relatif, RR : 2,01 ; intervalle de confiance à 95 %, IC : 1,40-2,89) et dans les pays appartenant à la classe de revenu inférieure de la Banque mondiale (RR : 1,55 ; IC à 95 % : 1,32-1,82). On n'a relevé aucune tendance significative de l'insuffisance du traitement de l'épilepsie au cours du temps (RR : 0,92 ; IC à 95 % : 0,79-1,07).

Conclusion Il existe à travers le monde des disparités considérables dans les soins dispensés aux épileptiques, et notamment entre les pays à revenu faible et élevé et entre les environnements ruraux et urbains. Notre compréhension des facteurs influant sur l'insuffisance du traitement est limitée : dans le cadre d'investigations futures, il conviendrait d'étudier d'autres explications possibles de cette insuffisance.

Resumen

Disparidades mundiales en la brecha de tratamiento de la epilepsia: revisión sistemática

Objetivo Describir la magnitud y las diferencias de la brecha de tratamiento de la epilepsia a nivel mundial.

Métodos A través de PubMed y EMBASE, se hizo una revisión sistemática de los artículos revisados por homólogos publicados entre el 1 de enero de 1987 y el 1 de septiembre de 2007. La finalidad era encontrar estudios poblacionales sobre la prevalencia de la epilepsia que informaran acerca de la brecha de tratamiento de esa enfermedad, definida como la proporción de personas afectadas que necesitan pero no reciben tratamiento. Las tendencias y relaciones se evaluaron mediante modelos de regresión binomial negativa.

Resultados La brecha terapéutica era superior al 75% en los países de ingresos bajos, y superior al 50% en la mayoría de los países de ingresos medios bajos y medios altos, mientras que muchos países de ingresos altos presentaban brechas inferiores al 10%. Sin embargo, la magnitud de la brecha terapéutica difería ampliamente tanto entre los países como en cada país. Era significativamente mayor en las zonas rurales (razón de tasas, RT: 2,01, intervalo de confianza del 95%: 1,40–2,89) y en los países incluidos en la categoría de ingresos bajos del Banco Mundial (RT: 1,55, IC95%: 1,32–1,82). No se observó ninguna tendencia significativa de la brecha a lo largo del tiempo (RT: 0,92, IC95%: 0,79–1,07).

Conclusión En lo referente al tratamiento de la epilepsia, existe una enorme disparidad mundial entre los países de altos y de bajos ingresos, y entre las zonas rurales y las urbanas. Nuestros conocimientos sobre los factores que determinan esa brecha terapéutica son limitados, y en las investigaciones futuras se deberían estudiar otras posibles explicaciones de la misma.

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Table 1. **Studies used for estimating epilepsy treatment gap based on the prevalence of active epilepsy, by country**

Country	Location	Year	No. of cases	% treatment gap	Setting/ population	Study
Argentina	Junin	1991	64	22	Town	Kochen S, Melcon MO. Prognosis of epilepsy in a community-based study: 8 years of follow-up in an Argentine community. *Acta Neurol Scand* 2005;112:370-4. doi:10.1111/j.1600-0404.2005.00519.x PMID:16281918
Argentina	Buenos Aires	1991	84	7	Urban, primary school	Somoza MJ, Forlenza RH, Brussino M, Licciardi L. Epidemiological survey of epilepsy in the primary school population in Buenos Aires. *Neuroepidemiology* 2005;25:62-8. doi:10.1159/000086285 PMID:15947492
Brazil	Mato Grosso state	2000	9	67	Rural, Bakairi indians	Borges MA, Barros EP, Zanetta DM, Borges AP. Prevalence of epilepsy in Bakairi indians from Mato Grosso State, Brazil. *Arq Neuropsiquiatr* 2002;60:80-5 [Portuguese.]. PMID:11965413
Brazil	Rio de Janeiro	2000	5	0	Urban, low-income	Gomes M, Zeitoune R, Kropf L, Van Beeck E. A house-to-house survey of epileptic seizures in an urban community of Rio de Janeiro, Brazil. *Arq Neuropsiquiatr* 2002;60:708-11. PMID:12364934
Brazil	Barao Geraldo, Campinas; Jaguare and Santo Antonio, Sao Jose do Rio Preto, south-eastern Brazil	2002	290	38	Mixed	Noronha AL, Borges M, Marques L, Zanetta D, Fernandes P, De Boer H, et al. Prevalence and pattern of epilepsy treatment in different socioeconomic classes in Brazil. *Epilepsia* 2007;48:880-885. doi:10.1111/j.1528-1167.2006.00974.x PMID:17326788
China	5 provinces: Heilongjiang, Ningxia, Henan, Shanxi, Jiangsu	2003[a]	257	63	Mixed	Wang WZ, Wu JZ, Wang DS, Dai XY, Yang B, Wang TP, et al. The prevalence and treatment gap in epilepsy in China: an ILAE/IBE/WHO study. *Neurology* 2003;60:1544-5. PMID:12743252
China, Province of Taiwan	20 districts and townships in Ilan County, NE Taiwan	1993–95	25	4	Mixed, adults > 40 yrs old	Su CL, Chang SF, Chen ZY, Lee CS, Chen RC. Neuroepidemiological survey in Ilan, Taiwan (NESIT): Prevalence of epilepsy. *Acta Neurol Taiwan* 1998;7:75-84.
China	Tibet Autonomous Region	2006	35	97	Rural	Zhao Y, Zhang Q, Tsering T, Sangwan, Hu X, Liu L, et al. Prevalence of convulsive epilepsy and health-related quality of life of the population with convulsive epilepsy in rural areas of Tibet Autonomous Region in China: An initial survey during a verbal episodic memory task. *Epilepsy Behav* 2008;12:373-81. doi:10.1016/j.yebeh.2007.10.012 PMID:18180204
Ecuador	Atahualpa	2003	18	28	Rural	Del Brutto OH, Santibanez R, Idrovo L, Rodriguez S, Diaz-Calderon E, Navas C, et al. Epilepsy and neurocysticercosis in Atahualpa: a door-to-door survey in rural coastal Ecuador. *Epilepsia* 2005;46:583-7. doi:10.1111/j.0013-9580.2005.36504.x PMID:15816956
Ecuador	El Carchi and Imbabura regions, northern Ecuador	1992[a]	575	79	Rural	Placencia M, Shorvon SD, Paredes V, Bimos C, Sander JW, Suarez J, et al. Epileptic seizures in an Andean region of Ecuador. Incidence and prevalence and regional variation. *Brain* 1992;115:771-82. doi:10.1093/brain/115.3.771 PMID:1628201 Placencia M, Sander J, Roman M, Madera A, Crespo F, Cascante S, et al. The characteristics of epilepsy in a largely untreated population in rural Ecuador. *J Neurol Neurosurg Psychiatry* 1994;57:320-5. doi:10.1136/jnnp.57.3.320 PMID:8158180
Ethiopia	Zay society	2006[a]	34	53	Rural	Almu S, Tadesse Z, Cooper P, Hackett R. The prevalence of epilepsy in the Zay Society, Ethiopia – an area of high prevalence. *Seizure* 2006;15:211-3. doi:10.1016/j.seizure.2006.01.004 PMID:16488161
Ethiopia	Meskan and Mareko sub-district, Haykoch and Butajira district	1986–1988	306	98	Rural	Tekle-Haimanot R, Forsgren L, Abebe M, Gebre-Mariam A, Heijbel J, Holmgren G, et al. Clinical and electroencephalographic characteristics of epilepsy in rural Ethiopia: a community based study. *Epilepsy Res* 1990;7:230-9. doi:10.1016/0920-1211(90)90020-V PMID:2289482
Ethiopia	Meskan and Mareko sub-district, Haykoch and Butajira district	1990	139	87	Rural	Tekle-Haimanot R, Forsgren L, Ekstedt J. Incidence of epilepsy in rural central Ethiopia. *Epilepsia* 1997;38:541-6. doi:10.1111/j.1528-1157.1997.tb01138.x PMID:9184599
France	Paris, Seine et Marne, Seine Saint-Denis, Val de Marne	1987–1988	149	7	Urban	Jallon P. Evaluation of epilepsy prevalence rate in young recruits in a military selection centre. *Rev Neurol* 1991;147:319-22. PMID:2063084

Country	Location	Year	No. of cases	% treatment gap	Setting/ population	Study
Gambia	Farafenni	1997, 1999	69	100	Rural	Coleman R, Loppy L, Walraven G. The treatment gap and primary health care for people with epilepsy in rural Gambia. *Bull World Health Organ* 2002;80:378-83. PMID:12077613
Honduras	Salama County	1997	100	58	Rural	Medina MT, Duron RM, Martinez L, Osorio JR, Estrada AL, Zuniga C, et al. Prevalence, incidence, and etiology of epilepsies in rural Honduras: the Salama Study. *Epilepsia* 2005;46:124-31. doi:10.1111/j.0013-9580.2005.11704.x PMID:15660778
India	Parsi community of Bombay	1985	50	22	Urban	Bharucha NE, Bharucha E, Bharucha A, Bhise A, Schoenberg B. Prevalence of epilepsy in the Parsi community of Bombay. *Epilepsia* 1988;29:111-5. doi:10.1111/j.1528-1157.1988.tb04405.x PMID:3258234
India	Calicut district, Kerala	1997[a]	26	50	Mixed	Hackett RJ, Hackett L, Bhakta P. The prevalence and associated factors of epilepsy in children in Calicut District, Kerala, India. *Acta Paediatr* 1997;86:1257-60. doi:10.1111/j.1651-2227.1997.tb14857.x PMID:9401524
India	Kuthar Valley, Anantnag district, South Kashmir	1986	157	75	Rural	Koul R, Razdan S, Motta A. Prevalence and pattern of epilepsy (Lath/Mirgi/Laran) in Rural Kashmir, India. *Epilepsia* 1988;29:116-22. doi:10.1111/j.1528-1157.1988.tb04406.x PMID:3258235 Razdan S, Kaul R, Motta A, Kaul S, Bhatt R. Prevalence and pattern of major neurological disorders in rural Kashmir (India) in 1986. *Neuroepidemiology* 1994;13:113-9. doi:10.1159/000110368 PMID:8015664
India	Yelandur, Karnataka, south India	1990–1991	457	78	Rural	Mani KS, Rangan G, Srinivas HV, Kalyanasundaram S, Narendran S, Reddy AK. The Yelandur study: a community-based approach to epilepsy in rural South India – epidemiological aspects. *Seizure* 1998;7:281-8. doi:10.1016/S1059-1311(98)80019-8 PMID:9733402
India	West Bengal	1995–1996	90	90	Rural	Pal DK, Das T, Sengupta S. Comparison of key informant and survey methods for ascertainment of childhood epilepsy in West Bengal, India. *Int J Epidemiol* 1998;27:672-6. doi:10.1093/ije/27.4.672 PMID:9758124
India	Thrissur, Palakkad, Malappuram districts, Kerala, south India; High literacy and health awareness	1996	1175	38	Semi-urban	Radhakrishnan K, Pandian JD, Santhoshkumar T, Thomas SV, Deetha TD, Sarma PS, et al. Prevalence, knowledge, attitude, and practice of epilepsy in Kerala, South India. *Epilepsia* 2000;41:1027-35. doi:10.1111/j.1528-1157.2000.tb00289.x PMID:10961631
India	Baruipur block, west Bengal, east India	1992–1993	75	65	Rural	Saha SP, Bhattacharya S, Das SK, Maity B, Roy T, Raut DK. Epidemiological study of neurological disorders in a rural population of Eastern India. *J Indian Med Assoc* 2003;101:299-300. PMID:14575218
India	Churu Tehsil, Rajasthan	2005	517	40	Rural	Sureka RK, Sureka R. Prevalence of epilepsy in rural Rajasthan – a door-to-door survey. *J Assoc Physicians India* 2007;55:741-2. PMID:18173034
Kenya	Kilifi district	2003	408	85	Rural	Edwards T, Scott AG, Munyoki G, Odera VM, Chengo E, Bauni E, et al. Active convulsive epilepsy in a rural district of Kenya: a study of prevalence and possible risk factors. *Lancet Neurol* 2008;7:50-6. doi:10.1016/S1474-4422(07)70292-2 PMID:18068520
Lao People's Democratic Republic	District Hinheub	2003–2004	33	97	Rural	Tran DS, Odermatt P, Le TO, Huc P, Druet-Cabanac M, Barennes H, et al. Prevalence of epilepsy in a rural district of central Lao People's Democratic Republic PDR. *Neuroepidemiology* 2006;26:199-206. doi:10.1159/000092407 PMID:16569936
Madagascar	Grand Antananarivo	2001	25	32	Urban	Andriantseheno L, Ralaizandriny D. Prevalence communautaire de l'epilepsie chez les Malgaches. *Epilepsies* 2004;16:83-6.
Mali	18 villages in Tyenfala, Baguineda	2000	70	65	Rural	Farnarier G, Diop S, Coulibaly B, Arborio S, Dabo A, Diakite M, et al. [Onchocerciasis and epilepsy. Epidemiological survey in Mali]. *Med Trop (Mars)* 2000;60:151-5. PMID:11100441
Mali	Comune IV and Comune VI, Bamako district	1998	46	76	Urban	Traore M, Tahny R, Sacko M. Prevalence de l'epilepsie chez les enfants de 3 a 15 ans dans 2 communes du district de Bamako. *Rev Neurol (Paris)* 2000;156: Suppl 1:S18.

Country	Location	Year	No. of cases	% treatment gap	Setting/ population	Study
Nigeria	Igbo-Ora	1982	101	96	Town	Osuntokun BO, Adeuja A, Nottidge V, Bademosi O, Olumide A, Ige O, et al. Prevalence of the epilepsies in Nigerian Africans: a community based study. *Epilepsia* 1987;28:272-9. doi:10.1111/j.1528-1157.1987.tb04218.x PMID:3582291
Norway	Vaga community, southern Norway	1995–1997	12	0	Rural	Brodtkorb E, Sjaastad O. Epilepsy prevalence by individual interview in a Norwegian community. *Seizure* 2008;17:646-50. doi:10.1016/j.seizure.2008.03.005 PMID:18434213
Norway	Oppland county	2001	35	3	Mixed	Svendsen T, Lossius M, Nakken KO. Age-specific prevalence of epilepsy in Oppland County, Norway. *Acta Neurol Scand* 2007;116:307-11. doi:10.1111/j.1600-0404.2007.00909.x PMID:17922724
Pakistan	Sind Province, Mirpur Sakro	1987	126	98	Rural	Aziz H, Ali S, Frances P, Khan M, Hasan K. Epilepsy in Pakistan: a population-based epidemiologic study. *Epilepsia* 1994;35:950-8. doi:10.1111/j.1528-1157.1994.tb02539.x PMID:7925166
Pakistan	Karachi	1987	115	73	Urban	Aziz H, Ali S, Frances P, Khan M, Hasan K. Epilepsy in Pakistan: a population-based epidemiologic study. *Epilepsia* 1994;35:950-8. doi:10.1111/j.1528-1157.1994.tb02539.x PMID:7925166
Panama	Changuinola, Bocas del Toro province	1988	19	100	Small town, Guaymi Indians	Gracia F, deLao S, Castillo L, Larreategui M, Archbold C, Brenes M, et al. Epidemiology of epilepsy in Guaymi Indians from Bocas del Toro Province, Republic of Panama. *Epilepsia* 1990;31:718-23. doi:10.1111/j.1528-1157.1990.tb05512.x PMID:2245802
Senegal	Pikine Health District, suburb of Dakar	2005	64	23	Suburban	Ndoye NF, Sow AD, Diop AG, Sessouma B, Sene-Diouf F, Boissy L, et al. Prevalence of epilepsy its treatment gap and knowledge, attitude and practice of its population in sub-urban Senegal an ILAE/IBE/WHO study. *Seizure* 2005;14:106-11. doi:10.1016/j.seizure.2004.11.003 PMID:15694563
South Africa	Bushbuckridge, Northern Province	2000	45	51	Rural, children	Christianson AL, Zwane ME, Manga P, Rosen E, Venter A, Kromberg JG. Epilepsy in rural South African children – prevalence, associated disability and management. *S Afr Med J* 2000;90:262-6. PMID:10853404
South Africa	Nkalukeni village	2003	38	88	Rural	Del Rio-Romero A, Foyaca-Sibat H, Ibanez-Valdes L, Vega-Novoa E. Prevalence of Epilepsy and General Knowledge about Neurocysticercosis at Nkalukeni Village, South Africa. *Internet Journal of Neurology* 2005;3:1-12.
Spain	Madrid	1984	9	56	Urban	Cruz Gutierrez-del-Olmo M, Schoenberg BS, Portera-Sanchez A. Prevalence of neurological diseases in Madrid, Spain. *Neuroepidemiology* 1989;8:43-7. doi:10.1159/000110164 PMID:2643061
Togo	10 of 13 villages in Nadoba, Batamariba district; Batamariba or Tamberma tribe	2002	92	100	Rural	Balogou AA, Grunitzky K, Belo M, Sankaredja M, Djagba D, Tatagan-Agbi K, et al. Managment of Epilepsy Patients in Batamariba District, Togo. *Acta Neurol Scand* 2007;116:211-6. doi:10.1111/j.1600-0404.2007.00871.x PMID:17824896
Togo	Tone	1995	170	78	Mixed	Balogou AA, Doh A, Grunitzky K. Affections neurologiques et endemie goitreuse: analyse comparative de deux provinces du Togo. *Bull Soc Pathol Exot* 2001;94:406-10. PMID:11889943
Turkey	Central Anatolia (Elmadag township and Kutludugun village) and Demirlirbahce district of Anakara city	1987	59	70	Mixed	Aziz H, Guvener A, Akhtar SW, Hasan KZ. Comparative epidemiology of epilepsy in Pakistan and Turkey: population-based studies using identical protocols. *Epilepsia* 1997;38:716-22. doi:10.1111/j.1528-1157.1997.tb01242.x PMID:9186255
Turkey	Sivas	1997	33	76	Urban	Topalkara K, Akyuz A, Sumer H, Bekar D, Topaktas S, Dener S, et al. Siva il Merkezinde Tabakali Ornekleme Yontemi ile Gerceklestirilen Epilepsi Prevalans Calismasi. *Epilepsia* 1999;5:24-9.
Turkey	Bursa city center	2004–2005	18	50	Urban	Calişir N, Bora I, Irgil E, Boz M. Prevalence of Epilepsy in Bursa City Center, an Urban Area of Turkey. *Epilepsia* 2006;47:1691-9. doi:10.1111/j.1528-1167.2006.00635.x PMID:17054692
Turkey	Silivri	1994	49	45	Mixed	Karaagaç N, Yeni SN, Senocak M, Bozluolcay M, Savrun FK, Ozdemir H, et al. Prevalence of epilepsy in Silivri, a rural area of Turkey. *Epilepsia* 1999;40:637-42. doi:10.1111/j.1528-1157.1999.tb05567.x PMID:10386534
Turkey	47 villages in Ulas town, Sivas city, middle Anatolia region of Turkey		125	78	Mixed	Sahin A, Bolayir E, Sumer H, Tas A, Mollaoglu M, Dener S. Epidemiologic evaluation of epileptic and nonepileptic seizures in Sivas region of Middle Anatolia. *Neurol Psychiatry Brain Res* 2004;11:97-102.

[a] Prevalence year not reported in manuscript, therefore publication year substituted.

Country	Location	Year	No. of cases	% treatment gap	Setting/ population	Study
Uganda	Kabende parish, Kabarole district	1994	61	100	Rural	Kaiser C, Kipp W, Asaba G, Mugisa C, Kabagambe G, Rating D, et al. The prevalence of epilepsy follows the distribution of onchocerciasis in a west Ugandan focus. *Bull World Health Organ* 1996;74:361-7. PMID:8823957
United Kingdom of Great Britain and Northern Ireland	National child survey	1988	124	2	National, children only	Kurtz Z, Tookey P, Ross E. Epilepsy in young people: 23 year follow up of the British national child development study. *BMJ* 1998;316:339-42. PMID:9487166
United Republic of Tanzania	Nachingwea district	1999	42	95	Rural	Dent W, Helbok R, Matuja WB, Scheunemann S, Schmutzhard E. Prevalence of active epilepsy in a rural area in South United Republic of Tanzania: a door-to-door survey. *Epilepsia* 2005;46:1963-9. doi:10.1111/j.1528-1167.2005.00338.x PMID:16393163
United Republic of Tanzania	Ulanga district	1989–1990	185	100	Rural	Rwiza H, Kilonzo G, Haule J, Matuja W, Mteza I, Mbena P, et al. Prevalence and incidence of epilepsy in Ulanga, a rural Tanzanian district: a community-based study. *Epilepsia* 1992;33:1051-6. doi:10.1111/j.1528-1157.1992.tb01758.x PMID:1464263 Rwiza H. The Muhimbili epilepsy project, a three pronged approach. *Trop Geogr Med* 1994;46 Suppl;22-4.
United States of America	Washington Heights, Inwood, New York City	2004–2005	42	7	Urban	Kelvin EA, Hesdorffer DC, Bagiella E, Andrews H, Pedley TA, Shih TT, et al. Prevalence of self-reported epilepsy in a multiracial and multiethnic community in New York City. *Epilepsy Res* 2007;77:141-50. doi:10.1016/j.eplepsyres.2007.09.012 PMID:18023147
United States of America	California	2003	322	10	Mixed	Kobau R, Zahran H, Grant D, Thurman DJ, Price PH, Zack MM. Prevalence of active epilepsy and health-related quality of life among adults with self-reported epilepsy in California: California Health Interview Survey, 2003. *Epilepsia* 2007;48:1904-13. doi:10.1111/j.1528-1167.2007.01161.x PMID:17565591
United States of America	19 states	2005	919	7	Mixed	Kobau R, Zahran H, Thurman DJ, Zack MM, Henry TR, Schachter SC, et al. Epilepsy surveillance among adults — 19 States, Behavioural Risk Factor Surveillance System, 2005. *MMWR Surveill Summ* 2008;57:1-20. PMID:18685554
Zambia	Chikankata catchment area	2000–2001	799	97	Rural	Birbeck GL, Kalichi EM. Epilepsy prevalence in rural Zambia: a door-to-door survey. *Trop Med Int Health* 2004;9:92-5. doi:10.1046/j.1365-3156.2003.01149.x PMID:14728612

[a] Prevalence year not reported in manuscript, therefore publication year substituted.

Table 2. **Studies used for estimating epilepsy treatment gap based on the lifetime prevalence of epilepsy, by country**

Country	Location	Year	No. of cases	% treatment gap	Setting/ population	Author
Bangladesh	Attempts to be representative of country; 3 rural, 2 urban areas	1992[a]	67	86	Mixed, children	Durkin MS, Davidson L, Hasan K, Hasan Z, Hauser W, Khan N, et al. Estimates of the prevalence of childhood seizure disorders in communities where professional resources are scarce: results from Bangladesh, Jamaica and Pakistan. *Paediatr Perinat Epidemiol* 1992;6:166-80. doi:10.1111/j.1365-3016.1992.tb00758.x PMID:1584719
Bolivia	Cordillera Province, Santa Cruz Department	1994	124	100	Rural	Nicoletti A, Reggio A, Bartoloni A, Failla G, Sofia V, Bartalesi F, et al. Prevalence of epilepsy in rural Bolivia: a door-to-door survey. *Neurology* 1999;53:2064-9. PMID:10599782
Cameroon	Bilomo, west bank of Mbam river in Centre Province of Cameroon	1998	93	32	Rural	Njamnshi AK, Sini V, Djientcheu VDP, Ongolo-Zogo P, Mapoure Y, Yepnjio FN, et al. Risk factors associated with epilepsy in a rural area in Cameroon: A preliminary study. *African J Neurol Sci* 2007;26:18-26.
China	4 towns, 6 villages in Dongning County, Mundanjiang City, Heilongjiang Province	2000	81	36	Rural	Ma GY, Li ZQ, Lu S, Wang LH, Wen SR, Li GZ, et al. Survey of etiological factors of epilepsy in Mudanjian rural population by randomly cluster sampling. *Chin J Clin Rehabil* 2004;8:3178-9. Tang Y, Li GZ, Ma GY, Wang DS. Epidemiological survey of epilepsy in Dongning county, a rural area in Heilongjiang Province of China. *Chin J Clin Rehabil* 2004;8:770-1.
Colombia	Medellin	1983	77	73	Urban	Zuloaga L, Soto C, Jaramillo D, Mora O, Betancur C, Londono R. [Prevalence of epilepsy in Medellin, Colombia, 1983]. *Bol Oficina Sanit Panam* 1988;104:331-44. PMID:2971372
France	Haute-Vienne, Limousin region	1986–87	20	55	Mixed	Munoz M, Boutros-Toni F, Preux PM, Chartier JP, Ndzanga E, Boa F, et al. Prevalence of neurological disorders in Haute-Vienne department (Limousin region-France). *Neuroepidemiology* 1995;14:193-8. doi:10.1159/000109796 PMID:7643954
Guatemala	Small rural village	1996[a]	16	31	Rural	Mendizabal JE, Salguero LF. Prevalence of epilepsy in a rural community of Guatemala. *Epilepsia* 1996;37:373-6. doi:10.1111/j.1528-1157.1996.tb00574.x PMID:8603643
India	PHC cachement area, Haryana, North India	1992–4	126	53	Rural	Singh A, Kaur A. Epilepsy in rural Haryana – prevalence and treatment seeking behaviour. *J Indian Med Assoc* 1997;95:37-9, 47. PMID:9357239
Italy	Riposto (Catania Province); Santa Teresa di Riva (Messina Province); Terrasini (Palermo Province) Sicily	1987	111	39	Semi-urban	Rocca WA, Savettieri G, Anderson DW, Meneghini F, Grigoletto F, Morgante L, et al. Door-to-door prevalence survey of epilepsy in three Sicilian municipalities. *Neuroepidemiology* 2001;20:237-41. doi:10.1159/000054796 PMID:11684899
Jamaica	May Pen and Lionel Town, Clarendon parish	1992[a]	32	62	Rural, children	Durkin MS, Davidson L, Hasan K, Hasan Z, Hauser W, Khan N, et al. Estimates of the prevalence of childhood seizure disorders in communities where professional resources are scarce: results from Bangladesh, Jamaica and Pakistan. *Paediatr Perinat Epidemiol* 1992;6:166-80. doi:10.1111/j.1365-3016.1992.tb00758.x PMID:1584719
Netherlands	Elderly, Rotterdam Study	1991–1993	85	52	Suburb	de la Court A, Breteler MM, Meinardi H, Hauser WA, Hofman A. Prevalence of epilepsy in the elderly: the Rotterdam Study. *Epilepsia* 1996;37:141-7. doi:10.1111/j.1528-1157.1996.tb00005.x PMID:8635424
Pakistan	Greater Karachi; 43 urban and 16 rural	1992[a]	99	62	Mixed, children	Durkin MS, Davidson L, Hasan K, Hasan Z, Hauser W, Khan N, et al. Estimates of the prevalence of childhood seizure disorders in communities where professional resources are scarce: results from Bangladesh, Jamaica and Pakistan. *Paediatr Perinat Epidemiol* 1992;6:166-80. doi:10.1111/j.1365-3016.1992.tb00758.x PMID:1584719

Country	Location	Year	No. of cases	% treatment gap	Setting/ population	Author
Singapore	National	1995	89	6	National; 18 year old men	Kun LN, Ling LW, Wah YW, Lian TT. Epidemiologic study of epilepsy in young Singaporean men. *Epilepsia* 1999;40:1384-7. doi:10.1111/j.1528-1157.1999.tb02009.x PMID:10528933
Spain	Guillena municipality	1981	40	18	Mixed, children	Nieto Barrera M. Neuroepidemiology of epilepsy. *An Esp Pediatr* 1988;29:59-63. PMID:3250297
Sri Lanka	218 villages belonging to 12 Gramodaya Centres	1983	690	49	Mixed	Senanayake N. Epilepsy control in a developing country-the challenge of tomorrow. *Ceylon Med J* 1987;32:181-99. PMID:3506450
United States of America	Copiah County	1978	246	40	Rural	Haerer AF, Anderson D, Schoenberg B. Prevalence and clinical features of epilepsy in a biracial United States population. *Epilepsia* 1986;27:66-75. doi:10.1111/j.1528-1157.1986.tb03503.x PMID:3948820
United States of America	US population	2004	123	50	Mixed	Kobau R, Gilliam F, Thurman DJ. Prevalence of self-reported epilepsy or seizure disorder and its associations with self-reported depression and anxiety: results from the 2004. *Health Styles Survey Epilepsia* 2006;47:1915-21. doi:10.1111/j.1528-1167.2006.00612.x
United States of America	South Carolina	2003–5	379	50	Mixed	Prevalence of epilepsy and health-related quality of life and disability among adults with epilepsy – South Carolina, 2003 and 2004. *MMWR Morb Mortal Wkly Rep* 2005;54:1080-2. PMID:16251865 Ferguson PL, Chiprich J, Smith G, Dong B, Wannamaker BB, Kobau R, et al. Prevalence of self-reported epilepsy, health care access, and health behaviours among adults in South Carolina. *Epilepsy Behav* 2008;13:529-34. doi:10.1016/j.yebeh.2008.05.005 PMID:18585962

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