

The incidence and prevalence of epilepsy

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Epilepsy is the commonest neurological condition affecting people of all ages, race and social class. There are an estimated 50 million people with epilepsy in the world, of whom up to 75% live in resource-poor countries with little or no access to medical services or treatment^{1,2}.

Early epidemiological studies in epilepsy up to the 1960s were carried out in tertiary referral centres which favoured the belief that epilepsy was a chronic, progressive incurable condition with little chance of remission famously expressed by Gowers writing in 1881 that ‘The spontaneous cessation of the disease is an event too rare to be reasonably anticipated in any given case’³.

Since then many epidemiological studies have been published from both developed and resource-poor countries but methodological differences, lack of standardised classification, problems with case ascertainment and diagnostic accuracy have resulted in disparity in study findings, as well as reflecting the heterogeneous nature of a diagnosis of epilepsy⁴.

Diagnostic accuracy is a particular problem in epilepsy as seizures are a symptom of diverse underlying cerebral aetiologies and normally do not have any physical manifestations⁴. Consequently a definitive diagnosis of epilepsy is often only made after an extended period of follow up, as evidenced in the Rochester study⁵ and the National General Practice Study of Epilepsy (NGPSE), a community-based study of epilepsy in the United Kingdom⁶. Moreover it has been found that 20–30% of those attending tertiary referral centres with refractory epilepsy do not in fact have epilepsy⁷, with the most common differential diagnoses being dissociative seizures and syncope. As expected, neurologists are better at the diagnosis of epilepsy than non-specialists (mistake rate 5.6% vs 18.9%)⁸, but a misdiagnosis rate of 5% should be considered as the absolute minimum.

Many people with epilepsy may not come to medical attention, either through ignorance or lack of awareness of the symptoms. This is particularly true of absence and minor complex partial seizures, which may only be recognised in retrospect following presentation with a generalised seizure⁹. Indeed in one study of general practices only 20% of patients with seizures suspected the diagnosis prior to medical consultation¹⁰.

Incidence studies

While many people presenting with seizures do so with a prior history of events, between one-third and half present with a single unprovoked seizure^{6,11}. Most studies combine the incidence rates for

all newly diagnosed unprovoked seizures (single seizures and newly diagnosed epilepsy) but would be expected to be higher than the incidence of epilepsy in a population followed over a long period of time, as not all people with a single seizure go on to develop epilepsy (defined as at least two recurrent seizures). This was demonstrated in the Rochester study which followed a population over a 50-year period. The incidence of a first unprovoked seizure was 61 per 100,000 compared to the incidence of epilepsy of 44 per 100,000¹². Overall, while difficult to confirm, the incidence of first single unprovoked seizures is likely to lie somewhere in the range of 50 and 70 per 100,000 in industrialised countries but may be much higher in developing countries¹³.

In general, the incidence of epilepsy in developed countries is taken to be around 50 per 100,000 (range 40–70 per 100,000/year)¹⁴ while the incidence of epilepsy in resource-poor countries is generally higher in the range of 100–190 per 100,000/year¹⁵. While many factors may be contributing to this disparity, it has been shown that people from a socio-economically deprived background are at higher risk of developing epilepsy¹⁶.

In a systematic review of incidence studies carried out, 40 studies were identified, nine of which were prospective, and seven studies identified were from resource-poor countries. The median incidence rate of epilepsy and unprovoked seizures was 47.4 and 56 per 100,000. When the analysis was limited to studies of the highest quality, the median incidence rates for epilepsy and unprovoked seizures decreased to 45 and 50.8 per 100,000¹⁷. In a systematic review of European epidemiological studies, annual incidence rates in studies of all ages ranged from 43–47 per 100,000 person years¹⁸.

A more recent systematic review and meta-analysis identified 33 cohort studies with the median incidence of epilepsy being 50.4 per 100,000 person years (interquartile range (IQR) 33.6, 75.6). The median incidence was lower in high income countries (45.0; IQR 30.3, 66.7) compared to that in low- and middle-income countries (81.7; IQR 28.0, 233.5)¹⁹.

The incidence of epilepsy in Italy in 2011, using a nationwide database (the Health Search CSD Longitudinal Patient Database), was 33.5 per 100,000 person years with a higher incidence in women (women 35.3, men 31.5) and the incidence being highest in people aged <25 years and ≥75 years. This represents one of the lowest incidence rates reported in a European population²⁰.

While there are only few incidence studies from low- and middle-income countries, two recent studies from rural Kenya²¹ and Benin²² provide important data on the incidence of epilepsy in sub-Saharan Africa. In rural Kenya, in a cohort of 151,408 people, 194 developed (convulsive) epilepsy over five years giving a minimum crude incidence rate of 37.6/100,000 person years (95% CI 32.7, 43.3) and adjusted for loss of follow-up an incidence of 77.0/100,000 person years (95% CI 67.7, 87.4). Incidence was highest in children aged 6–12 years (96.1/100,000 person years; 95% CI 78.4, 117.9)²¹. In the study from Benin²², 11,688 people were surveyed and 148 people with epilepsy were identified over an 18-month period, with the prevalence estimated to be as high as 38.4 per 1000 (95% CI 34.9, 41.9). The mean annual incidence was 69.4 per 100,000 person years with an estimated cumulative incidence of 104.2 per 100,000 person years.

Prevalence studies

Studies have shown prevalence rates for active epilepsy in developed countries of between 4 and 10 per 1000¹⁵, although most studies give a prevalence rate of active epilepsy of 4–7 per 1000. In a systematic review¹⁸ it was found that the range for prevalence rates in Europe was 3.3–7.8 per 1000 with a median prevalence rate of active epilepsy of 5.2 per 1000. Studies with the lowest

prevalence rates reported were from Italy; 3.3 per 1000 in Sicily²³ and 3.01 per 1000 in the Aeolian Islands²⁴, although the authors of both studies suggest that prejudice towards people with epilepsy and the low prevalence rates may result from patients' desire to conceal the diagnosis to avoid perceived social disadvantages. In the Rochester study the prevalence of active epilepsy, calculated at 10-year intervals over 50 years, ranged from 2.7 per 1000 in 1940 to 6.8 per 1000 in 1980²⁵.

More recent studies using patient reports from Norway (crude prevalence rate 11.7 per 1000; active epilepsy 6.7 per 1000)²⁶ and Ireland (life prevalence 10 per 1000; treated epilepsy 8.3–9.0 per 1000)²³ suggest higher prevalence rates in western countries. The median lifetime prevalence in developed countries has been estimated to be 5.8 per 1000 (range 2.7–12.4) with a median prevalence of active epilepsy of 4.9 per 1000 (range 2.3–10.3)². In the Italian study the crude prevalence of epilepsy in 2011 was 7.9 per 1000 (men 8.1, women 7.7) with the prevalence being highest in those aged <25 years and ≥75 years²⁰.

The lifetime prevalence of seizures (the risk of having a non-febrile epileptic seizure at some point in an average lifetime) is between 2 and 5%. The difference between the lifetime prevalence and prevalence of active epilepsy implies that for the majority either the condition remits or the patient dies.

Evidence from community-based studies have shown that 70–80% of people with epilepsy will achieve remission, usually in the early course of the condition and indeed the longer epilepsy remains active the poorer the prognosis²⁸. (Prognosis is reviewed in Chapter 36.)

Factors influencing incidence and prevalence

Most incidence studies show that epilepsy is more common in males than females, both in developed and resource-poor countries but this difference is rarely significant²⁹.

In the systematic review of incidence studies, the median annual incidence of epilepsy was 50.7 per 100,000 for males and 46.2 per 100,000 for females¹⁷. Incidence rates also vary considerably with age. Studies in the industrialised world consistently show a bimodal distribution. There is a very high incidence in the first year of life and in early childhood, with a relative decrease in adolescence. Incidence is at its lowest between the ages of 20 and 40 and steadily increases after age 50, with the greatest increase seen in those over age 80. There is evidence that the incidence of epilepsy is now higher in elderly people than children³⁰.

The temporal changes in incidence of epilepsy in Finland between 1986 and 2002 were examined using a nationwide database. The total incidence decreased significantly from 71.6 to 52.9 per 100,000 per year during that time. The incidence decreased in children and adults but increased in the elderly, particularly in women³¹.

Incidence and prevalence rates of epilepsy tend to be higher in resource-poor countries. The highest reported rates of epilepsy have been found in South America; in a well designed study in Ecuador the incidence rate was 122 per 100,000/year³².

The prevalence of epilepsy appears to be lower in Africa, while studies from Asia (mainly China and India) have demonstrated rates similar to those in the Western world. Moreover there can be marked variation in incidence and prevalence rates between different regions within the same country, although most but not all studies have shown that rates are higher in rural than in urban areas¹⁵. No consistent racial differences in epilepsy have been found and in a study of incidence in

a low-income community in New York, the incidence among Hispanics (36.5 per 100,000) was similar to that of non-Hispanic whites (39.4 per 100,000) and non-Hispanic blacks (37.6 per 100,000). Lower income was, however, associated with a higher incidence of epilepsy in all ethnic groups³³.

The median prevalence of lifetime epilepsy in developing countries has been estimated to be 15.4 per 1000 (range 4.8–49.6) in rural areas and 10.3 per 1000 in studies in urban areas (range 2.8–37.7). The corresponding figures for active epilepsy were 12.7 per 1000 (range 3.5–45.4) and 5.9 per 1000 (range 3.4–10.2)².

Characteristics of epilepsy in a general population

Based on a prevalence rate of 6 per 1000, it has been estimated that in the UK there are about 96,000 people with epilepsy who require continuing hospital-based medical treatment. Of those, 15,000 will have more than one major seizure a month and 36,000 more than one seizure a month. Overall it has been estimated that there are approximately 12,000 patients with severe epilepsy and additional handicaps who may require institutional care.

In population-based studies the most frequent causes of epilepsy are cryptogenic (presumed symptomatic) or idiopathic (presumed genetic), ranging from 44.5%³⁴ to 67%³⁵, with the proportion of identified causes (symptomatic or localisation-related epilepsy – remote or progressive) increasing with age. The number of cases classified as cryptogenic has remained broadly similar over the past 20 years despite significant improvements in neuroimaging. In a study in New York³³ 55% of cases were defined as idiopathic/cryptogenic, similar to the 61% of cases in the NGPSE⁶ almost 20 years ago. Risk factors or associated factors linked to the subsequent development of epilepsy such as cerebrovascular disease, head trauma, neurodegenerative disease, CNS infections, neoplasms and learning disability predominate in identified aetiologies in population-based incidence studies. Aetiologies tend to be age specific with cerebral palsy, congenital brain damage and learning disability predominating in the young, while tumours, neurodegenerative disorders and especially cerebrovascular disease dominate in the elderly. In resource-poor countries, infective causes (e.g. parasitic infestation, malaria, tuberculosis) are an important risk factor for epilepsy. However, as in developed countries, cryptogenic cases predominate.

Based on community-based studies^{6,12,36} proportions (%) of presumed identified causes of epilepsy are the following: cerebrovascular disease 11–21%, trauma 2–6%, tumours 4–7%, infection 0–3%, and idiopathic 54–65%.

Partial seizures predominate in most studies from developing countries: NGPSE (59% vs 39%)⁶, the Rochester study (57% vs 40%)¹², the Umeå study (Sweden) (68% vs 16%)³⁶ and the CAROLE study (France) (46.2% vs 31.9%)³⁷. A systematic review¹⁷ found that partial seizures occurred in 55% of patients compared to 45% with generalised seizures. In the Rochester study age-specific incidences of generalised and partial seizures were compared; generalised seizures were more common in the first five years of life, the incidence was similar for both between the ages of 6 and 24, and partial seizures were at least twice as common as generalised onset seizures in adults over 24 years¹². Interestingly a predominance of partial seizures has also been demonstrated in a community-based study of children with newly diagnosed epilepsy (55% had partial seizures compared to 45% with generalised seizures)³⁸.

In contrast, many studies from the resource-poor countries have found more people with generalised seizures (80.5% in Pakistan and 65.4% in Turkey)³⁹. The combined use of EEG and

clinical data allows the reclassification of some cases clinically diagnosed as generalised seizures to partial seizures with secondary generalisation, as was shown in a study from Bolivia⁴⁰. Two-thirds of cases were clinically diagnosed with generalised seizures (34% partial seizures) but, on the basis of electro-clinical data, the proportion with partial seizures increased to 53%.

Epilepsy syndromes are classified according to the ILAE classification⁴¹ which is based on age, clinical semiology and electrophysiological findings. However many cases in epidemiological studies are unclassifiable according to the current classification⁴². A community-based study from Iceland³⁵ showed the following syndrome frequencies in the cohort (with calculated incidence rates): juvenile myoclonic epilepsy (JME) (1%; incidence 0.7 per 100,000 person years), childhood absence epilepsy (1%; incidence 0.8 per 100,000 person years), benign rolandic epilepsy (5%; incidence 2.8 per 100,000 person years), West syndrome (1%; incidence 0.007 per 100,000 person years), Landau-Kleffner syndrome (0.4%; incidence 0.2 per 100,000 person years), benign familial infantile convulsions (0.6%; incidence 0.3 per 100,000 person years), primary reading epilepsy and benign occipital epilepsy (0.1%; incidence 0.2 per 100,000 person years), respectively (Table 1).

The use of medical services over a 12-month period has been studied in a series of 1628 prevalent cases identified randomly in a population-based survey, the cases ascertained being on antiepileptic drug (AED) therapy⁴⁵. In the prior 12-month period 28% had been seen by a specialist (and 81% had been seen by a specialist at some point), 87% had been seen by their general practitioner for epilepsy and 9% had not been seen by any doctor. In the previous 12 months, 18% had attended an accident and emergency (A&E) department and 9% had been admitted to hospital because of their epilepsy. A total of 43% had attended an A&E department and 47% had been admitted to a hospital, 2% more than 10 times, at some point because of their epilepsy. Most (65%) were on monotherapy, while 35% were on polytherapy.

Despite the fact that AED therapy is widely available, many people with active epilepsy go untreated, particularly in resource-poor countries. Reasons for this treatment gap (TG) are many and in a recent systematic review of this problem in resource-poor countries, the pooled mean of the TG prevalence was 56% (95% CI 33–100). When analysed by region, the mean prevalence of TG was 64.3% (95% CI 24.3–100) in Asia, 55.4 (95% CI 39.0–78.6) in Latin America and 48.9 (95% CI 14.3–100) in Africa. The TG was higher in rural areas (73.3; 95% CI 49.5–100) compared to urban areas (46.8; 95% CI 34.1–64.2). The principal causes identified for TG were inadequate skilled manpower in the local health service (median 70%; range 64–76), cost of treatment (median 62%; range 11–90) and unavailability of drugs (median 53%; range 18–84)⁴⁶.

Effective strategies aimed at reducing the TG in developing countries need to be identified and implemented in order to improve the prognosis of people with epilepsy living in such countries⁴⁷.

Conclusions

Further epidemiological studies should be prospective population-based incident cohort studies. Such studies should focus on the temporal changes in the incidence of epilepsy in defined populations. Furthermore research should focus on differences (real or perceived) between people of different ethnicity and social background. This may, in turn, lead to the identification of inherent risk factors in particular sub-populations for the subsequent development of epilepsy.

Table 1. Incidences of epileptic syndromes (per 100,000 person years).

		South-West France ⁴³	Rochester, USA ⁴⁴	Iceland ³⁵
Localisation-related epilepsies	Total	15.3	34.9	18.6
	Idiopathic partial epilepsies	1.7	0.2	1.6
	Symptomatic partial epilepsies	13.6	17.2	8.4
	Cryptogenic partial epilepsies	–	17.5	8.6
Generalised epilepsies	Total	7.2	7.7	3.9
	Idiopathic	6.1	3.7	3.1
	Cryptogenic or symptomatic	1.1	1.7	0.7
	Symptomatic	–	2.3	0.1
Epilepsies with both generalised and focal features		–	1.7	0.8
Epilepsies without unequivocal focal or generalised features		1.9	8.0	8.5
Isolated unprovoked seizures		18.3	–	22.8

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