Assessing the Disease Burden Due to Epilepsy by Disability Adjusted Life Year in Rural China

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Summary: Purpose: To demonstrate the application of Disability Adjusted Life Year (DALY) as an aid in health outcome measures to evaluate the epilepsy disease burden in rural China and to provide Chinese data to achieve a better understanding of disease burden due to epilepsy.

Methods: The DALY is the sum of the number of years of survival with disability (Years Lived with Disability, YLD) and the number of years lost because of premature mortality (Years of Life Lost, YLL). We calculated the YLD based on the prevalence survey of epilepsy among 66,393 people sampled in Heilongjiang, Henan, Jiangsu, Ningxia, Shanghai, and Shanxi provinces in 2000. The epilepsy mortality data from Chinese literature provided the YLL due to epilepsy. We applied sensitivity analysis to evaluate the influence of uncertainty on the epilepsy mortality value and disability weight in the study.

Results: In 2000, epilepsy caused 1.83 and 2.48 DALY lost per 1,000 population in Henan and Ningxia province, which had the lowest and the highest DALY lost among the six study areas. Overall, epilepsy caused 1.41 YLLs and 0.67 YLDs per 1,000 population; thus the DALY's lost because of epilepsy was 2.08 per 1,000 population, representing the epilepsy disease burden in rural China.

Conclusions: The DALY measure, which includes the extent of disability from epilepsy, provides a useful tool for the epilepsy disease burden assessment. The disease burden of epilepsy in China is considered higher than previous estimations.

Key Words: Epilepsy—Disability Adjusted Life Year (DALY)—Disease burden.

Both disease-specific measures, such as prevalence and incidence, and the non–disease-specific denominator, the mortality, have been used to measure the disease burden of epilepsy in China. The lifetime prevalence of epilepsy is between three and five per 1,000 population, and the incidence of epilepsy is between 30 and 40 per 100,000 population (Sichuan Medical School, 1981; Li et al., 1985; Zhang 1986, 1987; Xue et al., 1987; Kong et al., 1989; Li, 1989; Yang et al., 1989; Li et al., 1989; Liu et al., 1990; Shan et al., 1992; Kleinman et al., 1995; Zhang et al., 1997; Li et al., 1997; Da, 1997; Hong et al., 2000; Huang et al., 2002; Meng and Hong, 2002). A few studies carried out in China indicate that epilepsy-related mortality is between 3 and 7.9 per 100,000 population (Sichuan Medical School, 1981; Li et al., 1985; Li et al., 1989).

The Global Burden of Disease (GBD) study evaluated the global burden of >200 diseases or injuries by a nonmonetary composite index, Disability Adjusted Life Year (DALY), which could be used to evaluate the impact of mortality and morbidity together. One can also use DALY to compare the impacts of various interventions and health care approaches (Murray and Lopez, 1996). The GBD study estimated the DALYs lost because of epilepsy in the world and in the WHO subregions. The Chinese data used by the GBD study, however, were limited and relied largely on experts’ opinions. These limitations are expected to affect the reliability of the results. Additionally, China is a large country with 33 provinces, which have highly variable climate, geography, and socioeconomic characteristics. The epidemiologic statistics for epilepsy differed greatly in previous studies (Sichuan Medical School, 1981; Li et al., 1985; Zhang 1986,
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Xue et al., 1987; Kong et al., 1989; Li, 1989; Yang et al., 1989; Li et al., 1989; Liu et al., 1990; Shan et al., 1992; Kleinman et al., 1995; Zhang et al., 1997; Li et al., 1997; Da, 1997; Hong et al., 2000; Huang et al., 2002; Meng and Hong, 2002). It may be more appropriate to calculate and analyze the disease burden in different provinces rather than to use one number to represent all of China.

From 2000 to 2004, a WHO supported demonstration project, “Epilepsy Management at Primary Health Level” (EMPHL), was carried out in six study areas in rural China. The prevalence of epilepsy was investigated in each study area with populations about 10,000. Using the latest and most reliable prevalence data obtained from the epidemiologic survey, our study assessed the burden of epilepsy by DALY measurement in these six study areas. The study applied the DALY as an aid to evaluate disease burden and to provide data for a better understanding of the disease burden due to epilepsy in China.

MATERIALS AND METHODS

Case definitions

The EMPHL study involved people with unprovoked seizures (epileptic seizures not associated with a clear precipitant or triggering factor, such as: drugs, fever, acute head injury, acute cerebro-vascular accident, and acute metabolic imbalance) meeting ILAE definitions, including convulsive and non-convulsive types (Wang et al., 2003). The cause category codes of epilepsy were GBD 2000 code: U085; ICD-9 code: 345; and ICD-10 code: G40-G41 (Murray and Lopez, 1996).

Convulsive epilepsy referred to primarily or secondarily generalized tonic clonic (GTC) convulsions, with or without other seizure types. Nonconvulsive seizures included simple partial, complex partial and absence-like seizures.

Study setting and population

The EMPHL study chose six study areas, located in rural areas in Heilongjiang, Henan, Jiangsu, Ningxia, Shanghai, and Shanxi provinces (Figure 1), for the prevalence survey. 66,393 of the total population of 70,462 (94%) in these six rural areas were surveyed (Wang et al., 2002; Wang et al., 2003; Ding et al., 2004).

Age-group definition

We used 7 age groups as follows: 0-4, 5-14, 15-29, 30-44, 45-59, 60-69 and 70+ years (Murray and Lopez, 1996).

Prevalence of epilepsy

The EMPHL study calculated both the lifetime and period prevalence of epilepsy; however the DALY calculation used only the period prevalence (Murray and Lopez, 1996). The period prevalence of epilepsy was defined as the number of people with active epilepsy during the 24 months before the survey date divided by the surveyed target population size.

The prevalence of epilepsy is presented by sex, age group, and study area in table 1. The prevalence of epilepsy ranged from 3.5 (Shanxi) to 6.4 (Ningxia) per 1,000 population within six areas. Except in Shanxi, the prevalence of epilepsy was higher for females than for males. The age-specific epilepsy prevalence was different in the six areas. In Jiangsu and Ningxia, the highest prevalence of both sexes was in the “0–4” year (11.49/1,000) and “5–14” year (8.64/1,000) age groups respectively. In other four areas, however, the peaks of prevalence of both sexes were in the “45–59” or “60–69” year age groups.

Mortality estimates of epilepsy

Epilepsy mortality ranging from 1 to 4.5 per 100,000 population have been reported worldwide; however Chinese studies have reported rates between 3 and 7.9 per 100,000 population (Sichuan Medical School., 1981; Li et al., 1985; Shorvon and Farmer, 1988; Li et al., 1989; Pal et al., 1999). Since mortality could not be obtained from the prevalence survey, we used the average mortality of 6 per 100,000 population reported by Chinese literatures for the calculation of YLLs due to epilepsy according to sex and age group in each of the study areas.

Disability weight

Disability weight (DW) is the parameter used for the severity and classification of disability (Murray and Lopez, 1996). In this study, we used GBD 1990 DW values for epilepsy. For those epilepsy patients with appropriate treatment, DW is 0.041 for the “0–4” year age group, and 0.065 for the other age groups. Appropriate treatment definition includes the diagnosis and management of underlying causes and management of recurrent seizures according to national standards, using antiepileptic drugs.

FIG. 1. Map showing six study areas in China: “1”-Heilongjiang; “2”-Henan; “3”-Jiangsu; “4”-Ningxia; “5”-Shanghai; “6”-Shanxi.
(AEDs) and surgery where indicated (Wang et al., 2003). For those without appropriate treatment, DW is 0.099 for the “0–4” year age group and 0.150 for other age groups (Murray and Lopez, 1996).

**Estimating DALYs**

The Disability Adjusted Life Year (DALY) is an indicator of the time lived with a disability (Years Lived with Disability, YLD) plus the time lost due to premature mortality (Years of Life lost, YLL). YLDs are the disability component of DALYs. The basic formula for calculating YLD is: $\text{YLD} = 1 \times \text{DW} \times \text{L}$, where I is the number of incident cases in the reference period, DW is the disability weight (in the range 0–1) and L is the average duration of disability (measured in years) (Murray and Lopez, 1996).

A general formula for the number of YLDs and YLLs lost by one individual is calculated as:

$$\text{YLD}(L) = \int_{x=a+L}^{x=a} DC_{xe^{-r(x-a)}} dx$$

(Murray and Lopez 1996)

We used the prevalence-based YLD calculation based on the available prevalence data from the EMPHL study. In the YLD formula, a is the age of the epilepsy patient at the survey time; L equals to 1; D is the DW for the age group with/without appropriate treatment to which the individual belongs to.

For the YLL calculation, a is the age at death of the epilepsy patient; D equals to 1; L is the estimated life expectancy of each patient according to age. We used age-specific life expectancies estimated by the WHO in the China life table, 1999 (Lopez et al., 1999).

In the specific form used for calculating DALYs, $r$ refers to the discount rate, (0.03), $\beta$ is the parameter from the age-weighting function (0.04), and $C$ (0.16243) is the age weighted correction constant (Murray and Lopez, 1996). Based on the Dynamic Data Linking (DDL) function of the Microsoft Office Excel, this formula was written in a spreadsheet cell to facilitate calculation of DALYs.

The total loss of YLDs, YLLs and DALYs due to epilepsy were the aggregated results for all the individuals surveyed with epilepsy. The measurement “DALYs per 1,000 population” was used to compare the disease burden by sex and age groups, as well as study area. We used the population of China in 2000 to adjust for the sex and age structures of the population of each study area (National Bureau of Statistics of China, 2000).

**Sensitivity analysis**

We used one-way sensitivity analysis to evaluate the influence of uncertainty about the epilepsy mortality value in the study. We considered the extremes of the plausible range of 3 to 7.9 per 100,000 population as published in the Chinese literature on this subject (Sichuan Medical School, 1981; Li et al., 1985; Li et al., 1989). We also referred to the assessment of epilepsy mortality (1.07/100,000) in China by GBD study (GBD, 2000). We assumed that the sex and age structure remained unchanged when mortality varied within the plausible range.

It’s important to measure the DW of different epilepsy states, as defined by seizure type, seizure frequency, and other variables related to functional status and quality of life (Langfitt and Wiebe, 2002). The EMPHL study found that the mean seizure frequency of epilepsy patients was 10 (4–24) times per year, and the percentage of cases with primarily and secondarily GTC was 68–79% (Wang et al., 2002, Ding et al., 2004). Besides these, the emotional and cognitive problems of people with epilepsy should also be considered although we did not obtain these data from the EMPHL study. To clarify the impact on baseline results by DW variation, we did a one-way sensitivity analysis by using a group of higher DW parameters: 0.082 (treated, “0–4” year age group), 0.13 (Treated, other age groups), 0.3 (untreated, “0–4” year age group), and 0.3 (untreated, other age groups) (Chisholm, 2005).

**RESULTS**

**Estimates of the DALYs**

Table 2 shows that epilepsy caused 1.31 to 1.52 YLLs per 1,000 population in the six study areas in 2000. The YLDs caused by epilepsy ranged from 0.46 to 1.01 per 1,000 population. There were 1.83 and 2.48 DALYs per 1,000 population caused by epilepsy in Henan and Ningxia, which had the lowest and highest DALY lost respectively in six areas. Overall, the YLLs lost for males were higher than those for females, while the YLDs lost for males were lower than those for females except in Shanxi.

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**TABLE 1. The prevalence (cases per 1,000 population) due to epilepsy in six study areas in China, 2000**

<table>
<thead>
<tr>
<th>Areas</th>
<th>Males in age group (years)</th>
<th>Females in age group (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0–4</td>
<td>5–14</td>
</tr>
<tr>
<td>Heilongjiang</td>
<td>0.00</td>
<td>1.21</td>
</tr>
<tr>
<td>Henan</td>
<td>0.00</td>
<td>0.65</td>
</tr>
<tr>
<td>Jiangsu</td>
<td>23.26</td>
<td>2.84</td>
</tr>
<tr>
<td>Ningxia</td>
<td>4.32</td>
<td>8.89</td>
</tr>
<tr>
<td>Shanghai</td>
<td>0.00</td>
<td>2.29</td>
</tr>
<tr>
<td>Shanxi</td>
<td>2.56</td>
<td>3.15</td>
</tr>
</tbody>
</table>

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province. Using the total population of six study areas, we estimated the overall YLLs, YLDs, and DALYs lost due to epilepsy to represent the disease burden of epilepsy in Chinese rural population by adjusting to sex and age structures of the population of China in 2000. As summarized in table 2, epilepsy caused 1.41 YLLs and 0.67 YLDs lost per 1,000 population, thus the DALYs lost due to epilepsy was 2.08 per 1,000 population, representing the epilepsy disease burden in rural China.

The distribution of disease burden within age groups is shown in table 3. The YLLs lost per 1,000 population varied from 0.03 (“0–4” year age group) to 2.53 (“15–29” year age group), whereas the YLDs lost per 1,000 population varied from 0.16 (“70+” year age group) to 0.91 (“45–59” year age group). Over 3.2 DALYs lost per 1,000 population in people with 15–44 years old, indicating that epilepsy caused large disease burden especially in young population with physical labor.

Comparing with GBD study 2000

In the classification of the WHO subregions, China belongs to the subregion of WPRO B. The DALY lost due to epilepsy in rural China, based on the combined data of six study areas, was 2.08 per 1,000 population, which is 2.89 times higher than that of the WPRO B subregion (0.72/1,000) and 1.73 times higher than the worldwide burden (1.20/1,000) as assessed by the GBD study (GBD 2000).

Sensitivity analyses

Table 4 shows the different YLLs and DALYs lost caused by the diverse values of epilepsy mortality and DW. The YLLs and DALYs lost per 1,000 population increased by the mortality. If we use the mortality of 1.07 per 100,000 population provided by the GBD study, the YLLs and DALYs lost due to epilepsy would be 0.25 and 0.93 per 1,000 population respectively in the entire population. The total disease burden, however, would be ranged from 1.37 to 2.53 DALYs (include 0.70 to 1.85 YLLs) lost per 1,000 population based on the lower and upper limits of mortality of 3 and 7.9 per 100,000 population provided by Chinese literatures, respectively. If we use higher DW parameters as shown in table 4, the YLDs and DALYs lost due to epilepsy would be 1.35 and 2.76 per 1,000 population respectively, which is 67% and 33% enhancement of the baseline of the disease burden.

DISCUSSION

We used the prevalence-based calculation methods and estimated that the DALYs lost due to epilepsy per 1,000 population in the six study areas in China ranged from 1.83 in Henan province to 2.48 in Ningxia province in 2000. The overall DALYs lost due to the disease was 2.08 per 1,000 population, representing the epilepsy disease burden in rural China.

### TABLE 2. YLL, YLD and DALY lost per 1,000 population by sex due to epilepsy in six study areas in China

<table>
<thead>
<tr>
<th>Areas</th>
<th>YLL/1,000</th>
<th>YLD/1,000</th>
<th>DALY/1,000</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Total</td>
</tr>
<tr>
<td>Heilongjiang</td>
<td>1.64</td>
<td>1.38</td>
<td>1.52</td>
</tr>
<tr>
<td>Henan</td>
<td>1.39</td>
<td>1.22</td>
<td>1.31</td>
</tr>
<tr>
<td>Jiangsu</td>
<td>1.51</td>
<td>1.19</td>
<td>1.35</td>
</tr>
<tr>
<td>Ningxia</td>
<td>1.53</td>
<td>1.42</td>
<td>1.47</td>
</tr>
<tr>
<td>Shanghai</td>
<td>1.57</td>
<td>1.22</td>
<td>1.39</td>
</tr>
<tr>
<td>Shanxi</td>
<td>1.49</td>
<td>1.29</td>
<td>1.39</td>
</tr>
<tr>
<td>Total^a</td>
<td>1.52</td>
<td>1.30</td>
<td>1.41</td>
</tr>
</tbody>
</table>

^aSum of six study areas adjusted by the sex and age structure of China population in 2000.

### TABLE 3. YLL, YLD and DALY lost per 1,000 population by age group due to epilepsy in the entire population of the six study areas in China

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>YLL/1,000</th>
<th>YLD/1,000</th>
<th>DALY/1,000</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Total</td>
</tr>
<tr>
<td>0–4</td>
<td>0</td>
<td>0.06</td>
<td>0.03</td>
</tr>
<tr>
<td>5–14</td>
<td>0.57</td>
<td>0.33</td>
<td>0.46</td>
</tr>
<tr>
<td>15–29</td>
<td>2.42</td>
<td>2.64</td>
<td>2.53</td>
</tr>
<tr>
<td>30–44</td>
<td>2.88</td>
<td>1.93</td>
<td>2.40</td>
</tr>
<tr>
<td>45–59</td>
<td>0.67</td>
<td>0.60</td>
<td>0.64</td>
</tr>
<tr>
<td>60–69</td>
<td>0.17</td>
<td>0.29</td>
<td>0.23</td>
</tr>
<tr>
<td>70+</td>
<td>0.12</td>
<td>0.34</td>
<td>0.24</td>
</tr>
<tr>
<td>Total^a</td>
<td>1.52</td>
<td>1.30</td>
<td>1.41</td>
</tr>
</tbody>
</table>

^aSum of six study areas adjusted by the sex and age structure of China population in 2000.
TABLE 4. Sensitivity analysis of YLDs, YLLs and DALYs lost per 1,000 population by the plausible range of mortality and a higher DW due to epilepsy in the entire population of the six study areas in China.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>YLD/1,000</th>
<th>YLL/1,000</th>
<th>DALY/1,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.07/100,000b</td>
<td>0.67</td>
<td>0.25</td>
<td>0.92</td>
</tr>
<tr>
<td>3.0/100,000c</td>
<td>0.67</td>
<td>0.70</td>
<td>1.37</td>
</tr>
<tr>
<td>7.9/100,000d</td>
<td>0.67</td>
<td>1.85</td>
<td>2.52</td>
</tr>
<tr>
<td>Disability Weight (DW)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.083±0.13; 0.198±0.3b</td>
<td>1.35</td>
<td>1.41</td>
<td>2.76</td>
</tr>
</tbody>
</table>

- ^a^Sum of six study areas adjusted by the sex and age structure of China population in 2000.
- ^b^Epilepsy mortality in China provided by GBD study based on the national registration data (GBD, 2000).
- ^c^-^d^Lower and upper limit of epilepsy mortality rate published in Chinese literatures (Sichuan Medical School, 1981; Li et al., 1985; Li et al., 1989).
- ^e^-^h^Treated, age group “0–4;” ^f^Treated, other age groups; ^g^Untreated, age group “0–4;” ^h^Untreated, other age groups (Chisholm 2005).

Previous reports relied on incidence, prevalence and mortality data, to reflect the disease burden of epilepsy. The GBD study is the only assessment of the epilepsy disease burden using the DALY measurements. Leonardi et al. reported the only published disease burden for epilepsy which presented detailed YLD, YLD and DALY lost worldwide (Leonardi and Ustun, 2002). Their results were referenced from GBD 2000 study. In 1990, the GBD study estimated the DALYs lost due to epilepsy as 0.81 per 1,000 population in China (Murray and Lopez, 1996). No other DALY-related data in China, however, have been published.

In China, few epidemiologic investigations of epilepsy were conducted between 1980 and 2000 due to difficulties in administration and training for the survey for large sample populations. The studies that were conducted, with different study objectives, screening tools, and diagnostic criteria, showed widely divergent prevalence and incidence of epilepsy (Sichuan Medical School, 1981; Li et al., 1985; Zhang, 1986; Xue et al., 1987; Kong et al., 1989; Li, 1989; Yang et al., 1989; Li et al., 1989; Liu et al., 1990; Shan et al., 1992; Kleinman et al., 1995; Zhang et al., 1997; Li et al., 1997; Da, 1997; Hong et al., 2000; Huang et al., 2002; Meng and Hong, 2002). Even using the same method and criteria in one survey, prevalence still differed among localities (Li et al., 1985; Wang et al., 2002; Ding et al., 2004). This kind of prevalence difference might be related to different economic levels and medical conditions treating causes of epilepsy, such as trauma, infection of the CNS, and cerebrovascular diseases, etc.

The EMPHL study provides reliable epidemiologic data due to its study design and diagnostic criteria with respect to epilepsy. The screening questionnaires of the study were based on the ICBERG screening instrument and the WHO screening questionnaires previously used in China. These questionnaires were validated at the Beijing Neurological Institute with a specificity of 78.5% and a sensitivity of 100%. The epilepsy cases were screened by trained physicians, diagnosed by neurologists and experts at a diagnostic workshop. Both convulsive types and nonconvulsive types of epilepsy were diagnosed in the study (Wang et al., 2002). The study areas were representative not only of the different geographical areas (middle [Henan and Shanxi], southeast [Jiangsu and Shanghai], northeast [Heilongjiang], and northwest [Ningxia]), but also of the different economic levels of China (high [Jiangsu and Shanghai], middle [Henan, Shanxi, and Heilongjiang], and low [Ningxia]). Furthermore, the EMPHL epidemiologic survey provided the age-specific epilepsy prevalence that could be directly used for the prevalence-based calculation of DALY lost due to epilepsy. Comparing to the relatively low epilepsy prevalence and mortality used as the parameters for the DALYs assessment in GBD study, our data seems more reliable and representative of the disease pattern in China. Therefore, the disease burden of epilepsy in China is considered higher than the estimation of GBD study.

There are potential limitations to our study. YLL, which is calculated based on mortality data, was a very important part of DALY assessment. In Chinese literature reports, the mortality of epilepsy is between 3 and 7.9 per 100,000 population, which is higher than that used in the GBD study (1.07/100,000). We therefore performed a sensitivity analysis to consider the impact of this plausible range of mortality to the total disease burden (Table 4). Since the EMPHL study could not survey epilepsy mortality and other recent studies did not provide age and sex specific mortality, we could increase the accuracy of the YLL estimate by obtaining mortality data from investigations of larger sample sizes and longer follow-up in multiple areas of China.

The EMPHL epidemiologic survey was a cross-sectional study in rural areas in China. Although the screening tool had high specificity and sensitivity, and the diagnosis procedure was strict, the prevalence of epilepsy might be underestimated if the subjects conceal or deny their seizure history because of barriers of traditional prejudice, or, for children under 4 years old, partial seizure can not be noticed by the parents. Our results, therefore, might underestimate the disease burden by DALY measurement.

The classification of the disability weight of epilepsy offered by the GBD study seems inappropriate as it did not consider the different types of epilepsy (convulsive and non-convulsive) and the seizure frequency, which affect the quality of life. In the sensitivity analysis, we found 33% enhancement of the baseline of the disease burden by DALY measurement if we used higher DW parameters with double value of that in GBD study, indicating that the result of disease burden was impacted by the DW of epilepsy. Although we used the DW provided by GBD in our study for data comparison with other studies, the DW of epilepsy should be reconsidered.

For the complete assessment of the epilepsy disease burden, DALY measurements should be acquired not only for neurological diseases, but also for all the diseases in different areas of China. Unfortunately, this has not been done. Compared to the disease burden due to neurologic diseases in WPRO B subregion provided by GBD study, however, our result of 2.08 DALYs lost per 1,000 population is lower than that of cerebrovascular disease (9.86 DALYs lost per 1,000 population), and higher than that of Alzheimer’s disease and other dementia (1.76 DALYs lost per 1,000 population) or Parkinson’s disease (0.21 DALYs lost per 1,000 population) (GBD 2000).

Our study demonstrates a method which can be used to assess disease burden and which can be the basis for economic analysis of epilepsy treatment. According to our measurement, there was an overall size of burden of 1,681,410 DALYs lost in rural China based on the rural population of 808,370,000 in 2000 (National Bureau of Statistics of China, 2000). This entire burden can be massively reduced at low cost via effective treatment such as Phenobarbital (Chisholm, 2005; Wang, 2006).

The information provided in this study can help policy planners to allocate resources and identify strategies and interventions for the reduction of the burden of epilepsy in China.

REFERENCES


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