The purpose of this article is to review important studies of the epidemiology of neurological disease in the United Kingdom, and some of the difficulties encountered in conducting them. We will also explain the background to two exciting studies in progress. For a review of the basic methodology of neuroepidemiology the reader is referred to a number of seminal articles.1-5

Two of the key measurements used in descriptive epidemiology are the prevalence and incidence of a disease.2 The prevalence measures the number of current cases of a disease in a defined population at a given time and place. The incidence of a disease is the number of new cases occurring in a defined population for a given time interval, usually one year, and place. The determination of incidence or prevalence figures for a particular disease requires the precise ascertainment of all cases of the disease in the target population. It is worth emphasising that incidence and prevalence figures are measures of rates of disease, and therefore the selection and demographic characterisation of the denominator population is important. The incompleteness of case ascertainment can be a major source of error, and this poses problems that appear to be more significant in neurological disease in four particular ways.

First, to ascertain patients with a specific neurological disorder it is essential to have a clear and rigid diagnostic definition. This is often lacking in neurology compared with diseases in other specialities, because the diagnosis is often made on clinical grounds alone with a limited number of useful clinical and laboratory diagnostic tests available. For example, contrast the rigid diagnostic definition laid down by the World Health Organisation for diabetes,4 and the diagnostic criteria for multi-system atrophy.7 As new technologies become available, however, more reliable diagnostic definitions should be possible by incorporating investigations into diagnostic definitions, as shown by the recent application of MRI in multiple sclerosis (MS).6 Diagnostic validity also may be poor. For example in one UK study of 19 untreated patients with clinically diagnosed Parkinson’s disease, 20% later turned out on post mortem to have another diagnosis.8

Second, is what might be called the “iceberg” effect. This refers to sub clinical or hidden cases that evade case ascertainment, and in neuroepidemiology there are several reasons for this. There is a stigma attached to having a disease of the nervous system,9 so that patients may conceal their condition. In a field survey of people with definite epilepsy diagnosed from their hospital records, nearly 25% concealed the diagnosis when sent a questionnaire.10 The insidious nature of many neurological disorders means that people may not recognise that they are affected and so stay away from medical attention. In a twin study of MS, siblings of affected patients were contacted, and nearly 5% were found on clinical and MRI examination to have MS who previously had not suspected their diagnosis.11 There may be a similar undetected group of patients with diseases of the basal ganglia, as shown by studies using positron emission tomography that can demonstrate presymptomatic nigral involvement in subjects before the development of Parkinsonism.12 Cases will also evade case ascertainment if diagnosis is delayed. In one UK study of epilepsy, it took more than two years for a diagnosis to be reached in more than 25% of patients,13 obviously affecting incidence and prevalence rates.

The third problem is that there are so many neurological diseases (indeed there are many more individual diseases listed in the International Classification of Diseases than for any other medical speciality14), and yet they are often relatively rare. To arrive at incidence of rare conditions, a large population needs to be surveyed, carrying generally large logistic and financial costs. This partially explains why the last comprehensive study of the incidence of all the neurological diseases occurring in a UK population was over 26 years ago in Carlisle.15

Finally, the late development of neurology as a medical speciality has had an important impact on the pattern of neurological care, which has itself affected neuroepidemiological research. For instance, the majority of stroke patients in the UK never come into contact with a neurologist, and patients with multiple problems, often the elderly, are usually looked after by general physicians, even if there is a neurological component. It is clear therefore that for valid investigations of common neurological disorders, patients have to be recruited at population level, and not from the highly selected groups seen in neurological clinics. The failure to recognise this led to false ideas about the prognosis of epilepsy.16

Incidence and prevalence studies provide the most important measure of disease burden and give a broad picture of disease patterns. However, neuroepidemiology is not only concerned with incidence and prevalence figures, and can advance the knowledge of a disease by determining risk factors, defining prognosis and calculating attack rates, mortality rates, and case fatality rates.

Neuroepidemiology in the United Kingdom

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Incidence and prevalence studies provide the most important measure of disease burden and give a broad picture of disease patterns. However, neuroepidemiology is not only concerned with incidence and prevalence figures, and can advance the knowledge of a disease by determining risk factors, defining prognosis and calculating attack rates, mortality rates, and case fatality rates.
Such investigations require the assiduous application of the key epidemiological principles of investigating large numbers of people to achieve statistical power, and using control populations where appropriate. The organisation needed is often formidable. In the UK, risk factor data have recently been obtained on the risk factors for stroke in middle aged men, the risk of serious vascular events after a TIA, and the risk of developing MS in the UK West Indian population.

The prospective cohort study from the time of diagnosis is the epidemiological gold standard for investigating prognosis. The chronic, and fluctuating, nature of many neurological disorders, like MS which is characterised by relapses and exacerbations which can be decades apart, means that the study must be long term, with facility for regular, active follow up. A recent study from the North East of Scotland used information from data collected on patients with prevalent MS since 1970, producing results on prognostic indicators. Nevertheless, to date, there have been no large prospective studies of incident cases of MS in this country. The prospective approach has been successfully applied in the UK to common disorders such as, epilepsy, and cerebrovascular disease, and to specific aspects of prognosis, such as the risk of relapse of epilepsy following antiepileptic drug withdrawal.

There have been few population based investigations of mortality in the UK. Care should be taken when assessing mortality statistics using death certificate data which have well-known limitations. In chronic neurological conditions, inaccuracies may be particularly prominent as the cause of death is often an intercurrent illness such as bronchopneumonia, and the neurological condition may be omitted from the death certificate. Assessing the contribution of the neurological condition to the cause of death in this situation is highly subjective.

Neuroepidemiology in the UK has not been as well supported as in the USA, where the National Institute of Neurological Disorders and Stroke (NINDS) set up programmes of research to encourage development in this area. Between 1980 and 1990 there was a 101% increase in articles on Neuroepidemiology in the American medical press. Much of the NINDS funding initially went to the flagship of epidemiological research in the USA, the Mayo clinics record linkage system in Rochester, Minnesota. This utilises a system where all the population (approximately 90 000) have their medical contacts recorded on a central data base. This has enabled extensive analysis of all the neurological conditions that have occurred in that community over the last 40 years, and numerous studies have been produced from work using this data. The major drawback to this system is that all the information is retrospective and this introduces problems with diagnostic validity, accuracy of follow up, and completeness of data. Also, only patients attending the clinics linked to the system will be included, and the extent to which findings from such a small and homogenous population can be extrapolated to the general population is uncertain.

Advantages of the structure of the UK health care system for neuroepidemiology
Facets of our health care system makes the UK a potentially fertile territory for neuroepidemiological research. The most important is the general practitioner (GP) primary health care system, which is ideally suited to the surveillance of common diseases. There is high coverage of the population with over 98% registered with a GP. Information about neurological disorders occurring in a population of 300 000 served by 48 practices was produced as part of the Third National Morbidity Survey, and in a single year 65% of men and 77% of women saw their family doctor at least once.

The GP is usually the first medical practitioner to see a patient, and is the gatekeeper for hospital referral. The GP case notes contain a patient's lifetime medical history. Even if the patient goes straight to hospital (for example, in an emergency), the GP is still informed of the contact at discharge or death. If the patient moves to a new area, the notes are transferred to the new GP, and the NHS central register, run by the Office of Population Censuses and Surveys (OPCS), is able to track each patient. Everyone in the UK has a unique NHS number that can be monitored in the event of change of address or name. Death certification is linked via computer to the NHS number, and a patient can be flagged so that death and/or its certified causes can be available to the researcher. The GP is responsible for all but emergency prescribing, and this can assist with case ascertainment, and other health service research, by accessing GP surgery prescription data.

Demographic data is also readily available in this country at local or national level. The OPCS provides regular comprehensive national reports. The Family Health Service Authorities are able to supply local demographic data, and now, with the trend towards computerisation, most practices themselves are able to give demographic information on their own lists.

Care has to be exercised if raw GP data are used, however, in view of the potential problems of diagnostic validity. In one survey of GP diagnosis the range of confidence each practitioner has in their own conclusion ranged from 15–84%. This problem was tackled in the Oxford Community Stroke Project, in which each patient was seen by a trained neurologist after being diagnosed by their GP as having a possible stroke. Similarly in the National General Practice Study of Epilepsy, GP assessment was supplemented by hospital follow up data, and then subjected to a diagnostic panel review.

The benefits of using data from primary care were demonstrated by the Third National Morbidity Survey mentioned above. More detailed analysis of this has been reported and reviewed in this journal, and it was found that 9.5% of the population consulted their GP about a neurological symptom per year.

The specialist neurological services in the UK have some characteristics which are also important to consider in neuroepidemiological research, that confer advantages when studying rare diseases. First, the number of neurologists is small and the services highly centralised into a few neurological centres. Thus the logistical problems of surveying specialist practice are greatly eased. Whilst patients with common neurological conditions are often not referred to these neurological services, rare diseases usually are. The neurologist provides a consulting role for diagnosis rather than long-term follow up, and thus has a relatively large case register of uncommon diseases.

The burden of neurological illness in the UK
We have summarised the incidence, prevalence, and mortality data from the most important neuroepidemiological studies in the UK in table 1. The list is not exhaustive, as many diseases have not been adequately studied, but does give an illustration of the relative frequency of those diseases that have been surveyed. The table does not include descriptive categories, such as back pain, headaches, and neurological symptoms without an underlying cause, that are covered well else-


Table 1  Annual incidence, point prevalence, and annual mortality rate* of selected neurological diseases in the UK per 100 000 population. All ages.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Annual incidence</th>
<th>Point prevalence</th>
<th>Annual mortality rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine</td>
<td>N/A</td>
<td>3300 (a)</td>
<td>N/A</td>
</tr>
<tr>
<td>Stroke</td>
<td>200 (d)</td>
<td>570 (d)</td>
<td>230</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>30 (d)</td>
<td>2000 (d)</td>
<td>3 (d)</td>
</tr>
<tr>
<td>Demenrial</td>
<td>184 (b)</td>
<td>86 (d)</td>
<td>62 (d)</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>12 (b)</td>
<td>160 (b)</td>
<td>14 (b)</td>
</tr>
<tr>
<td>MS</td>
<td>5 (b)</td>
<td>110 (b)</td>
<td>3 (b)</td>
</tr>
<tr>
<td>Brain tumour</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) malignant</td>
<td>9-3 (b)</td>
<td>21 (b)</td>
<td>11 (b)</td>
</tr>
<tr>
<td>b) benign</td>
<td>2-8 (b)</td>
<td>28 (b)</td>
<td>9 (b)</td>
</tr>
<tr>
<td>MND</td>
<td>2-4 (b)</td>
<td>4-6 (b)</td>
<td>1-1 (b)</td>
</tr>
<tr>
<td>Huntington’s disease</td>
<td>N/A</td>
<td>4-9 (b)</td>
<td>1-1 (b)</td>
</tr>
<tr>
<td>Guillain-Barre syndrome</td>
<td>1.1 (b)</td>
<td>N/A</td>
<td>0-095</td>
</tr>
<tr>
<td>Myasthenia</td>
<td>0-22 (b)</td>
<td>2-3 (b)</td>
<td>0-08 (b)</td>
</tr>
<tr>
<td>Myotonic dystrophy</td>
<td>14 (b)</td>
<td>7-14 (b)</td>
<td>0-13 (b)</td>
</tr>
<tr>
<td>Muscular dystrophy</td>
<td>1-2 (b)</td>
<td>18 (b)</td>
<td>0-81 (b)</td>
</tr>
<tr>
<td>Hereditary neuropathy</td>
<td>0-2 (b)</td>
<td>13 (b)</td>
<td>0-13 (b)</td>
</tr>
</tbody>
</table>

* Rates given are to nearest two significant digits based on data quoted from references.

**Mortality data are from OPCS.21**

Incident figures are for first ever stroke of any aetiology.

Incident figure excludes isolated seizures, prevalent figures include.

Figures were calculated by assuming 20% of UK population >65 years old.

Incident rates are for Parkinsonism, prevalent rates for idiopathic Parkinson’s disease.

Includes primary and secondary tumours.

where.29 Many of the incidence figures come from the large survey in Carlisle.18 Thus some figures are relatively old, but the study still provides some of our most comprehensive data.

The findings vary between studies and inconsistencies arise. For instance the incidence of myotonic dystrophy is unlikely to be greater than its prevalence. Such variation is due to different methodologies and case ascertainment accuracy. The figures are in general agreement with those from the USA,33 and any differences are again probably due to differences in study methodologies rather than any intercontinental variation.

Neuroepidemiological data should be used to inform health service research about manpower needs. The second table (table 2) is an extrapolation from table 1, and shows the number of cases occurring in the population cared for by an average consultant neurologist in the UK. Out of this total burden only a certain percentage is ever seen by a neurologist. Figures from the National Morbidity Survey give the referral rates for individual conditions, for example, only 3-5% of patients with migraine and 13-7% with epilepsy were referred.22 This indicates the huge potential workload that would fall on the hospital consultant if GP referral patterns change, or patient demand increases. In the USA, neuroepidemiological evidence has been used to press for a large increase in the number of neurologists,24 but in the UK it has been cogently argued that much of the work carried out by American neurologists could satisfactorily be undertaken by British general practitioners.29 There is, however, a pressing need for studies measuring the relative clinical outcome, cost effectiveness, and quality of care in specialist clinics compared with primary care, so that realistic referral recommendations and therefore long-term manpower needs planned.

The future

We have reviewed the current status of neuroepidemiology in the UK. For common diseases the trend, for good epidemiological reasons, has been towards greater community based studies and away from hospital based case series, often via information from general practice. In spite of the advantages the UK has to offer neuroepidemiology, there are still gaps in the overall picture. A particular need is for an ongoing survey of neurological disease at the population level, similar to the Mayo Clinic record linkage system in the USA, yet more firmly population based, and conducted on a prospective basis. A pilot study has started coordinated from the Neuroepidemiology Research Group of the National Hospitals for Neurology and Neurosurgery, and will collect data on all the neurological diseases seen in a population of 25 000 served by two GP group practices. This system will record all the incident cases seen and will form the basis for prospective studies on all common neurological disorders. If this pilot study is successful then the population base increases to 100 000 from six or eight group practices.

Such an arrangement, however, will be of little benefit where cases have a low incidence (<1/100 000), or prevalence, as even large-scale community-based studies will ascertain only a small number of cases. Although the total burden of rarer disorders is small, the study of such disorders is still important. Accurate assessments of the incidence of some rare diseases are of public health relevance in order to plot their eradication (that is, polio), or possible rise (that is, Jacob-Creutzfeldt disease). The elucidation of the pathophysiology of rare diseases will also expand our basic science knowledge base, with potential to help patients affected with more common disorders. Patients with rare disorders are more difficult to treat because of unfamiliarity with the condition, lack of basic prognostic data, and inability to carry out controlled clinical trials. The rarity of the condition is of little comfort to either clinician or patient, and improvement in the care of these rarer disorders is required.

To address the problem of rare disease case ascertainment, the British Neurological Surveillance Unit (BNSU) has been launched. The BNSU will be run by the Association of British Neurologists (ABN), with the help of the Communicable Disease Surveillance Centre, the National Hospitals for Neurology and Neurosurgery, and the Institute of Neurology. The aim is to establish a nationwide case ascertainment scheme of rare neurological diseases, by a system of prospective active surveillance. The system operates by sending every member of the ABN a blue monthly reporting card which lists the diseases currently being surveyed. The notifying neurologist has simply to tick a box if he or she has or has not seen a case and then returns the card. The report card is postcard size and can be sent anonymously in the post as each ABN member is identified by an index number on the card. Up to nine diseases will be dealt with by the unit at any one time. Any ABN member can submit a study which will be vetted by a scientific advisory
committee. The model is the British Paediatric Surveillance Unit (BPSU),\textsuperscript{35} which has been running successfully for five years, with impressive results. Previously, ABN members were asked to identify patients with rare disorders by an unregulated and often haphazard method of passive surveillance. The BNSU will help to act as a coordinator, reducing the overall number of requests for patients from individual neurologists, and making sure that the studies being run are valid for this type of surveillance. Better surveillance will be achieved for those studies that are on the reporting card because the surveillance is active, and the simple reporting system should ensure good compliance. The BNSU will benefit the whole neurological community in the UK, but its success also hinges on the collective enthusiasm.

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