Epilepsy is a significant, but often underappreciated, health problem in Asia. Here, we systematically review the literature on epidemiology, aetiology, and management of epilepsy in 23 Asian countries. Prevalence estimates are available for only 11 countries from door-to-door surveys and are generally low. Figures for annual incidence in China and India are similar to those in the USA and Europe but lower than those reported from Africa and Latin America. There is a peak in incidence and prevalence in childhood, but a second peak in elderly people, as seen in developed countries, has not been documented. The main causes are head injuries, cerebrovascular disease, CNS infections, and birth trauma. Availability of epilepsy care depends largely on economic factors. Imaging and neurophysiological facilities are available in most countries, but often only in urban centres. Costly drugs, a large treatment gap, limited epilepsy surgery, and negative public attitude to epilepsy are other notable features of management in Asia. An understanding of the psychosocial, cultural, economic, organisational, and political factors influencing epilepsy causation, management, and outcome should be of high priority for future investigations.

Introduction
Epilepsy is a disorder of the brain that is characterised by an enduring predisposition to generate seizures and by its neurobiological, cognitive, psychological, and social consequences.1 WHO estimates that eight people per 1000 worldwide have this disease.2 The prevalence of epilepsy in developing countries is usually higher than in developed countries.3–5 Although substantial economic development and improvement of health services have occurred, Asia is a heterogeneous and resource-constrained continent. Over half of the 50 million people with epilepsy worldwide are estimated to live in Asia. Although much research is done in Asia, information about the recognition of the burden created by the disease is scarce. In 1997, Jallon6 reviewed studies from Asia, mostly done in the 1980s, and showed a prevalence varying from 1·5 per 1000 in Japan to 10·0 per 1000 in Pakistan. Here, we provide an update on prevalence, incidence, demographic data, types of epilepsy, aetiology, treatment, and prognosis in recent years to give a comprehensive view of epilepsy in this region.

Methods
Search strategy and selection criteria
We searched the PubMed database by using the keyword “epilepsy”, combined with each of the following: “epidemiology”, “prevalence”, “incidence”, “aetiology”, and “treatment” for each Asian country. Other words were also used in association with the keywords. These were “malaria”, “neurocysticercosis”, “cysticercosis”, “encephalitis”, “classification”, “mortality”, “therapy”, “antiepileptic”, “AEDs”, “surgery”, “chirurgical”, “recurrence”, “prognosis”, “stigma”, “stigmatization”, “knowledge”, and “awareness”. Asian countries (n=23) were defined as the countries of the WHO Western Pacific region and WHO Southeast Asian region: Bangladesh, Bhutan, Brunei, Cambodia, China, North Korea, India, Indonesia, Japan, Laos, Malaysia, Maldives, Mongolia, Burma, Nepal, Pakistan, the Philippines, South Korea, Singapore, Sri Lanka, Thailand, East Timor, and Vietnam. All issues of Neurology Asia and of the national medical journals of Korea (Journal of Korean Medical Science), Singapore (Singapore Medical Journal) and India (Neurology India) were hand-searched with the same criteria. Articles were included if they had at least an abstract in English or French. We included only studies reaching the recommendations of the International League Against Epilepsy (ILAE) 1993 Commission.8 Background references were identified through these searches and through searches of the authors’ own files.

Data collection and analysis
A total of 1348 articles from 20 countries were found using PubMed. No publications were found from Bhutan, Brunei, or North Korea. Most articles originated from Japan (460 articles), India (343 articles), and China (165 articles). Articles were assessed by the first two authors searching in each survey for methods and results on prevalence, incidence, demographic, classification, causes, treatment, and knowledge, attitudes, and practice. Data from 119 articles were collected for this Review (see figure for more detail on the selection process).

Results
Prevalence
The lifetime prevalence of epilepsy varied among countries from 1·5 to 14·0 per 1000 (table 1).13–30 This wide variation could partly result from the use of different methods and different types of questionnaire. Screening questionnaires were mainly derived from WHO questionnaires, but two studies used Limoges’ questionnaire.29,30 The median lifetime prevalence is estimated at 6 per 1000, which is lower than in developing countries in other areas of the world (15 per 1000 in sub-Saharan Africa and 18 per 1000 in Latin America).43 An understanding of these differences could generate

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hypotheses for studies aimed at identifying ways to prevent this disease: for example, is there a protective factor in Asia or specific risk factors in Africa or Latin America?

Incidence
Incidence rates were available from only two countries, China and India; of the five estimates, three were based on retrospective analyses of collections of prevalence data (table 2).9,12,17,18,31 The epilepsy incidence rates reported from China were low—from 28·8 per 100 000 person-years9 to 35·0 per 100 000 person-years in the general population.12 The results from India were higher, and reached 60·0 per 100 000 person-years.31 Overall, the results were not different from those in developed countries where the age-adjusted incidence of epilepsy is 24–53 per 100 000 person-years.32 Some authors report an incidence rate in developing countries that is as high as 190 per 100 000 person-years.33,34 Confirmation of low incidence rates in Asia would be very important, and rigorous population-based prospective studies are needed.

Demographic indicators
Age
The publications included in this Review show one peak age for incidence in children19,26 and one peak age for prevalence in young adults.12–13,16,19,35–38 However, one study, done in Shanghai, showed two prevalence age peaks: one between 10 and 30 years old and one in people over 60 years old.11 These figures are summarised in table 3.11,13,16,19,26,35–38

In developed countries, the incidence and prevalence of epilepsy both follow a bimodal distribution with a first peak in childhood and another in old age.32,39,40 The most probable reason for the missing peak in the older age groups in many Asian countries is the relatively young population compared with that in more developed regions.

Sex
Epilepsy is slightly more common in men than in women but the sex-specific prevalence is not, in general, significantly different (table 4).23,31,36,37,39–41 However, one study, done in Shanghai, showed two prevalence age peaks: one between 10 and 30 years old and one in people over 60 years old.11 These figures are summarised in table 3.31,36,37,39–41

In developed countries, the incidence and prevalence of epilepsy both follow a bimodal distribution with a first peak in childhood and another in old age.32,39,40 The most probable reason for the missing peak in the older age groups in many Asian countries is the relatively young population compared with that in more developed regions.

Location
Two studies (in Pakistan and in India) indicated that the prevalence was higher in rural areas than in urban areas.9,29 Although not significant, a meta-analysis of published and non-published community-based studies in India showed a higher prevalence of 5·5 per 1000 (95% CI 4·0–6·9) in rural areas than that of 5·1 per 1000 (3·5–6·7) in urban areas.9 Indeed, a higher prevalence in rural areas is a common tendency in developing countries.9

Mortality
Data on mortality rate in Asian people with epilepsy are scarce, and those that are available indicate high rates in

Table 2: Prevalence of epilepsy in Asia

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>N</th>
<th>Prevalence/1000</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>China (five provinces)</td>
<td>2002 and 2003</td>
<td>55 000</td>
<td>7 0</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>China (Shanghai)</td>
<td>2002</td>
<td>48 628</td>
<td>3 6*</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>China (six cities)</td>
<td>1985</td>
<td>63 195</td>
<td>4 4</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>India (West Godavari)</td>
<td>2004</td>
<td>74 086</td>
<td>6 2</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>India (Kerala state)</td>
<td>2000</td>
<td>238 102</td>
<td>4 7†</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>India</td>
<td>1998</td>
<td>64 963</td>
<td>3 9†</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>India</td>
<td>2006</td>
<td>50 617</td>
<td>3 8†</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>Laos</td>
<td>2006</td>
<td>43 10</td>
<td>7 7†</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>Turkey</td>
<td>1997</td>
<td>11 457</td>
<td>7 0†</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>Pakistan</td>
<td>1994</td>
<td>24 130</td>
<td>10 0†</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>Vietnam</td>
<td>2005</td>
<td>66 17</td>
<td>10 7†</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>Nepal</td>
<td>2003</td>
<td>46 36</td>
<td>7 3</td>
<td>Community-based</td>
</tr>
<tr>
<td>Taiwan</td>
<td>1997</td>
<td>10 058</td>
<td>2 4</td>
<td>Community-based</td>
</tr>
<tr>
<td>Taiwan</td>
<td>2001</td>
<td>15 663</td>
<td>2 8†</td>
<td>Community-based</td>
</tr>
<tr>
<td>Thailand</td>
<td>2002</td>
<td>20 69</td>
<td>7 2</td>
<td>Community-based</td>
</tr>
<tr>
<td>Singapore</td>
<td>1997</td>
<td>20 542</td>
<td>5 0</td>
<td>Men at 18 years old</td>
</tr>
<tr>
<td>Singapore</td>
<td>1997</td>
<td>96 047</td>
<td>3 5</td>
<td>Review &lt;5 years</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>2003</td>
<td>NA</td>
<td>1 5</td>
<td>Estimation in adult patients (≥15 years)</td>
</tr>
<tr>
<td>Vietnam</td>
<td>2003</td>
<td>NA</td>
<td>1 40</td>
<td>Estimation</td>
</tr>
<tr>
<td>India</td>
<td>14</td>
<td>2002</td>
<td>NA</td>
<td>5 6</td>
</tr>
<tr>
<td>India</td>
<td>17</td>
<td>2002</td>
<td>NA</td>
<td>5 0</td>
</tr>
</tbody>
</table>

N=sample size. NA=not available. *Active epilepsy (seizures within the previous year). †Active epilepsy (seizures within the previous 5 years). Otherwise, details of disease duration were not available.

Figure: Study selection for the systematic review
*Articles that were not specifically on epilepsy in Asia, except analytical studies on epilepsy risk factors. †Articles that were not within the framework of this review.

Table 1: Prevalence of epilepsy in Asia
developing countries in this region. In one study in Laos, there was a very high case-fatality rate of 90·9 per 1000 person-years. This study was in a mountainous region, in which very few people had access to antiepileptic drugs. These data came from a management project after door-to-door screening. The number of patients followed-up was small, but the results might not be too far from the real mortality rate, because almost all patients in Laos were not adequately treated and Laos is one of the least developed countries in this region. A recent study found a standardised mortality ratio of 3·9 among 2455 people with epilepsy who participated in an assessment of epilepsy management at the primary health-care level in rural China. Mortality is also usually high in developing countries in other regions of the world: 28·9 per 1000 person-years in a rural area of Cameroon and 31·6 per 1000 person-years in rural central Ethiopia. Other studies should be done to confirm this higher mortality rate in Asia, which might partly explain the low prevalence rate.

By contrast, mortality in the most developed countries in Asia is low. A study of childhood epilepsy in a Japanese general population showed a mortality of 45·0 per 1000 people accumulated over a long follow-up period (mean: 18·9 years). Another study in adult Taiwanese patients showed a mortality of 9 per 1000 person-years. Patients with epilepsy in Taiwan had a nearly 3·5 times higher risk of death than the general population (standardised mortality ratio 3·47, 95% CI 2·46–4·91).

**Table 2: Incidence of epilepsy in Asia**

<table>
<thead>
<tr>
<th>Reference Year</th>
<th>N</th>
<th>Incidence/100 000 person-years</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>China (five provinces) 9 2002</td>
<td>55 616</td>
<td>28·8</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>China 12 1985</td>
<td>61 195</td>
<td>35·0</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>India 18 1998</td>
<td>64 963</td>
<td>49·3</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>India 1999 NA 60·0</td>
<td>Estimation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>India 17 2002</td>
<td>38 0-49·3</td>
<td>Review</td>
<td></td>
</tr>
</tbody>
</table>

N=sample size. NA=not available.

**Table 3: Age distribution of patients with epilepsy in Asia**

<table>
<thead>
<tr>
<th>Reference Year</th>
<th>Age peak (years)</th>
<th>Mean age of onset (years)</th>
<th>% children (&lt;18 years)</th>
<th>N</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>China (Shanghai) 11 2002</td>
<td>10–30, &gt;60</td>
<td>NA</td>
<td>NA</td>
<td>151</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>India 16 2000</td>
<td>10–19</td>
<td>NA</td>
<td>NA</td>
<td>1175</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>Laos 19 2006</td>
<td>11–20</td>
<td>NA</td>
<td>NA</td>
<td>33</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>Pakistan 26 1997</td>
<td>NA</td>
<td>NA</td>
<td>74·3</td>
<td>241</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>Turkey 26 1997</td>
<td>NA</td>
<td>NA</td>
<td>72·0</td>
<td>81</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>Hong Kong 13 2003</td>
<td>25–30</td>
<td>19·9</td>
<td>NA</td>
<td>736</td>
<td>Adult patients in hospital</td>
</tr>
<tr>
<td>India 37 1999</td>
<td>14·3</td>
<td>NA</td>
<td>972</td>
<td>Hospital-registered patients</td>
<td></td>
</tr>
<tr>
<td>India 35 1999</td>
<td>10–19</td>
<td>NA</td>
<td>NA</td>
<td>525</td>
<td>Review</td>
</tr>
<tr>
<td>Bangladesh 36 2004</td>
<td>16–31</td>
<td>NA</td>
<td>NA</td>
<td>Review</td>
<td></td>
</tr>
<tr>
<td>Hong Kong 38 1997</td>
<td>NA</td>
<td>NA</td>
<td>2952</td>
<td>Review of outpatient records</td>
<td></td>
</tr>
</tbody>
</table>

N=number of patients with epilepsy. NA=not available.

**Table 4: Gender proportions and gender-adjusted prevalence in patients with epilepsy in Asia**

<table>
<thead>
<tr>
<th>Reference Year</th>
<th>Male (%)</th>
<th>Female (%)</th>
<th>Male prevalence (%)</th>
<th>Female prevalence (%)</th>
<th>N</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>China (Shanghai) 11 2002</td>
<td>NA</td>
<td>NA</td>
<td>3·6</td>
<td>25</td>
<td>151</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>Turkey 26 1997</td>
<td>54·3</td>
<td>45·7</td>
<td>8·7</td>
<td>6·3</td>
<td>81</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>India 18 1998</td>
<td>NA</td>
<td>NA</td>
<td>4·4</td>
<td>3·4</td>
<td>254</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>Laos 19 2006</td>
<td>66·6</td>
<td>33·4</td>
<td>NA</td>
<td>NA</td>
<td>33</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>Pakistan 26 1997</td>
<td>49·8</td>
<td>50·2</td>
<td>9·2</td>
<td>10·9</td>
<td>241</td>
<td>Door-to-door survey</td>
</tr>
<tr>
<td>Nepal 20 2003</td>
<td>NA</td>
<td>NA</td>
<td>6·8</td>
<td>7·9</td>
<td>34</td>
<td>Community based</td>
</tr>
<tr>
<td>Hong Kong 13 2003</td>
<td>57·1</td>
<td>42·9</td>
<td>NA</td>
<td>NA</td>
<td>736</td>
<td>Adult patients in hospital</td>
</tr>
<tr>
<td>Hong Kong 38 2001</td>
<td>54·3</td>
<td>45·7</td>
<td>NA</td>
<td>NA</td>
<td>2952</td>
<td>Review of outpatient records</td>
</tr>
<tr>
<td>Singapore 23 1997</td>
<td>50·1</td>
<td>49·9</td>
<td>3·5</td>
<td>3·5</td>
<td>336</td>
<td>Review &lt;5 years</td>
</tr>
<tr>
<td>India 35 1999</td>
<td>NA</td>
<td>NA</td>
<td>5·9</td>
<td>5·5</td>
<td>3207</td>
<td>Meta-analysis</td>
</tr>
</tbody>
</table>

N=number of patients with epilepsy. NA=not available.
convulsions in 23·7 per 1000.\textsuperscript{a} The most common cause, febrile convulsions, was documented in 396 (44·9%) deaths. Neonatal and infantile convulsions accounted for 186 (21·1%) deaths. Other causes of death associated with seizures included chest complications (60; 6·8%), drowning (28; 3·2%), asphyxia (20; 2·3%), status epilepticus (19; 2·2%), burns (7; 0·8%), and poisoning (2; 0·2%).\textsuperscript{47} In this study, deaths due to convulsive disorders showed a decrease from 37·3 per 1000 people in 1967 to 9·5 per 1000 people in 1987.\textsuperscript{47} Mortality from status epilepticus in patients in a large community hospital in Hong Kong from 1996 to 2001 was 16·0%. Predictors of mortality were older age (OR 1·04, 95% CI 1·01–1·07), a delay in starting treatment (3·52, 1·01–12·18), status epilepticus due to cerebrovascular disease (9·73, 1·58–59·96), and CNS infection (30·27, 3·14–292·19).\textsuperscript{46} Complications related to steroid treatment for intractable epilepsy were also an important cause of death as seen in Hong Kong.\textsuperscript{47} Specific mortality rates for the main causes of death must be estimated in Asia to enable better prevention.

**Prognosis**

In general, a third to two-thirds of patients will have recurrent seizures within 5 years of the first unprovoked seizure.\textsuperscript{34,35} Similar recurrence rates are seen in Asia. A study in Thai children showed a cumulative risk of recurrence of 25% at 14 days, 50% at 4 months, 51% at 6 months, and 66% at 12 months.\textsuperscript{31} In children treated for epilepsy, follow-up after withdrawal of antiepileptic drugs (average duration 43·5 months) showed a cumulative risk of recurrence of 10% at 12 months and 12% at 36 months.\textsuperscript{52} The need for two AEDs to control seizures was a risk factor for recurrence (incidence 0·025 vs 0·001, \(p=0·002\)). Another study in India noted seizure recurrence in 31% of patients (of all ages) during a follow-up period of 18 months. Longer duration of active epilepsy (relative risk 2·86, 95% CI 2·35–3·48) and a higher number of seizures before seizure control (1·50, 1·30–1·73) increased the risk of recurrence. Seizure-free duration before beginning drug withdrawal (2 years vs 4 years) did not significantly influence this risk.\textsuperscript{34}

Surgery for intractable temporal-lobe epilepsy led to good results in a study in Indonesia.\textsuperscript{35} Of 56 patients who had anterior temporal lobectomy with amygdalo-hippocampectomy, 46 patients (82·0%) were seizure-free (Engel I). Six patients (11%) had fewer than two seizures per year (Engel II), and seizures decreased by more than 75% (Engel III) in four patients (7%). Complications included extradural empyema in five patients (9%), depression in two patients (4%), and transient hemiparesis in one patient (2%). 31 patients were able to stop taking antiepileptic drugs. The follow-up varied between 12 and 76 months. This is the only description found in Asia on epilepsy surgery, an efficient solution for intractable epilepsy. Few patients in Asia can benefit from this therapy even if it is available in several countries (see Surgery section).

**Clinical classification**

Numerous clinical studies have been published but few have described the distribution of seizure types in community-based studies. In addition, comparison of the results from different studies is difficult because classifications used are not homogeneous. Here, we present only the results based on the 1981 ILAE classification (table 5).\textsuperscript{13,16,19,22,49,54–59}

The range of patients with generalised seizures was 50–69%, and 31–50% had partial seizures.\textsuperscript{13,19,22,26} The prevalence rates of symptomatic, idiopathic, and cryptogenic epilepsy were 22–53%, 4–42%, and 13–60%, respectively.\textsuperscript{13,19,38,40,41,57} The predominance of generalised epilepsy and wider range of cryptogenic epilepsy may be

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Seizure type classification</th>
<th>Aetiological classification</th>
<th>N</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>16</td>
<td>2000</td>
<td>GS 58.8</td>
<td>FS 30.6</td>
<td>US NA</td>
</tr>
<tr>
<td>Laos</td>
<td>19</td>
<td>2006</td>
<td>GS 63.6</td>
<td>FS 27.3</td>
<td>US 9.1</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>13</td>
<td>2002</td>
<td>GS NA</td>
<td>FS NA</td>
<td>US NA</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>19</td>
<td>2002</td>
<td>GS NA</td>
<td>FS NA</td>
<td>US NA</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>19</td>
<td>2002</td>
<td>GS NA</td>
<td>FS NA</td>
<td>US NA</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>19</td>
<td>2002</td>
<td>GS NA</td>
<td>FS NA</td>
<td>US NA</td>
</tr>
<tr>
<td>India</td>
<td>57</td>
<td>2005</td>
<td>GS 42.0</td>
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<td>Malaysia</td>
<td>58</td>
<td>1993</td>
<td>GS 86.0</td>
<td>FS 14.0</td>
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</tr>
<tr>
<td>Malaysia</td>
<td>58</td>
<td>1993</td>
<td>GS 92.0</td>
<td>FS 8.0</td>
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<td>1993</td>
<td>GS NA</td>
<td>FS NA</td>
<td>US NA</td>
</tr>
<tr>
<td>Singapore</td>
<td>22</td>
<td>1997</td>
<td>GS 69.0</td>
<td>FS 31.0</td>
<td>US NA</td>
</tr>
<tr>
<td>Singapore</td>
<td>22</td>
<td>1997</td>
<td>GS 29.0</td>
<td>FS 64.0</td>
<td>US 7.0</td>
</tr>
</tbody>
</table>

GS=generalised seizures. FS=focal seizures. US=unclassified seizures or multiple seizure types. IE=idiopathic epilepsy. CE=cryptogenic epilepsy. SE=symptomatic epilepsy. N=number of patients with epilepsy. PWE=people with epilepsy. EEG=electroencephalogram. *This figure applies to IE and CE combined.
due to differences in the extent of imaging studies and the lack of standardised classification and terminology in epilepsy research in Asia. Electroencephalographic data were often not available, which could also have influenced the proportions of idiopathic epilepsy reported in several studies. Population-based studies with electroencephalographic recording are required to enable accurate clinical classification of epilepsy in Asia.

Causes
There are very few studies on the causes of epilepsy in Asian populations, and there are particularly few case–control studies or cohort studies. From the available literature, causes seem to be dominated by head injury, birth trauma, and intracranial infections, such as neurocysticercosis or meningoencephalitis. Where socioeconomic development is better, head trauma and stroke are the leading causes of epilepsy. In China in the 1980s, brain injury, intracranial infection, and cerebrovascular disease, in that order, were the leading putative causes of epilepsy.12 Cases reported from China during 1994–2003 allowed the estimation of an average incidence of 8.7% for epilepsy with cerebrovascular disease and of 8% with post-traumatic epilepsy.40 In patients in Hong Kong, the commonest causes were cerebrovascular disease (26.2%), a history of CNS infection (26.0%), head trauma (11.4%), perinatal insult (9.7%), congenital brain malformation (7.4%), hippocampal sclerosis (5.9%), and intracranial neoplasm (5.6%).41 By contrast, in 300 incident cases of epilepsy in Nepal 42% were caused by neurocysticercosis, 9% by tumour, 4% by vascular disease, and 2% by head injury.42 In this section, we elaborate on these causes of epilepsy in Asia.

Head injury
In Asia, post-traumatic epilepsy is one of the most common complications of head injury. One study claimed that post-traumatic epilepsy accounted for 5% of total epilepsy and 20% of symptomatic epilepsy.40 A history of major brain trauma (20.9%) was also the leading cause of epilepsy in surgically treated patients in China.42

CNS infections
In developing countries in other regions of the world, such as sub-Saharan Africa or Latin America, CNS infections seem to explain the high prevalence of epilepsy. The Commission on Tropical Disease of the International League Against Epilepsy listed several diseases as causes of epilepsy, including malaria, tuberculosis, schistosomiasis, AIDS, and cysticercosis—among these, the latter seems to be the most common cause of epilepsy.42 In Asia, there is a lack of rigorous analytical studies to assess the effect of these infections in epilepsy.

An association between neurocysticercosis and epilepsy was found in numerous studies in Africa43 and Latin America.44-46 Neurocysticercosis was the cause of epilepsy in about 50% of patients in some studies,45,46 and seizures occur in 50–80% of patients with parenchymal cysticercosis.47 In Asia, many studies report the presence of cysticercosis (taeniasis).48-52 However, there are few studies on the relation between neurocysticercosis and epilepsy in Asia, and their results vary widely. Neurocysticercosis is probably an important cause of seizures and epilepsy in regions with a high prevalence of Taenia solium infection in human beings. In Asia, this includes India, Nepal, Bali, Papua and Sulawesi in Indonesia, and parts of Vietnam and China. Cysticercosis is only rarely detected in the most economically advanced countries of Asia, such as South Korea,53 but the prevalence might also be low in poor regions.54,55 In a meta-analysis, seizures were the most common symptom (56.2%) of cysticercosis in China.56 Another study noted that between 8.7% and 50.0% of cysticercosis-infected patients had recent seizures.57 Single CT enhancing lesions and neurocysticercosis together accounted for 67% of the provoking factors of acute symptomatic seizures.58 Conversely, in some studies, the cysticercosis seropositivity was not higher in patients with epilepsy in regions with either a low prevalence (eg, Laos59) or a high prevalence (eg, Indonesia60).

Paragonimiasis is endemic in several Asian countries: China, South Korea, the Philippines, Japan, and Vietnam.61,62 During migration, the causal lung fluke may reach the brain and may cause seizures, epilepsy, and other neurological syndromes.63-65 However, no study has quantified the importance of Paragonimus infection in epilepsy.

Malaria is still widely endemic in Asia, with more than 3 million cases per year. India, Burma, Indonesia, Pakistan, Cambodia, Papua New Guinea, and Bangladesh each have more than 50 000 cases per year.66 Malaria causes various symptoms, such as fever and convulsions. 7.7% of patients with childhood malaria (with or without the presence of cerebral malaria) in a retrospective survey in Thailand had convulsions.67 In cerebral malaria, convulsions present in 60% of cases.68 However, we did not find any analytical study reporting the relation between malaria and epilepsy in Asia. Nevertheless, the link between epilepsy and malaria was recently supported by a case–control study in Gabon and a cohort study in Mali in Africa.69-71

Japanese encephalitis is one of the most common encephalitic disorders worldwide. Most of China, southeast Asia, and the Indian subcontinent are affected.72 65% of patients with Japanese encephalitis have acute symptomatic seizures and 13% have chronic epilepsy.73 In a study in India, 30 of 65 patients with Japanese encephalitis had seizures in the first weeks of illness; 19 of them had two or more seizures.74

Genetic factors
Two studies in India found no relation between being a twin and epilepsy, and twins of people with epilepsy did not have a high risk of epilepsy.75,76 Case–control studies in
China have found no relation between epilepsy and susceptibility genes, such as \textit{GABAB1}, \textit{KHDRBS3} (T-STAR), and \textit{CACNA1G} (calcium channel, voltage dependent, T-Type, alpha 1G subunit). However, numerous studies have confirmed familial history of epilepsy and parental consanguinity as risk factors. In Kerala, south India, a family history of epilepsy was three times more common in patients with epilepsy than in controls (OR 3·2, 95% CI 2·1–4·7) and two times higher in another study in north India (2·1, 1·1–4·3). Family history was also a risk factor for epilepsy in studies in Laos and China. This level of risk is similar to that in studies from Africa.

In Asia, consanguineous marriage is common in certain cultures, in particular among Indian and Muslim populations. Consanguinity of parents was significantly more common among patients than among controls (13·1% vs 6·6%). The odds ratio for parental consanguinity was higher in patients with generalised epilepsy than for controls (2·6; 95% CI 1·5–4·4). Another study of 316 patients with epilepsy of Indian origin in Malaysia showed that 29·5% of them had a parental consanguineous marriage, and that there was a significant association with parental consanguinity in idiopathic and cryptogenic epilepsies. Consanguinity could be a target for a campaign to prevent epilepsy.

Epilepsy care

Typically, there is great variability in the case management of epilepsy among different countries. In southeast Asia, this variability depends on factors such as the economic status, the quality of the health system and peripheral services, rural or urban residence, and the cultural frameworks of societies.

\textbf{Health-care facilities}

According to WHO, the median number of hospital beds for epilepsy care per 100 000 population is very low in Asia: 0·05 in southeast Asia and 0·46 in the Western Pacific—fewer than in Africa (0·55) and far fewer than in Europe (1·65). Similarly, the number of neurologists is extremely low in most Asian countries. In 2004, in India, Laos, and Bangladesh, WHO estimated that there was fewer than one neurologist per million inhabitants. In Japan, there are between one and 50 neurologists per million people, and a proportion of these neurologists work in the public sector. In 2001, a comparative study of epilepsy reference centres in Europe and Asia showed that medical specialists in Asia examined more patients per day in walk-in clinics than did their European counterparts. The development of epilepsy care is commonly driven by epileptologists—neurologists with a special interest in epilepsy. If an epileptologist is defined as someone who has had a period of fellowship after training in general neurology, only Japan, South Korea, Singapore, and Taiwan have at least one epileptologist per million people. Paramedical professionals, such as nurses, occupational therapists, and educators rarely participate in the management of epilepsy in Asia—another difference from epilepsy care in Europe.

Technologies such as electroencephalography, CT, and MRI used in epilepsy diagnosis are widely available in Asian countries, but their accessibility varies in the different geographical regions. In developed economies, such as Japan, South Korea, Singapore, and Taiwan, sophisticated facilities are highly accessible to most of the population, whereas almost no electroencephalography or imaging facilities are available in other countries, such as Cambodia, East Timor, Laos, or Mongolia. In addition, many of these facilities are privately operated and available only in big cities, with MRI being mainly used for assessments for epilepsy surgery. However, the development of these facilities is changing rapidly.

Currently, there are 15 ILAE chapters in Asia. They are located in Bangladesh, China and Hong Kong, India, Indonesia, Japan, South Korea, Malaysia, Mongolia, Nepal, Pakistan, the Philippines, Taiwan, Thailand, and Singapore. These chapters are absent in the less developed nations.

\textbf{Antiepileptic drugs}

Antiepileptic drugs are the simplest and the safest means of controlling epilepsy. Various first-generation antiepileptic drugs—phenytoin, carbamazepine, valproic acid, phenobarbital, clonazepam, primidone, and ethosuximide—are used widely in Asian countries (table 6), and monotherapy is common. The particular drug used depends on the medical culture and practices in each country.

Second-generation antiepileptic drugs, such as lamotrigine, gabapentin, tiagabine, felbamate, vigabatrin, or topiramate, are used widely in China, India, and Singapore and in some of the economically less developed countries, including the Philippines and Vietnam. Clobazam, oxcarbazepine, and levetiracetam are available in large Asian countries, such as India, but are prohibitively expensive. Access to drugs is probably easier in Asia than in Africa but this varies widely according to the context (degree of development, urbanisation, etc). Although first-generation antiepileptic drugs are predominant, there are availability and accessibility problems in several places. In 2003, a study in Long Xuyen, Vietnam, showed that drugs were available but only for a short period of time. Moreover, these antiepileptic drugs were sold in pharmacies that were located in only a small area in the city centres. In most parts of Asia, there are limited amounts of or no subsidised antiepileptic drugs. The patients and families have to pay beyond their means for even the most common first-generation drugs. For example, the yearly cost of 100 mg daily phenobarbital, one of the cheapest drugs, is about US$30 in Laos, which is about the monthly salary of a school teacher; in north India, this cost is US$11. In consequence, almost all patients would not be able to have long-term treatment if it...
is not funded. The average annual cost (direct and indirect) of outpatient treatment of epilepsy is US$47 per patient. In general, the cost of phenobarbital in southeast Asia is 2.7 times higher than in Europe, and two to six times higher than in sub-Saharan Africa. The annual cost incurred in emergency and inpatient management in India is estimated to be US$810.50 and US$168.30, respectively, for all the patients attending a secondary hospital. In general, the cost of treatment is much lower than productivity losses, and it would be cost efficient for governments or societies to invest in epilepsy treatment.

Epilepsy control assessment

Treatment with phenobarbital was assessed in 2455 Chinese patients from rural areas in a community-based intervention trial. In 68% of patients who completed 12 months’ treatment, seizure frequency was decreased by at least 50%, and a third of patients were seizure-free. 72% of patients who completed 24 months’ treatment had at least 50% reduction in seizure frequency and a quarter of patients remained seizure-free. 597 patients discontinued treatment before the end of the study. Many of those withdrew because of a misunderstanding that they were cured on becoming seizure-free (28%); others withdrew because they perceived the treatment to be ineffective (16%). Only 5% discontinued the treatment because of adverse events. Another study in India showed that strict drug compliance and early treatment (with phenobarbital or phenytoin or both) were important predictors of a 2 year terminal remission.

Treatment gap

The treatment gap was defined by a workshop of the ILAE as the difference between the number of people with active epilepsy (defined in this case as two or more unprovoked seizures on different days in the previous year) and the number whose seizures are being appropriately treated in a given population at a given point in time, expressed as a percentage. In developing countries in sub-Saharan Africa and Latin America, up to 90% of people with epilepsy receive inadequate treatment or no treatment at all. In Asian countries, the treatment gap was 29–98%, with values for most countries between 50% and 80%. The treatment gap was higher in rural areas than in urban areas (table 7).

Table 6: Use of antiepileptic drugs in Asian countries

<table>
<thead>
<tr>
<th>Reference</th>
<th>First or second-generation AEDs</th>
<th>Monotherapy or polytherapy</th>
<th>AEDs used</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hong Kong</td>
<td>61 First and second</td>
<td>Monotherapy: 57.4%</td>
<td>Phenytoin used in 38.7%</td>
<td></td>
</tr>
<tr>
<td>India</td>
<td>39 First</td>
<td>Polytherapy: 57.8% (entry) and monotherapy: 76.4% (follow-up)</td>
<td>Carbamazepine used at entry and at follow-up</td>
<td></td>
</tr>
<tr>
<td>India (secondary level hospital)</td>
<td>105 NA</td>
<td>Polytherapy: 20.8%</td>
<td>Phenytoin used in 93.0%</td>
<td></td>
</tr>
<tr>
<td>India (university medical centres)</td>
<td>106 First and second</td>
<td>Polytherapy: 24.5% and monotherapy 75.5%</td>
<td>Carbamazepine used in 47.4%</td>
<td></td>
</tr>
<tr>
<td>Indonesia</td>
<td>107 First and second</td>
<td>NA</td>
<td>NA</td>
<td>Availability of AEDs depending on urban or rural area</td>
</tr>
<tr>
<td>Nepal (hospital)</td>
<td>20 First</td>
<td>NA</td>
<td>NA</td>
<td>AEDs used depending on geographical location. Monotherapy: with carbamazepine used at &gt;92% in one hospital</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>108 First</td>
<td>Monotherapy: 75.0%</td>
<td>Carbamazepine used in 48.0%</td>
<td></td>
</tr>
<tr>
<td>Sri Lanka (hospital)</td>
<td>109 First</td>
<td>Monotherapy: 70.8%</td>
<td>Carbamazepine</td>
<td></td>
</tr>
<tr>
<td>Taiwan</td>
<td>110 First</td>
<td>Polytherapy: 0.6% and monotherapy: 29.4%</td>
<td>Carbamazepine used in 78.4%</td>
<td></td>
</tr>
<tr>
<td>Taiwan</td>
<td>111 First</td>
<td>Monotherapy: 61.0%</td>
<td>Carbamazepine used in 56.9%</td>
<td></td>
</tr>
<tr>
<td>Thailand</td>
<td>112 NA</td>
<td>Polytherapy: 58.6%</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

First-generation antiepileptic drugs (AEDs): phenytoin, carbamazepine, valproic acid, phenobarbital, clonazepam, primidone, ethosuximide. Second-generation AEDs: lamotrigine, gabapentin, tiagabine, felbamate, vigabatrin, topiramate. NA=not available.

References Year Treatment gap (%)
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China 9,10 2002 (and 2003) 62.6
India 120 2003 50.0–70.0
India 121 2002 73.0–78.0
India (semi-urban) 16 2000 38.0
India (rural) 25 1999 >70.0
India (rural) 121 1999 54.0
India (rural) 122 1997 78.0
India (semi-urban) 123 1997 57.0
India (rural) 124 1988 74.5
India (urban) 125 1988 29.0
Nepal 126 2004 >70.0
Pakistan (rural) 21,26 1994 (and 1997) 98.0
Pakistan (urban) 21,26 1994 (and 1997) >72.0
Turkey 26 1997 70.0
Surgery

The ILAE reported the presence of epilepsy surgery centres in 26 countries worldwide from 1980 to 1990; at that time, only four Asian countries were on the list: Japan, China, Taiwan, and Vietnam. More recent reports revealed some others in Hong Kong, India, Iran, North Korea and South Korea, the Philippines, Singapore, Thailand, and Turkey. A cohort study of patients with medically refractory temporal-lobe epilepsy in India showed a significantly better outcome of surgery (77.0% seizure-free, 32.7% off medication) compared with medical treatment (11.5% seizure-free, 0.8% off medication). There was no statistically significant difference in mortality between the two groups.

Concepts of disease and use of traditional, complementary, and alternative medicine

There are few dedicated studies on the concepts of disease and use of traditional, complementary, and alternative medicine among patients with epilepsy in Asia, although many clinicians practising in the region have reported widespread use of traditional medicine and spiritual medium, particularly in rural areas. Tan and Lim reported prevalence of syncretism (i.e., simultaneously holding to concepts from different schools of thought) in concepts and practice among the ethnic Chinese patients with chronic epilepsy in Kuala Lumpur, with some patients attributing the illness to epilepsy as well as to the traditional concepts of “weakness” (xu), “hotness” (re), “wind” (feng), and “supernatural cause” (xie). Rajbhandari reported that 69% of the newly diagnosed patients with epilepsy in Kathmandu worshipped family gods, 66% wore mantra butti, jantar, and beets (items believed to protect patients from evil spirits), and 58% made animal sacrifices. Tsai reported from Taiwan that 50% of their patients used Chinese traditional medicine, and 47% sought folk healing methods including Qian interpretation, fortune telling, Qigong, geomancy, and shamanism. The use of these traditional treatment modalities is probably related to the large treatment gap in large parts of Asia. Some of the so-called traditional preparations are adulterated with conventional antiepileptic drugs, which complicates the management of these patients. This situation is comparable to that in sub-Saharan Africa. As long as traditional beliefs exist, patients with epilepsy are not likely to be correctly treated.

Knowledge, attitudes, and practice

Numerous studies on knowledge, attitudes, and practice have been done, particularly in Chinese communities within and outside China (table 8). Stigma was least important but evident in some advanced regions, such as Hong Kong or Singapore. In Hong Kong, 94.1% of respondents thought that people with epilepsy could be married, but only 67.8% would allow their child to marry a person with epilepsy; from the reports discussed in this Review, it seems that people in Hong Kong have the most open-minded attitudes towards epilepsy. In another study in China, only 13.0% of the respondents would allow their child to marry a person with epilepsy. Lack of awareness may be a factor explaining stigma. In almost all studies, a third to a half of responding people thought that a person with epilepsy cannot work like other people, and a quarter thought that epilepsy is a mental illness or a form of insanity. As in other parts of the world, epilepsy is believed to be a contagious disease, and some people avoid touching patients, especially during seizures, when some simple forms of help may avoid dangerous situations. Health education campaigns are necessary to rehabilitate.
patients with epilepsy in the community and to improve their quality of life.

Conclusion

There have been significant advances in understanding the epidemiology of epilepsy in Asia over the past 20 years. The median lifetime prevalence rate is estimated to be six per 1000 people, which is lower than in other developing regions. However, the number of affected patients in the region is large and much remains poorly documented or unknown. There are few data on incidence and mortality (in particular in elderly people), the treatment gap, public understanding and attitudes, patients’ concepts of disease, and help-seeking behaviour. What distinguishes epilepsy in Asia from other regions is probably not so much genetics or biological differences of Asians or environmental factors that influence the causes of symptomatic epilepsy, but most likely, the psychosocial, cultural, economic, organisational, and political factors that influence epilepsy causation, management, and outcome. These areas should be the focus of further study, and governments must give a higher priority to the fight against epilepsy in Asia. Some of the countries included in this Review are no longer poor, and could make free or subsidised antiepileptic drugs available to the general public, as the cost of even phenobarbital can be a burden on some of these communities. Nurturing of epileptologists who can spearhead improvements in epilepsy care in the community is also important. Moreover, governments should give high priority to the development of epilepsy surgery to treat drug-resistant epilepsy and should identify centres to be equipped with physical facilities such as video-electroencephalography and MRI.

Contributors

TLM and DST contributed equally in reviewing all the publications and analysing data. FQ and PO participated in interpretation, and the work was coordinated by PMP and CTT. All authors contributed to the writing of the paper.

Conflicts of interest

We have no conflicts of interest.

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