The contribution of British general practice to our knowledge of epilepsy and its effects on people

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Introduction: British general practice is a good base for epidemiological research which is evidenced by the study of epilepsy.

Sources of data: A comprehensive search of PubMed using various keywords for articles on epilepsy research performed in British general practice.

Areas of agreement: Studies in the setting of general practice have contributed significantly to knowledge in the field of epilepsy, especially in relation to epidemiology, studies of prognosis and treatment patterns and psychosocial aspects.

Areas of controversy: The extent to which epilepsy can be managed in general practice.

Growing points: The importance of primary care research and the importance of collaborative studies between general practice, hospital and university departments.

Areas timely for developing research: The effects of interventions at general practice level on seizure control, morbidity and mortality.

Keywords: epilepsy/general practice/prognosis/mortality/psycho-social

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One of the authors became a partner in a practice in Tonbridge in 1977. It was quite a few years before it was appreciated that an antecedent in the practice was Dr William James West. In 1841 he wrote a famous letter to the Lancet entitled ‘On a peculiar form of infantile convulsions’, the first symptoms of his son James Edwin West at an age of about 4 months.1 This was the first objective description of Infantile Spasms which is also known as West Syndrome (Infantile Myoclonic Encephalopathy with Hypsarrhythmia). In 1848, the year his father died, James was admitted to
Park House in Highgate, a home for the mentally subnormal. James is one of four case histories mentioned by Dr William Newnham, in 1849, who used the term ‘eclampsia nutans’. In 1854 all the patients were transferred to Earlswood Hospital and James came under the care of John Langdon Down. He died from tuberculosis in 1860 and was buried in his father’s grave in Tonbridge. At a distance of 170 years, it has been possible to note the life history of one patient with a rare type of epilepsy. The prevalence is around 1:3500 of live births. Dr West showed the value of observation which is ideally suited at a general practitioner (GP) level where most patients present with disease, and which is then followed up by general practice despite hospital attendance.

In a lecture in 1921, Sir James MacKenzie, who is the father of general practice-based research, said that ‘if you do not recognize the early symptoms of disease you can never recognize the circumstances that favour or cause its onset’. He added that ‘there is only one person’, who can do this, ‘and that is the general practitioner’. In the same lecture, he noted that, ‘In medical practice one question arises incessantly and persistently, implied or expressly demanded of the doctor, and that question is ‘What is to be the outcome of my complaint?’ The patient or his friends want to know if the illness is temporary or is it to result in ill health or in death’. Later he said that ‘the chief purpose of records is to lay the basis of prognosis’.

In this article, we assess the contribution of British General Practice to research in epilepsy since 1948, based on a comprehensive review of the literature. We chose to look at the post-1948 literature as this was when the National Health Service was founded with all patients having their medical records kept by their GP.

**Method**

Using PubMed, searches were made using the keywords epilepsy, epileptic and seizure with general practice, group practice, primary care, community care, general practitioner(s), NICE and by review of reference lists from these articles. All articles found were analysed to find research articles on epilepsy in which British general practices’ populations had contributed to the research. Only articles contributing new relevant data are cited in this article. A small number of references were picked up through personal recommendation.

**Early general practice epidemiological research on epilepsy**

General practice is ideally placed to do epidemiological work, because of its resident population. Research in epilepsy in general practice has
been able to record incidence, prevalence, prognosis, mortality and other factors like treatment and care. Fry\textsuperscript{4} saw ‘the potentialities’ of epidemiological and clinical research in general practice and recorded diseases in his Beckenham practice including epilepsy. In 1982, he reported a cumulative incidence, over 22 years, of epilepsy of 10.5 per 1000 patients and that 67\% of his patients had had no seizures for over 3 years. The College of General Practitioners was formed in 1952 and in 1953 with the General Register Office started the work needed for a morbidity study\textsuperscript{5}. One hundred and eighty general practices in England and Wales with a population of 400 000 collected data over a year in 1955–56. This gave the first figures from general practice on the estimated prevalence of epilepsy in this country and found this to be 3.3/1000. This evolved into a decennial series of surveys from 1958 to 1991. The fourth national survey provided data showing higher rates of a range of comorbidities. In 1957–58 the Research Committee of the College of General Practice carried out the first detailed study of epilepsy in the community and recorded, over a year, first seizures and patients with repeated seizures or on medication for more than one seizure for over 2 years.\textsuperscript{6} One hundred and thirty-four GPs participated, recording an incidence of 0.63/1000, and noted the increase in epilepsy in childhood and the elderly. Their prevalence figure for epilepsy was 4.19/1000. They also looked at admission rates to hospital, the degree of control of seizures and treatment, and noted hospital admissions, social problems and unemployment. They estimated that 4\% of patients are likely to have a seizure during their lifetime. They calculated that the chances of a first fit being repeated at intervals and requiring continuous treatment as about 1 in 8, and that 1 in every 160 persons having had a first fit would be severely disabled by their epilepsy. The College’s Records and Statistical Unit was formed in 1957 and the Birmingham Research Unit subsequently collected annual prevalence figures for epilepsy. The most recent figures, for instance, were in a sample population equal to \(\sim 1.6\%\) of the national population of England and Wales, in the years 2001–07 and varied between 3.4 and 5.1/1000. Desmond Pond, a consultant psychiatrist, with the help of a psychiatric social worker, investigated the epilepsy patients in 14 of the practices.\textsuperscript{7} Brewis \textit{et al}.\textsuperscript{8} in 1966 investigated the prevalence of neurological disease in Carlisle which had a prevalence of epilepsy of 5.5/1000 persons. Similar figures were found by others.\textsuperscript{9–11} In 1979, the prevalence of epilepsy was estimated to be 7.6/1000 in the paper by Zander \textit{et al}.\textsuperscript{12} and similar figures on prevalence and incidence have been given by a variety of later studies of epilepsy in general practice (referenced later in the review) give prevalence and incidence figures.
The general practice research database and other large-scale computerized databases

Since 1998, the computerized UK General Practice Research Database, owned by the Department of Health, was made available to researchers, covering 6.0% of the national population (it has now metamorphosed into the Clinical Practice Research Datalink). The incidence and prevalence of epilepsy, deprivation, SUDEP and mortality have been investigated. The age-standardized prevalence of epilepsy was found to be 5.15 and 7.3 per 1000 persons, with higher rates found particularly in older people. Higher mortality rates were found to be associated with active epilepsy, alcohol misuse, treated depression, recent accidents or injuries and non-adherence to medication. One study also looked at the association of epilepsy and stroke and found the occurrence of late-onset epileptic seizures were a strong predictor of a subsequent stroke. The database was also used to investigate co-morbidities, with findings similar to that of the 1991 national morbidity survey. The database also revealed a higher incidence, especially in women, of fractures especially of the hip and femur. Women’s health issues have been extensively researched. Low fertility rates were noted in women aged 25–39 treated with anticonvulsants and poor standards of co-prescribing of antiepileptic drugs and oral contraceptives, and rates of major congenital malformations in infants of mothers treated with antiepileptic drugs.

The database also provides excellent data for studying prescribing patterns over time for instance showing, between 1994 and 1998, a large increase in the use of the newer anticonvulsants, lamotrigine and gabapentin, and of lamotrigine and levetiracetam especially in the young including women aged 15–44. There is a higher incidence of self-harm and suicide by users of the newer antiepileptic drugs. Research has also looked to see whether there is a risk of seizures with the use of tramadol (there is not), a link between antiepileptic medication and blood dyscrasias (rare), and a link between carbamazepine and Parkinson’s disease (unlikely).

Another large general practice database, QResearch, with 13 million people registered has been used to study variations in the reported prevalence of epilepsy in different practices. The most recent database is the Health Improvement Network (THIN), with a population base of 11 million, and this has shown a decline of 47% in cumulative incidence and a 9% decline in annual incidence in epilepsy in children. Another study analysed prescribing trends of antiepileptic drugs during pregnancy and noted the increase in the use of lamotrigine and the decrease in carbamazepine and valproate.
Prognosis in epilepsy: Tonbridge study and the National General Practice Study of Epilepsy

In his Tonbridge general practice, one of the authors, from 1977, kept a disease register of all his registered patients and noted a high prevalence of epilepsy but a low incidence of active epilepsy. It was at a time when figures published from the Rochester Records Linkage system of the Mayo clinic also suggested a high rate of remission. The contemporary view at the time was that epilepsy was usually a chronic condition with a poor outlook for seizure control. The authors decided to survey retrospectively the notes of 6000 patients in the Tonbridge practice to look at the prognosis from the onset of epilepsy and published the results in 1983. There was a prevalence of 20.3/1000 patients with a seizure history (excluding febrile convulsions), while only 5.3/1000 had active epilepsy. One hundred and twenty-two patients were identified and 114 of them were interviewed. Phenytoin, phenobarbitone and valproate were the main anticonvulsants used by the 38.5% of patients who were on drug treatment. It was determined that 19% had partial seizures, 61% generalized seizures and 13% with a mixed seizure type. In 25% of cases, an aetiological diagnosis could be made. The major findings in this study related to prognosis. It was found firstly that 80% of persons who had a first seizure had a recurrence and were then treated with antiepileptic drugs, but ~40% of these patients went into remission within a year, later reaching a figure by 20 years of 80%. Patients with frequent seizures and partial or mixed partial seizures had a worse prognosis. The pattern of epilepsy over time was reported for the first time. After the first seizure most patients had further seizures, usually within a year, though often limited up to 10 seizures in total. 18% of patients had single seizures, 49% had a ‘burst’ pattern (seizures recurring for a period of time and then remission with no further relapse), 12% had an intermittent pattern (periods of remission followed by relapse) and 21% had a continuous pattern (continuing seizures with no remission). This was one of the first longitudinal community cohort studies of the prognosis of epilepsy in the UK and the first to report seizure patterns over time. This methodology has become very influential in elucidating our views of prognosis.

In 1993, in the same Tonbridge practice, another 6000 patient notes were analysed and showed a roughly similar incidence and prevalence to the earlier Tonbridge study. 61% of the 126 patients had a 2-year remission reaching 81% remission at 4 years. Overtime it was noted that there had been an increase in the number of elderly patients presenting with a first seizure, while there was a decrease in the number of children.

In 1984, the National General Practice Study of Epilepsy (NGPSE) was initiated to follow a large prospective cohort study of people from the
time of diagnosis of epilepsy. Two hundred and seventy-five GPs were recruited to help the study and 1195 patients with a first diagnosed possible seizure were recruited to the study between 1984 and 1987. The cohort has been followed ever since. The first paper was published in 1989, and a further 18 papers presenting the primary data have been published with a final paper awaiting publication. It has been the basis of nine PhD or MD research projects and one MSc project. The primary aim of the study was to determine the long-term seizure prognosis and mortality of people with new onset of seizures, with secondary aims to identify clinical features of epilepsy and its investigation, patterns of epilepsy and patterns of treatment, the prognosis of febrile seizures, the cost of epilepsy and its life expectancy.  

Five hundred and sixty-four of the cohort were classified as having definite epileptic seizures, 228 patients as having possible seizures, 220 with febrile seizures and 183 patients were excluded for various reasons. The cohort has been followed up intermittently with analysis of their epilepsy outcome and prognosis and other factors. The NGPSE is now reporting the results of ~25 years prospective follow-up and there is no comparable large prospective cohort study of this duration.

The overall study results are given elsewhere, where the following summary of the findings of the NGPSE in relation to prognosis is given: (i) epilepsy has an often good prognosis with 65–85% of cases eventually entering long-term remission, and an even higher proportion of cases entering a short-term remission; (ii) the likelihood of long-term remission of seizures is much better in newly diagnosed cases than in patients with chronic epilepsy; (iii) the early response to treatment is a good guide to longer term prognosis (although not inevitably so); (iv) the longer is the remission, the less likely is subsequent recurrence; (v) the longer an epilepsy is active, the poorer is the longer term outlook; (vi) that delaying treatment, even for many years, does not worsen long-term prognosis; (vii) the ‘continuous’ and ‘burst’ patterns are much commoner than the ‘intermittent’ seizure pattern; (viii) epilepsy has a mortality which is highest in the early years after diagnosis, and in the early years is largely due to the underlying cause. However, higher mortality rates than expected are observed throughout the course of an epilepsy; (ix) the prognosis of febrile seizures is generally good, with ~6–7% developing later epilepsy; (x) clinical factors associated with outcome have been well studied, and those consistently found to predict a worse outcome include the presence of neurodeficit, high frequency of seizures before therapy (seizure density), poor response to initial therapy, some epilepsy syndromes.

Other aspects were also studied. In 1991, a psycho-social survey of 216 patients with epilepsy, with a good response rate of 89%, showed that 91% of the patients had psychological problems though only about 10% were severe. The most significant concerns amongst newly diagnosed
patients were the fear of seizures, fear of stigma in employment problems with accepting the diagnosis, fear of failure and concern about medication. Throughout, the study has shown a higher standardized mortality rate than would be expected in the general population. At over 20 years follow-up there had been 301 deaths in a cohort of 792 with an SMR of 2.2 and the risk of premature death was found to be persistently raised throughout the follow up period. Life expectancy was also reported and was found to be decreased by 2 years for people with a diagnosis of cryptogenic/idiopathic epilepsy and up to 10 years with a history of symptomatic epilepsy.

The treatment status of the cohort was surveyed over time. Antiepileptic drugs were started in 77% of the patients diagnosed with definite epilepsy, while follow-up at over 10 years showed that only 37% were still on treatment with 7% having restarted because of seizure recurrence. The follow-up of 220 children with a history of a febrile convulsion at 12 years showed that 6% of them had subsequently developed epilepsy and 10% had other neurological sequelae.

The NGPSE spawned general neurological research in general practice. In 1995, the Tonbridge practice and another practice audited new neurological diagnoses and this study acted as a model to start for the National Hospital for Neurology and Neurosurgery Linkage Study to which again, the Tonbridge practice contributed. The linkage study lasted 18 months and showed that 0.6% of patients have a neurological condition diagnosed each year with a lifetime prevalence of 6% (the only other previous population-based study had been conducted in Carlisle in 1968). The commonest neurological diseases in the descending order of incidence found were cerebrovascular events, herpes zoster, diabetic neuropathy, compressive neuropathies, epilepsy, Parkinson’s disease and peripheral neuropathies.

**Social and Psycho-social aspects of epilepsy**

Bond and Bidwell were the first to investigate this area in 1960. They noted the difficulties with education, employment, psychological problems and a higher number with deprivation. Lloyd Jones, as a vocational GP Trainee in 1980, carried out a medical audit in one group practice and noted that patients remembered little advice except free prescriptions. A Northern Ireland study in 1983 found that many young adults were not confident enough to tell others about their seizure condition. Many patients were distressed by nocturnal seizures, and patients felt that they needed better explanation about their diagnosis and reassurance. Only 50% of the patients were employed.
An association of deprivation with epilepsy is apparent. A raised unemployment rate has been noted in many studies, and patients had increased benefit claims. Many patients have psychosocial problems. Research in 1999 carried out in the Tonbridge and one other practice found a third of the patients with active epilepsy were significantly handicapped with psychological problems, though this was unknown to the GP in two-thirds of the patients. Subjective handicap was less in those patients in remission. In the NGPSE study of newly diagnosed patients, the problems were mild but were still present in 91% of the patient’s studied. The problems were worse for those with frequent or recent seizures and less for people aged over 60. Depression and anxiety are common in people with epilepsy, often unrecognized by GPs. The incidence of depression and anxiety is increased for patients with active epilepsy, the elderly, and psychiatric cases are commoner in patients with focal seizures.

Perceived stigmatization was found to be common in many studies matters were worsened and worse amongst those with a history of active epilepsy, and those of a younger age. A concern about stigmatization often involved employment issues. Stigma is interconnected to concealment of reporting seizures, driving with a history of active epilepsy, and not informing employers of the diagnosis.

Patients with epilepsy have the feeling that the advice and information given to them is not adequate. This is compounded by the finding that there is often poor communication between the GP and patient. The Clinical Standards Advisory Group (CSAG) found the major impacts of epilepsy on life were work and school difficulties, driving and psychological and social life.

**Improving standards of care**

There have been numerous audits in general practice concerned with care for patients with epilepsy, and almost all have shown deficits and deficiencies which could be improved. The first study was that of Hopkins and Scambler, who, in 1977, recruited GPs through the Faculties of the RCGP. Lloyd Jones in 1980 noted the stigma of epilepsy and the lack of serum drug level measurement (which is now needed much less), and that follow up was not related to patient’s needs. Cooper and Huitson found that doctors were often not aware of the effect of epilepsy on patients, while Dalrymple and Appleby noted that a significant proportion of patients with epilepsy under-report their seizures to GPs.
Taylor et al. recorded how care could be improved over time by careful drug treatment, better coordination between hospitals and general practice and better diagnosis. Mant and Tulloch noted the importance of accurate disease registers for it is difficult to provide good medical care without having an accurate disease register. Redhead et al. showed that repeated audits and the use of standards were beneficial to good care in two practices in King’s Lynn. The Chester City Primary Care Group in 2001 appointed a GP to conduct a comprehensive audit of patients with epilepsy registered in 13 practices serving the city of Chester. It was noted that there were inadequate review arrangements, a surprisingly low remission rate (probably due to lack of documentation) and a high rate of diagnostic uncertainty. Re-audit in 2004–05, following the introduction of the Quality Outcomes Framework (QOF) of the new GP contract in 2004, which included payment for an annual review of patients with epilepsy and a record of seizure frequency, and an educational session for the GPs, showed a significant increase in documented remission, a significant decrease in A&E attendance, improved recording of seizure frequency, and a reduction of inappropriate use of therapeutic drug monitoring.

Although there have been no studies measuring seizure frequency directly and showing that better care within general practice has led to a significant decreased seizure frequency, there have been findings which indicate a significant and relatively strong relationship between the quality of epilepsy management in primary care (proportion of seizure-free patients) and an important care outcome (epilepsy-related emergency hospitalization). Also one study on the impact of QOF found that improved processes of care had resulted in improvements in patient outcomes in epilepsy by 29.1%. The cooperation between 26 practices and an epilepsy clinic at Wrexham led to the referral of patients with active epilepsy to specialist care resulting in 17 out of 55 (30.7%) of the patients obtaining at least 1-year seizure freedom. Poor self-management behaviour can be detected using medication records, patterns of medication ordering and self-reported questions. However for the generality of GPs, the care of epilepsy patients is problematic as exemplified by the TIGER Trial where despite some GPs receiving guidelines and a nurse specialist, there was a failure to improve the patient’s quality of life or quality of epilepsy care.

The introduction of the specially trained epilepsy nurses in primary care has led to an increase in information and advice to patients. Dellaportas piloted this service in his practice over 2 years prior to 1993 which provided patients with support and counselling, and better liaison with secondary services.

A CSAG study was set up by the Department of Health to survey the quality of care received by patients with epilepsy in the UK. It was partly
based in general practice and included a survey of 1652 people with epilepsy from 80 general practices. The study resulted in a series of recommendation from the Department of Health on epilepsy care including recommendation on primary care management and the links which should be made with primary care. These have been influential in the organization of care for patients with epilepsy in the UK.

In recent years, after the CSAG report, there have been a number of studies of epilepsy specialist nurses and epilepsy mortality. Other aspects of care have been reported from studies in West Cheshire. In 2013, the Royal College of General Practitioners appointed Dr G Rogers to act as a Clinical Champion for Epilepsy Care. He was working with seven other local East Kent GPs to run epilepsy clinics in their surgeries and has analysed a series of local projects designed to promote greater involvement of primary care in the treatment of epilepsy and to determine the extent to which high capacity programs of care in general practice are possible to achieve. The importance of an increasing prevalence of epilepsy in the elderly has been recently emphasized, and this increased prevalence is probably largely due to the increased number of persons with cerebrovascular disease in the population. There is an interesting finding in Bradford that patients of a South Asian origin have a prevalence of epilepsy of half the general population and this may be due to under-reporting of epilepsy due to stigma and emphasizes the importance of cultural sensitivity when devising care strategies for epilepsy.

Conclusions

There are a number of conclusions that we can draw from this review of the contribution of UK General Practice to the study of epilepsy.

First, the unique structure of the NHS has facilitated cohort studies which, being undertaken at a general practice level, have good epidemiological validity. The important characteristics of the structure of British General Practice relevant to such research are: that each general practice has a registered population with age/sex data: that almost all persons in that population have only a single general practice; that there is a medical record covering all GP and hospital episodes and that when the patient moves, the record is transferred to the new practice. This is an ideal system for cohort studies, and a system which cannot be replicated in most other countries. Such cohort studies have made valuable contributions to a better understanding of the prognosis and mortality of epilepsy. It is to be hoped that the major reorganization in the NHS at the current time will not compromise this potential.
Secondly, James McKenzie’s wise remarks, cited in the opening part of this paper, still have resonance. There are aspects of disease which can be particularly satisfactorily studied from general practice—for instance, the ascertainment of precipitating cause and the study of co-morbidity. This is often best studied at general practice level, where medical records from the various specialities are centralized, and which is the first port of call for patients with diverse medical problems.

Thirdly, studies of long-term care and healthcare utilization can be conducted best at a population level.

Finally, general practice, population-based studies are also fundamental when it comes to understanding the psycho-social aspects of epilepsy, the consequences of epilepsy on everyday life and the community attitudes to epilepsy. The key challenge for general practice is to improve the knowledge and outcomes for people with epilepsy. The GP is also key to understanding the best needs of patients. However, good care and good research require GPs to have a good working knowledge of epilepsy and the skills to manage patients with epilepsy.

Two other observations are apparent from our survey. First, the partnership of general practice with specialized university research departments provides a mixture of expertise which is fruitful from the point of view of general practice research. Most of the important studies on epilepsy were conducted from such a base. Secondly, the advent of large computerized databases over the last three decades has revolutionized general practice research. This has been possible by the advance of computing power and memory, the computerization of general practice and other community-based record systems, and the availability of searchable database. The result has been a massive increase in the denominator of health studies of all types, and also in longitudinal and cohort studies. This is a welcome development, but inevitably means the loss of personal oversight of individual cases. The validity of an epidemiological study is only as good as the quality of the data and the quantity does not substitute for this. Here the early Research Committee of the Royal College of GPs sets a good example.

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Conflict of interest

Both authors were involved with the Tonbridge Study and the National General Practice Study of Epilepsy. Articles by the authors were found on searching PubMed for keywords for epilepsy and either general practice, general practitioners, group practice, primary care or community care.

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