Occasional review

Incidence and prevalence studies in epilepsy and their methodological problems: a review

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SUMMARY Epidemiological studies in epilepsy have a number of specific problems, discussed here with reference to the published literature. Case ascertainment may pose difficulties because of deficiencies in patients reporting and in the diagnosis of seizures, and inherent methodological problems; the classification of epilepsy is often arbitrary and definitions variable; unsuspected selection bias may markedly influence incidence and prevalence rates. The major published incidence and prevalence studies are reviewed and the factors influencing these rates discussed.

The interpretation of vital statistics in epilepsy is often complicated and unsatisfactory, and this is largely due to difficult methodological problems which have frequently been overlooked in the published epidemiological literature. Whilst this is true of epidemiological investigations in many areas of medicine, there are problems peculiar to epilepsy, and these form the substance of this review. We shall discuss problems relating mainly to case ascertainment, classification and definition and to patient selection bias, and appraise their impact on published incidence and prevalence figures. A brief appendix is also given, outlining the findings from the most comprehensive published studies and those that are frequently cited.

Incidence is the measure of the rate of occurrence of new cases of a given disease per unit time, within a specified population. The numerator is the number of new cases and the denominator is the number of persons at risk of acquiring the disease, but in practice the total population is often used. It can be derived only from longitudinal investigation, and because of this has been reported in relatively few publications. Prevalence is defined as the proportion of a population with a given disease at a specified time. The numerator is all cases of the disease, new and old, and the denominator is the total population from which

the cases are drawn. Prevalence may be obtained from cross-sectional surveys and so data are more often available. With all chronic diseases, the number of patients accumulates with time and so prevalence tends to be high in spite of low incidence. Both prevalence and incidence vary with age, and age specific rates are often a more helpful measure than are the crude rates. Prevalence rates are higher than incidence rates, and so meaningful studies of prevalence can be made on smaller populations than are necessary for incidence studies. Point prevalence is defined as the prevalence at a specific point in time, and period prevalence as the prevalence over a defined period. The cumulative incidence rate is a cumulation of age specific incidence rates adjusted to fit the age range of a population to define the numbers of persons in a population who will have ever developed the condition at any point in their lives. In a truly chronic condition, which never recovers, assuming that incidence rates do not vary significantly over time, cumulative incidence figures should approach prevalence rates, the difference being largely explained by differential death rates in the cases and in the general population.

Case ascertainment

(a) Deficiencies in patient reporting

Unlike many ailments, the bulk of seizure disorders do not have physical manifestations, and are of a transient and unpredictable nature. For most of the time the disorder is "not there", so can be diagnosed

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only historically or by the chance observation of a seizure. Ideally (at least for epidemiological studies) all seizures should be recorded immediately in medical records, but this seldom happens. Some patients never seek medical attention, either because they ignore or misinterpret the symptoms, or indeed may be unaware of them, and this is particularly true of absence and some minor complex partial seizures.¹

Sometimes, the patient may conceal or deny the condition. Social customs may also influence patient notification and for example nocturnal convulsions have a seemingly higher prevalence in societies where the whole family sleeps together, as in Japan or the Mariana Island, and this may partly account for the high incidence of nocturnal seizures reported by mothers in their offspring.² The problem of patient underreporting is not confined to countries with poor medical surveillance. In a sample of 17 general practices in Metropolitan London, for instance, only 20% of patients with epileptic seizures had suspected the diagnosis before deciding to consult a doctor.³ Miller *et al*⁴ found that 20% of convulsive children in Newcastle-upon-Tyne had never been seen by a doctor and Tsuboi² found that 14% of 1649 children in Japan suffering seizures had no previous medical contact. Gudmundsson⁵ found that a significant proportion of the epileptics in Iceland never received medication for their condition and this is further illustrated by Zielinski¹ who, in a community survey in Warsaw observed that 1/3 of patients had never been treated and about 1/4 had never consulted a doctor. So it should be expected that in all community based studies a substantial number of cases will be present who are unknown to even the most sophisticated medical record system. As this applies particularly to mild or inactive cases, studies which show a high proportion of active cases should be viewed with circumspection. To be comprehensive, therefore, a community study should be undertaken, in which case ascertainment is essentially independent of existing medical records (although this may be used to augment case finding) and for this a highly sensitive questionnaire will be required.

(b) Deficiencies in the diagnosis of seizures

Epilepsy is a condition defined by the occurrence of epileptic seizures. The diagnosis is therefore essentially clinical and may be often difficult or delayed. The differential diagnosis encompasses all causes of transient alterations of consciousness, and in practice both false positive and false negative diagnoses are common. Syncope was, in one review, misdiagnosed as epilepsy (at least initially) in about 1/3 of cases,⁶ and it has also been estimated that up to 20% of chronic cases referred to specialised epilepsy units have in fact psychogenic attacks.⁷ By contrast, many

patients with epilepsy have the condition for months or years before the correct diagnosis is achieved, and confusion is particularly likely with the more minor attacks. In a study of 106 newly diagnosed hospital cases, for instance, 24 months or more elapsed before the diagnosis was made in 25% of cases, and this may have an important impact on incidence and prevalence rates.⁸ There has been almost no acknowledgement of the problem in published epidemiological surveys, and diagnostic criteria have been, almost without exception, unspecified or loosely defined. Commonly the operational definition of "a specialist confirmed diagnosis" is used, but no one should doubt the variability of subjective specialist opinion. This diagnostic method has been utterly rejected in epidemiological studies in other diseases states (such as angina and schizophrenia) and yet in epilepsy is commonplace.

(c) Case ascertainment methods

The most common published method of case ascertainment is that of a retrospective review of medical records. For all the reasons discussed above, there are major sources of inaccuracy and underreporting is common. The extent of this is well shown by Zielinski¹ who found a prevalence rate of 5.1/1000 based on a survey of medical records alone which rose to 10.4/1000 when a sample of 0.5% of the community with their households was added. Similarly, in the studies of Stanhope, *et al*⁹ in Guam, incidence rates ranged from 17/100,000 to 35/100,000, and the rates in the field surveys were twice as high as those based on medical records only. Usually, the case records are reviewed for a mention of fits, prescription of anticonvulsants, request for EEG, or a diagnostic index is used. Differing diagnostic or therapeutic practices and temporal changes within or between different centres are invariably ignored. The record reviews have covered total populations,^{5 10-12} a random sample,^{1 13} or selected groups such as sick funds,⁷ policy holders,¹⁴ army draftees,¹⁵ school children,¹⁶⁻¹⁸ government employees,¹⁹ or general practitioners' lists.^{20 21} A retrospective case record review may be supplemented by an interview of positively identified cases.^{22 23} A second approach has been the use of a register of cases such as in Rochester, Minnesota²⁴ or Aarhus, Denmark,²⁵ but unless careful precautions are taken, these may suffer exactly the same diagnostic problems as a simple review of existing records. An advantage of a register set up for research purposes is that the methodology may be planned in advance.

An approach, which does not rely on prior diagnosis, is to carry out a community or house to house survey using a screening questionnaire, and this has been done in various locations.²⁶⁻³⁷ Again, some

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studies have included the entire population or random samples, and others have selected racial or demographic sub-groups or specific age groups. In some investigations, hospital and medical records, public health, school and institutional records are also surveyed. Of course, such surveys depend crucially on the adequacy of the screening methods (usually administered by non-medically qualified persons), and these are difficult to design. It is crucial to achieve a balance between sensitivity and specificity, and to date we feel this has not been satisfactorily achieved. Some published examples indeed show astonishing naivety, with screening questions which are ambiguous, brief and non-specific. Other studies have included "epileptic equivalents", nightmares, minimal brain damage and abnormal EEG tracings in their case findings methods.^{29 30 32} The sensitivity of the screening method can be partly tested by a comparison with existing records, and the specificity by medical examination of positively identified patients. The questionnaire should also be piloted in a group of known cases. In spite of these problems, this should be (in theory at least) the optimum method for the detection of all active cases. In practice, inactive cases have often been overlooked by all these methods, and a review of primary care records, where these are comprehensive, supplemented by patient examination is probably the optimum method of identifying inactive patients.²² The fact that many patients conceal, deny or forget their seizures can be illustrated by the Warsaw field study in which patients who were known from medical files to have had seizures refused to answer a questionnaire more often than the rest of the population (8% versus 1.4%)¹ and by Beran's finding that approximately one in four people, proven to have epilepsy, denied this fact when sampled by questionnaire.³⁸ Confidentiality compounds this problem, as epilepsy carries a considerable social stigma, and may have important socio-domestic implications, for instance for employment or driving.

Studies in non western populations are prone to a different problem. The traditional views of illness, symptoms and aetiology are often very different from the western medical model and questionnaires framed in a medical format might well be meaningless to these other cultures. To the anthropologists this is self evident, but medical literature does not acknowledge this point.

CLASSIFICATION AND DEFINITION

In epidemiological work, even if case ascertainment is excellent and epileptic seizures accurately identified, serious problems may arise in the classification of epilepsy. Commonly cases are categorised according to seizure type and to aetiology. As with the diagnosis of epilepsy itself, the classification of seizure type

depends primarily on a skilfully obtained seizure description, and diagnostic mistakes are common. Laboratory tests (especially EEG) contribute to but do not confirm the diagnosis. All epidemiological surveys should have fixed criteria on which to base the diagnosis of seizures, although these have seldom been published. An example is the definition of tonic clonic seizures, in current use in Ecuador and in Kenya; 10 criteria are specified, and a tonic clonic convulsion is considered to have occurred if criteria i-iii are present with any two criteria iv-x. The criteria used were as follows: (i) loss of consciousness for one minute to 30 minutes; (ii) tonic phase; (iii) clonic movements; (iv) sphincter disturbance; (v) tongue biting; (vi) fall; (vii) injury due to fall; (viii) postictal muscular soreness; (ix) postictal drowsiness, sleep or confusion; (x) transient postictal focal paralysis.

An internationally agreed classification of seizure type has been proposed³⁹ which incorporates EEG data in a way which is inadequately defined and this is a source of major confusion. Even when presented with extensive EEG and clinical data, hospital specialists very often fail to agree on seizure type classification⁴⁰ and disagreements concerning seizure classification are frequently voiced.⁴¹ Furthermore, the use of EEG in field surveys or retrospective reviews of medical records is very often impractical, in which case the international classification of seizure type is strictly speaking inapplicable. Many recent published studies however have reported the apparent use of this system, without EEG data. There is an urgent need for a classification system suitable for epidemiological work.

Epilepsy may be a manifestation of many disease entities and an aetiological classification is often of great interest. The relative frequency of different causes varies in different locations and this may be an important potential influence on incidence and prevalence rates. Cystercercosis is, for instance, the commonest identified cause of epilepsy in Mexico^{42 43} but is virtually unknown in Europe and the rates for head injury also may vary considerably. The use of the term idiopathic epilepsy is a particular source of confusion. This is used by some authors to refer to primary generalised epilepsy, a genetic syndrome with strictly defined clinical and EEG findings,⁴⁴ but by others to refer to any case in which aetiology has not been established. This may make comparisons impossible, as the majority of the cryptogenic epilepsies differ widely in many respects from primary generalised epilepsy. It is self evident moreover that the successful detection of an aetiological factor depends upon the extent of investigation, and unless this is standardised and specified in any large scale study, evaluation is problematic.

A final problem in classification concerns the actual

definition of epilepsy. The inclusion of single seizures, neo-natal seizures, febrile seizures and seizures in acute illness may vary from study to study, and this may alter incidence and prevalence figures by two or three fold. A published report should specify whether these seizures are included. Moreover if single seizures are to be excluded a minimal time since the attack should be specified, as a second attack may occur months or even years after the first.

A particular source of difficulty in prevalence studies is the patients with inactive epilepsy. It is now clear that in most people with epilepsy the seizures cease^{23 45} but there is no general agreement as to what length of remission should occur before a patient is no longer designated "epileptic". Some studies have taken the view that "once an epileptic always an epileptic"⁴⁶ others have defined epilepsy as a condition in which a seizure has occurred in the preceding year, two years, three years or five years. Some investigators have taken treatment status into account, with patients in remission included if they are still taking antiepileptic drugs. Most reports however appear not to have considered this problem, and in our view it is this failure to define activity which may be particularly responsible for the observed major differences in prevalence data.

How epilepsy should be defined depends on the purpose of a study, but clearly the definition used should be stated. It should include the clinical criteria on which the epileptic seizure is diagnosed, the EEG criteria, the inclusion or otherwise of single seizures, neonatal seizures, febrile seizures, symptomatic seizures and seizures in acute illnesses, the degree of activity of the epilepsy accepted by the authors, and the aetiological categories used and the extent of investigations.

SELECTION BIAS IN THE STUDY POPULATION

Even if case ascertainment, classification and definition are satisfactory, population selection bias may have an important influence on incidence and prevalence statistics. There are almost certainly true regional differences in vital statistics reflecting geographic, ethnic and genetic, environmental and socioeconomic factors. For this reason the demographic characteristics of the population sample should be well described, and the analysis should account for such differences. The selection bias may be occult, and the presence of an institution for the mentally handicapped, the sampling of only those accepted into the armed services, or sampling in an area endemic for cystercercosis are all examples from the published literature of uncontrolled bias. Age is the most important demographic variable and age specific rates should be given where possible. Standardisation of incidence and prevalence rates are

preferable in many situations, if standardised data on the population are available. In practice standardised rates have seldom been reported.

Finally, the natural history and the role of treatment in epilepsy needs to be considered. The significance of prevalence figures in any disorder is dependent to some extent on an appreciation of the natural history and basic clinical characteristics of the condition. Surprisingly, although epilepsy has been a well recognised condition for centuries, the natural history of the untreated condition is almost entirely unknown. This is largely because of the long availability of effective therapy. Bromides were introduced into clinical practice in 1857, and were used widely (by the mid 1870s for instance, 2.5 tons (2550 kg) of the drug were used annually at the National Hospital in London).⁴⁷ Any doubts about the efficacy of bromides may be dismissed by the work of Arieff⁴⁸ who found a 6 months terminal remission rate of 83% in 140 patients treated with bromides alone, and bromides were as efficacious as phenobarbitone. So the information we have of the longitudinal characteristics of the condition is almost entirely that of the treated disease. It has also been suggested that early treatment may alter the long term course of the condition, and that effective early treatment may prevent the development of chronic epilepsy.^{49 50} If this is the case, then treatment intervention may influence prevalence and prognostic indices, although the extent of this influence is quite unknown.

PUBLISHED INCIDENCE AND PREVALENCE STATISTICS

(a) Incidence rates:

A selection of studies of incidence rates in epilepsy is summarised in Appendix 1. Case ascertainment has usually been carried out from medical records, as for instance in the studies from Nigata City,⁵¹ Iceland,⁵ Warsaw¹ and Copparo.¹² In some investigations, these were augmented by a medical re-examination to check the accuracy of the original diagnosis.¹⁻⁵ In the Warsaw studies of Zielinski,¹ a representative household sample was also included to identify missed cases. The studies from Rochester and Aarhus have used a retrospective research register.^{24 25} Studies from groups of general practitioners have been carried out in the UK^{20 21} and they have used the number of patients registered in each practice as denominators instead of the more usual census figures. A particular problem in these investigations was the wide variation from practice to practice, suggesting that some general practitioners were more assiduous in their registration than others.

The incidence rates published vary between 11/100,000 to 134/100,000, although most fall between 20 to 70/100,000. The lower figures are found

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in studies in which only recurrent non-febrile seizures are included and in studies on which case ascertainment methods have been largely through medical records. The highest figure was in a study of school children, and in this study the rate fell to 82/100,000 if febrile seizures were excluded.⁵² The classic study of incidence and prevalence rate in epilepsy is from Rochester Minnesota²⁵ in which meticulous attention was paid to problems of methodology. In this survey, a combined rate for recurrent, febrile and single convulsions of almost 120/100,000 was found, which fell to 54/100,000 when only recurrent seizures were included. In our opinion, the studies with the highest incidence rates are the most satisfactory, and the low incidence rates found in some studies are probably due largely to inadequate case ascertainment methods. Of course, true incidence rates may differ from place to place, but because of methodological difficulties, we do not consider this point to have been proved. It is noted that in few studies was there evidence that the problems of case ascertainment, classification, definition and patient selection had been considered in any detail. In some studies incidence rates were gathered retrospectively, by determining the date of onset of the seizure disorder in the population studied and this is a practice particularly to be deprecated as the deficiencies in case ascertainment and selection bias are of course magnified with this approach.

(b) Prevalence rates

As cross sectional data are more easily obtained there are, of course, more studies of prevalence than of incidence. Most papers presenting data on incidence also report prevalence, and there are additional investigations some of which have been restricted to selected populations such as army draftees,¹⁵ sick fund policy holders,¹⁴ mine workers,⁵³ school children⁵⁴ or birth-cohorts of children.^{4 55} As with incidence rates, reported prevalence rates are also very variable and rates as high as 31/1000 and as low as 1.5/1000 have been given. The rates are generally higher in studies of children, but in very few cases have rates been standardised. The problems of case ascertainment have again been largely ignored in these studies, and no doubt this is partially responsible for the 30 fold range in prevalence rates. The importance of definition can be illustrated by the study of 6000 patients from one general practice in southern England, where a prevalence of 20.3/1000 was found for all cases (including single, recurrent, active and inactive cases but excluding febrile seizures) and 17.0 for those with recurrent seizures only, 10.5 for those with active epilepsy (defined as a seizure in the previous two years) and/or on treatment and 5.3/100,000 for those with active epilepsy only.²² In

relatively unselected populations, most studies have found the prevalence of chronic epilepsy to lie between 4 to 10/1000. As with incidence studies higher rates have been found in studies with intensive or sophisticated case ascertainment methods. For prevalence studies, case finding methods may be usefully combined, and the population investigated at both community and hospital levels by questionnaire and medical examination. It seems clear that most investigations have underestimated the prevalence of epilepsy, and even if single seizures, febrile convulsions, seizures with acute illnesses, neonatal seizures and inactive epilepsy are excluded, rates for chronic epilepsy of around 10/1000 are probably applicable to all general western populations. Cumulative incidence or lifetime prevalence rates are much higher, and on the basis of available figures it is generally agreed that between 2 to 5% of any population will have a non febrile seizure at some point in time,^{22 23 56 57} and seizures will recur in over 50%. A comparison of incidence and prevalence figures will show, however, that in many cases (perhaps 60–70%) the epilepsy will cease, and this is usually after a relatively short period of activity.^{22 23}

(c) Specific incidence and prevalence rates

A number of variables may affect both prevalence and incidence rates and details of these should be included in epidemiological studies in epilepsy.

(1) *Sex* Almost all reports show higher rates in males than in females, exceptions being the study of Pond, Bidwell and Stein²¹ in 14 general practices and the report of Gomez, *et al*³¹ from Bogota. The suggestion that this is due to a higher incidence of head trauma has never been formally confirmed, and the low overall incidence of post traumatic epilepsy makes this unlikely. Syncope and psychogenic attacks are much more common in females than in males, and the potential for misdiagnosis in epilepsy in females is greater. Consultation rates from general practices in the United Kingdom, for instance, show that women consult their general practitioner for episodes of disturbed consciousness of any sort twice as often as males.⁵⁸

(2) *Age* The relative age specific incidence rates are similar in all studies. Incidence rates are highest in the first decade, and within this decade in the first year of life. Neonatal seizures are said to occur in about 1% of all neonates, but these are usually not included in large scale community surveys of epilepsy. The rates fall in the second decade, and remain low in early and mid adult life. In patients over 50 years of age rates have varied. In Iceland, Carlisle and Great Aarhus for instance, the rates in the elderly remain low,^{5 13 25} while in Rochester and Warsaw a marked increase in the older age groups was found.^{1 24} Prevalence rates

increase with age, and in most studies reach their highest levels in the third and fourth decade.⁵¹⁻⁵⁹ In the Rochester study they continue to rise with increasing age.²⁴ In this study the authors felt that the increased rate in the older age groups did not necessarily reflect a higher incidence of brain tumour or cerebrovascular disease, since in 70% of their late onset cases no aetiology was established. From more recent CT studies, however, it is now evident that occult cerebrovascular disease is responsible for a much higher proportion of late onset cases than previously recognised, at least in developed countries.⁶⁰

(3) *Seizure type* Many studies have found the majority of patients to have generalised seizures and rates as high as 88% have been reported.³⁶ Exceptions to this are the Rochester study in which 66% of the patients had partial seizures²⁴ and the Warsaw field study in which 65% of patients had partial seizures.¹ The present schemes for seizure classification are unsatisfactory, and the categorisation of seizure type is often difficult, and there seems to be little doubt that partial seizures are often under reported. Many so-called generalised seizures are in fact secondarily generalised, and therefore should be categorised as partial, and the detection of a partial onset may depend on the skill of the investigator or the extent of investigation. The studies showing the highest proportion of partial seizures are those in which medical services are the most sophisticated. The internationally accepted classification of seizure types is singularly difficult to apply in large scale epidemiological surveys, based as it is upon intensive observation of individual seizures (often requiring EEG telemetry). Thus, although this classification has often been said to have been used in large scale surveys, the reported seizure classification should be viewed with caution. Another point to note is the almost complete absence of unclassified convulsions in published reports which purport to have used the international classification. In hospital practice about one third of cases are unclassifiable.

(4) *Aetiology* In most investigations, a specific aetiology for the epilepsy was found in only about 1/4 or 1/3 cases. In the Rochester study, 5% were due to head trauma, 5% to cerebrovascular diseases, 4% to brain tumour, 4% to congenital or genetic abnormalities and 3% to infectious diseases,²⁴ while in the study from Copparo (which has one of the highest percentages of cases with known aetiology) 20% were said to be secondary to perinatal injuries, 7% to head trauma, 5% to infective diseases, 4% to cerebrovascular diseases, 2% to brain tumour, and in 61% no cause was found.¹²

It is self evident that the more extensive the investigation, the more likely are aetiological factors to be identified. To what extent this would modify the

findings of a large scale epidemiological investigation is uncertain. CT scanning for instance, has resulted in a higher rate of positive aetiologies in hospital based surveys, but in field surveys or in retrospective record reviews it is of course inapplicable. In all reports the extent of investigation should be documented and where possible should be standardised.

(5) *Geographic variations and socio-economic status* Epilepsy is widespread in all countries and all cultures. Rates almost certainly differ from location to location although reliable information on this point is scarce.

There are several uncontrolled reports showing high rates in black African populations.⁶¹⁻⁶⁵ Nelson and Ellenberg⁶⁶ found a higher prevalence for blacks than for whites in a study of 7 year old American school children, as did Shamansky and Glaser⁶⁷ in their study of childhood epilepsy in the New Haven area; and Haerer, Anderson and Schoenberg⁶⁸ in their census of neurological diseases in a biracial population of Copeh County. Similarly, US mortality data,⁶⁹⁻⁷⁰ suggest that the prevalence of epilepsy in non-whites is twice that of whites in America. The lower standard of perinatal care might be relevant, and the infant mortality rates amongst blacks in America is twice that of whites.⁶⁷⁻⁷¹ Data from other developed countries also show higher prevalence rates in the lower socio-economic classes.⁵⁻²¹⁻⁷² The high prevalence rates in some Latin America countries³¹⁻³²⁻³⁷ may relate to the high local prevalence rates of cysticercosis.⁷³⁻⁷⁵ Other parasitic disorders such as malaria⁷⁶ or schistosomiasis⁷⁷⁻⁷⁸ may also contribute to the high rates in the tropics, but the exact extent of this contribution is unclear. Even in the absence of such influences, rates may vary from location to location, and Tsuboi found differences in five separate villages on Myake Island in Japan.² In cross cultural comparisons, studies in which the same protocol has been used may provide useful information. Examples of this approach are those from the current WHO studies in the US, Africa, South America and Asia,³⁴⁻³⁶⁻⁷⁹ and from Maryland, Oregon and Chile using the same questionnaire in school-children aged 8/9 years, in which a significantly higher prevalence rate was found in Chile.²⁹⁻³⁰⁻³²

Appendix: Selected studies of incidence and prevalence

Author:	Baumann, Marx and Leonidakis, 1978 ⁵⁴
Country:	USA
Prevalence:	5.7/1,000 (epilepsy)
	1/1,000 (single seizure)
	17/1,000 (febrile seizures)

Observations: Survey by questionnaire of 3822 children between the ages of 4 and 16 years in Kentucky, including those in special schools. Supplemented by a medical examination of a sample of positive and negative cases. Inclusion

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criteria not defined, but febrile seizures analysed separately. The problems of false positive and negative questionnaire responses discussed, and the rates considered an underestimate.

Author: Bird, 1962⁵³
Country: South Africa
Prevalence: 3.7/1,000

Observations: Review of medical records of approximately 367,000 Bantu mine workers for dismissal or discharge from work due to epilepsy. 1347 individuals identified. Diagnostic criteria not specified.

Author: Blom, Heijbel and Bergfors, 1978⁵²
Country: Sweden
Incidence: 82/100,000 (recurrent)
134/100,000 (including febrile seizures)

Observations: Medical records review of 52,252 children in a special clinic up to 15 years of age. Seventy four children identified who had their first seizure during a 12 month incidence period, three years previously. Epilepsy defined by the presence of seizures in the previous three years. Seizure type, EEG changes, aetiology were analysed. The rates were not standardised. Prognosis discussed.

Author: Brewis *et al* 1966¹³
Country: United Kingdom
Incidence: 30/100,000
Prevalence: 6.0/1,000

Observations: Review of the hospital records, GP records, Medical Officer of Health records, death certificates in an English city (Carlisle) with 67,798 inhabitants, supplemented by a household survey of 11.5% of the inhabitants. No definition of epilepsy given for prevalence studies. Incidence rates calculated from 140 cases over a seven year period. Those with stroke and tumours and single seizures excluded and febrile seizures analysed separately for incidence studies. Seizure type analysed with a high proportion of grand mal found. Age adjusted rates given.

Author: Cavazutti 1980¹⁸
Country: Italy
Incidence: 82/100,000
Prevalence: 4.4/1,000

Observations: Case note review covering a 5 year period from a special epilepsy clinic in Modena. One hundred and seventy eight children were identified, the denominator was the total school population of about 22,000 persons, and the region included an institutionalised population. Incidence rates were calculated retrospectively. The pattern of age of onset of seizures is unusual perhaps reflecting case ascertainment bias. Age specific rates, aetiology and seizure type given. Prognosis discussed.

Author: Chiofalo *et al*, 1979³²
Country: Chile
Prevalence: 31/1,000 (epilepsy)
40/1,000 (febrile convulsions)

Observations: Survey by questionnaire and interview of

2,085 children in Melipilla, with an examination and EEG in a proportion of the children. Forty four cases identified and a further 22 estimated. Febrile convulsions, single seizures with a positive family history or EEG abnormalities and cases of minimal brain dysfunction (without overt seizures) included.

Author: Crombie *et al*, 1960²⁰
Country: United Kingdom
Incidence: 63/100,000
Prevalence: 4.2/1,000 (active cases)

Observations: Information collected during a single year in 67 practices, with total list size of 288,830 patients. Febrile seizures included. Diagnoses registered by GPs. Prevalence excluded "inactive" cases (not defined). Patients not seen for interview by the investigators. Marked variation in rates between practices. Age specific rates calculated, and seizure type divided into two categories. An estimated lifetime prevalence rate of approximately 5% was calculated.

Author: de Graaf, 1974⁵⁹
Country: Norway
Incidence: 33/100,000
Prevalence: 3.5/1,000

Observations: Review of medical and EEG records of specialised service in the Tromso region covering an isolated population of 213,116, which included an institution for the mentally handicapped. Seven hundred and forty nine patients identified with previously identified seizures, diagnosed by a neurologist. Age, sex and aetiology given. Not clear whether single seizures included, and febrile convulsions with normal EEG excluded. Incidence rates calculated retrospectively.

Author: Goodridge and Shorvon, 1983^{22 23}
Country: United Kingdom
Prevalence: 20/1,000 (all seizures)
17/1,000 (recurrent seizures)
5/1,000 (active epilepsy)

Observations: Medical records review of 6,000 cases from a single general practice in Tonbridge, Kent. Supplemented by a medical examination of positive cases. One hundred and twenty two patients identified. Febrile seizures excluded. Detailed discussion of definition, diagnosis and case ascertainment. Age, sex, aetiology, seizure type, investigations and treatment analysed. Treatment and prognosis discussed. High proportion of inactive cases found, and estimated that over 2% of the population will have experienced a non-febrile seizure at some point in time.

Author: Gomez *et al*, 1978³¹
Country: Colombia
Prevalence: 19.5/1,000

Observations: Questionnaire of an unspecified sample of

an urban population of 8,500 with medical examination of identified cases. Includes only recurrent attacks. Excludes febrile convulsions occurring at less than four years. Rates higher amongst females, and in the lower socio-economic strata.

Author: Granieri *et al*, 1983¹²
Country: Italy
Incidence: 33/100,000
Prevalence: 6.2/1,000

Observations: Review of medical records, and records from EEG departments, private doctors, laboratories, pharmacists and schools in the city of Copparo. Two hundred and seventy eight persons from a population of 45,203 identified and examined. Incidence rates calculated retrospectively, and rates standardised. Active epilepsy or those taking anticonvulsant drugs only included. Single seizures, febrile seizures and symptomatic epilepsy excluded. Aetiology, seizure type and occupational status discussed.

Author: Gudmundsson, 1966⁵
Country: Iceland
Incidence: 26/100,000
Prevalence: 5.2/1,000

Observations: Information from district doctors, review of medical and social records covering the entire population of 190,000. Much detail about epilepsy and related problems, although it is not clear how complete was case ascertainment. Incidence and prevalence rates exclude febrile convulsions and convulsions in acute diseases. Includes active cases, inactive cases, single seizures and other transitory disturbances of cerebral function. Nine hundred and eighty seven patients identified, of whom 56 had a single convulsion only. Incidence calculated over a five year period. Age, sex, aetiology, and seizure type reported and analysed. One of the most comprehensive early epidemiological studies.

Author: Hauser and Kurland, 1975²⁴
Country: USA
Incidence: 54/100,000
Prevalence: 5.7/1,000

Observations: Medical register of the Mayo Clinic, covering the entire population of Rochester, Minnesota; a city of 55,000 inhabitants. Five hundred and sixteen patients identified, who received a diagnosis of epilepsy over a 32 year period. Includes all the recurrent active seizures. Active defined as a seizure in the previous five years, or on anti-convulsants. Excludes febrile and single fits. Age adjusted rates given. Febrile seizures dealt with separately. This is the most comprehensive of all the epidemiological studies, and one of the few in which detailed consideration given to the problems of diagnosis, definitions, and case ascertainment and in which sophisticated epidemiological techniques have been applied. Prognosis discussed in detail in a later report (Annergers, Hauser and Elveback, 1979).⁴⁵

Author: Jilek-Aall 1965⁶²
Country: Tanzania
Prevalence: 20/1,000

Observations: Cases with Kifafa presenting to a mission clinic in an isolated African population. Acknowledged underestimate of incidence. Degenerative disease accounting for many cases. Denominator estimated in the absence of complete data (see also report by Jilek-Aall, Jilek and Miller, 1979).⁶³

Author: Juul-Jensen and Foldspang, 1983²⁵
Country: Denmark
Incidence: 34/100,000
Prevalence: 13.0/1,000

Observations: Figures taken from a research register kept since 1963, and also a medical record review since 1940. One thousand, eight hundred and seventy patients were identified, including 365 febrile seizures, from a population of 244,800 persons in the city of Aarhus. The register comprised all patients admitted to hospital with seizures, febrile convulsions or isolated fits. The rates are an admitted underestimate. Age, sex, seizure type, aetiology and precipitating factors reported and analysed. Cumulative incidence rates according to seizure type made. Detailed discussion of problems in analysing vital statistics in epilepsy. It was estimated that 2.54% of the population had an epileptic seizure at some point in time.

Author: Krohn, 1961¹⁰
Country: Norway
Incidence: 11/100,000
Prevalence: 2.3/1,000

Observations: Information from district doctors and review of medical records covering an isolated population of 416,000. Nine hundred and fifty one cases identified, some mild or inactive cases, and single seizures excluded, and febrile seizures not separated out. Incidence rates gathered retrospectively. Figures were considered to be an underestimate. Seizure type and age of onset analysed. Pattern of age of onset unusual.

Author: Leibowitz and Alter, 1968¹¹
Country: Israel
Prevalence: 4/1,000

Observations: Review of hospital, private practice, and insurance fund medical and EEG records of 170,000 persons in Jerusalem, supplemented by an interview of positive cases. One thousand and twenty seven patients identified. Febrile seizures and epileptic equivalents analysed separately. Rates analysed for sex, age, age of onset, ethnic background, social class, duration of epilepsy and EEG. This is an authoritative and comprehensive report.

Author: Li *et al*, 1985³⁶
Country: China
Incidence: 35/100,000 (age adjusted)
Prevalence: 4.4/1,000

Observations: House to house survey with examination of

Incidence and prevalence in epilepsy

positive cases in 63,195 persons in six Chinese cities. Two hundred and eighty nine cases identified. Incidence calculated on the basis of 16 persons developing epilepsy in a 12 month period. Epilepsy defined as recurrent nonfebrile seizures, unrelated to an acute illness. Age adjusted rates given. Age, aetiology, and seizure type analysed. A high proportion of generalised seizures and a very low proportion of complex partial seizures found.

Author: Mathai *et al*, 1968²⁷
Country: Mariana Islands
Incidence: 30/100,000
Prevalence: 3.4/1,000 (recurrent nonfebrile seizures)

Observations: House to house survey, with examination of positive cases by a neurologist. Six thousand, nine hundred and sixty seven persons surveyed; 182 febrile seizures, and 32 nonfebrile seizures identified. Incidence rates calculated over a five year period. Under-estimate of partial seizures. Seizures related to acute illnesses excluded. EEG in a proportion of cases. Seizure type and age of onset analysed. Standardised rates given. High rates for grand mal seizures and symptomatic epilepsy.

Author: Pond, Bidwell and Stein, 1960²¹
Country: United Kingdom
Incidence: 70/100,000
Prevalence: 6.2/1,000

Observations: A review of case notes of 39,500 persons in 14 general practices in South East England, supplemented by an interview of positive cases. Two hundred and forty five patients identified. Previously identified active cases only included, and single seizures and symptomatic seizures. Some febrile seizures probably also included. Incidence calculated by counting cases developing epilepsy over a single year, and rates varied considerably from practice to practice. Prevalence rates calculated for active cases only. Age, sex, social class, aetiology and seizure type reported and analysed. Rates not standardised.

Author: Rose *et al*, 1973²⁹
Country: USA
Prevalence: 18.6/1,000

Observations: Mailed questionnaire with 1,866 replies, of children of third grade age (approximately 8–9 years of age) and a telephone survey of institutions in Washington, County Maryland. Random sample examined. Twenty nine cases identified. Single seizures and inactive epilepsy included.

Author: Sato, 1964⁵¹
Country: Japan
Incidence: 17/100,000
Prevalence: 1.5/1,000

Observations: Information from a review of hospital records (including institution for mentally handicapped), interview of teachers and public health nurses in Nigata City. Some positively identified patients examined. Private practitioners records not included. Three hundred and forty

four cases identified from a population of about 22,000. Incidence rate based retrospectively on cases with diagnoses made over a five year period. Included were "epileptic migraine" and some EEG abnormalities without a history of overt seizures. Febrile convulsions and symptomatic epilepsy excluded. Age, sex, aetiology and seizure type reported and analysed. Surprisingly low rates found.

Author: Stanhope *et al*, 1972⁹
Country: Mariana Islands
Incidence: 46/100,000
Prevalence: 5.3/1,000

Observations: Review of medical records supplemented by questionnaire of all the population, and medical examination of the identified patients in the population of an isolated island. Rates include only recurrent active seizures. Febrile seizures analysed separately. Aetiology and age reported and analysed, with an unusually high proportion of symptomatic cases.

Author: Tsuboi, 1984²
Country: Japan
Prevalence: 9/1,000 (non febrile seizures)
83/1,000 (febrile seizures)

Observations: Examination of 17,044 3 year old children attending a routine medical examination in urban and rural island populations. Nine hundred and eighty two cases identified. Febrile and single seizures were included. Analyses of geographic differences made. Intensive efforts made to maximise case ascertainment and the problems of definition and diagnoses discussed in detail. This is a well documented and comprehensive survey.

Author: Wajsbort, Haral, Alfandary, 1967¹⁴
Country: Israel
Prevalence: 2.3/1,000

Observations: Review of case records of an insurance fund, covering 316,017 persons (male preponderance) in Northern Israel. Seven hundred and thirty five patients taking medication identified. Patients with single seizures and those with several negative EEGs excluded. Aetiology, age, age of onset, sex, and ethnic origins analysed. Seizure type divided into two categories. High rates found in those of European or American origin, especially in the older age groups. The atypical population structure of Israel thought to be responsible for some unusual findings.

Author: Zielinski, 1974¹
Country: Poland
Incidence: 20/100,000 (first attendance rates)
Prevalence: 8/1,000 (active epilepsy)

Observations: This is an extensive investigation covering almost all epidemiological and social aspects of epilepsy. It was based on a random sample of 10% of 3983 known cases of epilepsy, in which the diagnosis was confirmed by medical examination in 85%, and a random sample of 0.5% of Warsaw residents and their households, covering 14,858 persons. Incidence rates were calculated from first attendance rates

over a 12 month period. Two separate questionnaires were used, one for children and one for adults. Ninety eight cases were identified from the community sample after interview of all suspected cases. Sophisticated case ascertainment methods were used, and the point amply made that many mild and inactive cases are missed by a less intensive methodology. A high rate of partial seizures was found, and the rates were standardised. The problems of diagnosis, definition and case ascertainment were discussed in detail. This is an authoritative and thorough paper.

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