PROVISION OF CARE TO PEOPLE WITH EPILEPSY: STANDARDS AND MORTALITY

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ABSTRACT

Background

Audits of service provision for people with epilepsy in the UK have shown care to be substandard. People with epilepsy may die prematurely, and substandard care may contribute to this.

Methods

The Chiltern audit is a records audit of people taking anti-epileptic drugs in 12 general practices in Buckinghamshire. The National Sentinel Clinical Audit of Epilepsy-related death is an audit of deaths certified as being epilepsy-related in one year in the UK; the primary and specialist care sections were further explored in this thesis. In both audits documented care was compared with published standards.

Data from an incident cohort of people with epilepsy were examined to investigate which details predicted inclusion of epilepsy on the death certificate. The standardised mortality ratio (SMR) for epilepsy in England and Wales was calculated from death certificates including epilepsy. A re-analysis of a previously published meta-analysis of suicide in epilepsy was performed.

Results

The primary care audits found evidence of recent epilepsy review in fewer than two thirds of people with epilepsy. These audits suffered from lack of evidence in the clinical records. The overall standard of specialist care was adequate in under half, but there was no evidence of different standards of care in people with and without learning disability.

Epilepsy is indicated in seven percent of death certificates of people with epilepsy, confirming that they do not provide appropriate case ascertainment for studying death in people with epilepsy. The investigation of suicide in England and Wales shows that they are similarly unsuitable for investigating deaths from suicide in people with epilepsy. The SMR for suicide in epilepsy is significantly increased.

Conclusion

Poor record keeping hampers assessment of care by audit. Epilepsy care may often be substandard, but death as outcome is far removed from delivery of care; other outcomes are considered.

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ABBREVIATIONS

A&E	Accident and Emergency
AED	Anti epileptic drug
CI	Confidence interval
CIA	Central Intelligence Agency
CNS	Central nervous system
CT	Computerised tomography
DALE	Disability adjusted life expectancy
EEG	Electroencephalography
GDP	Gross domestic product
GP	General Practitioner
GTCS	Generalised tonic-clonic seizure
HDI	Human Development Index
HIS	Health Insurance Scheme (Germany)
HIV	Human Immunodeficiency Virus
HMO	Health Maintenance Organisations (United States of America)
ICD	International Classification of Diseases
IHSD	Institute for Health Sector Development
ILAE	International League Against Epilepsy
IMR	Infant mortality rate
KAWE	Kenya Association for the Welfare of Epileptics
MRI	Magnetic resonance imaging
NatPact	National Primary and Care Trust Development Programme
NGO	Non-governmental organisation
NGPSE	National General Practice Study of Epilepsy and Epileptic Seizures
NHIF	National Hospital Insurance Fund (Kenya)
NHS	National Health Service
NHSCR	National Health Service Central Register
NICE	National Institute for Clinical Excellence
NIS	National Insurance Scheme (Norway)

NSF	National Service Framework
PPO	Preferred Provider Organisations (United States of America)
SIGN	Scottish Intercollegiate Guidelines Network
SMR	Standardised mortality ratio
SUDEP	Sudden unexpected death in epilepsy
SUS	Unified Health System (Brazil)
US$	United States Dollar
WHO	World Health Organisation

PERSONAL CONTRIBUTION

The inspiration behind most of the work in this audit was Prof Ley Sander

1. The Chiltern audit

The audit was designed by Mrs Annette Russell, Prof Ley Sander and Prof John Duncan. The data were extracted from the primary case records by Annette Russell, Anita March and Alison Nixon. The original data entry into Microsoft Excel was designed by the author and performed by Annette Russell. Further data entry and checking were performed by the author. The author performed all the analyses and is responsible for writing up the study.

2. The National Sentinel Clinical Audit of epilepsy-related death

The National Sentinel Clinical Audit of epilepsy-related death was instigated by the charity Epilepsy Bereaved and the Royal Colleges. Audit record development was by the steering committee of the project. Data extraction was performed by five audit officers who also entered the data into Microsoft Excel.

The author researched the standards against which to assess care. The author prepared summaries of the primary, specialist and pathology audit records for the specialist care panel and recorded the decisions. She checked all the data entry and designed and performed the analysis for the adult specialist care section of the report and for both sections presented in this thesis.

3. Use of death certificates as case ascertainment for epilepsy

The National General Practice Study of Epilepsy was set up over 20 years ago. The author and Dr Thanasis Gaitatzis hand searched the records for details of death certificates and the author hand searched them for all clinical details and for the details of the physician who certified death. The author designed and performed the analysis, with advice from Dr Tony Johnson of the MRC Biostatistics Unit in Cambridge. The author was responsible for the publication of this study.

4. Suicide in England and Wales

This study was designed by the author, Prof Ley Sander and Dr Thanasis Gaitatzis. The author and Dr Gaitatzis independently reviewed the death certificates in which epilepsy was recorded and sought deaths by suicide. Dr Gaitatzis calculated the Standardised Mortality Ratios (SMRs). This calculation was checked by the author who also calculated the confidence intervals. The author and Dr Gaitatzis were responsible for writing up the study.

5. Meta-analysis of suicide in epilepsy

The author was responsible for all aspects of this study. She and Dr Andrew Bell independently reviewed all the studies in the original paper to ascertain the number of suicides and patient-years at risk. The author extracted the national rates of suicides from the relevant data sets and calculated the SMRs. She performed all the analyses with advice from Dr Tony Johnson and is responsible for writing up the study.

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INTRODUCTION

This thesis concerns the provision of services for people with epilepsy in the UK and its relationship to standards of care and the implications, particularly for mortality. It starts by providing a snapshot of the provision of services for people with epilepsy in the world and then reviews services for people with epilepsy in the United Kingdom (UK).

Epilepsy is one of the most common serious neurological conditions, affecting between five and ten people per thousand. It can be defined as "the occurrence of transient paroxysms of excessive or uncontrolled discharges of neurons, which may be caused by a number of different aetiologies, leading to epileptic seizures" (Sander and Hart, 1997). There are many causes of epilepsy, and in many ways seizures can be regarded as a symptom of many diseases rather than as a single disease (Sander and Hart, 1997). Epileptic seizures represent the clinical manifestations that result from excessive, synchronous, abnormal firing patterns of cerebral neurons.

People with epilepsy have increased morbidity from other causes (Gaitatzis et al., 2004a), as well as an increase in mortality rate. Substandard care could contribute to this. Work carried out for this thesis is an initial assessment to look into these concerns. It comprises an assessment of mortality, and of some of the methodological problems in the study of this. It looks into the standard of care in two ways; a national audit carried out to determine the role of care in people who died from a cause related to epilepsy and a thorough audit of the provision of services in 12 general practices.

SECTION 1. REVIEW OF THE LITERATURE

1.1. PROVISION OF CLINICAL SERVICES FOR PEOPLE WITH EPILEPSY AROUND THE WORLD – A SNAPSHOT OF CARE

People's expectations for health vary from country to country and from culture to culture (Gumnit, 1997a). While expectations may indeed vary, this may be related far more to lack of health facilities than to the basic desire for good health. Unless knowledge of facilities for epilepsy care and accurate figures for both morbidity and mortality around the world are available, it will not be possible to ascertain how the two relate. In terms of health provision in general, studies are beginning to evaluate the impact of reforms on health. A discussion paper from the Global Programme on Evidence for Health Policy (Evans et al., 2006) compared the efficiency of national health systems delivery. Using total health expenditure per capita as a surrogate for physical inputs to the health system, and Disability Adjusted Life Expectancy (DALE) as outcome, the authors established the expected positive correlation between the two (ie as expenditure on health increases, so does the DALE). Income per capita is highly collinear with health expenditure per capita (Evans et al., 2006); thus it is not possible to consider the impact of services for health independently of the financial resources of the country and the way in which they are allocated.

In 2000 almost 200 nations committed, in the United Nations Millennium Declaration, to rid the human race of want. To help track progress, a set of time-bound and measurable goals and targets was established– the Millennium Development Goals. The first of these is to halve, between 1990 and 2015, the proportion of people whose income is less than one US dollar (US$) a day (United Nations Statistics Division, 2005).

In resource-poor countries, much of the focus of healthcare is on the prevention, management and control of communicable diseases (Gourie-Devi et al., 2003).

This chapter provides a snapshot overview of services for people with epilepsy in a small number of countries around the world. Countries were not chosen at random, but were selected to provide a broad spectrum in terms of geographical distribution, as well

as population size and wealth. Wherever possible *bona fide* texts have been used, from government sources, the World Health Organisation (WHO) and the International League Against Epilepsy (ILAE). For many countries, however, it was extremely difficult to find such information. Thus, occasionally, less reliable sources have been used, such as newspaper articles or web-sites biased towards a particular viewpoint (for example, the '50 years is enough' campaign (US Network for global economic justice, 2005)). The information provided is as up-to-date as possible; nevertheless, some older sources have been used where more recent material is not available.

Countries are grouped according to the WHO regions. For most countries the infant mortality rate (IMR) and the life expectancy at birth are provided, usually from data from the US Central Intelligence Agency (CIA, 2006). These are given in an attempt to assess the general state of health of the population. It should be noted that in some countries, particularly those in Africa, life expectancy has been reduced by up to 20 years by the Human Immunodeficiency Virus (HIV) (Mathers et al., 2001). For the less developed countries the Human Development Index (HDI) rank has also been given. The HDI is a composite index of human well-being, and is calculated as a function of life expectancy at birth, adult literacy rate (and amount of schooling) and per capita gross domestic product (GDP) (United Nations Development Programme, 2005).

The section on Africa includes some information on the Bamako Initiative, as this is central to some of the problems and proposed solutions in Africa.

COUNTRIES DISCUSSED, GROUPED ACCORDING TO WHO REGIONS

Africa
Burkina Faso
Kenya
Lesotho
Nigeria
Senegal
South Africa
Uganda

Eastern Mediterranean
Islamic Republic of Iran
Morocco
Saudi Arabia
Sudan
Yemen

Europe
Denmark
France
Germany
Italy
The Netherlands
Norway
Russian Federation
Slovenia

The Americas
Argentina
Brazil
Canada
Chile
Panama
Peru
United States of America

South-East Asia
Bangladesh
India
Nepal

Western Pacific
Australia
China
Japan
New Zealand
Samoa

1.1.1. Africa

In most African countries, fees are charged for health services, reducing accessibility of services for the poor. Even in systems of 'free' public healthcare, it is rarely free in reality. Additionally, the distribution of services is unequal in Africa, favouring urban areas. Many African countries are very poor; the percentage of the population of Lesotho described as indigent in 1985 was 50% in cities and 55% in the rural areas (World Bank 1994, quoted in Stierle et al., 1999). Figures show that the percentage living on or below one US$ per day, when most recently estimated (between 1990 and 2003) was 11% in South Africa, 23% in Kenya, 26% in Senegal, 36% in Lesotho, 70% in Nigeria, (United Nations Development Programme, 2005) and 69% in Uganda (World Bank, 1999). Recently the percentage of people living in absolute poverty in Sub-Saharan Africa has risen from 42% to 47%, while in the world as a whole the percentage has dropped. Of the countries discussed here, only Uganda and South Africa are on track to halve the number of people living on less than one US$ per day by 2015 (United Nations Industrial Development Organisation, 2004).

Some African countries have introduced measures to protect the poor from charges for health services. In Senegal, indigent people are exempt from some fees, and this is administered locally. In Lesotho, there is a national policy to exempt the 'poor without means' although, in practice, few are exempt. Nigeria and Uganda each have various policies throughout the country, but Burkina Faso has no such system (Stierle et al., 1999).

Another mechanism which can improve access to healthcare by vulnerable groups is price differentiation, based on demographic, geographical or socio-economic factors, health status, or a mixture. Subsidies are recommended for various health-related activities, but in many cases funds intended for subsidies are, in fact, spent on urban health facilities providing secondary and tertiary care and mainly benefiting the richer segments of society (Stierle et al., 1999).

Some countries have introduced prepayment and health insurance to overcome problems in financing healthcare. In general they require the existence of some form of individual

or collective saving capacity, mutual confidence between members, and the presence of functioning and credible healthcare services. One advantage of these schemes is that payment does not occur at the time of need. They are, however, difficult to design and implement in low-income countries and rural areas. Additionally, indigent people may not be able to afford to pay at all, and may miss out on the benefits. Excluding public servants (whose health services may be provided by the state), under five percent of the population of Burkina Faso was covered by such insurances in 1989 (Stierle et al., 1999).

The exacerbation in the 1980s of many of the problems of healthcare in Africa has been blamed on the World Bank (Samba, 2004). A combination of natural and manmade factors, together with general worldwide economic depression, left many African countries with increasing debts. These countries turned for loans to the World Bank and the International Monetary Fund, who, in return, demanded stringent conditions, including cuts to health, education and housing programmes. Before this time many African countries provided medical services and essential drugs free of charge, but by the end of the 1990s, the health systems in most sub-Saharan countries had virtually collapsed (Samba, 2004). A different view is that user-fees were introduced in the 1980s as an alternative way of financing healthcare on the assumption that they would extend the coverage of services and promote the appropriate use of care (International Labour Organisation, 2000).

1.1.1.1. The Bamako Initiative

In September 1987, at a meeting in Bamako, Mali, the United Nations Children's Fund proposed a scheme to help solve the drug supply and maternal and child health problems of sub-Saharan Africa. This involved supplying patients with essential drugs at two to three times the cost price, and using the funds so raised to improve public health services (Anonymous, 1988). The African Health Ministers agreed with the proposal, which is based on eight principles:

- Improving primary healthcare services for all
- Decentralising the management of primary health services to district level

- Decentralising the management of locally collected patient fees to community level
- Ensuring consistent fees are charged at all levels for health services – whether in hospitals, clinics or health centres
- High commitment from governments to maintain and, if possible, expand primary healthcare services
- National policies on essential drugs should be complementary to primary healthcare
- Ensuring the poorest have access to primary healthcare
- Monitoring clear objectives for curative health services (McPake et al, quoted in Tearfund International learning zone, 2005).

Many people had misgivings about the initiative (Chabot, 1988; Garner, 1989), and countries varied considerably in the ways they tried to put these principles into action (McPake et al, quoted in Tearfund International learning zone, 2005). A study published in 2000 suggested that, although there were initial gains in some countries, these were not sustained over time. Additionally, none of the countries studied had effective exemption mechanisms to protect the poorest from the burden of payment (Gilson et al., 2000). Others, however, see the advantages of the Bamako Initiative, seeing it as an example of 'user-fees that work' (Vandemooretele et al., 1997). For example, phenobarbital and phenytoin are available in most healthcare establishments in Africa via the Bamako Initiative drug supply system (Stierle et al., 1999).

1.1.1.2. Burkina Faso

Burkina Faso (population 13 million) is one of the world's poorest countries, with literacy rates of less than one in three males and one in eight females. Education is free, but not compulsory, and less than one third of children receive basic education (Family Heath & AIDS, 1994). Life expectancy is 48 years, and the IMR is 92 per thousand live births (CIA, 2006).

Healthcare is organised into several tiers. The primary health posts, staffed by paramedical workers, provide small communities with essential treatment (Family

Heath & AIDS, 1994; Laafi, 2000). The second level, the centre of health and social promotion, treats more severe cases, and care is provided by nurses. Medical centres cater for small towns, usually having a physician and often an attached operating theatre. Hospitals are found in larger towns.

In theory, patients are referred to the next level according to the severity of their condition (Laafi, 2000). In practice, however, very few communities have a working primary health post, as these require the voluntary work of community health workers, and essential drugs are often not available. The nearest medical centre is often far away, and costs prohibitive.

Burkina Faso has only one neurologist (WHO, 2001a), but essential anti-epileptic drugs (AEDs) are available, as is Computerised Tomographic (CT) scanning. Primary care workers are responsible for follow-up and for education (Dua, personal communication). Many people with epilepsy are treated by traditional healers, although phenobarbital costs less than most traditional treatments (Millogo et al., 2004).

1.1.1.3. Kenya

Kenya (population 33 million) has a life expectancy of 47 years, and IMR of 61 per thousand live births (CIA, 2006). Since independence in 1963, Kenya has attempted to promote coverage and access to healthcare by the population (Owino, 1997). Non-Government Organisations (NGOs), mostly located in rural and underserved areas, provide services, helped by partial government grants, donations and user-fees. Private practitioners provide treatment to those who can afford it, and local government provides primary and preventative healthcare. There is a pyramid system of care, with dispensaries and health posts at the bottom of the pyramid, through health centres and subdistrict hospitals, eventually to Kenyatta National Hospital in Nairobi at the top (Owino, 1997).

Initially the government committed itself to free health services and, in 1964, abolished user-fees. Many services were free to unemployed people; employers met the expenses of those in employment. This proved unsustainable, however, and in 1989 cost-sharing

was introduced. This was supposed to generate additional revenue, strengthen the referral system and improve equity and access to health (Institute of Policy Analysis and Research, 2003). The scheme included a system of waivers and exceptions to cushion the poor and other vulnerable groups. The cost-sharing programme was decentralised, however, and this led to an arbitrary and uncoordinated fee structure (Owino W et al., 2000).

The National Hospital Insurance Fund (NHIF) was established in 1968. Contributions were compulsory for those earning above a certain limit, and aimed to assist workers to gain access to private hospitals and to relieve congestion in public hospitals (Owino, 1997). A study in 2005 found that the fund covered only 20-30% of the population, and that it was inaccessible to many (Institute of Policy Analysis and Research, 2005). Although the monthly premiums are low, many are not able to join NHIF due to high poverty levels.

Studies in Kenya have shown that patients with convulsive epilepsy can be identified and treated by primary healthcare workers, and that over half can be rendered seizure-free with the use of AEDs (Feksi et al., 1991). An NGO, the Kenya Association for the Welfare of Epileptics (KAWE) was established in 1982. Its work includes providing clinics, but also publicity to educate the population that epilepsy is a treatable, medical condition (Dekker, 2002). It depends on local and international donations (Dua, personal communication). Despite this, in 2002 it was reported that only one percent of people with epilepsy in Kenya were receiving medical care (Epilepsy Action, 2002). Basic AEDs are available, as are electroencephalography (EEG) and Magnetic Resonance Imaging (MRI). Primary care workers are involved with diagnosis, treatment and follow-up, maintenance of AED supply and education (Dua, personal communication).

1.1.1.4. Lesotho

Almost all of the two million people in Lesotho are poor (Wiskin and Torbe, 2001). The IMR is 88 per thousand live births, and life expectancy is only 34 years (CIA, 2006).

The country is divided into nine different health service areas, each covered by a hospital, most of which have satellite clinics. There is one national referral hospital to which patients are transferred if necessary (Wiskin and Torbe, 2001). Further transfer to hospitals in South Africa is sometimes necessary. At a local level, health centres have a catchment population of 6,000 to 10,000 people (World Bank, 1995). The most basic level of services is provided at the village level, through a network of village health workers. Traditional practitioners are the most common medical practitioners in Lesotho, mostly providing herbal remedies. Flying Doctors serve remote clinics (World Bank, 1995).

Poor people do not have the same access to basic services and good healthcare as those better off, and the life expectancy in the richer urban areas is almost seven years longer than in rural areas, with a similar inequity in the infant mortality rate. This may be, in part, a result of the policy to enforce user-fees (World Bank, 1995).

There is little information available on the care for people with epilepsy in Lesotho. In 2002 the country received a loan and grant to finance support to the health sector reforms programme. Part of this was intended to strengthen the mental care system, and to create standards of care and develop clinical protocols for epilepsy (Strategis, 2002). There is one neurologist in Lesotho, and the basic AEDs are available at primary care level (WHO, 2001a). Primary care workers are responsible for the initial detection of symptoms, of encouraging the patient to attend the clinic, and then for follow-up and education (Dua, personal communication).

1.1.1.5. Nigeria

Nigeria has a large population (128 million), with life expectancy of only 46 years, and a very high IMR of 98 per thousand live births (CIA, 2006). Primary healthcare in villages is provided by the village health service (manned by volunteer village health workers) and district health centres (manned by community health officers) (Adamolekun, 1997). Recently new health centres have been built, and a basic package of minimum health services has been established (Management Sciences for Health,

2002). The National Primary Health Care Development Agency, formed in 1992, is responsible for the delivery of primary healthcare services and the construction of the new health centres (Adamolekun, 1997).

Many public health institutions lack basic facilities such as medicines and dressings. The population per physician ratio is better than many in Africa, although the spread is not uniform throughout the country. In 1995, there were as many Nigerian hospital specialists practising in the US as in Nigeria (Africa Recovery, 1999).

Traditional medicine is the indigenous healthcare system in Nigeria. People with epilepsy have a strong preference for traditional herbal medicine over conventional medicine, particularly in rural areas. In a survey, of 101 patients with epilepsy, all had been treated with herbal remedies while only four were receiving conventional AEDs. The village surveyed had good primary healthcare facilities. Most patients with epilepsy seen for the first time in a conventional hospital facility have spent up to five years in traditional therapy (Adamolekun, 1997).

People with epilepsy must be referred to health centres and thence to the general hospitals, as the health centres may only use paraldehyde or diazepam as treatment. The hospitals usually have a full range of AEDs available, as well as EEG and CT scanning (Adamolekun, 1997).

1.1.1.6. Senegal

Senegal has a population of 11 million, an IMR of 54 per thousand live births, and a life expectancy of 58 years (CIA, 2006). In Senegal, micro-health organisations, which are non-profit, mutual, community-based health insurance schemes, have been formed. Several such schemes exist in and around Dakar (Organisation for Economic Co-operation and Development, 2001). Here, the health insurance organisations cooperate closely with the local regional hospital. The health insurance organisations pay for 100% of hospital costs for two weeks, while the hospital offers the organisations and their members the services at reduced cost (Novartis Foundation, 2004). Each scheme has around 500 members, but does not include all members of the community; in

particular, the very poorest still cannot afford to pay regular membership contributions. The schemes do not provide primary healthcare (Organisation for Economic Co-operation and Development, 2001).

Senegal has a chapter of the ILAE, and has been the site of a WHO epilepsy demonstration project. This found the prevalence of epilepsy to be 14 per thousand, with only 23% either not treated or treated only by traditional healers (Ndoye et al., 2005). The authors report that the prevalence appears to have increased since a similar study in 1989 and postulate that this increase may be accounted for by population changes due to the establishment in nearby Dakar of the Senegalese League against Epilepsy, which has provided people with information about epilepsy, and attracted people with epilepsy from rural areas to the suburbs of Dakar. Carbamazepine, phenobarbital and sodium valproate are generally available at primary healthcare level in Senegal (WHO, 2001a). There are epilepsy specialists in Dakar, but only limited investigations available (EEG and CT scanning). Most epilepsy care is paid for out-of-pocket. Primary care workers are responsible for follow-up and education of people with epilepsy (Dua, personal communication).

1.1.1.7. South Africa

Before the abolition of apartheid, there was no real attempt to deliver primary healthcare to the majority of the 44 million people in South Africa (International Marketing Council for South Africa, 2001). With the end of apartheid in 1994, the healthcare system in South Africa underwent changes to erase inequities in service and access, and to fund a higher level of healthcare. The aim is to provide a decentralised system that offers an equally accessible and free basic package of primary healthcare to all (Connolly, 2002). The IMR is 61 per thousand live births, and life expectancy is only 43 years (CIA, 2006).

The public sector is under-resourced and over-used, while the fast-growing private sector has most of the resources, yet cares for only 20% of the population. Many of the nation's health professionals work in the private hospitals (International Marketing Council for South Africa, 2001).

Mental health is part of the primary healthcare system in South Africa (WHO, 2001a). A study of the management of non-communicable diseases found that 80% of people with epilepsy achieved 'acceptable' control (as defined by the patient or carer) when treated by doctors at primary care clinics (Coleman et al., 1998). Investigations are available in the major cities, and AEDs are available on general practitioner (GP) prescription. The major roles of primary care include diagnosis and treatment, as well as education (Dua, personal communication).

1.1.1.8. Uganda

The population of Uganda (27 million) has a life expectancy of 51 years, and an IMR of 67 per thousand live births (CIA, 2006). Healthcare is beyond the reach of over half the households in Uganda (WHO, 2001e). In 1989 there were 79 hospitals, and in 1990 about 700 doctors, in the country. A little over half the hospitals were provided by the government (Federal Research Division of the Library of Congress, 1990). In the north of the country the facilities were poorer, and people needed to travel further to reach them. There is a structure to the health services provided, with minimal facilities at village level to meet immediate needs (WHO, 2001e).

In 1993, after years of indecision, user-fees were introduced in Uganda as a condition of a World Bank loan (Okuonzi, 2004); they were abolished in 2001 (Kajula et al., 2004). User-fees were expected to generate resources and improve quality and equity of health services. They generated less than five percent of total expenditure, and were associated with a dramatic drop in the uptake of health services. Although the system included decentralisation of delivery of services, the earmarking of many funds dictated that the district health authorities were not able to deploy them to meet local needs; hence specific local priorities frequently were not addressed (Okuonzi, 2004).

The Epilepsy Support Association of Uganda provides training for people with epilepsy as volunteers to raise awareness of the condition. They also become community-based counsellors for individuals with epilepsy and their families.

There is a shortage of basic drugs for epilepsy in Uganda (International Bureau for Epilepsy, 2002), and the cost of those that exist is prohibitive for many people (Warf, 2004). In areas of Uganda people use traditional medicine, and this seems to be particularly the case for epilepsy (Tabuti et al., 2003). Most epilepsy care is paid for out-of-pocket. Primary care is responsible for referring and counselling patients, distributing AEDs and providing education (Dua, personal communication).

Paediatric neurosurgery is available in Mbale. In 2004 there were plans to develop an epilepsy surgery programme in 2005, which would make it the only comprehensive epilepsy centre in east or central Africa (Warf, 2004).

1.1.2. Eastern Mediterranean

This WHO region mostly covers the Muslim third world. The countries described here, with the exception of Saudi Arabia (position 77 of 177), come in the lower half of the world in human development rank (United Nations Development Programme, 2005). The data for the percentage of the population surviving on less than one US$ per day are not available for Saudi Arabia or Sudan, but fewer than two percent of the population does so in Iran and Morocco, compared with 13% in Pakistan, and 16% in Yemen (United Nations Development Programme, 2005). IMRs are higher than those in the western world, and life expectancy somewhat shorter (CIA, 2006).

1.1.2.1. Islamic Republic of Iran

The population of Iran is 68 million, and life expectancy is 69 years (CIA, 2006). Over the last twenty years the rural health system has been transformed by the introduction of a primary healthcare system; the IMR in 1974 was 120 per thousand live births in rural areas and 62 in urban areas and it decreased to 30 in rural areas and 28 in the cities by 2000 (World Bank, 2005).

The basis of the primary health system is the establishment of health houses in villages with each designed to cover about 1500 people. The health house is run by health workers, whose role includes record keeping, public health education, antenatal, perinatal, and postnatal care, care of children, family planning, immunisation and

disease control. There is backup for the health houses with diagnostic and treatment services, and those needing more specialised care can be referred to district health centres or hospitals. There is a similar setup in urban areas, and the system is funded entirely by the national government (World Bank, 2005).

Mental healthcare (including epilepsy care) became integrated into the primary healthcare system in the late 1980s, and now covers the whole country. There are four neurologists per million inhabitants. Carbamazepine, ethosuximide, phenobarbital, phenytoin and sodium valproate are all generally available at primary healthcare level (WHO, 2001a). At least some care is available for people with epilepsy in hospital outpatient clinics (Baker et al., 2005). A pilot study of mental health activities in the late 1980s found that, at the point of identification, the duration of illness in 70% of people with epilepsy was more than ten years, and that most were not on regular treatment (WHO, 2001b). Epilepsy investigations are available, but there are no epilepsy specialists. Epilepsy care is paid for directly or by social or private insurance (Dua, personal communication).

1.1.2.2. Morocco

The literacy rate in Morocco (population 33 million) is under 50% (WHO, 2001c), and the IMR is high at 42 per thousand live births. Life expectancy is 71 years (CIA, 2006).

The national health system is organised in three sectors. The public sector aims to implement prevention, promotion of health and treatment strategies. Within the public sector the primary healthcare network consists of dispensaries, community health centres, local hospitals and urban health centres. Specialised and general hospitals consist of public health polyclinics, regional hospitals and academic hospitals (WHO, 2001c). There is also a private (profit making) sector and a private, non-profit sector. The health system has done much to improve the health standards in Morocco. However, there is uneven distribution of health cover and insufficient manpower and practical resources (Archane, 1994).

There are three neurologists per million population, and in 1999 there were 80 neurosurgeons in Morocco (El, 1999). Epilepsy is covered by the mental health programme. Some AEDs are available at primary healthcare level (WHO, 2001a) and there are epilepsy specialists, and epilepsy investigations. The roles of primary healthcare workers include diagnosis, maintenance of AEDs and education of patients (Dua, personal communication).

1.1.2.3. Saudi Arabia

The 26 million people of Saudi Arabia have a life expectancy at birth of 75 years, and the IMR is 13 per thousand live births (CIA, 2006).

Primary healthcare centres were established in the early 1980s (Al-Yousuf et al., 2002). They are distributed throughout the country and are the patient's first point of contact with the health system. The centres refer to general hospitals, which provide secondary care and are linked to tertiary care services. Each health centre provides preventive, curative and rehabilitative functions, as well as the provision of drugs, environmental health and health education.

Saudi Arabia is a welfare state. Healthcare, including drugs, is free (Abduljabbar et al., 1998), and most drugs can be prescribed by primary care physicians (WHO, 2001a). Most healthcare is provided from government revenues; the remaining health services are financed through private sources and through occupational health insurance premiums. There is also a pilgrimage health service which provides care for both acute and chronic illnesses of pilgrims performing the Haj (Al-Yousuf et al., 2002). There is an essential drugs list within primary care which reduces expenditure on pharmaceuticals.

Epilepsy is the second most common neurological disorder in Saudi Arabia. Specialised neurological services with modern investigations are found at some hospitals. There is less than one neurologist per million population, although there are five neurosurgeons per million (WHO, 2001a). Primary care workers are responsible for arranging tertiary

care, follow-up of patients and prescription of AEDs, education of patients and pre-marital counselling (Dua, personal communication).

1.1.2.4. Sudan

The 40 million people in Sudan have a life expectancy of 58 years, and an IMR of 62 per thousand live births (CIA, 2006). In the 1960s, medical care was free (Abdu et al., 2004), but civil war for most of the time since 1956 has caused the healthcare system to disintegrate. Healthcare facilities have been drastically reduced in the south by the war, and in the north by the economic situation, as Sudan lacks the hard currency to buy drugs and equipment (Federal Research Division of the Library of Congress, 1991).

In the 1970s, the Ministry of Health began a national programme to provide primary care, with emphasis on preventative medicine. The primary healthcare centre was to be staffed by community health workers, who would receive a few months of training (Federal Research Division of the Library of Congress, 1991). The programme had virtually disappeared by 1991. In 1992 a user fee system was introduced, meaning that uninsured patients had to pay the full cost of every consultation, laboratory service and treatment. No exemption policy was developed to protect poor or vulnerable groups; over 60% of the population is estimated to live below the poverty line. Despite an increase in gross domestic product (GDP) since 1990, government spending on health has steadily declined (Abdu et al., 2004).

A survey amongst school children in Khartoum in the 1980s found that most children with epilepsy were receiving treatment (Younis, 1983). There is little other information available. The ILAE proposed to integrate epilepsy services into the primary healthcare services in Sudan (Newsletter of the Global Campaign against Epilepsy, 2004), but this has not been followed up.

1.1.2.5. Yemen

Yemen is one of the poorest Middle Eastern countries, with a large disparity between urban areas (47% poor) and rural areas (82% poor) (Yemeni development foundation,

2002). The people of Yemen (20 million) have a life expectancy at birth of 61 years, and an IMR of 61 per thousand live births (CIA, 2006).

The government aims to improve the health status of the population and to reduce regional disparities in access to healthcare (Al-Ghabiry, 2002); in 2001, only 45% of the population had access to primary healthcare (Yemeni development foundation, 2002). Nonetheless, the public health facilities have increased since the 1970s, when only ten percent of the population had access to basic healthcare (Al-Ghabiry, 2002). There is a large public health sector as well as a private health sector. The public health sector has three tiers: the primary tier has healthcare units, staffed by primary healthcare workers, and healthcare centres staffed with one or two physicians and some nurses; secondary care is provided by district hospitals; tertiary care is provided in specialised and university hospitals in two cities (WHO, 2001d). Many primary healthcare facilities in rural areas are short of qualified staff and of drugs, whereas the secondary and tertiary levels, largely in urban areas, are better financed and better equipped. Therefore the majority of hospital patients are self-referred (Al-Ghabiry, 2002). Out-of-pocket expenses are high, and may be an important disincentive to accessing healthcare (United Nations Development Programme, 2001).

There is little information available on the care for people with epilepsy in Yemen. Commonly used AEDs are available on GP prescription, and EEG and CT are available, but not MRI. Most epilepsy care is paid for out-of-pocket (Dua, personal communication).

1.1.3. Europe

Most countries in Western Europe are well-developed, with low IMRs (between 3.7 and 5.9 per thousand live births in the countries studied here) and relatively long life expectancies (between 76 and 79 years). Conversely, those in the Russian Federation have shorter life expectancy (67 years) and relatively high IMR (15 per thousand live births) (CIA, 2006). None, however, counts as a developing country in the United Nations Development Programme report.

The western European countries investigated here have good healthcare provision, funded either through taxes or through compulsory insurance. In some countries there are out-of-pocket co-payments, but there is usually a ceiling above which patients need pay no more. Some countries use GPs as gatekeepers to the secondary care system, while others do not. All have at least reasonable epilepsy care. The Russian Federation attempted to provide compulsory health insurance, but this has not worked well in practice.

1.1.3.1. Denmark

Denmark, with 5.5 million residents, has a tax-based decentralised health system, with care free at the point of use (European Observatory on Health Care Systems, 2004). About 30% of the population purchases voluntary health insurance to cover the costs of co-payments for physiotherapy, pharmaceuticals etc. Primary care is provided by self-employed GPs. Residents choose between two options: in the first option they may access a GP free of charge, but the GP will act as gatekeeper to specialist care; in the second option they may visit any GP or specialist without referral, but will have to pay part of the cost.

The 30 to 40 thousand people with epilepsy in Denmark are treated by the approximately 250 neurologists and 300 paediatricians in that country (Gram, 1997). Paediatric neurology is not recognised as a specialty, but some paediatricians have particular interest in epilepsy. There is easy access to specialists. Any GP can request an EEG, but only hospitals can request CT scans. GPs may write repeat prescriptions for people with epilepsy. Patients are reimbursed for 75% of the costs of AEDs, but if drugs are expensive the patient can apply for additional reimbursements, so that there is a ceiling for drug costs to an individual.

Denmark has a National Epilepsy Centre, but access to the centre is limited, as referrals outside the local area need to be funded. Although GPs can refer patients to the Epilepsy Centre, traditionally those referred have intractable epilepsy, and most will have been seen by specialists in the regional neurological or paediatric wards (Schubart and Jensen, 2003).

1.1.3.2. France

Healthcare for the 60 million people in France is based on a national social insurance system complemented by voluntary insurance (European Observatory on Health Care Systems, 2004). There are three main schemes within the statutory health insurance system; the general scheme covers 84% of the population, the agricultural scheme seven percent and the self-employed scheme five percent. At the end of the last century universal health insurance coverage was established; anyone who is legally living in France and not covered by insurance has medical expenses (including any co-payments) covered (Elkan, 2003).

People can see a specialist without being referred (Elkan, 2003), and changing physician is easy. France has more physicians per thousand population than Britain, but fewer than most countries in Europe (European Observatory on Health Care Systems, 2004). Patients pay to consult a physician, but 75% is refunded by the National Sickness Insurance Funds. Most of the population takes out supplementary insurance to cover the co-payments. Some chronic diseases, such as tuberculosis, psychosis and severe learning disability, are covered fully by the state insurance, and no co-payments are required (Dulac and Jallon, 1997). Although most people with epilepsy are not exempt from co-payments, those with associated handicaps and with cognitive impairments may be exempt.

People with new onset of seizures are often seen in A&E; however, epilepsy care is often initiated by the GP and followed-up by a neurologist (Dulac and Jallon, 1997). Almost all people with new onset seizures will have an EEG and a CT scan. Although patients may choose their own physician, they are only reimbursed at the rate for their local physician unless the local physician refers them further, when reimbursement will be provided by the national insurance. About half of neurologists have specialised training in epilepsy care. In 1997 six centres in France performed epilepsy surgery. The national insurance covers all costs for this (Dulac and Jallon, 1997).

1.1.3.3. Germany

Over eighty million people live in Germany (CIA, 2006), 90% of whom are covered by insurance through the Statutory Health Insurance Scheme (HIS), which is based on income (European Observatory on Health Care Systems, 2004; Pforzheim University, 2004). Most of the rest are covered by private health insurance, as it is obligatory to have adequate health insurance. The HIS pays doctors' fees, and also for hospital treatment and medication; in the Statutory HIS, the patients pay a small fee. Ambulatory healthcare is mainly delivered by GPs; patients have free choice of physicians. There is no formal gatekeeping system by GPs and therefore referral is not necessary for visiting a specialist. In 2004 co-payments were introduced for outpatient visits.

After a first seizure, the patient is usually referred by the GP to a neurologist. Over ten percent of neurologists have additional training in epilepsy (Pfafflin and Thorbecke, 1997). If control is good, the patient will be followed-up by the GP, but can be referred back if there are further seizures or complications. Those with refractory epilepsy will receive care from a specialist at an epilepsy centre, although access to these centres is restricted. In 1993 there were over 80 epilepsy clinics for children and 39 for adults, and five comprehensive epilepsy centres (Pfafflin and Thorbecke, 1997). Surgery is carried out at 16 epilepsy centres, but (in 1997) limited to approximately 300 patients per year.

1.1.3.4. Italy

Italy has a population of around 58 million (CIA, 2006). In 1978, health insurance funds were abolished and the National Health Service (NHS) was established (European Observatory on Health Care Systems, 2001). Reorganisation in the late 1990s reinforced central state control over the NHS, but at local level, local health units are responsible for assessing needs and providing comprehensive care. In 1999 approximately 30% of the population was covered by private health insurance.

Outpatient costs are paid by the patients, with a ceiling to prevent excessive costs. People with chronic diseases and disability, as well as some people on low income, are

exempt. Private healthcare services and over-the-counter drugs also incur a cost to the user.

Primary healthcare is provided by GPs and paediatricians, who act as gatekeepers for access to secondary services. Secondary and tertiary care is provided either directly by the local health units or by contracted-out facilities. Once secondary care is authorised by the GP, the patient can choose a provider from those accredited. High co-payments, long waiting lists and low quality of services lead many people to seek private care.

Italy has more neurologists per person than any other country in Europe (one neurologist for fewer than 9,000 people) (Humphrey et al., 2002). Despite this, a study in 1992 showed that the healthcare of people with epilepsy involved a wide range of specialists, and that GPs were responsible for the diagnosis of epilepsy in 10% of patients and for its management in 22% (Giuliani et al., 1992). A more recent survey by the WHO suggests that the major task of primary care physicians in Italy is maintenance of drug therapy (Dua, personal communication).

1.1.3.5. The Netherlands

The health service for the 16 million people in the Netherlands is based on health insurance (European Observatory on Health Care Systems, 2004). There is national health insurance for exceptional medical expenses associated with long-term care or high-cost treatment, financed by payroll deductions and government funds, and most people are covered by this. Standard medical care for anyone whose income is below a certain level is provided by insurance from sickness funds. Anyone with earnings above this level is insured by private health insurance, and a further scheme exists for public servants.

Patients enrol with a GP, who acts as gatekeeper for specialist and inpatient care. Referral rates are low. The Netherlands has 100 general hospitals, eight teaching hospitals and 28 specialist hospitals. Nearly all medical specialists work in hospitals; some are salaried, but most work on a fee-for-service basis (Scholten et al., 1998).

There are three special epilepsy centres in the Netherlands, which together run 13 outpatient clinics (De Boer and Muller, 2003). Around one quarter of people with epilepsy are referred to the epilepsy centres at some stage, by neurologists, paediatric neurologists or paediatricians, and occasionally by GPs. Most people are seen only in outpatient clinics, but short stay and long stay care facilities exist. Epilepsy surgery is carried out, where indicated, at Utrecht University Hospital.

The majority of the population, with obligatory health insurance, needs to consult the GP for referral to an epilepsy specialist. The specialists tend to advise on treatment, but GPs can prescribe AEDs (Dua, personal communication).

1.1.3.6. Norway

In Norway (population four million) healthcare is predominantly provided by a tax-financed scheme, supplemented by out-of-pocket payments. The compulsory National Insurance Scheme (NIS) covers all residents. Hospital inpatient treatment is free, but most other forms of treatment require co-payment. For example, patients are charged a small amount for each consultation and each investigation. However, there is an annual ceiling for cost-sharing, and once the ceiling is reached, free treatment and benefits are provided for the rest of the calendar year (European Observatory on Health Care Systems, 2000).

Most GPs are either employed by the municipality or have a contract with the municipality which provides a basic grant and a fee-for-service from the NIS. Since 2000, all patients have needed to register with a single GP (European Observatory on Health Care Systems, 1999). GPs refer patients for secondary care as, without the referral, the specialist cannot be paid thought the NIS (European Observatory on Health Care Systems, 2000). Norway has many small hospitals, at least in part owing to the dispersed population in the north of the country. There are a few private clinics in densely populated areas, and five private hospitals. Treatment in these hospitals is financed by the NIS and by user charges.

An adult with newly suspected epilepsy will be referred to a neurologist, and followed up by either the neurologist or the GP. The most difficult cases are referred to the National Centre for Epilepsy; tertiary referral can only be made from a regional hospital. Most people with newly suspected epilepsy will have an EEG at onset, and most will have CT scanning and an MRI if the CT is normal. The epilepsy surgery service is small and centralised. Plans introduced in the 1990s may reduce referrals to the National Centre for epilepsy, and limit the availability of epilepsy surgery (Henriksen, 1997).

1.1.3.7. Russian Federation

The population of the Russian Federation, is 143 million, but declining. The IMR is 15 per thousand live births and life expectancy is 67 years (CIA, 2006).

At the time of the break-up of the Soviet Union, spending on healthcare had declined to about three percent of the budget, as more was spent on military and industrial development (Tragakes and Lessof, 2003). (Health expenditure in European countries is generally more than eight percent of GDP (Epidemiology Statistics and Health Information Unit, 1999)). Changes in policy in Russia aimed for equity in provision, and a system of compulsory health insurance was proposed to provide universal access and comprehensive cover, while giving patients freedom to choose both insurer and provider. This was to be financed by payroll contributions and was to supplement the budgetary provision. Additional voluntary insurance was to be permitted to cover services beyond those provided by the basic compulsory insurance, or people could pay directly for healthcare. In practice, health insurance financing has failed to be purely supplementary, as the budgetary provision has been reduced. In some areas no insurance companies have been set up, and in others the area is divided into sectors with insurance companies allocated to these sectors, eliminating the right to choose (Tragakes and Lessof, 2003).

In rural areas the first point of contact is a nurse-run health post. More complex problems are referred to a rural health centre, providing a mixture of primary and routine secondary care. More complex cases still are referred to polyclinics or hospitals.

Each region also has a tertiary referral hospital. In urban areas the primary care givers are doctors working out of polyclinics. There is a failure to communicate between primary and secondary care, which encourages inappropriate referrals and lack of continuity of care. Patients are assigned to a primary care doctor and although they have a technical right to change their doctor, in practice this rarely happens. There is a lack of confidence in the primary healthcare system and many self-referrals to secondary care are made; thus gatekeeping does not work in practice (Tragakes and Lessof, 2003).

There is little information available on care for people with epilepsy in Russia. The vast majority of any published information in the medical journals is in Russian, and abstracts are rarely available. The setting up of a regional epileptological centre has been described (Gromov et al., 1990). There is a Russian chapter of the ILAE. AEDs are available on specialist prescription. EEG, CT and MRI imaging are also available, and there are epilepsy specialists in the Russian Federation (Dua, personal communication).

1.1.3.8. Slovenia

The IMR in Slovenia (population two million) is low at four per thousand live births, and life expectancy is 76 years (CIA, 2006).

In 1899 a sickness fund was established, making Slovenia one of the first countries in Europe to establish compulsory health insurance. When Slovenia became part of the Socialist Federal Republic of Yugoslavia in 1945, healthcare was based on the principles of universal coverage. Private practice was prohibited and all physicians became salaried employees of the state. However, the country experienced periods of high inflation, and by 1990 the healthcare system was on the verge of financial collapse (European Observatory on Health Care Systems, 1996)

In 1991 Slovenia became independent. In early 1992 legislation was changed to introduce a compulsory and a voluntary health insurance system, and private practice was reintroduced. People are obliged to insure themselves against health risks, and virtually the entire population is covered. Those who are unemployed are covered by

payments from the local authorities (European Observatory on Health Care Systems, 1996).

The compulsory plan covers a full range of basic benefits, either in total or with co-payment; this includes treatment of epilepsy. To cover the difference between the share of healthcare costs paid by compulsory insurance and the full price, people may take out voluntary supplementary health insurance (European Industrial Relations Observatory on-line, 2005).

At the primary level, healthcare centres provide healthcare to the local community. Specialist care at the secondary levels is organised in regional general hospitals. Tertiary care, generally organised at the national level, includes university hospitals and institutes, providing highly specialised services, education and research (European Observatory on Health Care Systems, 2002c).

Personal physicians generally refer patients with epilepsy to secondary care where necessary. Fees for AEDs are fully reimbursed, and most established AEDs (except ethosuximide) are available. There are some epilepsy specialists in Slovenia, but no postgraduate education. Primary care providers are responsible for fast-track referrals, prescription of drugs and follow-up of treatment (Dua, personal communication).

1.1.4. The Americas

The countries of South America investigated here are all relatively poor; they are classed as resource-poor countries, but all appear in the upper half of the HDI ranks. Peru has 18% of its population living on less than one US$ per day; the others have less than ten percent (United Nations Development Programme, 2005). Despite poverty, Peru and Panama appear to have fairly well-structured healthcare systems, while the other South American countries investigated have less successful schemes.

Canada and USA both have high human development indices. While Canada provides healthcare that is free at the point of use, the US has private health insurance and a

variety of schemes for those who cannot afford healthcare; some people seem to have little access to healthcare.

1.1.4.1. Argentina

Almost one fifth of the 39 million people who live in Argentina live in a situation of poverty (International Development Research Centre, 1995). The IMR is 15 per thousand live births and life expectancy at birth is 75 years (CIA, 2006).

There are three main providers of healthcare; the public sector, social plans and the private sector (International Observatory on End of Life Care, 2002). The public sector, which supplies free clinical care for inpatients and outpatients, covers about 50% of the population. Outpatients are charged for medicines. The private sector, where patients meet the total cost of care, covers about five percent of the population. The Social Plans are group insurance schemes based on occupation. Employers and employees each pay a fixed fee. The plans function as sickness insurance funds, financing healthcare services of employees and their families. The patient may need to provide the difference between the fixed fee and the actual cost of treatment (International Observatory on End of Life Care, 2002).

In Argentina, patients can, without being referred, choose to see any GP or specialist. There has been very little use of gate keeping within the system (International Development Research Centre, 1995).

Mental health is part of the primary healthcare system, but facilities are not uniform across the country. There are about 1.6 neurologists per million population (WHO, 2001a). Basic AEDs are available at primary care level. MRI and EEG are available, as are epilepsy specialists. Primary care workers are responsible for monitoring treatment and provision of drugs (Dua, personal communication).

1.1.4.2. Brazil

Brazil is one of the top ten world economies, but has huge social inequalities. The population is 186 million, IMR is 29 per thousand live births and life expectancy is 71 years (CIA, 2006).

In 1990 the SUS (the Unified Health System) was created, theoretically offering total health coverage to the population (Guerreiro, 1997). This was in response to the constitution which states that health is the right of every citizen and the duty of the state to provide. There are problems with the SUS, particularly in the poorest parts, and in practice less than 80% of the population is covered. The SUS owns and runs most of the outpatient services in Brazil, but most of the hospitals are private (IHSD, 1999a). Most Brazilians, therefore, use private hospital services funded by the public sector, but with difficulties. Unofficial co-payments are common. The money the federal government disburses for services is frequently below the actual cost of those services (Guerreiro, 1997). There is unequal access to healthcare, and it is estimated that about ten million people in northern Brazil have no access (IHSD, 1999a).

The primary healthcare system in Brazil consists of home care, health clinics and diagnostic and therapeutic support services. Secondary healthcare includes specialist outpatient clinics and local and regional hospitals. Tertiary healthcare adds university hospitals. Over half of neurologists practise in the private sector. The higher income areas have more neurologists than the low-income areas. Most psychiatrists in Brazil will treat some patients with epilepsy, but a survey of Brazilian psychiatrists found that one third had no formal training in epilepsy, and most lacked knowledge on some aspects of epilepsy (Marchetti et al., 2004).

The cumulative prevalence of epilepsy in Brazil is estimated as between 12 and 21 per thousand population. The treatment gap (the percentage difference between the number of people with active epilepsy and the number whose seizures are being appropriately treated (Meinardi et al., 2001)) for epilepsy is around 50%. A recent house-to-house survey of over 55,000 people in three areas of Brazil confirmed epilepsy in nine per thousand, of whom almost 60% had active epilepsy; the prevalence of active epilepsy

was higher in poorer socio-economic groups. Almost two fifths of those with active epilepsy were on inadequate treatment, of whom half were on no treatment (Li, personal communication).

1.1.4.3. Canada

Canada has a population of 32 million, with a life expectancy of 80 years, and with an IMR of four per thousand live births (CIA, 2006).

Healthcare is provided by Medicare, which is publicly financed, but privately run. Care is free at the point of use, and the healthcare system is based on five principles; care should be universal, portable, comprehensive, accessible and publicly administered (Irvine and Ferguson, 2002). Theoretically patients have free choice of physician and hospital. The healthcare system is funded by taxes; the federal government transfers cash to provinces, but the latter may levy their own taxes to supplement the money. Although Canadians may buy private health insurance, this is limited to services that are not available under the public health system.

Healthcare providers are predominantly private, but are publicly funded. Physicians are mostly in private practice, receiving fee-for-service payments, but a few opt out of the system. In order to limit the demand for expensive treatments, Canada introduced the Canadian Coordinating Office for Health Technology Assessment, similar to (but pre-dating) the UK's National Institute for Clinical Excellence Technology Assessments. Hospitals are also limited by budgets, and in 2002 waiting time for a cranial MRI scan was an average of five months.

There are approximately 30,000 primary care physicians in Canada, providing basic medical treatments and preventative care. Patients have the right to choose their GP, and can change as often as they wish (Keene, 1997). Primary care physicians refer patients to specialists when required, and hospitals deal with these referrals as well as emergencies (Canadian Health Care, 2004).

Family physicians in more isolated areas of Canada are likely to be more involved in the care of people with epilepsy than those in urban areas (Keene, 1997). There are neurologists located in larger Canadian urban centres, and centres of excellence for people with epilepsy in almost all provinces. Patients need to be referred to these centres of excellence by their physicians. Most AEDs are available at primary healthcare level (WHO, 2001a), and EEG and MRI are available in the country. The major roles of primary care in caring for people with epilepsy are referring to specialists, monitoring AEDs and their side-effects, and counselling (Dua, personal communication).

1.1.4.4. Chile

The population of Chile is almost 16 million. The IMR is eight per thousand live births, and the life expectancy 76 years (CIA, 2006).

The National Health Service began in 1952, and provided care free of charge for people who had previously held accounts in various pension funds, to workers and their families in the social security system, and, for a fee, to the population at large (Federal Research Division of the Library of Congress, 1994). However, standards of care deteriorated, due to decreasing funding. Following decentralisation and privatisation a two-tier system resulted, with the wealthy and healthy in the private system and the poor and sick in the public system. The return to democracy resulted in public health expenditure more than doubling (Bailey, 2003).

Currently the mixed health system allows people in Chile to opt for their preferred system. About 30% opt for the private health insurance, and the rest are covered by the public system (the SNSS) (Bailey, 2003). The SNSS provides treatment free of charge to those whose income falls below a certain level, and up to 50% is payable by those with higher incomes. The private health insurance system requires that employees pay a premium in addition to that paid by employers. Medical services are then reimbursed to users at a percentage of the cost. The companies, however, may refuse to cover those at higher risk of illness, and may drop those who become higher risk. Consequently, the

SNSS covers the healthcare of most high-risk individuals (Federal Research Division of the Library of Congress, 1994).

There has been interest in epilepsy amongst professionals for many years, and epilepsy is well catered for. There are epilepsy specialists and post-graduate education in epilepsy, and there is an epilepsy surgery programme. Primary care includes the diagnosis, follow-up and education of people with epilepsy (Dua, personal communication).

1.1.4.5. Panama

In 1995 it was estimated that 40% of the population of Panama (now three million) lived in poverty, and 18% lived in extreme poverty (Pan American Health Organisation, 2001). The IMR is 16 per thousand live births, and life expectancy is 75 years (CIA, 2006).

The aim of the current health policy is to offer universal access to comprehensive health programmes. The model emphasises primary healthcare and the use of family physicians, so that health problems can be solved at the appropriate level, with the result that national hospitals no longer have to deal with problems that could be solved at the local level (Latin America and Caribbean Regional Health Sector, 2001).

There are approximately three neurologists per million population (WHO, 2001a). Basic AEDs are available at primary healthcare level, and there are facilities for EEG and MR imaging. The aims of primary care for epilepsy include follow-up of treatment, introducing a national policy for the treatment of epilepsy and promoting suitable environments for people with epilepsy (Dua, personal communication).

1.1.4.6. Peru

Peru is characterised by extreme inequalities in income distribution, with corresponding inequalities in life expectancy. About 50% live in poverty with some in extreme poverty (IDHS, 1999). The IMR is 31 per thousand live births, and overall life expectancy is 69 years. The current population is 27 million (CIA, 2006).

Peru has a well-developed service infrastructure for health, with the Ministry of Health providing the largest hospitals and most primary healthcare establishments. The Peruvian Institute of Social Security, funded by employers and employees, delivers some hospital-based services, mostly in urban areas, and the private sector provides services to the wealthiest part of the population, either through insurance schemes or through direct fees for service. The government has attempted to improve primary care availability, particularly in areas previously under-served (IDHS, 1999).

In the mid 1990s it was found that although the number of primary care facilities had been increased, costs, inefficiencies and a weak information system meant that many primary care facilities were underused. The Ministry of Health therefore introduced Local Health Administration Committees, to transfer administrative responsibility for rural health services to communally owned and administered institutions. By 1998 there were over 500 such committees, as well as 650 minor health posts. The committee facilities have higher rates of community participation (Bowyer, 2004).

There is little information available on services for people with epilepsy. Basic AEDs are available, as are facilities for neuroimaging and EEG. Primary care is responsible for diagnosis, initial treatment and follow-up, and referral to specialists when needed (Dua, personal communication).

1.1.4.7. United States of America

There are 195 million people in the USA, with a life expectancy at birth of 77 years. The IMR is 6.5 per thousand live births (CIA, 2006).

The health sector in the US is diverse, with a mix of public and private funding and provision (Irvine, 2002). The very poor have no health insurance (Gumnit, 1997b), and much healthcare is provided by Accident and Emergency (A&E) departments. As a consequence, many postpone seeking medical care, and are less likely to receive preventative care (Kaiser Commission, 2004). The major public health programme for people with low income is Medicaid (Kaiser Commission, 2004). To qualify for

Medicaid an individual must meet financial criteria and must also fit into a category such as children, pregnant women, the elderly, people with disabilities and parents. Medicaid pays for a broad range of services but pays a very low percentage of costs and therefore many practitioners will not accept its patients (Willmore, 1997).

People over 65 years old, and certain people with disabilities, are eligible for Medicare. One part of Medicare covers inpatient care, nursing and hospice care. Although there is no premium charge, there is a charge for most of these services. Another part of Medicare pays for doctors' services and outpatient care and laboratory tests. There is a monthly premium to be paid, and also some co-payments required. From 2006 some outpatient prescription costs will be covered (Kaiser Foundation, 2005).

Many Americans are covered by private health insurance, often through employment-based health insurance (Irvine, 2002). Various managed care plans have appeared in an attempt to control costs; these put administrators and 'gatekeepers' in charge of guiding patients through the healthcare network, in order to manage costs. Patients are often required to check with their health plan for approval prior to visiting a physician. Examples of these managed care plans are Health Maintenance Organisations (HMOs) and Preferred Provider Organisations (PPOs). HMOs generally provide care through hospitals and clinics that the plans own, with physicians, nurses and other personnel employed by the HMO. It is in the best interest of the HMO to enrol healthy people and provide the least amount of care (Willmore, 1997). PPOs are networks of doctors and hospitals that have agreed to treat participants in these plans for reduced fees based on pre-negotiated contracts (Irvine, 2002).

Treatment of patients with epilepsy is influenced by their health insurance plan (Willmore, 1997). Those with low income will often use hospitals with open access to emergency departments. The emergency physician will assess the patient, and then select an AED. Treatment is thus often provided by the physician with the least education. Those people enrolled in HMOs may fare little better. There is a tendency not to refer to specialists (who might require expensive tests and prescribe expensive medication). The primary care provider is not allowed to make a referral to a

neurologist until persistent demands are made or the patient develops complications (Willmore, 1997). Practice guidelines have been developed which offer a systematic process for treating patients (Montouris, 2000). Some managed care plans require practitioners to adhere to guidelines, while others offer incentives. The insistence of the insurance companies and managed care organisations that primary care practitioners manage all aspects of a patient's health means that only 17% of patients with new onset epilepsy are seen by neurologists (Montouris, 2000). However, the National Association of Epilepsy Centres recommends that, after three months of unsuccessful treatment at primary care level, the patient should be referred to a neurologist, and that after nine months of unsuccessful treatment by a neurologist, the patient should be referred for subspecialty evaluation (Montouris, 2000). In a study reported in 2003 of people who had epilepsy surgery, the average duration of epilepsy before being seen at the epilepsy referral centre was 18 years; 22 of 36 patients operated on were referred by neurologists, while 14 were self-referred (including five who had been specifically advised not to consider surgery) (Benbadis et al., 2003).

The A&E department is the source of initial, primary and ongoing care for many children (Clancy, 1997). When a child has a first seizure, the diagnostic evaluation will vary depending on the type of health insurance, and there is no consensus for minimal diagnostic evaluation (Clancy, 1997). Children with epilepsy may be cared for by the family physician or a paediatrician; access to an epilepsy specialist is often dependent on insurance. There are relatively few comprehensive paediatric epilepsy centres. Although EEGs can be ordered by any physician, there is variability in the quality of recordings and interpretation.

1.1.5. South-East Asia

In many parts of the world, beliefs about epilepsy are based on myths and misconceptions. In parts of Asia, faith healers may be consulted in preference to medical doctors (Gourie-Devi et al., 2003).

Bangladesh, India and Nepal all occur in or near the bottom half of the HDI, with over one third of the population estimated to live on less than one US$ per day (data from

1990 to 2003) (United Nations Development Programme, 2005). Much of the population has access either to primary care only, or to no healthcare at all.

1.1.5.1. Bangladesh

The population of Bangladesh is large (143 million). Life expectancy is 62 years (CIA, 2006), and illiteracy is widespread. Less than 40% of the population has access to basic healthcare; many trained staff are unwilling to work in rural areas, hence access to services is inequitable (Pearson, 1999).

Primary health centres were established over 20 years ago, and initially included operating theatres and x-ray, pharmacy and inpatient facilities. An essential package of services has been defined for primary health centres, and includes reproductive healthcare, child healthcare, communicable disease control and limited curative care. The facilities in the health centres often deteriorated and many doctors are unwilling to work in them. The hospital system is overused, as many people bypass the primary health centres (Pearson M, 1999).

There are an estimated 1.5 million people with epilepsy in Bangladesh (Mannan, 2004). The Epilepsy Association of Bangladesh organises seminars and workshops about epilepsy for health professionals, and also runs free epilepsy clinics; however, only a small proportion of people with epilepsy is treated. Many people have alternative beliefs which influence their attitudes towards epilepsy; only about 20% of people with epilepsy will seek medical advice. Even when advice is sought, drug supply is not satisfactory and many patients cannot afford the drugs (Mannan, 2004). Theoretically phenobarbital and phenytoin are available with a prescription from a GP, and carbamazepine and sodium valproate with a prescription from a specialist. The only source of funding for epilepsy treatment is out-of-pocket. Primary care workers are able to refer patients to higher levels within the health system, and sometimes follow-up the patients themselves. All investigations are available within the country. There are epilepsy specialists but there is no post-graduate education available (Dua, personal communication).

1.1.5.2. India

Between the early 1950s and the 1980s healthcare facilities and personnel in India increased substantially, but the increase was outstripped by the growth in population (Indian Child, 2000). The IMR of the population (one billion) is estimated at 57 per thousand live births and life expectancy at about 66 years (WHO Regional Office for South-East Asia, 2000).

Primary healthcare is provided by subcentres manned by health workers, and by primary health centres (Gourie-Devi et al., 2003) staffed by primary care practitioners, supported by nurses and health assistants. Although 70% of the Indian population lives in villages, only 30% of medical personnel practises there (Mani and Subbakrishna, 2003). Complicated cases are referred from primary health centres to sub-district hospitals, and from there to district hospitals or to the large government hospitals (Mani and Rangan, 1997). Tertiary care is provided by the hospitals of medical colleges and specialised centres (Gourie-Devi et al., 2003).

Healthcare in India is funded by both the federal and state governments (Mani and Rangan, 1997), but only a little over two percent of the government budget is given to healthcare. More recently a general health insurance system has been introduced; this covers only people between five and 70 years old and specifically excludes epilepsy from its cover. Some employees are entitled to free or reimbursable services in certain hospitals; private insurance companies barely exist.

Many people consult traditional or spiritual healers for their illnesses. The treatment gap for epilepsy in India is between 50 and 70% (Gourie-Devi et al., 2003). Various groups have attempted to improve care for people with epilepsy. Suggestions include teaching simple practical epilepsy-related medicine to primary healthcare physicians and also providing sufficient teaching to paramedical workers to enable them to be able to identify cases (Mani and Rangan, 1997). In 2003 there were fewer than 700 neurologists in India, about one per 7,000 people with epilepsy (Gourie-Devi et al., 2003). Epilepsy surgery is being developed in a few large centres (Mani and Rangan, 1997).

The main AEDs available are phenobarbital and phenytoin. MRI, CT scanning and EEG are available in the country. The primary method of paying for epilepsy care is out-of-pocket (Dua, personal communication).

1.1.5.3. Nepal

Nepal is one of the poorest countries in the world, and has a population of around 27 million. There is one doctor per 20,000 population (Rajbhandari, 2004). Around 70% of the burden of disease is due to communicable diseases. Life expectancy is about 62 years and the IMR is around 60 per thousand live births (WHO Regional Office for South-East Asia, 2000). Many rural communities are distant from health centres, and health services are fragmented. Governmental health facilities are more widespread than mission and private facilities. In government health facilities patients pay subsidised rates (Rajbhandari, 2004), whereas user-fees are commonplace in mission and private facilities (IHSD, 1999b).

The prevalence of epilepsy is around seven per thousand population (Nepal et al, quoted in Rajbhandari, 2004). In one study almost half of new onset seizures were caused by neurocysticercosis (Rajbhandari, quoted in Rajbhandari, 2004). In 2003 there were seven neurologists in the country, and some investigations are available. Most basic AEDs are available in some situations. The treatment gap in rural areas is between 74 and 80%. In Nepal, primary healthcare workers are involved in health education and referral, and treatment of people with uncomplicated epilepsy (Dua, personal communication).

Many Nepali people do not attribute seizures to a disease, but to evil spirits and weakness. As a result, the practice of traditional treatment of epilepsy is prevalent (Rajbhandari, 2004).

1.1.6. Western Pacific

There is a wide range of healthcare availability in the Western Pacific Region. Australia and New Zealand are both well-developed countries with good systems of health

provision. GPs act as gatekeepers in both systems. Japan is one of the most developed countries, and has good access to healthcare with mandatory insurance cover, and thorough epilepsy care. China is a relatively poor country, with 17% living on less than one US$ per day (United Nations Development Programme, 2005) and access to medical care is limited. Samoa is a small nation with a poor economy; most tertiary care is provided in Australia or New Zealand.

1.1.6.1. Australia

The people of Australia (20 million) have a long life expectancy at over 80 years and low IMR at four per thousand live births (CIA, 2006).

The healthcare system is financed through general taxation and a health insurance levy (European Observatory on Health Care Systems, 2002a). It offers universal access to healthcare through the government health insurance system, Medicare. Medical treatment is mainly free and its use is largely unlimited. Self-employed GPs provide most medical care. Patients are free to choose their GP, and may consult more than one, as there is no need to enrol with a practice. Most GPs 'bulk-bill' the health insurance commission so that their services effectively are free to patients. Alternatively the GP may charge the patient a higher amount and the patient may then reclaim an 85% rebate. GPs act as referral gatekeepers to the rest of the healthcare system. Medicare reimburses 85% of the schedule fee for outpatient appointments. There is also, however, a large private sector in the health service, as the government provides a 30% subsidy to individuals who acquire private health insurance (Australian government: Department of Health and Ageing, 2005).

The GP is usually the first point of contact for a patient with a first seizure (Averis, 1997), and may refer the patient to a specialist neurologist where necessary; epilepsy is the second most common reason for referral to neurologists. People with epilepsy commonly see both the GP and the neurologist. Occasionally people with epilepsy may be referred to a comprehensive epilepsy centre for initial diagnostic evaluation, particularly if there are complications. GPs are responsible for the long-term follow-up

of people with epilepsy, including monitoring of seizure control and side-effects of medication.

Most GPs will initiate AEDs on occasions, and more than half of these do so frequently. Patients with refractory epilepsy or with complex problems may be reviewed at the comprehensive epilepsy centre, but a recent questionnaire showed that very few GPs knew of the existence or role of the comprehensive epilepsy service.

1.1.6.2. China

China has the largest population in the world (1.3 billion). It has a relatively low IMR at 24 per thousand live births, and relatively high life expectancy (72 years) (CIA, 2006).

Prior to the 1980s, funding for healthcare in rural areas was arranged through the collective, and in urban areas through medical insurance or direct provision of health services by employers (Walford, 2000). Since then, however, public sector healthcare providers have had to generate revenues to cover the difference between costs and the government's allocation (Liu, 2004). In rural areas this meant that the system of referral (village health station, township health centre and country hospital) became fragmented, with different health facilities competing for revenues from patients. For many patients, the village health practitioner is the first and only point of contact with the medical system. The rural doctors have little supervision or professional training.

Despite rising medical costs, fewer people are now covered by medical insurance. In regions where many people live in poverty the admission rate of people without insurance is seven-fold lower than that of people with insurance. Many people in hospital in rural China are discharged against medical advice, frequently because they cannot afford to stay any longer (Liu, 2004).

More recently, insurance schemes have been developed to try to increase healthcare utilisation. The subsidised insurance is, however, intended only to help cover catastrophic medical expenses (Liu, 2004).

People with epilepsy face stigmatisation, such that they become withdrawn from society. An epidemiological estimation in 2000 found the prevalence of epilepsy was seven per thousand, and the number of people with active epilepsy almost five per thousand. Over 40% had never received any treatment for epilepsy (Wang et al., 2003). Phenobarbital, phenytoin, carbamazepine and sodium valproate are all available on GP prescription, and investigations are available. The tasks of primary care workers include diagnosis, treatment, follow-up and education of patients and the community. Both epilepsy specialists and postgraduate education are available in China. The primary source of finance of epilepsy care is out-of-pocket (Dua, personal communication), although a National Epilepsy Programme is being set up and will cover the cost of AEDs (Wang et al., 2006).

1.1.6.3. Japan

Japan is a country with 125 million residents, of whom 75% live in urban areas (Seino and Yeh, 1997). It has one of the longest life expectancies in the world, at 81 years, and a low IMR (three per thousand live births) (CIA, 2006). Access to healthcare is readily available. The government began providing health insurance in the 1920s and it was extended to the whole population in the 1960s. There are two main forms of health insurance – employee insurance and the national health insurance (Yeh and Seino, 1997), and it is mandatory to have a policy (Ikeda S, 2004). Neither system provides over-the-counter drugs, and reimbursement is provided only for those drugs listed on the drug price list. Although the insurance premiums are supposed to finance the health insurance system, there is also a system of public support (Japan Pharmaceutical Manufacturers Association, 2005).

In 1997, Japan had 170 physicians per 100,000 people. There are almost no GPs. People with epilepsy are cared for by neuropsychiatrists (almost half), neurologists and paediatricians (almost one quarter), with a small number being cared for by neurosurgeons (Seino and Yeh, 1997).

In about one quarter of adults with epilepsy it is refractory to treatment, and specialists in epilepsy usually manage these. Those with the most severe epilepsy reside in mental

hospitals. The National Epilepsy Centre, Shizuoka, provides comprehensive epilepsy care with a multidisciplinary team, and supplies training and research (Seino and Yeh, 1997).

All patients with epilepsy have an EEG at diagnosis, usually including sleep deprivation. At Shizuoka, outpatients who are seizure-free also have an annual EEG to ascertain the need for continued medication. Patients are usually seen at least four times a year, and many are seen more frequently. Patients with newly diagnosed epilepsy are usually started on monotherapy, with polytherapy reserved for treatment refractory patients. Surgical treatment of epilepsy was started in 1983, and by 2001 almost 500 operations had been performed (Mihara et al., 2004).

1.1.6.4. New Zealand

New Zealand has a population of four million people, with long life expectancy (78 years) and a fairly low IMR (almost six per thousand live births) (CIA, 2006).

The structure of the health service has been changed many times in recent years. The healthcare system is largely financed through taxation, whilst out-of-pocket payments provide much of the rest. Primary care, provided by GPs, is charged on a 'fee-for-service' basis, with subsidies for people on low incomes (European Observatory on Health Care Systems, 2002b). Drugs are provided free for inpatients, but in the community a co-payment is charged. Private insurance exists, but mainly insures people against the supplementary costs; most insurers do not offer comprehensive health cover. Hospital outpatient and inpatient services are provided free of charge. Most hospital specialists are paid a salary, but many also work in private practice (European Observatory on Health Care Systems, 2002b). Patients may choose their GP who will act as a gatekeeper, as patients are not able to access free specialist services without referral.

New Zealand has facilities for investigations, and AEDs are available (WHO, 2004). The major role of GPs is to review the patient, maintain the treatment and educate on first aid and seizure prevention (Dua, personal communication). The Maori population

apparently has an excess of hospitalisations for seizures, whilst Epilepsy New Zealand field officers report few Maori clients using their services of support and information (Hills MD et al., 2005).

1.1.6.5. Samoa

Samoa is a small group of islands in the South Pacific Ocean, with a population of 177 thousand people. The IMR is 27 per thousand live births, and life expectancy is 70 years (CIA, 2006).

The economy of Samoa is dependent on development aid and overseas remittance, as well as on agriculture and fishing. Approximately six percent of GDP is spent on the health sector. The Ministry of Health provides primary, secondary and limited tertiary care, financed by public sources. Most tertiary care is provided in New Zealand or Australia. There is some private healthcare available, and some of the population uses traditional healers. Non-communicable diseases are the major cause of death. Many patients, particularly from the rural areas, present late with advanced disease (WHO Regional Office for the Western Pacific, 2005).

There are no epilepsy specialists in Samoa, and no facilities for investigations (Dua, personal communication). Phenytoin, carbamazepine and sodium valproate are available (WHO, 2004). The role of primary care in epilepsy is to prescribe AEDs, review the patients and educate them on first aid and seizure prevention (Dua, personal communication).

1.1.7. Conclusion

Healthcare systems around the world vary according to the way in which they are financed (private insurance, social insurance, tax-based or out-of pocket), and in the way in which they are structured. Most countries seem to have, at least in theory, a tiered system, with referral from primary to specialist care. Some countries provide care which is free at the point of use, although some rely on out-of-pocket payments for some expenses. In other countries compulsory health insurance ensures care. The resource-poor countries frequently rely on user-fees, which prohibit many people from accessing

healthcare. Inequalities in distribution of healthcare services and in access to it persist in many parts of the world.

In 1999 estimates of health life expectancy were produced for the 191 WHO member countries. It was found that there was a striking relationship between healthy life expectancy at birth and average health expenditure (Mathers et al., 2001). Other investigations of the same countries attempted to measure the efficiency of countries in providing care. It is notable that all the African countries investigated here are in the least efficient one third of countries, along with Russia and Samoa (ranked 127 and 131 of 191 respectively) (Evans et al., 2006).

Thus healthcare throughout the world depends not only on the budget available, but also on the efficiencies of the systems. This is a complex area. In all countries health services are stretched, but in the resource-poor countries the effect of this is much greater and healthcare is relatively poor in terms of budget and of efficiency; care provided for people with epilepsy reflects this.

1.2. PROVISION OF CLINICAL SERVICES FOR PEOPLE WITH EPILEPSY IN THE UNITED KINGDOM

The provision of medical care for people with epilepsy in the UK is reviewed here. Any analysis of the adequacy of services for epilepsy needs to take into account both the clinical needs of the patient and the patient's preferences.

1.2.1. Brief history of the National Health Service

People who live in the UK have most of their healthcare provided by the National Health Service (NHS). The NHS was set up in 1948, and is the largest organisation in Europe. The most important part of the new service was the GP who, as provider of primary care, was the gatekeeper to the rest of the NHS, referring patients to secondary care when necessary, and prescribing drugs. From its outset the NHS aimed to provide care free at the point of delivery (NHS Act, 1946), on the basis of need and not on the ability to pay. The service was financed through central taxation, meaning that the rich paid more than the poor for comparable benefits (Rivett, 2005). From the start, however, it had financial problems, as public expectations rose, and the innovations of medical science increased costs. Prescription charges were introduced in 1952, together with a flat rate fee for dental treatment.

In the early 1990s, in an attempt to address the problems resulting from limited resources and increasing demands, it was decided to establish an 'internal market' in which Health Authorities would purchase care for their populations from providers. At the same time, many GPs elected to hold their own budgets with which to buy healthcare for their patients, becoming 'Fund Holders'. Later in the same decade, but with a new government, a white paper entitled 'The new NHS - Modern, Dependable' was enacted, attempting to replace the internal market with integrated care. This introduced the National Institute for Clinical Excellence (NICE), the Commission for Health Improvement, and National Service Frameworks (Rivett, 2005). In 2000 the NHS Plan was published, a ten year plan for investment in the NHS (Binley, 2005). It focused attention on the patient, and, whilst it allocated investment to the NHS, it also planned for devolution of power from the government to the local health service

(Department of Health, 1999). Various government publications since then have sought to clarify how the NHS plan was put into action. In 2004 the NHS Improvement Plan was published, setting priorities for the NHS, and in 2005 the Department of Health published 'Creating a Patient-led NHS' (Binley, 2005). The new primary care contracts in 2004 were designed to reward general practices for the quality of care they provided rather than the number of patients under their care (NHS, 2005). More recently, patients have been given the choice of where and when their hospital treatment takes place (NHS, 2006).

The NHS is constantly evolving, and is different over the four nations of the UK.

In England the Secretary of State for Health is responsible for the NHS and the Department of Health is responsible for the overall planning, regulation and inspection of the health service. There are 28 Strategic Health Authorities, each concerned with the healthcare of one region; they need to ensure that trusts achieve national objectives whilst keeping services in line with local needs. Primary Care Trusts (PCTs) provide primary care and commission hospital services; as such they are responsible for much of the NHS budget. Secondary care services in England are organised in almost 300 NHS trusts. Some NHS trusts have opted out of NHS control to become Foundation Trusts; these are accountable through performance contracts with PCTs and through independent inspections (Binley, 2005).

In Scotland, the Scottish Executive Health Department oversees the work of the 15 area health boards which are responsible for health service planning. There are both primary care and acute hospital trusts. The Scottish Intercollegiate Guidelines Network (SIGN) (SIGN, 2003), aiming to improve quality of care by reducing variation in practice, develops national clinical guidelines based on current evidence (Binley, 2005).

The NHS Wales Department sets healthcare policy in Wales. The 22 local health Boards buy services from healthcare professionals in primary, secondary and tertiary care.

In Northern Ireland, healthcare is overseen by the Department of Health, Social Services and Public Safety. Specialist care is provided by 15 acute hospitals and primary care by local health and social care groups, centred around general practices (Binley, 2005).

People in the UK may choose to use private healthcare; this sector is much smaller than the NHS. Most people are registered with an NHS GP, but may use the private sector for specialist care. Whilst some people pay directly for private healthcare, more are members of health insurance schemes, sometimes funded by employers (BBC Action Network Team, 2005). Private healthcare is thus more often used for one-off specialist treatment, or specific operations, than for chronic conditions (Medic Direct, 2006).

1.2.2. Provision of care for people with epilepsy

Epilepsy is one of the most common neurological conditions yet in the UK provision of care for patients with epilepsy is patchy. Since 1948 there have been six government-sponsored reports into epilepsy services (Hanna et al., 2002). The Clinical Standards Advisory Group (CSAG) report, published in 2000 (CSAG, 2000), stated that still 'there is a lack of focus for services for people with epilepsy and lack of co-ordination between primary care, secondary care, specialist centres and the voluntary sector'.

In 1997 the Scottish Intercollegiate Guidelines Network produced guidelines for the management of epilepsy (SIGN, 1997), and these were updated in 2003 (SIGN, 2003). The National Sentinel Clinical Audit of epilepsy-related death was published in 2002, and reported that a majority of people had received inadequate secondary care and that many deaths were potentially or probably avoidable (Hanna et al., 2002). In response to this, the Department of Health published its Action Plan (Department of Health, 2003b) which focussed the attention of health departments on epilepsy. Since then, numerous government initiatives and reports have included epilepsy in their recommendations. Particularly relevant are the NICE guidelines on the diagnosis and management of the epilepsies in adults and children in primary and secondary care (NICE, 2004c) and the NICE technology appraisals on newer drugs for epilepsy (NICE, 2004a; NICE, 2004b). As a result of the Action Plan, the 'Be epilepsy aware' card was produced by the Department of Health (Department of Health, 2004); this includes information on the

risks of epilepsy, and provides contact details of epilepsy organisations. The Medicines Partnership also produced a leaflet for people with epilepsy encouraging them to ask for an epilepsy review (Medicines Partnership, 2004). Other government initiatives have involved care for people with epilepsy amongst others (for example, the guidelines for the appointment of GPs with a special interest (Department of Health, 2003a) and Standards for Better Health (Department of Health, 2005c)). The National Service Framework into long-term conditions specifically mentions epilepsy (Department of Health, 2005b). Recent publications, including the Expert Patients Programme (Department of Health, 2005a), and the new white paper 'Our health, our care, our say' (Department of Health, 2006) encourage the participation of patients in their care. The National Primary and Care Trust Development Programme (NatPact) included a competency framework for epilepsy services encouraging the use of practice epilepsy registers, regular check ups of people with epilepsy and effective links with secondary care providers (NatPact, 2005). Various non-government organisations have also published recommendations to improve epilepsy care. For examples of these and of national and governmental recommendations, see appendix 1.

Modern understanding of the nature of epilepsy began in the middle of the 19th century (Taylor, 2000). It was then recognised that epilepsy was a symptom of a variety of brain disorders. Despite the fact that most of the founding fathers of British neurology had an interest in epilepsy, their successors became disinterested in the subject (Sander et al., 1993). Indeed, at the time of the inception of the NHS in 1948, there were about 50 consultant neurologists in the UK, mainly in and around London, of whom only one or two had a major interest in epilepsy. By the time of the CSAG report there were about 330 consultant neurologists in the UK, relatively few of whom had a specialist interest in epilepsy. In 2002 the Association of British Neurologists found that there were 358 consultant neurologists in the UK, less than eight neurologists per million population, whilst France had 26 per million, the Netherlands 39 and Italy 123 (Humphrey et al., 2002). By early 2005 the number of UK consultant neurologists had risen to approximately 460 (British Association of Neurologists, personal communication).

The new contract for GPs was introduced in 2004, and brought about a major change in funding. The contract includes quality markers, and associated financial incentives, for the management of ten conditions in primary care; epilepsy is one of these conditions. Practices wishing to gain this funding should be able to produce a register of patients receiving drug treatment for epilepsy. They also receive funding for the percentage of patients aged 16 and over who have a record of seizure frequency, for those aged 16 and over with a record of medication review and for those aged 16 and over who are seizure-free, all in the previous 15 months (NHS Confederation and British Medical Association, 2003). It appears that many practices are taking up this option; in England in 2004-5 only approximately 50 practices did not have an epilepsy register (NHS Health and Social Care Information Centre, 2005). Intuitively it would seem that improved record keeping would translate into improved quality of care, and thence to improved quality of life for people with epilepsy; there are no randomised controlled trials available to support or refute this notion. The way in which the review is performed will impact on the effectiveness of the process. If the activity is seen merely as a 'tick-box' exercise, then little will change for the better for people with epilepsy. If, however, GPs undertake proper reviews and react to the problems they encounter, this may improve the lives of people with epilepsy.

The Department of Health Action plan suggested a specific framework to help develop more GPs and nurses with a special interest in neurology (Department of Health, 2003b). This is already happening in parts of the UK (Rogers, 2002), and there may be up to 100 GPs with a special interest in epilepsy now.

Most of the deficiencies perceived by GPs and patients in the CSAG studies related to the interface between primary and secondary/tertiary care. Suggested ways to improve this communication were: epilepsy co-operation cards, shared-care protocols, electronic patient records/healthcare records and the sharing of data sheets and information sheets with GPs. Pivotal to the care was seen to be the provision of epilepsy specialist nurses, acting as a contact point for GPs seeking advice, visiting general practices and holding outreach clinics, facilitating fast-track referral, acting as a resource for information about local services and training GPs, practice nurses and volunteers (CSAG, 2000).

NICE guidelines also reinforce the role of epilepsy specialist nurses, stating than they should be an integral part of the network of care for people with epilepsy (NICE, 2004c). In 2004 over 400 nurses were members of the Epilepsy Specialist Nurses Association (Epilepsy Specialist Nurses Association, personal communication). Many of these may include epilepsy as only a minor part of their role.

1.2.2.1. Primary care

1.2.2.1.1. New diagnosis

GPs are well placed to gain an accurate account of an initial episode suggestive of epilepsy. The diagnosis of epilepsy is largely based on the history of the attack (SIGN, 2003), and the GP may well be the best person to take a detailed history from the patient and any eye-witnesses before salient features are forgotten or (unintentionally) embellished. A GP with an average sized list can expect to see one or two patients with new-onset epilepsy each year (Hall et al., 1997). Because of the potential problems of diagnosis, however, it is recommended that a consultant neurologist, or other specialist with an interest in epilepsy should see patients with a possible diagnosis of epilepsy promptly; the 2003 SIGN and 2004 NICE guidelines both suggest that the diagnosis should be made by an epilepsy specialist, and that patients should be seen within two weeks (SIGN, 2003; NICE, 2004c). The SIGN guidelines also suggest that the 'shared care management system' should 'provide appropriate information' once a provisional diagnosis has been made, and the patient referred to a specialist centre (SIGN, 2003). The patient should be fully informed of the specialist's findings, as should the GP (Hall et al., 1997).

The Epilepsy Needs Revisited document (Brown et al., 1998) suggested that GPs should not usually initiate treatment, and the SIGN Guidelines confirm this, stating that the decision to start AEDs should be made by the patient and epilepsy specialist (SIGN, 2003). The NICE Guidelines suggest that an epilepsy specialist should recommend the appropriate treatment, and also plan its continuation in partnership with the patient. It is important that treatment is initiated with the most appropriate AED at diagnosis as, once patients become seizure-free, they may be reluctant to change AEDs, regardless of side-effects, particularly if driving licences have been obtained (Goodwin et al., 2002).

Once the diagnosis has been established, the primary care team can help the patient to understand the implications of epilepsy. The following checklist has been proposed for the first review of the patient by the primary healthcare team, after the diagnosis of epilepsy has been made (Hall et al., 1997):

- Discuss the diagnosis
- Review seizure frequency; consider the use of a seizure diary
- Discuss drugs – the benefits and side-effects
- Discuss the impact on the patient's lifestyle
- Find out what the patient knows and fill in the gaps
- Provide addresses of patient organisations
- Discuss contraception and pregnancy with women
- Agree a timetable for follow-up.

1.2.2.1.2. Active epilepsy

About 30% of patients who develop epilepsy will continue to have seizures despite treatment with AEDs, and the Epilepsy Needs Revisited document suggested that most of these will require further specialist follow-up (Brown et al., 1998). It is to the GP, however, that most patients will have ready access when problems arise. CSAG recommended that, for patients in whom seizure control is sub-optimal, a management plan should be formulated jointly by the hospital and general practice. This would help to alleviate the mismatch which could occur when the patient's epilepsy is being looked after by secondary or tertiary care, but when the patient has access only to the GP when acute problems occur. During routine visits, GPs should monitor drug dosages, seizure frequency, adverse drug effects, adherence to AED regimen and any other problems (CSAG, 2000). The NICE guidelines further propose that, for each person with epilepsy, there should be a comprehensive care plan that is agreed between the individual and primary and secondary care providers, and which includes medical and lifestyle issues (NICE, 2004c). Patients should receive appropriate information and education about all aspects of epilepsy, and some can be encouraged to manage their epilepsy more effectively through the Expert Patients Programme (Department of Health, 2005a).

1.2.2.1.3. Controlled epilepsy

It is generally accepted that those no longer experiencing seizures can be returned to primary care with provision for re-referral when necessary. Primary care services for epilepsy, however, vary from practice to practice, and many patients receive little epilepsy care, their care being reactive rather than proactive (Chappell and Smithson, 1998). The NICE guidelines suggest that patients should have a regular structured review, performed by either the GP or specialist depending on the circumstances and severity of epilepsy, which should occur at least once a year (NICE, 2004c). The GP should re-refer the patient to secondary care if the seizures are inadequately controlled, or if there are specific medical or lifestyle issues, such as pregnancy or consideration of withdrawal of AEDs.

1.2.2.1.4. Those not under current review

There may be problems in attempting to review all patients with epilepsy, particularly those who have not been reviewed for some years. Patients may not wish to be reminded of the diagnosis, which may have been denied or concealed (Taylor, 2000), and there may be anxiety about the prospect of change (Elwyn et al., 2003). It has been suggested that the best time to offer a review is when a prescription is due (Taylor, 2000). In keeping with the goal of patient-centred medicine, it is suggested that the first requirement is to define the main problems as seen by the patient; whether directly seizure-related, AED side-effects or psychosocial problems (Taylor, 2000). The correctness of the diagnosis should be challenged, the frequency and severity of seizures ascertained, and all aspects of AED therapy, including adherence to drug regimen, discussed. It has been shown that reviewing patients with epilepsy in general practice, reducing polypharmacy and changing treatment, can improve seizure control in over one quarter of patients, and reduce side-effects in almost one quarter (Taylor, 2000). In many cases, however, re-referral to specialist care for these alterations may be more appropriate.

1.2.2.2. Specialist Care

A major recommendation of the CSAG report was that hospital epilepsy services should be better organised, take a local population focus and have better links to other services; it suggested that the core of this service would be the epilepsy centre. Emphasis should be on shared care and better communication between general practice and hospital (CSAG, 2000).

The NICE guidelines do not specifically address models of care, nor recommend what form of service configuration can best provide the resources required. A Cochrane Review found that there were no controlled trials of suitable quality to compare epilepsy clinics versus general neurology or medical clinics for the treatment of people with epilepsy (Bradley and Lindsay, 2005). Nevertheless, several studies have shown that neurology opinions may contribute useful advice to, or change the diagnosis in, patients previously under the care of non-neurologists (Hillen and Sage, 1996; Steiger et al., 1996), and the Association of British Neurologists states that neurologists who specialise in epilepsy (or other conditions) are better at managing those conditions than neurologists without such a specialism (Humphrey et al., 2002). Whatever form the clinics take, there is agreement that people needing specialist care for epilepsy should be treated by a specialist with an interest in epilepsy.

1.2.2.2.1. New diagnosis

As long ago as 1969 the Reid report recommended that patients who develop seizures should be referred for specialist opinion (Reid, 1969). This recommendation has not altered. The function of the hospital-led service is to:

- Confirm the diagnosis
- Initiate treatment, if indicated
- Provide initial counselling and information to patients and their families
- Monitor the response to the initial treatment, and
- Refer the patient back to the GP if the condition is stable (Brown et al., 1998).

The NICE guidelines (NICE, 2004c) propose that the diagnosis of epilepsy should be established by specialist practitioners with training and expertise in epilepsy. (Misdiagnosis of epilepsy is common, occurring in up to one quarter of patients referred to a specialist clinic (Smith et al., 1999) and in at least one fifth of people from primary care who were assessed by a specialist (Scheepers et al., 1998); there may be physical, psychosocial and socioeconomic consequences of a misdiagnosis.) After a detailed history of the attack has been obtained from the patient and any eye-witnesses, a full physical examination, including cardiac, neurological and mental state, should be carried out. Appropriate investigations should be available where necessary. The guidelines stress that information on how to recognise a seizure, and first aid for seizures should be provided to the individual, to the family and to carers. Some information should be provided while the diagnosis is awaited. Once epilepsy is diagnosed, seizures and syndromes should be classified using a multi-axial diagnostic scheme. The decision to start AED treatment should be made after full discussion of the risks and benefits, taking account of the person's epilepsy syndrome, prognosis and lifestyle. Treatment (where appropriate) should be initiated by the specialist, who should also plan the continuation of treatment, and manage, or provide guidance for, withdrawal of AEDs. The National Service Framework (NSF) for Long-term Conditions (Department of Health, 2005b) requires that people suspected of having a neurological condition are to have prompt access to specialist neurological expertise for an accurate diagnosis and treatment as close to home as possible, and also supports the Public Service Agreement objective III (part of HM Treasury) to ensure that by 2008 no one waits more than 18 weeks from GP referral to hospital treatment.

1.2.2.2.2. Active epilepsy

Those with continuing seizures should benefit from continuing secondary care, with additional investigations and treatments being available. Video telemetry and high resolution MRI may be indicated, and the patient may need to try second-line or experimental drugs, or be assessed for epilepsy surgery (Brown et al., 1998). All people with epilepsy should be able to consult a tertiary care specialist (via the secondary care specialist) should the circumstances require this (NICE, 2004c). Suggested criteria for referral to tertiary care are:

- Epilepsy not controlled with medication within two years, or after two AEDs
- Unacceptable side-effects of AEDs
- Presence of a unilateral structural lesion
- Psychological or psychiatric comorbidity
- Diagnostic doubt (NICE, 2004c)

1.2.2.2.3. Controlled epilepsy

Although those adult patients who become seizure-free will probably not need ongoing secondary care, it is important that re-referral can be swiftly instigated should seizures recur, or circumstances changes (e.g. impending pregnancy). NICE suggests that AED withdrawal should be discussed with adults who have been seizure-free for at least two years; it is important that this decision is made by the patient and the specialist after a full discussion of the risks and benefits, and that the withdrawal be under the guidance of the specialist (NICE, 2004c). In children a regular structured review, occurring at least yearly, should be provided by a specialist (NICE, 2004b).

1.2.2.3. Accident and emergency care

A survey in Leeds in 1998 showed that less than a quarter of patients with epilepsy-related emergencies seen in A&E were referred for neurological follow-up, noted to be under regular specialist follow-up or admitted to the neurology ward (Reuber et al., 2000). A more recent audit of 38 patients with a first seizure seen in an accident and emergency department found that, of 22 patients discharged, either with an appointment to see a neurologist or a letter to the GP advising such referral, only 10 (45%) were seen by a neurologist (Bhatt et al., 2005). The mean wait was 21 weeks, and range six to 44 weeks. The NICE guidelines recommend that A&E departments should develop protocols to ensure that people with suspected seizures are properly assessed, and that, once initial screening has been performed by a suitable physician, onward referral to a specialist should follow whenever an epileptic seizure is suspected (NICE, 2004c).

1.2.2.4. Use of AEDs

Drug therapy is the most important part of the management of the epilepsies (NICE, 2004a). In the UK AEDs are generally not prescribed unless the person has had at least

two unprovoked seizures, unless there are other factors such as certain EEG abnormalities which make recurrence after a first seizure extremely likely. Therapy with a single AED is recommended wherever possible, but some people will need to try several different AEDs before the seizures are fully controlled, and a minority will need to be treated with two or more AEDs (NICE, 2004a). The most commonly prescribed AEDs in the UK are sodium valproate (often for generalised seizures) and carbamazepine (often for seizures with partial onset). Phenytoin and phenobarbital may be effective in partial onset seizures, but they are not recommended as first line treatment in the NICE guidelines (NICE, 2004c). A variety of other older AEDs are also sometimes used, often for specific indications.

Since the late 1980s, nine 'new' AEDs have been licensed in the UK, and two recent NICE technology appraisals (Newer drugs for epilepsy in adults (NICE, 2004a), and in children (NICE, 2004b)) have been published. In adults the use of these newer drugs is recommended in people who have not benefited from the older drugs, or in whom the latter are unsuitable for a variety of reasons such as drug interactions or in women who may become pregnant. The guideline for children also suggests other qualifications for newer AEDs, such as avoiding the introduction of sodium valproate in a young girl who may need to continue taking it for several years (NICE, 2004b).

The use of barbiturates (phenobarbital and primidone), phenytoin, sodium valproate and topiramate are considered further in this thesis. Neither carbamazepine nor lamotrigine is considered further as the clinical records audited did not generally provide enough information to assess their suitability. Most other AEDs were not taken by sufficient numbers of people in the audit to enable their usage to be assessed with any accuracy.

1.2.2.5. Investigations

1.2.2.5.1. EEG

In 1998 the Epilepsy Needs Revisited document suggested that every person with newly diagnosed epilepsy would need at least one standard EEG to assist in syndrome diagnosis (Brown et al., 1998). The 1997 SIGN pilot guidelines, whilst acknowledging the importance of syndromic classification, considered that in patients under 25 years

old, EEG should be performed to assist in the classification of the seizures (SIGN, 1997). The age cut-off was suggested as presentation with an idiopathic generalised epilepsy was thought rare after 25 years old. By the time of the publication of the SIGN guidelines in 2003, it was stated that EEG is not routinely indicated and should not be used to exclude a diagnosis of epilepsy, but can be used to support the classification (SIGN, 2003). It should be used in young people with generalised seizures to aid classification and detect a photoparoxysmal response. The NICE guidelines agree that an EEG should only be used to support a diagnosis of epilepsy, and should not be used to exclude the diagnosis in cases of probable syncope or non-epileptic attack (NICE, 2004c). Sleep or sleep-deprived EEGs, and video EEG monitoring may be required if diagnostic uncertainty persists.

1.2.2.5.2. Neuroimaging

In 1997 it was advised that best practice is to carry out MRI in all patients with epilepsy, with the exception of patients who have a definite electroclinical diagnosis of idiopathic generalised epilepsy, or benign epilepsy of childhood with centrotemporal spikes. It is particularly indicated where there is evidence of partial onset, evidence of a focal fixed deficit on examination, and difficulty in gaining or maintaining control of seizures (Wallace et al., 1997). The SIGN guidelines suggest that MRI is the current reference standard for epilepsy, but is not routinely required in idiopathic generalised epilepsy with complete response to a first line AED (SIGN, 2003). The NICE guidelines echo this advice, adding that MRI is also required in people who develop epilepsy under two years old, or in adulthood (NICE, 2004c). CT scanning is used where MRI is unavailable or contraindicated, and in some emergency situations (NICE, 2004c).

1.2.2.6. Surgery

Surgical treatment for epilepsy is sometimes suitable for people who have partial epilepsy resistant to drug treatment (having not gained seizure control with two appropriate AEDs in adequate dosage) (SIGN, 2003). Assessment for surgery should be carried out in a specialist unit, (SIGN, 2003) with experienced staff, and involves a multi-disciplinary approach including neurologist, neurosurgeon, psychologist, psychiatrist, neurophysiologist and radiologist (Walker and Fish, 2005b). In many

cases, the aim of surgery is to remove the epileptogenic focus; to be sure of accuracy in doing this it is recommended that congruent results are found in the clinical history and in the results of a variety of investigations, such as neuropsychometry, neuroimaging and EEG. Sometimes more invasive investigations are performed, including intracranial EEG monitoring (Walker and Fish, 2005b). It is also important to establish whether surgery is likely to disrupt other key areas of brain function, such as speech (Harkness and McEvoy, 2005).

1.2.2.7. Information provision

Most epilepsy publications stress the importance of information provision for people with epilepsy (Brown et al., 1998; Chappell and Hall, 1997; CSAG, 2000; Hall et al., 1997; Leeds Health Authority, 1999; Smith and Leach, 2003). Much information is crucial to the health and safety of the person with epilepsy, while other information is important in encouraging adherence to the AED regime and reducing the stigma of epilepsy.

1.2.2.8. Special Groups

1.2.2.8.1. Learning disability

Epilepsy and learning disabilities are both common conditions, but they both occur together more often than predicted by chance; this may be because the two neurodevelopmental disorders often have a common aetiology. The prevalence of epilepsy seems to increase as IQ decreases – about 15% of those with IQ between 50 and 69 have epilepsy, compared with 30% in those with more severe learning disability (EUCARE, 2003). Those with more severe learning disability are also more likely to have a more mixed seizure presentation (Clark et al., 2001). Epilepsy is said to be almost inevitable in those whose severe learning disability is caused by postnatal injury (Jenkins and Brown, 1992).

Both epilepsy and learning disability are indicators of early mortality and of psychiatric disorders (Branford et al., 1998a). The incidence of SUDEP is three-times higher in people with epilepsy and learning disability, compared with those with epilepsy in the general population (Lhatoo and Sander, 2001).

The treatment of epilepsy in those with learning disability is complicated. Patients often present with multiple seizure types, and behavioural problems are more frequent (EUCARE, 2003). The difficulty of diagnosing epilepsy in people with learning disability is recognised; difficulties arise through the presence of stereotypic and drug-induced movement disorders in people with learning disability (Bowley and Kerr, 2000). People with learning disability are entitled to the same degree of investigation and treatment as any other group (Jenkins and Brown, 1992; NatPact, 2005). The NICE guidelines add that the learning disability team should be involved in the care of people with epilepsy and learning disability (NICE, 2004c).

Epileptic syndrome diagnosis, identification of non-convulsive status, and the diagnosis of Non-Epileptic Attack Disorder almost always require EEG investigation (Jenkins and Brown, 1992). This may be difficult, but good quality recordings can usually be obtained, occasionally with the use of light anaesthesia. However, caution is required in interpreting the EEG of people with underlying brain damage, as it may be complicated by background changes. MRI may be required to make an aetiological diagnosis, to assess change and to aid future planning (Jenkins and Brown, 1992).

Drug treatment in people with epilepsy and learning disability is often complex. Seizures are often difficult to treat, or even intractable, leading to the use of polypharmacy (EUCARE, 2003). Although monotherapy is desirable, two studies 12 years apart in Leicestershire, with 138 subjects common to both, found both fewer patients on monotherapy or no AEDs and more patients with active epilepsy at the second time point (Branford et al., 1998b). This was contrary to expectations, and the authors postulated that this might be because at the earlier time epilepsy and AEDs were the focus of an expert team, whilst at the later date epilepsy was reviewed by GPs or by psychiatrists specialising in learning disability.

Drugs used in epilepsy can affect cognition because of sedative side-effects (e.g. phenobarbital, phenytoin, benzodiazepines), or can affect learning indirectly by causing side-effects such as diplopia and irritability (Besag, 2001b). Phenobarbital has been

shown to produce serious memory impairment, and phenytoin can cause moderate to large effects on cognitive function (Aldenkamp, 2001). Valproate may cause mild to moderate impairment of psychomotor and mental speed, but carbamazepine causes either no or mild cognitive impairment. Few controlled studies exist to interpret the cognitive effects of newer AEDs, but there is clear clinical evidence for topiramate-induced cognitive impairment, probably even when slow titration and relatively low doses are used (Aldenkamp et al., 2003). Lamotrigine has a selective positive effect on cognitive activation, which may be partially explained by its reduction of spontaneous epileptiform discharges. However, lamotrigine may have some negative effects such as restlessness and hyperactivity. Oxcarbazepine does not affect cognitive function in healthy volunteers and adult patients with newly diagnosed epilepsy and no definite conclusions can yet be drawn on the cognitive effects of levetiracetam. Tiagabine has no significant effect on cognitive function, and the only problem noted with gabapentin is drowsiness at higher doses (Aldenkamp et al., 2003).

Polypharmacy has a more marked negative impact on cognitive function than monotherapy, regardless of which AEDs are used (Aldenkamp et al., 2003). An audit of adult inpatients with learning disability found that 16% were being treated with three or more AEDs, and 37% patients were identified who might benefit from a reduction in the number of AEDs prescribed (Tiffin and Perini, 2001). Another problem in the treatment of people with epilepsy and learning disability is that doctors and patients may see side-effects differently. Treatment of people with learning disability is often by 'proxy' as the patient is not able to contribute views (Kerr, 2005). The NICE guidelines stress that in people with epilepsy and learning disabilities particular attention should be paid to the possibility of adverse cognitive and behavioural effects of AEDs (NICE, 2004c).

As in people without learning disability, for patients with learning disability and epilepsy that is refractory to treatment, the question of surgery arises. This is not an option in some patients, as they may have diffuse epileptogenic regions (Baker, 2001). Surgery must be likely to lead to a decrease in seizures and to an increase in quality of life, and any contraindications must be considered. However, it is also necessary to

determine whether the patient is able to understand the risks and benefits of surgery, and to have realistic expectations. The situation is further complicated by the fact that there are few neuropsychological tests available specifically for people with learning disability (Baker, 2001). Surgical ablation of the epilepsy focus may have positive or negative effects on the process of learning. Ablation generally produces positive effects, as it eliminates the negative consequences of the epileptic discharges that go from this area to other parts of the brain. However, it may lead to a functional deficit, causing negative postoperative results, if the brain area previously retained some of its own primary function (Cornaggia and Gobbi, 2001).

Overall it is important to assess the individual, and the impact of epilepsy on that individual, to assess treatment options and to apply a management plan, so that people with learning disability and epilepsy can live as inclusive a life as possible (Kerr, personal communication).

1.2.2.8.2. Women

In all people with epilepsy, the need for seizure control should be balanced against the side-effects of AEDs. Women with epilepsy have additional concerns with respect to interactions of AEDs with oral contraceptives and with the potential adverse effects of AEDs on the developing foetus, as well as any problems related to breast-feeding. Women with epilepsy may have additional problems, not directly related to AEDs: in some women seizures are affected by the menstrual cycle; fertility may be reduced in women with epilepsy; there may be an increased risk of foetal malformation in women with epilepsy compared with those without epilepsy; and a mother with epilepsy may have problems in caring for her baby. All women with epilepsy of childbearing age should be given information about epilepsy and pregnancy, and this should be repeated at review appointments. The advice on contraception should be given before young women are sexually active (NICE, 2004c; SIGN, 2003). Additionally, in young girls who may need to continue treatment into childbearing years, the risks and benefits of particular AEDs should be discussed with the child and carers when AEDs are prescribed (NICE, 2004c).

Several AEDs (notably phenytoin, phenobarbital, primidone, carbamazepine, oxcarbazepine and topiramate) interfere with the metabolism of the oral contraceptive pill, requiring the use of higher oestrogen doses to avoid possible contraceptive failure (Bell et al., 2002). It has recently been shown that lamotrigine may cause a fall in norethisterone concentrations, also increasing the risk of unplanned pregnancy if usual oral contraceptive doses are used (Crawford, 2005). Lamotrigine levels themselves may be altered by hormonal contraceptive pills (Stodieck and Schwenkhagen, 2004; Schwenkhagen and Stodieck 2004).

About ten percent of women have catamenial seizures (where seizures increase in frequency around the time of menstruation) (Crawford, 2005). The prevalence of polycystic ovary syndrome is thought to be higher in women with epilepsy than in those without, and is sometimes related to use of sodium valproate. Fertility is reduced in women with epilepsy; the reasons are probably multifactorial (O'Brien and Gilmour-White, 2005).

Most women with epilepsy have uneventful pregnancies, with over half of a large cohort recently reported being seizure-free throughout (EURAP epilepsy pregnancy registry, 2006). Pre-pregnancy planning is desirable for all women, but particularly so for women with epilepsy (Crawford, 2005); control of seizures should be optimised on the lowest effective dose of the most appropriate AED. Monotherapy should be used wherever possible, particularly as the incidence of foetal malformations increases with the number of AEDs taken during the first trimester of pregnancy (Nakane et al., 1980). Sometimes, if the woman has been seizure-free for several years, withdrawal of AEDs can be considered; this should be overseen by a specialist in epilepsy. Pregnancies exposed to sodium valproate, particularly as part of a polytherapy regime, seem to be especially at risk; the risk of major congenital malformation in the offspring of women taking valproate as part of a polytherapy combination is nine percent (Morrow et al., 2006). Women with epilepsy need to consider the safety considerations in looking after their babies, particularly as sleep deprivation may have detrimental effects on seizure control. Practical advice such as not bathing the baby while alone may be useful, although evidence of the effectiveness of advice is limited (Fox and Betts, 1999). The

decision whether or not to breast-feed has to balance the benefits to mother and child with the small risk of toxicity to the infant.

1.2.2.8.3. Care for other special groups

One major aim of the NHS is equity of care. A discussion paper from the London School of Economics reported that the evidence comparing NHS utilisation and morbidity with socio-economic groups is not clear-cut. Socially disadvantaged people, however, tend to present later to medical care, with more advanced disease and may be more likely to go to the A&E department instead of to the GP. They also tend to have higher drop out rates or non-compliance with management (Dixon et al., 2003). All of these are likely to have adverse consequences for people with epilepsy. One aim of good epilepsy services should be to provide equity of access and care.

1.3. MORTALITY IN PEOPLE WITH EPILEPSY

1.3.1. Introduction

More than two thirds of people diagnosed with epilepsy will cease to have seizures, either because the condition remits spontaneously, because of the use of AEDs or surgery, or both. There is little doubt, however, that people with epilepsy are more likely to die prematurely than those without it. There are several ways of quantifying the risk of death.

- The Standardised Mortality Ratio (SMR) uses the age-specific mortality rates of the population from which the study group came, and calculates the number of deaths expected in the study group if it experienced those age-specific mortality rates. The ratio of the observed number of deaths to the number expected is then calculated – this is the SMR.
- The case fatality is the ratio of the number of deaths among people with the disease over a defined period of follow-up to the number of newly incident cases of the disease at the start of the follow-up period.
- The proportionate mortality ratio is the number of deaths that occur in a defined population due to a specific cause divided by the overall deaths.
- Relative survivorship is the proportion of observed to expected number of survivors (Olafsson et al., 1998).

No one method is ideal. SMRs should not be compared across groups with different age structures in the study population (Forsgren et al., 2005), and PMRs are influenced not only by an increase of one cause of death, but also by decreases of other causes. The most useful and commonly used figure for epilepsy is the SMR. The risk of death is not uniform over the lifetime of a person with epilepsy, nor across different populations of people with epilepsy.

1.3.1.1. Accuracy of mortality data

There are many problems in calculating mortality figures for epilepsy. Epilepsy can be hard to diagnose; 12 of 92 people referred to a specialist clinic with 'refractory epilepsy' did not have epilepsy (Smith et al., 1999), and 21% of patients in a study of mortality from a hospital in Sweden were found to have been misdiagnosed, having had acute

symptomatic seizures, single seizures or non-epileptic attacks (Nilsson et al., 1997). Of 223 children referred to a tertiary epilepsy centre in Denmark with difficult to treat paroxysmal events, 87 (39%) did not have epilepsy (Uldall et al., 2006). Classification of epilepsy syndromes is also problematic, particularly in resource-poor countries, but also in industrialised nations (Loiseau et al., 2005) and the mortality rate is different for different epilepsy syndromes (see later).

Case ascertainment can also be extremely difficult. Any study of epilepsy will miss patients who do not present their symptoms to the medical services. In a UK hospital study the median number of seizures before referral was four for people with tonic clonic seizures and 44 for those with partial seizures (Shorvon, quoted in Hart et al., 1990). Some people may conceal their seizures to avoid stigma or other problems, while others may not realise that their symptoms could be epilepsy (Zielinski, 1974b). One commonly used method of case ascertainment for studies of death in epilepsy is the use of death certificates. Death certificates can be an unreliable source of information on cause of death (Hauser et al., 1980; Zielinski, 1974a) and, although autopsy and supplementary clinical data improve accuracy, certificates remain subject to bias and error. It has been pointed out that reliance on death certificates will underestimate the mortality of epilepsy (Morgan and Kerr, 2002). Although the underestimation is not controversial, its extent is unknown. Use of death certificates may identify many of the people who die from an epilepsy-related death, but it may miss many people with epilepsy who die of other causes. Another common method of case-ascertainment, use of AED prescriptions, is also liable to inaccuracies. Some people with epilepsy do not take AEDs, either because they choose not to do so (possibly because of side-effects), or because they do not adhere to the regimen. Additionally, AEDs can be used for diseases other than epilepsy, such as neuropathic pain, trigeminal neuralgia, bipolar affective disorders and migraine prophylaxis. In resource-poor countries there is a large treatment gap, with a majority of people with epilepsy not taking AEDs.

Another issue in case ascertainment is the definition of the study population. Early studies from institutions for people with epilepsy and hospital based populations showed epilepsy to be a progressive, incurable disease, as milder cases were not represented.

Population-based studies, however, may include people whose epilepsy has not been fully characterised.

It is difficult to disentangle the effects of epilepsy from those of the underlying conditions causing the epilepsy. For this reason some studies compare mortality rates in people with remote symptomatic epilepsy with people with the underlying condition (e.g. learning disability) but without seizures (Day et al., 2005; Strauss et al., 2003). Those with idiopathic epilepsy are usually compared with people in the general population, but it is difficult to account for all possible confounders. A recent editorial, in response to a paper considering life expectancy in people with epilepsy, asked whether life expectancy would be different for someone with a stroke who developed epilepsy and someone who did not (Tomson and Forsgren, 2005). Again, it would be almost impossible to eliminate confounders such as the location and severity of the stroke.

1.3.2. Mortality in epilepsy

Almost all studies show premature mortality in epilepsy, and the figure generally quoted is an SMR of two to three (Cockerell et al., 1996; Lhatoo and Sander, 2005). This overall figure, however, encompasses different study populations, with a variety of epilepsy syndromes, different ages of subjects, and different study durations, all of which have been shown to affect the mortality rate.

1.3.2.1. Time since diagnosis

In a study of patients with newly diagnosed epilepsy in Holland, the SMR was highest soon after diagnosis and decreased thereafter (being 16 in the first two years and 2.8 later) (Shackleton et al., 1999). In the population-based UK National General Practice Study of Epilepsy and Epileptic Seizures (NGPSE) the overall SMR in those with definite epilepsy was 6.6 (95% Confidence Interval [CI] 4.8 to 8.7) in the year after the index seizure (the seizure which led to identification of epilepsy), and decreased thereafter, remaining significantly raised until four years after the index seizure (Cockerell et al., 1994). Further follow-up of this cohort revealed a slight but significant rise in mortality after nine years after the index seizure (SMR 1.8 [95%CI 1.1

to 2.7] at nine to 14 years) (Lhatoo et al., 2001). A similar finding was shown in a study of people with newly diagnosed unprovoked epileptic seizures in Sweden, where the SMR was increased for the first 2 years after diagnosis, but not thereafter, until nine years after diagnosis when it was again raised to 5.4 (95% CI 2.7 to 11.2) (Lindsten et al., 2000). The early papers from Rochester (USA) found the mortality to be significantly raised for the first ten years after diagnosis, and again after 25 years (Hauser et al., 1980).

1.3.2.2. Type of epilepsy

This seems to be one of the most significant factors leading to the variation in SMRs quoted; it interacts with the time after diagnosis.

1.3.2.2.1. Idiopathic/cryptogenic epilepsy

In epidemiological studies idiopathic and cryptogenic epilepsies are frequently grouped together. Most studies show either no increase in SMR or a very modest, non-significant increase (Lindsten et al., 2000; Loiseau et al., 1999). A few studies show a borderline raised SMR (Cockerell et al., 1994) - although this was no longer significantly raised in the later report from the same patient group (Lhatoo et al., 2001) - or increased SMRs in selected groups only (Olafsson et al., 1998). The large study from the US found that the SMR for idiopathic epilepsy was slightly increased for the first ten years after diagnosis, then was at most marginally increased until 25 years after diagnosis, and then was raised to 3.2 (Hauser et al., 1980). One study shows minimal reduction of life expectancy in this group (Gaitatzis et al., 2004b).

1.3.2.2.2. Symptomatic epilepsies

Most studies show the SMR to be increased in symptomatic epilepsies, with a range of SMR from 2.3 after 30 years in Iceland (Olafsson et al., 1998) to 6.5 in a short-term follow-up of people with a first epileptic seizure in France (Loiseau et al., 1999). Relative survivorship was also confirmed to be lower than for people with idiopathic seizures in the Iceland study (Olafsson et al., 1998).

1.3.2.2.3. Epilepsy associated with congenital neurodeficit

This is associated with significantly raised SMRs, of between 11 (Hauser et al., 1980) and 50 (Cockerell et al., 1994). The longer follow-up of the latter study showed a lower SMR associated with these conditions, but it was still very high (Lhatoo et al., 2001).

1.3.2.3. Age

Both current age and age at diagnosis seem to affect the mortality rate in people with epilepsy. The NGPSE found the highest SMRs (over eight) in the 50 to 59 year age group, decreasing with increasing age thereafter (Lhatoo et al., 2001). The Swedish hospital-based study showed the highest SMR in those aged below 35 years; this also decreased with increase in age (Nilsson et al., 1997). The Dutch study showed an SMR of 48 in those aged up to four years, and this decreased fairly steadily until the age of 45 years, when it levelled off. It was significantly increased in all those under 65 years old. Age at diagnosis follows a similar pattern; the Dutch study showed an SMR of 24 in those aged under 20 years at diagnosis, compared with an SMR of 2.5 in those older at diagnosis (Shackleton et al., 1999).

In children in general the excess death rate seems to be due to the underlying pathology and not to the seizures. Three large studies in children all show a minority of deaths to be possibly seizure-related (Berg et al., 2004; Camfield et al., 2002; Shinnar et al., 2005).

1.3.3. Cause of death

The cause of death in people with epilepsy is often described as being either unrelated to epilepsy, related to the underlying condition causing epilepsy or related to epilepsy itself. It has been suggested that approximately half the deaths are epilepsy-related, and half not, and that only one fifth of the epilepsy-related deaths are seizure-related (Forsgren, quoted in Loiseau et al., 1999).

A few studies have shown rates of cause-specific mortalities (Hauser et al., 1980; Klenerman et al., 1993; Lhatoo et al., 2001; Lindsten et al., 2000; Rafnsson et al., 2001). Together they suggest that somewhere under one third of deaths are due to malignancy

(including primary brain tumours), one tenth to one quarter are due to ischaemic heart disease, just under one fifth to cerebrovascular disease, and under one quarter to pneumonia.

1.3.3.1. Death due to the underlying disease causing epilepsy

Death due to the underlying disease causing the epilepsy is relatively common, and accounted for 19% of deaths in those who died within the first two years of follow-up and 15% of deaths thereafter in the study from Holland. In that study the SMR was 16 in the first two years of follow-up and 2.8 thereafter (Shackleton et al., 1999). The marked trend of decreased SMR over time found in studies such as the NGPSE is thought to be due to the early death of patients from the underlying disease (Cockerell et al., 1994). In the study with short term follow-up after a first seizure, 25% of those dying with provoked seizures did so within the first week (Loiseau et al., 1999).

In an attempt to control for deaths due to the underlying disease, studies from California and Sweden have looked at large populations of people with learning disability, some of whom also had epilepsy (Day et al., 2005; Forsgren et al., 1996; Strauss et al., 2003). The Swedish study, a seven-year follow-up of almost 1,500 people with learning disability, 296 of whom had epilepsy, found the SMR to be 2 for those without epilepsy, and 5 for those with epilepsy, suggesting that part of the increased mortality rate is due to the underlying brain disorder (Forsgren et al., 1996). The study from California, including only relatively high functioning subjects, and excluding those with idiopathic epilepsy, compared 70 thousand people without epilepsy and eight thousand with epilepsy. There were 1523 deaths between 1988 and 1999. The mortality ratio of people with epilepsy *compared with those without* was only 1.1 for those with no seizures in the previous year, 2.4 for those with seizures (but no tonic clonic seizures) in the previous year and 2.9 for those with generalised tonic clonic seizures (GTCS) in the previous year. This suggests that seizures are relevant to the deaths; the study did not compare death rates with those in the general population (Strauss et al., 2003).

1.3.3.2. Death related to epilepsy

Death from status epilepticus (SE), sudden unexpected death in epilepsy (SUDEP), deaths due to accidents or drowning, treatment-related deaths and, sometimes, suicide are considered to be deaths related to epilepsy.

In some studies in institutionalised patients, the PMR due to epilepsy is up to 35% (Iivanainen and Lehtinen, 1979; Klenerman et al., 1993; Krohn, 1963; White et al., 1979). It is lower in population-based studies (between two and fourteen percent) (Lhatoo et al., 2001; Zielinski, 1974a).

1.3.3.2.1 Status epilepticus

SE can occur *de novo* in people without existing epilepsy, but around half of all cases of SE occur in people with epilepsy. In early studies from epilepsy institutions SE accounted for between six and nine percent of deaths (Iivanainen and Lehtinen, 1979; Krohn, 1963), and more recently it was shown to account for four percent of deaths in people with remote symptomatic epilepsy (Day et al., 2005).

SE can lead to profound systemic and neurological damage, and carries a significant short-term and long-term mortality rate (Logroscino et al., 2002; Simon et al., 1997), particularly in adults. The case fatality of SE is higher in those with acute symptomatic seizures and in the elderly, and is particularly high in myoclonic SE (Logroscino et al., 2001). The incidence of SE may be falling (Wu et al., 2002) .

In children, SE may be the first epileptic event, but in adults the data are conflicting; between 30 and 71% of all adults presenting in SE do not have pre-existing epilepsy (Shorvon, 1994). About five percent of all people with epilepsy have at least one episode of tonic-clonic SE, and a precipitating factor can be found in over half of these. Important precipitants are acute AED withdrawal (either due to poor adherence to drug regimen or under medical supervision), withdrawal of other drugs or alcohol, infections, intercurrent illness or progression of the underlying lesion (Sander and Hart, 1997). It is important to reduce these precipitants where possible. Adherence to drug regimen should be encouraged, and the risks of not doing so explained.

1.3.3.2.2. Sudden Unexpected Death in Epilepsy (SUDEP)

SUDEP can be defined as 'sudden, unexpected, witnessed or unwitnessed, non-traumatic and non-drowning death in patients with epilepsy, with or without evidence for a seizure and excluding documented status epilepticus, in which postmortem examination does not reveal a toxicological or anatomical cause for death' (Nashef, 1997). The other commonly used definition includes death occurring suddenly and unexpectedly, during normal activities and benign circumstances, excluding death from trauma or intractable status epilepticus, in an individual diagnosed with epilepsy; no obvious medical cause of death should be found (Leestma et al., 1997). In 1868 Bacon noted the occurrence of 'sudden death in a fit' (Nashef, 1997) and over 30 years later Spratling found that four percent of deaths in people with epilepsy were the direct result of a seizure, with no other explanation found (Terrence et al., 1975). Despite this, in the 1960s it was suggested that 'there is no reason why ...*someone with epilepsy*... should not live as long as he would if he did not have epilepsy' (O'Donoghue and Sander, 1997). Awareness has again increased over recent years, yet in many countries the medical profession has been reluctant to consider SUDEP (Lear-Kaul et al., 2005). Indeed, there is little comparative data on the incidence of SUDEP in different countries.

By definition, the causes of SUDEP are unknown. Nevertheless establishing risk factors can be useful; individual patients can be advised on minimising avoidable risks, and evaluation of risk factors can point to areas of future research to try to establish potential causes and mechanisms of SUDEP.

Most studies of SUDEP have been in selected populations. In the majority (about 70%) of people with newly incident epilepsy the seizures remit, with or without the use of AEDs; SUDEP is rare in these populations (Lhatoo et al., 1999). Whilst studying this group might provide valuable insights, searching for risk factors would require meticulous follow-up of large cohorts. Groups studied have therefore usually had a more severe form of epilepsy than most, with tertiary care clinics (Nashef et al., 1995b), people ever hospitalised (Nilsson et al., 1999), residential groups (Nashef et al., 1995a)

or surgical candidates (Hennessy et al., 1999) being followed. Some studies use AED prescriptions to identify people with epilepsy (Derby et al., 1996; Tennis et al., 1995).

In all studies the risk of sudden death in epilepsy is found to be elevated. It is usually estimated as between 1:500 and 1:1000 patient-years in community-based populations with epilepsy, and up to 1:100 in surgical series.

Of the many risk factors suggested for SUDEP, few have been proved conclusively. Evidence is frequently conflicting; the size of the cohort studied, the control group used, the methodology of the study and the definition of SUDEP may all affect the risk factors identified (O'Donoghue and Sander, 1997; Tellez-Zenteno et al., 2005). More consistent risk factors include young adulthood, early age of onset of seizures, presence of generalised tonic clonic seizures, higher frequency of seizures, polytherapy and poor adherence to AED regimen. Others suggested have been male gender, symptomatic epilepsies versus idiopathic, Afro-American background, frequent changes of dose or type of AED, alcohol abuse, presence of comorbid learning disability and presence of nocturnal seizures.

1.3.3.2.2.1. SUDEP: age at death

The definitions of SUDEP require no anatomical or toxicological cause for death found at post-mortem examination (Leestma et al., 1997; Nashef, 1997). Many elderly people have evidence of cerebrovascular or cardiovascular disease and it may be difficult to exclude this as a cause of death; as a result the elderly are less likely to fulfil this negative requirement of the definition, and so be classified as SUDEP. Thus the rate of SUDEP estimated in the elderly may be falsely low.

Different studies have found different decades of peak incidence of SUDEP; e.g. third and fourth decades (Antoniuk et al., 2001), second and fifth decades (Terrence et al., 1975). Mean ages of death range from 26 to 37 years (Langan et al., 2005; Langan et al., 1998; Lear-Kaul et al., 2005; Leestma et al., 1989; Leestma et al., 1997; Nashef et al., 1995b; Timmings, 1998). However, SUDEP may occur in children (Earnest et al., 1992; Nashef et al., 1995a).

1.3.3.2.2.2. SUDEP: age of onset of seizures

A retrospective study investigating deaths in a tertiary referral centre population with chronic refractory epilepsy found the age of onset to be slightly, but significantly, lower in the SUDEP group than in the group who died of causes other than SUDEP (mean age 8.2 years vs 12.7 years) (Kloster and Engelskjon, 1999). A case-control study in Sweden found that, in men, onset of epilepsy in childhood or early adolescence compared with onset after 45 years increased the relative risk of SUDEP almost 18 times. This association was not significant in women (Nilsson et al., 1999). Other studies have found long duration of epilepsy in people dying with SUDEP (Earnest et al., 1992; Lear-Kaul et al., 2005; Leestma et al., 1989; Leestma et al., 1997; Nashef et al., 1995b; Timmings, 1998). Young age of onset of seizures is often correlated with long duration of epilepsy. A study of mortality in AED development programmes did not, however, find that the SUDEP rate increased with the duration of the epilepsy (Racoosin et al., 2001).

1.3.3.2.2.3. SUDEP: presence of tonic-clonic seizures

SUDEP is usually unwitnessed, but when witnessed often follows a generalised tonic clonic seizure. Evidence for a seizure prior to death is frequently, but not always, found at post-mortem examination. In the study comparing patients with epilepsy who died with SUDEP with those dying from other causes there were signs of seizures occurring immediately before death in 67% of SUDEP patients compared with 35% in the non-SUDEP group (Kloster and Engelskjon, 1999). Of 15 witnessed cases of SUDEP in another study, 12 occurred in association with a generalised tonic-clonic seizure (Langan et al., 2000). Studies in both children (Donner et al., 2001; Nashef et al., 1995a) and adults (Ficker et al., 1998; Hirsch and Martin, 1971; Kloster and Engelskjon, 1999; Langan et al., 1998; Leestma et al., 1989; Terrence et al., 1975; Timmings, 1998) have found that most, if not all, cases of SUDEP in whom the seizure type was known, had a history of GTCS. Some of these seizures may have partial onset (Nashef et al., 1998). A prospective cohort study of patients at three American epilepsy centres found that higher numbers of GTCS in the year before the last hospital visit was a risk factor for women (Walczak et al., 2001).

1.3.3.2.2.4. SUDEP: seizure frequency

Many studies of death in epilepsy have been undertaken in different populations, and together they confirm SUDEP as a real phenomenon. Higher rates of SUDEP are reported from studies of individuals with intractable epilepsy, however, and it is suggested that seizure severity and frequency are risk factors (Annegers and Coan, 1999). However, some authors have suggested that seizures are often infrequent or rare in people dying with SUDEP (Hirsch and Martin, 1971; Leestma et al., 1989; Terrence et al., 1975), suggesting that seizure frequency is not a significant risk factor. Comparing these older studies with the more recently published Swedish nested case-control study (Nilsson et al., 1999) shows remarkably similar findings, but different conclusions were drawn. The studies show that seizures occurred at least monthly in 32% (Hirsch and Martin, 1971), 43% (Leestma et al., 1989) and 42% (Nilsson et al., 1999). The Swedish study compared subjects who died from SUDEP with three living controls per subject, matched for age, sex and assessment period. They found the seizure frequency to be the factor most strongly associated with an increased risk of SUDEP, showing the importance of using living subjects from the same population group with epilepsy as controls in this type of study. A case-control study conducted in the UK found that 11 to 20 or 21 to 50 tonic-clonic seizures in the previous three months was a risk factor compared with those with five seizures or fewer, although more than 50 seizures did not appear as a significant risk factor, perhaps due to small numbers (Langan et al., 2005).

1.3.3.2.2.5. SUDEP: AED therapy

Polytherapy

Several studies suggest increased risk of SUDEP with increasing number of AEDs used. One study used the number of simultaneous AEDs as a surrogate for persistent seizures (Tennis et al., 1995) whilst others found the increased risk associated with polytherapy was still significant after adjusting for seizure frequency (Nilsson et al., 1999; Walczak et al., 2001). However, neither the tertiary referral centre study comparing those dying with SUDEP with those dying from other causes (Kloster and Engelskjon, 1999), nor an Australian prospective coroners' study also comparing SUDEP deaths with those dying

from other causes (Opeskin and Berkovic, 2003) found any increased risk with polytherapy.

Specific AEDs

It has been suggested that the risk of SUDEP may be increased by certain AEDs. SUDEP occurred before modern AEDs were in widespread use (Timmings, 1998), but its frequency does not appear to have decreased with advances in therapy (Terrence et al., 1975). Some authors suggest that carbamazepine may be associated with SUDEP (Langan et al., 2005; Timmings, 1998), but this is disputed by others (Opeskin et al., 1999; Walczak et al., 2001). Carbamazepine has been shown to affect the conduction system of the heart, and to affect the autonomic nervous system (Stollberger and Finsterer, 2004).

Studies have been undertaken on the incidence of SUDEP in clinical trials (Leestma et al., 1997; Racoosin et al., 2001). These studies showed that SUDEP does not appear to be related to the use of specific AEDs, but that the higher rate in clinical trials of new drugs is due to the high-risk patients who are entered into such trials (Lathers and Schraeder, 2002; Racoosin et al., 2001).

Non-adherence to drug regimen, and subtherapeutic, or supratherapeutic AED levels

Studies have found subtherapeutic levels of AEDs in many patients dying from SUDEP (Earnest et al., 1992; Kloster and Engelskjon, 1999; Leestma et al., 1989; Lund and Gormsen, 1985; Terrence et al., 1975), sometimes associated with a history of poor adherence to drug regimen (Earnest et al., 1992), whilst others have found no difference between those dying from SUDEP and those dying from other causes (Opeskin et al., 1999) or from living controls (Walczak et al., 2001). Toxic levels in some patients have also been documented (Lund and Gormsen, 1985; Terrence et al., 1975). The Swedish case control study found the relative risk of SUDEP was elevated in those whose carbamazepine levels were above the therapeutic range at last drug monitoring, with an even higher risk if high carbamazepine levels were present in those on polytherapy or with frequent dose changes. This increased risk was not found in patients on phenytoin (Nilsson et al., 2001).

Change in AEDs

Anecdotal evidence suggests that SUDEP is also more likely to occur at times of AED change (Lip and Brodie, 1992; Shorvon, 1997) and mechanisms for this have been suggested (Hennessy et al., 2001). The Swedish study found that frequent changes of AED dosage was a risk factor (Nilsson et al., 1999), and also that patients who had had therapeutic drug monitoring performed during a two year observation period were less likely to die from SUDEP than those who had not (Nilsson et al., 2001). The UK case-control study found that lifetime use of four or more AEDs increased the odds of SUDEP compared with lifetime use of one or two, but also that having never taken AEDs increased the risk (Langan et al., 2005).

1.3.3.2.2.6. SUDEP: gender

Many studies have found more males than females in those dying with SUDEP, e.g. male:female 1.7:1 (Donner et al., 2001), 1.8:1 (Timmings, 1998), 2:1 (Langan et al., 1998), 2.3:1 (Antoniuk et al., 2001), 2.5:1 (Lear-Kaul et al., 2005), 3.3:1 (Leestma et al., 1989). However, other studies found no difference in the SUDEP rate between males and females (Birnbach et al., 1991; Kloster and Engelskjon, 1999; Racoosin et al., 2001). The Swedish case control study found different risk factors in males and females, but found the annual incidence rate of SUDEP was 1.4/1000 in both men and women, despite the male/female ratio in the deaths being almost 3:2 (Nilsson et al., 1999). The study population, who had been admitted to hospital with a diagnosis of epilepsy, included more men than women; people admitted to hospital may have additional diagnoses, and this may affect the sex distribution. A few studies, including an American study at three epilepsy centres (Walczak et al., 2001), have found the incidence of SUDEP to be higher in women than men. A study of the incidence of SUDEP in young people with epilepsy and learning difficulty investigated 14 deaths due to SUDEP of whom 71% were girls. However, the school had a preponderance of females due to a previous admissions policy, and the rate of SUDEP cases per pupil-year was similar for males (1:287) and females (1:298) (Nashef et al., 1995a).

1.3.3.2.2.7. SUDEP: race

Two early studies suggested that SUDEP is more common amongst Afro-American populations (Leestma et al., 1989; Terrence et al., 1975) but this could be due to selection bias. It has not been studied recently.

1.3.3.2.2.8. SUDEP: alcohol

Alcohol abuse has been suggested as a risk factor for SUDEP (Black and Graham, 2002; Leestma et al., 1989). This may in some cases be due to selection bias, as those with problems with alcohol have different hospital admission rates. The Swedish case-control study found no association with alcohol abuse (Nilsson et al., 1999).

1.3.3.2.2.9. SUDEP: epilepsy syndromes

Some authors have found SUDEP to be more common amongst those with remote symptomatic epilepsy and neurological deficits presumed present from birth (Annegers and Coan, 1999; Donner et al., 2001). However, a retrospective study of patients with chronic refractory epilepsy at a tertiary referral centre found more patients with primary generalised seizures in the SUDEP group than in the group of patients with epilepsy who died from other causes (Kloster and Engelskjon, 1999). Similarly the Swedish case control study found an increased risk of SUDEP among men with idiopathic generalised epilepsy compared with localisation-related symptomatic epilepsy (Nilsson et al., 1999).

1.3.3.2.2.10. SUDEP: presence of nocturnal seizures

Many people dying with SUDEP are found in or near the bed (Kloster and Engelskjon, 1999). It has been suggested that nocturnal seizures may, therefore, be a risk factor for SUDEP. However, this has not been clearly established. People are less likely to be with others during the night, and so seizures are more likely to be unwitnessed. Studies at a school for children with epilepsy (Nashef et al., 1995a), and a recent case control study (Langan et al., 2005) both suggest that supervision may be an important preventative factor; this needs to be studied further.

1.3.3.2.2.11. SUDEP: presence of learning disability

An American cohort study found that, compared with those with IQ of at least 80, those with an IQ of less than 70 were five times as likely to die from SUDEP (Walczak et al., 2001). A cohort study in Canada found that SUDEP incidence was higher in those with a history of hospitalisation for learning disability (Tennis et al., 1995). However, other studies have found no such association (Opeskin and Berkovic, 2003).

1.3.3.2.3. Accidents

People with epilepsy are more likely to have accidents and may die as a result of them. In one study over a third of subjects with seizures had had at least one injury in the previous 12 months (Buck et al., 1997); type, frequency and severity of seizures were the best predictors of all types of accidents. Another study in a tertiary referral centre found that over ten percent of subjects had had burns sufficient to require medical attention (Spitz et al., 1994). The risk was increased by the lifetime number of seizures, and decreased by the presence of neurological impairment. Most burns occurred during cooking or showering. It is likely that the same risk factors would apply to fatal accidents as to these non-fatal ones.

The Swedish study investigating mortality in people who had been hospitalised with epilepsy showed that deaths from injury and poisoning were five times higher than expected, and deaths from burning, drowning, and other accidents were also increased (Nilsson et al., 1997). A more recent study looked at the death certificates of people with epilepsy anywhere on the certificate (Jansson and Ahmed, 2002). Injury and poisoning were listed as the underlying cause of death in over five percent of subjects. The most frequent external causes of death were falling, drowning and accidental poisoning. These are usually assumed to be the result of seizures or postictal confusion, suggesting that improved seizure control might reduce the incidence.

Accidents are more common in people with frequent severe seizures, and falls not directly related to seizures are also more common in people with epilepsy, perhaps due to balance disturbances as a side-effect of AEDs (Jansson and Ahmed, 2002).

People with epilepsy may drown when suffering a seizure during swimming or bathing. It is imperative that people with epilepsy and their families are appropriately counselled and the risks associated with these activities explained to them. Risk factors for drowning accidents in epilepsy include tonic seizures (Besag, 2001a), and risk factors for having a seizure while bathing or swimming include high seizure frequency and number of drug-related adverse events (Buck et al., 1997). Previous studies reported that the relative risk of drowning in children with epilepsy, compared to those without epilepsy, is 96 in the bath and 23 in the swimming pool (Diekema et al., 1993). The SMR for deaths due to drowning and suffocation in the large study in Sweden was 8.2 (95% CI 5.2 to 12.1) (Nilsson et al., 1997). People with epilepsy are usually advised to use a shower instead of a bath, to minimise the risk of drowning (Ryan and Dowling, 1993).

1.3.3.2.4. Suicide

Suicide is considered by many people as being related to epilepsy as it seems to be more common in populations with epilepsy. Several attempts to ascertain the increased rate of suicide have been made but most have had methodological problems (see later).

Some report that rates of suicide are increased in people with epilepsy, and that suicide in epilepsy may occur at the same rate as that reported among patients with manic-depressive illness (Blumer et al., 2002). It has been reported that various studies give suicide rates of about three times that of the general population, and that this rate may be increased even further in people with temporal lobe epilepsy (Robertson, 1997). Suicide appears to be a serious problem particularly among those with chronic epilepsy who require treatment in specialty clinics (Blumer et al., 2002). One case control study, conducted in Sweden in the adults who had been hospitalised with epilepsy, found a marked increase in relative risk for suicide associated with psychiatric co-morbidity, and with the use of antipsychotic drugs (Nilsson et al., 2002). Risk also seemed to increase with high seizure frequency and AED polytherapy, although the associations were not statistically significant. In contrast to this, however, others have found that suicide may occur in patients with longstanding complex partial seizures and dysphoric disorder shortly after full control of seizures is achieved (Blumer et al., 2002). In Iceland, a

history of previous attempted suicide was shown to increase the risk of development of seizures, independent of major depression, suggesting that the mechanisms producing suicidal behaviour and depression may both be important in the development of epilepsy (Hesdorffer et al., 2006).

Little is known, however, of the risk of death from suicide in prevalent cases of epilepsy in the community. Using hospital cohorts for investigation of death may introduce a selection bias towards people with more severe epilepsy, and those with comorbid disorders which may influence mortality rates (Nilsson et al., 1997).

1.3.3.2.5. Treatment-related deaths

Fatalities caused by the treatment of epilepsy are rare (Tomson et al., 2004). The mortality of temporal lobectomy is less than five percent (Walker and Fish, 2005a). In a Swedish study of 651 surgical procedures in 596 patients, one patient died of post operative intracerebral haemorrhage (0.15% operations) (Nilsson et al., 2003). A UK study of 299 patients following surgery for temporal lobe epilepsy reported two early deaths related to the surgery and a third two years later (Hennessy et al., 1999). It is important to realise that pre-surgical investigations may also rarely lead to death (Walker and Fish, 2005a).

Drug-related mortality is also rare. Overdosage with phenobarbital or phenytoin can cause respiratory depression, and most AEDs are toxic in overdose. Stevens-Johnson syndrome and other idiosyncratic reactions are known to occur with several AEDs (Martindale, 2006).

1.3.3.3. Deaths probably unrelated to epilepsy

1.3.3.3.1. Malignancy

It is not surprising that the SMR is usually increased for central nervous system (CNS) tumours, as in many cases the brain tumour is the cause of the seizures. In many studies, however, the SMR for cancers other than primary brain tumours, is also increased to between 1.4 and 4.1 (Cockerell et al., 1994; Hauser et al., 1980; Nilsson et al., 1997; White et al., 1979). The later study from the NGPSE showed that the SMR

for malignant neoplasms excluding primary brain tumour was increased (2.5) in the first seven years after diagnosis but not in the second seven years (0.8) (Lhatoo et al., 2001), suggesting that, in some way, the neoplasm may have contributed to the development of seizures. The authors suggest that these SMRs argue against the proneoplastic effect of AEDs. In the early study from Rochester, USA, individuals who experienced a single seizure only were investigated separately. In the first two years after identification 13 of 158 patients died. In seven of these, death was caused by non-CNS neoplasms, but there was no indication of any metastasis to the brain, nor of any precipitating factors for the seizures (Hauser et al., 1980).

Early work considered the possibility of this increase in mortality rate being due to the carcinogenicity of AEDs (White et al., 1979). A recent review has again considered the relationship between AEDs and cancer (Singh et al., 2005). In animals, phenobarbital has been shown to promote liver tumours, although it is apparently not itself carcinogenic. Phenytoin has led to lymphoma in a few animal studies, and valproate administration has caused uterine adenocarcinomas in rats. More recently, however, an antitumour effect for valproate has been proposed. Human studies have reported an increased risk for lung cancer associated with phenobarbital, and of lymphoma and myeloma with phenytoin; both phenobarbital and phenytoin are considered to be possibly carcinogenic to humans (Singh et al., 2005).

1.3.3.3.2. Cerebrovascular disease

Death due to cerebrovascular disease seems to be common in cohorts of people with epilepsy, with SMRs ranging from 1.8 to 5.3 (Cockerell et al., 1994; Lhatoo et al., 2001; Lindsten et al., 2000; Nilsson et al., 1997; White et al., 1979). Cerebrovascular disease may be the underlying cause of epilepsy (Nilsson et al., 1997). The SMR for cerebrovascular disease in the NGPSE fell to a non-significantly raised level (1.9 [95% CI 0.8 to 4.0]) by the second seven years of follow-up, and was not raised in either time period in those with idiopathic epilepsy, again supporting this hypothesis (Lhatoo et al., 2001).

1.3.3.3.3. Ischaemic heart disease

Many studies show no impact in epilepsy of death due to ischaemic heart disease, with SMRs around one for ischaemic heart disease (Annegers et al., 1984; Cockerell et al., 1994; Lhatoo et al., 2001; White et al., 1979) or heart disease (Hauser et al., 1980). The Swedish hospital based study, however, found a significantly raised level at 2.5 (95% CI 2.3 to 2.7). The authors suggest that, as cerebrovascular disease is overrepresented as a possible aetiology of epilepsy, other manifestations of vascular disease may also be overrepresented (Nilsson et al., 1997). An alternative explanation could be that, as death certificates were used to categorise the cause of death in this study, there may be a degree of inaccuracy in this. A study from Rochester, however, while confirming a non-significantly raised SMR for heart disease overall (1.16 [95% CI 0.9 to 1.5]), reported significantly raised SMRs of 5.7 and 2.45 in the 25 to 44 year and 45 to 64 year age groups respectively, with these results echoed in those who died at least ten years after diagnosis (Annegers et al., 1984).

1.3.3.3.4. Pneumonia

Pneumonia is overrepresented as a cause of death in most cohorts of people with epilepsy (Cockerell et al., 1994; Hauser et al., 1980; Klenerman et al., 1993; Nilsson et al., 1997; White et al., 1979). In the NGPSE, ischaemic heart disease, cerebrovascular disease and pneumonia accounted for most deaths in people over 50 years old. The SMR for pneumonia was significantly raised in both the first and second seven years of follow-up, and was also significantly raised for the first seven years in those with idiopathic epilepsy (Lhatoo et al., 2001). In the past the effect of AEDs on pulmonary function was suggested (Moore MT, quoted in Cockerell et al., 1994), but never substantiated.

1.3.4. Conclusion

1.3.4.1. Role of seizures

In the Swedish study of people with learning disability, those with no seizures in the previous 12 months did not have a significantly raised SMR compared with those without epilepsy (although the SMR was two), but the SMR was 4.7 in those with seizures no more frequently than weekly, and 17 for those with seizures more frequently

than weekly (Forsgren et al., 1996). A study of newly diagnosed patients in Sweden with 850 patient-years of follow-up found that the presence of generalised tonic-clonic seizures increased the risk of death in both males and females, although the increase was not significant in females. For those with partial seizures, the SMR was significantly raised in both males and females (Lindsten et al., 2000). The study from Rochester, USA, however, found a significantly elevated SMR for the first five years after achieving a five-year seizure remission, although the SMR for the 30 years following remission was not significantly elevated. This suggests that it is not only seizures which contribute to the higher mortality rate. The NGPSE found that neither seizure recurrence nor AED use influences mortality, although this study was population based and included few seizure-related deaths (Lhatoo et al., 2001).

Some studies of mortality following epilepsy surgery have shown that the rate of death is increased in people with seizures recurring post-operatively compared with those who become seizure-free (Salanova et al., 2002; Sperling et al., 1999). This would suggest that attainment of seizure freedom is of paramount importance in the reduction of the mortality rate in epilepsy. However, other studies of surgery for epilepsy have reported no major differences in death rates between those seizure-free and those with recurrent seizures after surgery (Hennessy et al., 1999; Nilsson et al., 2003; Stavem and Guldvog, 2005). Even if those rendered seizure-free after surgery are shown conclusively to have a reduced risk of death it is, of course, possible that the factors which in others cause the surgery to be unsuccessful in controlling seizures may also contribute to the increased death rate.

Seizure frequency and severity are the strongest contenders for being risk factors in SUDEP, and are also implicated in deaths due to accidents and drowning. The chances of suicide seem to be increased in those with severe epilepsy as well as in those with recently controlled seizures, making the contribution of seizures to this cause of death difficult to assess.

1.3.4.2. Role of AEDs

AEDs are often successful in reducing seizure frequency and, as such, should be expected to reduce the risk of death if this is genuinely related to seizure frequency. The adverse effects of AEDs on sudden death and possibly on the development of malignancy need to be considered, particularly as AEDs are taken for prolonged periods.

1.3.4.3. Future work

More work needs to be done to establish the cause or causes of SUDEP and to investigate all the factors which may contribute to suicide. The roles of ischaemic heart disease and pneumonia as causes of death in epilepsy need to be clarified, and if they are found to be increased then ways of reducing these need to be sought. Clearly treatment of the underlying condition causing epilepsy may reduce the death rate, although the impact of epilepsy on these deaths is likely to be small.

SECTION 2. AIMS

2.1. THE AIMS OF THE CHILTERN AUDIT OF PRIMARY CARE IN EPILEPSY

1. To audit the documented care provided for people with epilepsy in 12 local general practices in the UK
2. To assess documented care provided with nationally available guidelines, where possible

2.2. The aims of the primary care section of the National Sentinel Clinical Audit of epilepsy-related death

1. To audit the documented primary care provided for people with epilepsy in the UK whose death was related to epilepsy
2. To assess documented primary care provided with nationally available guidelines, where possible

2.3. THE AIMS OF THE SPECIALIST CARE SECTION OF THE NATIONAL SENTINEL CLINICAL AUDIT OF EPILEPSY-RELATED DEATH

1. To audit the documented specialist care provided for people with epilepsy in the UK whose death was related to epilepsy, paying special attention to those with learning disability
2. To assess documented specialist care provided with nationally produced guidelines, where possible

2.4. THE AIMS OF THE INVESTIGATION INTO THE USE OF DEATH CERTIFICATES AS CASE ASCERTAINMENT FOR EPILEPSY

1. To assess the predictive value of death certification in the case ascertainment of epilepsy
2. To validate the methodology of the National Sentinel Clinical Audit of epilepsy-related death

2.5. THE AIMS OF THE CALCULATION OF THE SMR FOR SUICIDE IN PEOPLE WITH EPILEPSY IN ENGLAND AND WALES

1. To estimate the SMR for suicide for people with epilepsy using information from two sources to identify the population of people with epilepsy
2. To validate the methodology of the National Sentinel Clinical Audit of epilepsy-related death by using the same ascertainment to identify those with epilepsy dying from suicide

2.6. THE AIMS OF THE META-ANALYSIS OF SUICIDE IN PEOPLE WITH EPILEPSY

1. To re-analyse the data from a published meta-analysis of suicide in epilepsy, to overcome some of the problems with that meta-analysis
2. To quantify the number of people with epilepsy who die from suicide to investigate the validity of the data used in the study calculating the SMR from suicide in people with epilepsy in England and Wales

SECTION 3. METHODS

3.1. THE CHILTERN AUDIT

3.1.1. Audit design

The Chiltern audit was designed as a review of primary care for people with epilepsy in twelve general practices within one Primary Care Trust local to the National Society for Epilepsy. It was carried out by three experienced epilepsy specialist nurses between January 2001 and November 2002. One practice (75 patients with epilepsy) had an epilepsy specialist nurse attached.

3.1.2. Inclusion criteria

Only one practice had a disease register and so patients were identified from AED prescriptions. Each practice produced a list of patients prescribed AEDs; the epilepsy nurses conducting the audit scrutinised the clinical records and excluded those who took AEDs for reasons other than epilepsy. Some patients were identified who were on the list of people taking AEDs but had either never taken them or had stopped. These were included in the audit.

3.1.3. Information audited

The information required was extracted from any source available within the practice; this included Lloyd George records, A4 records, computerised records and letters from hospitals. Data were recorded on a specially prepared form before being transferred to computer file.

Information recorded included the date of birth and the year when the first seizure occurred. Any information indicating learning disability or possible problems with alcohol was sought, and, where present, this was noted in dichotomous form. The existence of a seizure description in the notes was audited, but the description itself was not recorded. The documentation of a seizure frequency at any time was noted and the most recent seizure frequency recorded, although the date of the documentation was not sought. Wherever possible the epilepsy was classified by the epilepsy audit nurses using any information available in the records. The AEDs taken at the time of the audit were recorded from the repeat prescription record.

The dates of last epilepsy review by a specialist, by an epilepsy specialist and by the GP were recorded. The date the patient last consulted the GP for any reason was also recorded. The date of the first and most recent EEG, the first and most recent CT scan and first and most recent MRI scan were recorded. The records were searched for any documentation about discussion of lifestyle issues, particularly alcohol, safety and leisure, and the driving regulations. In women of childbearing potential, documented advice on contraception, preconceptual counselling and pregnancy was sought.

The duration of epilepsy (from first seizure to the date of the audit) was calculated in completed years. The time periods between the last GP review for epilepsy and the audit, and between the last review by any specialist and the audit were calculated.

3.1.4. Criteria for primary care

The audit assessed care received against the following criteria:

- People with continuing seizures should continue to have access to specialist care (CSAG, 2000). Patients with severe epilepsy should continue to be supervised by a consultant (Winterton, 1986)
- Some form of planned shared care is the preferred model of care for patients with epilepsy (SIGN, 1997). These guidelines do not specify the timing of the planned care. In view of the Quality and Outcomes Framework indicators, in which payments are made to GPs for the percentage of people with epilepsy reviewed within 15 months, this was taken as the reference point for this audit (NHS Confederation and British Medical Association, 2003)
- Primary care should monitor seizures and side-effects of medication, provide information and counselling, and should re-refer to secondary care where necessary (SIGN, 1997)
- AEDs should be used in monotherapy where possible (Hall et al., 1997). The aim should be to maintain the patient on the minimum number of drugs required to achieve adequate symptom control (SIGN, 1997)
- EEG should be performed in patients aged under 25 years at diagnosis. It is not necessary in establishing a diagnosis if a clear clinical history is available (SIGN,

1997). EEG is indicated in patients with continuing seizures where there is diagnostic doubt (Wallace et al., 1997).

- Brain imaging is unnecessary if a firm diagnosis of an idiopathic generalised epilepsy syndrome has been made on the basis of the clinical history and EEG findings. Brain imaging should always be performed in patients aged over 25 years. If a firm diagnosis of an idiopathic generalised epilepsy has not been made, both an EEG and brain imaging are necessary (SIGN, 1997). MRI is indicated where there is evidence of a partial onset from the clinical history or EEG, at any age (Wallace et al., 1997).

3.1.5. Analysis

Most analysis was done using SPSS version 11.0. Some analysis of summary data was performed in Clinstat, a DOS-based software programme available from St George's Hospital Medical School.

For continuous data the t-test was used where the data were normally distributed, and the Mann-Whitney U test where they were not. For categorical data the Chi squared test was used. For 2 by 2 tables the difference between binomial proportions was used, and 95% Confidence Interval (CI) calculated. For 2 by 2 tables with small expected values, Fisher's exact test was used. All comparisons were 2-sided. A p-value of < 0.05 was taken to indicate statistical significance.

3.1.6. Confidentiality

All electronic data were irretrievably anonymised.

3.2. THE PRIMARY CARE SECTION OF THE NATIONAL SENTINEL CLINICAL AUDIT OF EPILEPSY-RELATED DEATH

3.2.1. Audit design

The intended study population was everyone who died from an epilepsy-related cause in the UK from 1 September 1999 until 31 August 2000.

3.2.2. Case ascertainment

The Office for National Statistics and the General Register Offices for Scotland and for Northern Ireland identified deaths during the study period where epilepsy was mentioned on the death certificate.

A panel, consisting of five physicians with interest and expertise in epilepsy, reviewed 20% of the death certificates in which epilepsy appeared only in part II. The conclusion was that those deaths in which epilepsy appeared only in part II were unlikely to be epilepsy-related deaths. The certificates with epilepsy on part I of the certificate were further reviewed by two members of the panel, and the deaths were divided into probably, possibly and unlikely to be related to epilepsy. The pre-mortem audits attempted to analyse the records of only those in whom epilepsy appeared in part I of the death certificate and in whom the death was considered as probably due to epilepsy.

In England and Wales, access to the clinical records was dependent on the cooperation of the coroner, who provided the name of the patient's GP. The GP was then asked to let the audit team have access to the case records. In Scotland, the team was provided with details of the GP by the General Register Office, and in Northern Ireland the team had authority to access primary care records centrally. The research team did not personally have access to any patient care records, but clinical records were audited by field workers.

The analysis reported here includes some audit records which were received too late to be included in the published report.

3.2.3. Audit tool development

Criteria for audit were developed using published guidelines, results of literature searches and views of the research team, and an audit tool was developed based on the criteria. The primary care tool was developed using seven sources of evidence (Bradford and Airedale Health Authority, 1998; Brown et al., 1993; Epilepsy Task Force, 1998; Hall et al., 1997; Leeds Health Authority, 1999; Taylor, 1996) (SIGN, 1997).

3.2.4. Information audited

Clinical records were audited by trained research nurses. The audit required that any data were taken only from the primary care records themselves; audit nurses were not permitted to use information extracted from letters from specialist care or other agencies. Different audit forms were used for those who had been, and those who had not been referred to specialist care.

Age at death was calculated from the date of birth and date of death. Seizure frequency was audited only in those not referred to secondary care. Seizure description was audited in any patient whose first seizure occurred less than five years before death. AEDs taken at the time of death were recorded. Data on some aspects of information provision were audited.

The time of the last review prior to death was calculated, and the type of professional performing that review recorded.

3.2.5. Criteria for primary care

The audit assessed care received against the following criteria:

- People with continuing seizures should continue to have access to specialist care (CSAG, 2000). Patients with severe epilepsy should continue to be supervised by a consultant (Winterton, 1986)
- Some form of planned shared care is the preferred model of care for patients with epilepsy (SIGN, 1997). These guidelines do not specify the timing of the planned care. In view of the Quality and Outcomes Framework indicators, in

which payments are made to GPs for the percentage of people with epilepsy reviewed within 15 months, this was taken as the reference point for this audit (NHS Confederation and British Medical Association, 2003)

- Primary care should monitor seizures and side-effects of medication, provide information and counselling, and should re-refer to secondary care where necessary (SIGN, 1997)
- AEDs should be used in monotherapy where possible (Hall et al., 1997). The aim should be to maintain the patient on the minimum number of drugs required to achieve adequate symptom control (SIGN, 1997)

3.2.6. Analysis

Most analysis was done using SPSS version 11.0. Some analysis of summary data was performed in Clinstat, a DOS-based software programme available from St George's Hospital Medical School.

For continuous data the t-test was used where the data were normally distributed, and the Mann-Whitney U and Kruskal-Wallis tests where they were not. For categorical data the Chi squared test was used. For 2 by 2 tables the difference between binomial proportions was used, and 95% CI calculated. All comparisons were 2-sided. A p-value of < 0.05 was taken to indicate statistical significance.

3.2.7. Ethics and confidentiality

All data were anonymised. Two Multi-centre Research Ethics Committees reviewed the proposal and each independently defined the project as audit.

3.3. THE SPECIALIST CARE SECTION OF THE NATIONAL SENTINEL CLINICAL AUDIT OF EPILEPSY-RELATED DEATH

3.3.1. Audit design

The intended study population was everyone who died from an epilepsy-related cause in the UK from 1 September 1999 until 31 August 2000.

3.3.2. Case ascertainment

Initial case ascertainment was as described in section 3.2.1. Specialist care records were obtained where possible after location of the primary care records.

3.3.3. Audit tool development

The specialist care audit tool used three sources of evidence (Wallace et al., 1997; Winterton, 1986; SIGN, 1997), and the analysis was based on these and the CSAG report (CSAG, 2000) when it was published.

3.3.4. Information audited

The analysis of specialist care in this thesis concentrates on the care provided to people with both epilepsy and learning disability. Overall care for adults and children was covered in the secondary care section of the published report (Hanna et al., 2002).

The age of each patient at death and the duration of epilepsy were, wherever possible, calculated. When only the year of first seizure was known, it was taken as June 30th of that year, and when only a month was known, it was taken as the 15th of that month. Wherever possible, time from last outpatient appointment to death was calculated from the date of the appointment and the date of death. The most senior clinician and the most appropriate specialty were also assessed from the last three outpatient appointments. Where a consultant was not seen in the last three appointments, the audit officers documented the date when a consultant was last seen. In some cases this calculation was not possible as the audit officers documented the last three specialist appointments relating to epilepsy, and both outpatient and inpatient episodes were documented. Time from EEG recording and MRI or CT scanning was also calculated

where these investigations had been performed. The presence or absence of a clear seizure description and of seizure frequency at the last consultation was noted. Seizure frequency at last consultation was calculated where possible. In those with two or more seizures per month, the audit officers assessed whether suitability for surgery had been considered.

The number of AEDs taken by each patient was calculated, taking into account information from both the primary care and secondary care audit files. The different items of information documented as discussed with each patient or family were calculated.

3.3.5. Criteria for specialist care

The audit assessed care received against the following criteria:

- People with continuing seizures should continue to have access to specialist care (CSAG, 2000). Patients with severe epilepsy should continue to be supervised by a consultant (Winterton, 1986)
- People who continue to be drug resistant should be referred for assessment for epilepsy surgery (SIGN, 1997). In most instances patients will be experiencing more than two seizures per month (Wallace et al., 1997)
- The basis of the patient record for use in the care of all patients with epilepsy should include a detailed history including a witness account of the frequency of attacks and of observations before and during the attacks (SIGN, 1997)
- EEG should be performed in patients aged under 25 years at diagnosis. It is not necessary in establishing a diagnosis if a clear clinical history is available (SIGN, 1997). EEG is indicated in patients with continuing seizures where there is diagnostic doubt (Wallace et al., 1997)
- Brain imaging is unnecessary if a firm diagnosis of an idiopathic generalised epilepsy syndrome has been made on the basis of the clinical history and EEG findings. Brain imaging should always be performed in patients aged over 25 years. If a firm diagnosis of an idiopathic generalised epilepsy has not been made, both an EEG and brain imaging are necessary (SIGN, 1997). MRI is

indicated where there is evidence of a partial onset from the clinical history or EEG, at any age (Wallace et al., 1997)

- The aim should be to maintain the patient on the minimum number of drugs required to achieve adequate symptom control (SIGN, 1997)
- The care and management of people with epilepsy is not complete without provision of clear and accurate advice and information (SIGN, 1997). Ensure that patients have clear information about the drugs they are taking, including information about possible side-effects and drug interactions. The importance of compliance should be stressed (Wallace et al., 1997)

3.3.6. Analysis

Most analysis was done using SPSS version 11.0. Some analysis of summary data was performed in Clinstat, a DOS-based software programme available from St George's Hospital Medical School.

For continuous data the t-test was used where the data were normally distributed, and the Mann-Whitney U test where they were not. For categorical data the Chi squared test was used. For 2 by 2 tables the difference between binomial proportions was used, and 95% CI calculated. For 2 by 2 tables with small expected values, Fisher's exact test was used. All comparisons were 2-sided. A p-value of < 0.05 was taken to indicate statistical significance.

3.3.6.1. Analysis of investigations according to available guidelines

To analyse use of EEG when appropriate, information was grouped, according to 1997 SIGN guidelines, into those who had EEG, those who had no EEG but in whom this was acceptable (e.g. first seizure at age over 25 years, and clear history available), those who had no EEG in whom this was not acceptable (e.g. aged under 25 at diagnosis), and those in whom need for EEG is unclear (e.g. aged over 25 at diagnosis in whom seizure history is unclear). The information regarding neuroimaging was grouped according to whether imaging status was satisfactory (either imaging had been performed, or it was not necessary due to a clear diagnosis of idiopathic generalised epilepsy, or imaging was not possible due to lack of co-operation), those in whom the need for imaging was

unclear due to the lack of a clear description of a seizure in the case records, those in whom it was unclear for other reasons, and those who should have had imaging (those with ongoing seizures in whom the probable diagnosis was not idiopathic generalised epilepsy, and those with a change in seizure type or pattern) but had not.

3.3.6.2. Analysis of care in those with learning disability

For those with learning disability, the specialty of clinician seen was considered. A consultant specialist in learning disability categorised the clinicians caring for the adults into 'good', 'satisfactory', 'not satisfactory' and 'unclear'. The clinicians caring for children with learning disability were categorised by a consultant paediatric neurologist into the same categories.

For the time between the last outpatient appointment and death, and suitability for surgery, the results are presented separately for those with and without learning disability. For the other criteria, results are compared between those with and those without learning disability, among those seen by the various categories of clinicians, and between those ever seen by a consultant and those not.

The people taking AEDs thought to have negative impact on cognition in people with learning disability (phenobarbital [and primidone], phenytoin, sodium valproate and topiramate) and those taking newer AEDs (lamotrigine, topiramate, tiagabine, gabapentin and vigabatrin) were identified.

3.3.6.3. Quality of care

In the National Sentinel Clinical Audit the completed audit tools were also assessed independently by at least two panel members. Summaries of the primary, specialist and pathology audit tools were prepared for each case by the author. The full panel met and discussed each case in detail, taking into account all information available from the primary care and pathology audit tools, and each others' expert opinions and guidelines where available. Each case was classified as having received adequate care, or care which failed to meet guidelines. Cases were screened for large errors, which were defined as major deviations from standard care. Where no information was available,

the information was insufficient, or where there was any doubt, the cases were classified as unclear. Each case was further classified as death unavoidable, potentially avoidable, probably avoidable or unclear. This information is presented comparing those with and without learning disability and, in those with learning disability, according to the categories listed above.

3.3.7. Ethics and confidentiality

All data were anonymised. Two Multi-centre Research Ethics Committees reviewed the proposal and each independently defined the project as audit.

3.4. INVESTIGATION INTO THE USE OF DEATH CERTIFICATES AS CASE ASCERTAINMENT FOR EPILEPSY

3.4.1. Initial study design

The National General Practice Study of Epilepsy and Epileptic Seizures was initiated in 1984. It aimed to identify 1200 people in whom a new diagnosis of epileptic seizures was suspected, and to monitor their progress. GPs, who volunteered for the study after it had been publicised in medical journals, were asked to notify the study of any patient in whom epileptic seizures were suspected, excluding babies with neonatal seizures. Initial registration of patients took place between June 1984 and October 1987, and 175 GPs registered 1195 patients. The form for the initial notification contained details of the medical history, family history, likely aetiology of the seizure and the circumstances and description of the seizure, and included a checklist. Six months after registration GPs were asked to complete follow-up forms with details of seizure recurrence, AED treatment and any other developments. The hospital consultants of any patients who had been referred were also asked to complete a form with details of diagnosis and any investigations. At this stage, patients were classified by an expert panel using all available information; 792 patients were classified as having either definite epilepsy (564) or possible epilepsy (228). A further 220 were classified as having had febrile convulsions and 79 as having non-epileptic events (such as syncope, non-epileptic attack disorder or breath holding attacks). In total 104 patients were excluded, and not followed further, due to either a previous diagnosis of epilepsy or the diagnosis being neonatal seizures (Hart et al., 1989; Sander et al., 1990).

From then on GPs were asked to complete follow-up forms on a yearly basis until the death of the patient or until early 2000. The follow-up form contained a summary of the information held by the study and asked for any neurological, medical or psychological developments, for details of seizure recurrence including dates, timing and any change in character of the seizures and for current AED treatment. If the patient had died, the GP was asked for any details about the death. The cohort was flagged by the National Health Service Central Register (NHSCR), and all deaths were notified to the study. Death certificates and any post-mortem reports were then obtained by the study.

3.4.2. The current study

Eight criteria were hypothesised which might influence whether or not epilepsy was included on the death certificate. These were:

- Classification at six months after study entry into 'definite' or 'possible' epilepsy
- Convulsive seizures
- Seizures during follow-up
- Average number of seizures/year in the five years before death, or average number of seizures/year during lifetime after seizure onset if seizure onset was less than five years before death
- Age at death
- Physician who certified death
- Cause of death
- Number of AEDs prescribed at the time of the last follow-up

The follow-up forms were examined to establish whether or not subjects had ever had convulsive seizures, and whether they had further seizures during the study. The average number of seizures per year during the last five years before death (or during lifetime, after onset, in those dying less than five years after onset) was calculated. In those with seizures occurring more frequently than daily the average number of seizures per year was taken as 365. Age at death was calculated from the date of birth and date of death. Patients were then divided into four groups according to age at death. The number of AEDs prescribed was taken from the most recent follow-up form.

Death certificates were examined manually to see whether epilepsy (or seizures or status epilepticus) was mentioned in either part of the death certificate. The name of the person who completed the death certificate (the certifying physician) was compared with the name of the physician who completed the most recent follow-up form (current physician), and with the name of the physician who initially registered the patient with the study (referring physician). The presumed cause of death was established from the death certificate and available clinical information, and classified into three groups: malignancy, vascular (including cerebrovascular and cardiovascular deaths), and other.

3.4.3. Analysis

Each of the eight categories was divided into subgroups and the number of death certificates indicating epilepsy was calculated as a percentage of the deaths.

The categories were then individually entered into a univariate logistic regression model, and the results expressed as odds ratios (and 95% CI) for epilepsy mentioned on the death certificate. Statistical analysis was performed using SPSS for Windows, release 11 (SPSS, Inc., Chicago, IL).

3.4.4. Ethics and confidentiality

All data were anonymised. NGPSE was approved by the Joint Ethics Committee of the Institute of Neurology and the National Hospital for Neurology and Neurosurgery.

3.5. SUICIDE IN PEOPLE WITH EPILEPSY IN ENGLAND AND WALES

3.5.1. Study design

The National Sentinel Clinical Audit of epilepsy-related death (Hanna NJ et al., 2002) used national registries to search for people with epilepsy who died from an epilepsy-related cause in the UK between 1st September 1999 and 31st August 2000. Specifically, the Office for National Statistics and the General Register Offices for Scotland and for Northern Ireland identified deaths during the study period where epilepsy was mentioned on the death certificate. The methodology of this audit has been detailed earlier (3.2. and 3.3.).

3.5.2. Analysis

The death certificates in England and Wales in which epilepsy was recorded (N = 2060) were reviewed. Deaths by suicide were sought using words such as "suicide", "self harm", and key words used to specify the ICD-9 subcategories for suicide and self-inflicted injury (ICD-9, E950-959). Deaths by hanging were also specifically sought.

The population of people with epilepsy in England and Wales was estimated by applying the 1998 prevalence rates of treated epilepsy in England and Wales per age group and sex (Purcell et al., 2002) to the resident general population (Office for National Statistics., 2001). The expected number of deaths in people with epilepsy was then calculated by applying the relevant year 2000 death rates for the population of England and Wales per age group (0-4, 5-14, 15-24, subsequent decades up to 84, and 85+) and sex (Office for National Statistics., 2001) to the population of people with epilepsy. The population of England and Wales in mid-2000 was 52.9 million (Office for National Statistics, 2001).

The total number of expected deaths and observed deaths in males and females in the population with epilepsy were then calculated using the age-specific rates. The SMR was calculated as the ratio of the observed to the expected number of deaths, and confidence intervals calculated using the Poisson distribution. An assumption was made that all deaths identified occurred amongst people with treated epilepsy.

All analysis was performed in Microsoft Excel.

3.6. A META-ANALYSIS OF SUICIDE IN PEOPLE WITH EPILEPSY

3.6.1. Overview

A published meta-analysis of suicide in epilepsy included 29 studies from various countries (Pompili et al., 2005). Seven of these, however, should have been excluded (see 3.6.3. below): some articles were later publications on the same set of patients as reported previously and included in the analysis, and in others the data are not available to calculate the person-years at risk. The authors concluded that 'our meta-analysis shows that suicide in patients with epilepsy is more frequent than in the general population', yet they did not produce an SMR despite pooling the data. A re-analysis of the eligible studies was performed to avoid these problems.

3.6.2. Included studies

Twenty two articles provided the information needed to perform the meta-analysis:

- Bladin, 1992
- Camfield et al., 2002
- Currie et al., 1971
- Dalby, 1969
- Guldvog et al., 1994a
- Guldvog et al., 1994b
- Hauser et al., 1980
- Hennessy et al., 1999
- Klenerman et al., 1993
- Lhatoo et al., 2001
- Lindsay et al., 1979
- Lip and Brodie, 1992
- Loiseau et al., 1999
- Nilsson et al., 1997
- Rafnsson et al., 2001
- Salanova et al., 2002
- Shackleton et al., 1999

- Sillanpaa, 1983
- Stepien et al., 1969
- Taylor and Falconer, 1968
- White et al., 1979
- Zielinski, 1974a

3.6.3. Excluded studies

Seven of the articles in the previous publication were not used in the current analysis of suicide. For four, it was not possible to determine the number of patient-years of follow-up:

- Blumer et al., 2002
- Iivanainen and Lehtinen, 1979
- Krohn, 1963
- Mendez and Doss, 1992

Two contained data that was repeated in a later follow-up of the same series:

- Cockerell et al., 1994
- Sillanpaa, 1973

One study was a case control study which was a follow on from a previous cohort study:

- Nilsson et al., 2002

3.6.4. Analysis

3.6.4.1. Unweighted SMR

The articles were each reviewed by two independent researchers, and deaths stated as suicide were ascertained. The number of patient-years follow-up in each paper was calculated from the number of patients in the study and the mean follow-up duration. If no mean was given, the median was used instead, or the mean was taken as the average of the maximum and minimum. If the paper gave the number of patient-years at risk, this was used in preference to a calculated rate

Expected deaths were calculated by applying the rates for each cause of death using WHO datasets for the country taken, where possible for the year at the midpoint of the study. Where this was not possible, data for the earliest year available were used. In the case of early studies from England and Wales, ONS data were used (Office for National Statistics, 2003). For two studies the authors provided expected number of deaths, and these were used instead of WHO data. Gender was rarely given in the papers, and so was not considered in calculating the expected values. The SMR was calculated as the ratio of the observed deaths to those expected, and the 95% CI for the SMR calculated using the Poisson distribution.

3.6.4.2. Weighted SMR

The data were also analysed using RevMan software (Cochrane Collaboration, v42. 2005); this software applies weighting to the SMR but does not allow for population sizes of greater than 999,999. The software also requires the numerator (the number of deaths from suicide) and the denominator data (the number of people in the population) and so the figures provided by two of the papers for the expected numbers of suicides could not be used. The analysis was therefore performed in RevMan using the number of population suicides and the total denominator population, both divided by 1,000 to allow for appropriate weighting. This allowed all 22 studies to be included. As the population numbers needed to be integers, these data were rounded. The unweighted analysis was also repeated using the population suicides and total population from WHO data sets.

3.6.4.3. Unweighted SMR by year of publication

The data were further analysed according to whether they were published in the last ten years or earlier. Eight studies were published after 1996 (Camfield et al., 2002; Hennessy et al., 1999; Lhatoo et al., 2001; Loiseau et al., 1999; Nilsson et al., 1997; Rafnsson et al., 2001; Salanova et al., 2002; Shackleton et al., 1999). Unweighted SMRs were calculated for each group.

SECTION 4. RESULTS

4.1. THE CHILTERN AUDIT

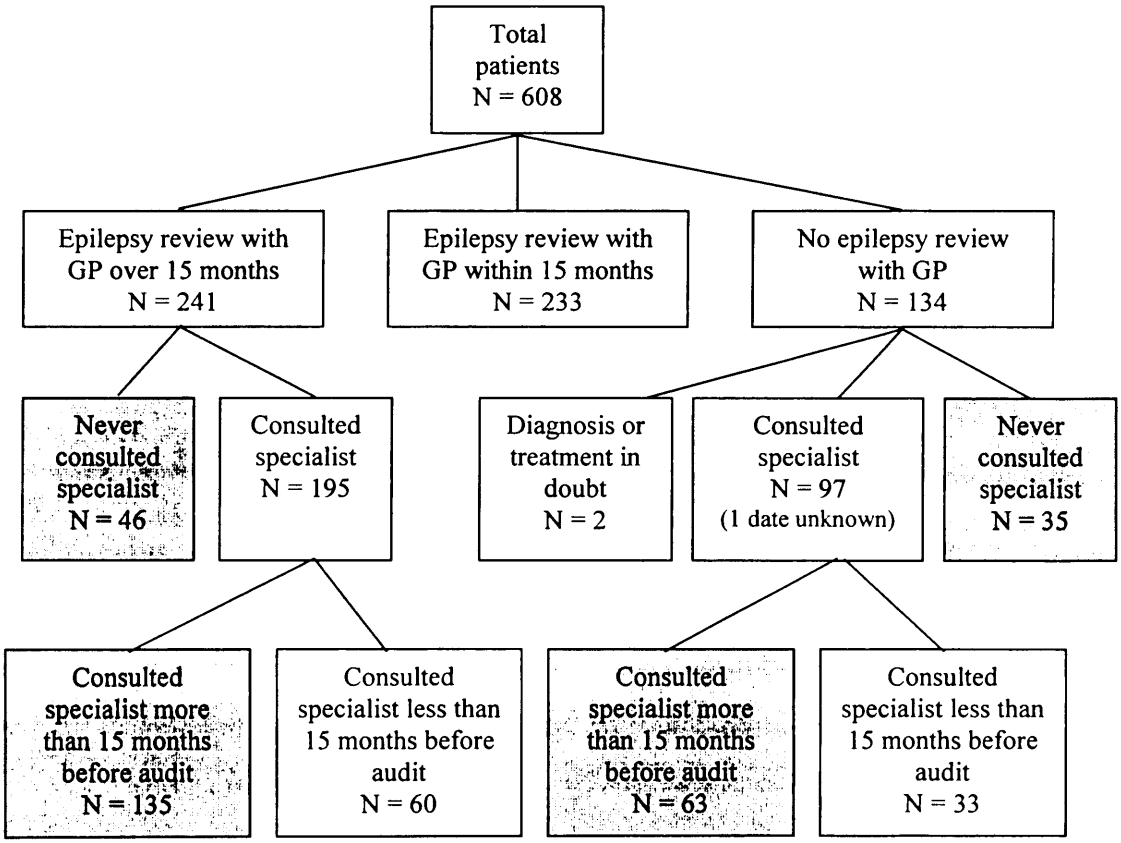
4.1.1. Demographic details

The notes of 608 patients (335 [55%] male) were audited. The mean age of patients was 47 years (median 46 years), range one to 97 years. Nineteen patients (3%) had documented problems with alcohol. Sixty three patients (10%) had documented learning disability.

4.1.2. Access to care

The documented evidence for epilepsy review is illustrated below. Those who do not appear to have had an epilepsy review within 15 months of the audit (highlighted in figure 1) are described in more detail, and illustrated in appendix 2.

Figure 1 Access to care within 15 months in the Chiltern audit



4.1.2.1. GP review

One hundred and thirty five patients (22%) had seen the GP for epilepsy review within six months of the audit, 205 (34%) within a year, and 233 (38%) within 15 months. One hundred and thirty four (22%) had no documented epilepsy review with the GP.

Of those who had never had epilepsy review with the GP, 44% had no seizure frequency documented or else the seizure frequency was unclear. Thirty seven percent were seizure-free and three percent had seizures at least weekly. Twenty percent were on no AEDs, 56% on monotherapy and 20% on polytherapy.

4.1.2.2. No epilepsy review documented

Thirty seven people (6%) appear to have seen neither a specialist nor a GP for epilepsy. In two of these, the situation is unclear: one was under a specialist neurological hospital for another illness; in the other, the diagnosis was in doubt (the patient collapsed many years previously and took no AEDs).

The situation of the other 35 people is illustrated in appendix 2 (figure A1). Four people probably had fewer than five seizures; two were taking AEDs, and in one AEDs are unknown. In 18 no seizure frequency has been documented, or was very unclear; five of these may have been seizure-free. Fourteen of these 18 were taking AEDs, including four on polytherapy. Fifty one percent had seen their GP for another reason within the 13 weeks before the audit, and a further 23% within a year. Fourteen percent appear never to have consulted the GP.

4.1.2.3. Last GP epilepsy review more than 15 months before the audit

Of all patients, 241 (40%) had last had a GP review for epilepsy more than 15 months before the audit. Of these 41% were seizure-free, and three percent had seizures weekly or daily. In 46% seizure frequency was unclear or not documented. Over half (55%) were on monotherapy, 22% on no AEDs, and 23% on polytherapy (up to 4 AEDs).

One hundred and ninety five (81%) of these people had seen a specialist. Forty three (18%) had seen a specialist within 6 months of the audit, 53 (22%) within a year and 60

(25%) within 15 months. The mean time since these 195 people had seen a specialist was over 6 years, and the median over 3 years. Maximum time since last specialist review was 41 years.

4.1.2.4. Last epilepsy review more than 15 months before the audit

One hundred and thirty five patients (22%) were last reviewed for epilepsy by anyone more than 15 months before the audit (figure A2). Of these, 60 (44%) were known to be seizure-free (19 on no AEDs, 37 on monotherapy and four on polytherapy), and a further 25 (19%) may have been seizure-free (six on no AEDs, 14 on monotherapy, four on two AEDs and one on three AEDs). In 29 there was no record of seizure frequency in the case notes; nine were on no AEDs, 16 were on monotherapy and four were on two AEDs.

Of those whose last epilepsy review by a GP was more than 15 months before the audit, 46 (19%) do not appear to have been reviewed by any specialist (figure A3). The majority of these (24, 52%) were either seizure-free, or had experienced fewer than five documented seizures. However, seven of these (29%) were on AED polytherapy.

4.1.2.5. No epilepsy review by GP

Of those who had no GP review, 97 (72%) were seen at some stage by a specialist. The date of one specialist appointment is not known. Of the other 96, 22 (23%) were seen within six months of the audit, 30 (31%) within 12 months, and 33 (34%) within 15 months. Sixty three (66%) were seen over 15 months before the audit (figure A4). Of the 63 seen by the specialist over 15 months before the audit, 32 were seizure-free (eight on no AEDs, 20 on monotherapy and four on two AEDs). Five had fewer than five seizures documented; three were on no AEDs. All of those with seizures occurring at least yearly were on AEDs, with the majority (three of five, 60%) on polytherapy, one of whom, with weekly seizures, was on three AEDs.

Of the 375 who had never seen a GP or who had seen a GP for epilepsy review more than 15 months before the audit, 307 (82%) had seen a GP for another reason in the previous 15 months.

4.1.2.6. No epilepsy review within 15 months of audit

In the whole group of case records audited, 279 (46%) patients had not had an epilepsy review by either a GP or specialist within 15 months of death. Of those, 72 (26%) were taking no AEDs, but 46 (16%) were on AED polytherapy.

The two whose diagnosis or review is in doubt are excluded from the following analyses.

4.1.2.6.1. Time of last review and use of AEDs

Those without review took significantly fewer AEDs (mean 0.9 AEDs, SD 0.7) than those with review (mean 1.4 AEDs, SD 0.77; Mann Whitney U = 29940, $p < 0.0001$). AEDs taken are shown in table 1.

Table 1 Chiltern audit: number of AEDs taken, where known, in those who had/had not been reviewed within 15 months of the audit

	No AEDs		Monotherapy		Polytherapy		Total
	N	%	N	%	N	%	
No review	72	26	157	57	46	17	275
Review	12	4	200	62	110	34	322
Total	84	14	357	60	156	26	597

4.1.2.6.2. Time of last review and age

Those who had no epilepsy review for at least 15 months before the audit were significantly older than those who had a review in that time; the mean age of those with no review was 52.0 years, SD 20.8 and in those with review was 42.9 years, SD 22.9 (difference = 9.0 years [95% CI 5.5 to 12.6 years], $t = 5.0$, $p< 0.0001$).

4.1.2.6.3. Time of last review and learning disability

A significantly higher percentage of those who were reviewed had learning disability (48/327 [15%] of those reviewed compared with 15/279 [5%] of those not reviewed; difference 9%, [95% CI 5 to 14%], $p = 0.0002$).

4.1.2.6.4. Time of last review and alcohol problems.

There was no difference in time of last review between those with and without documented alcohol related problems (13 of 327 [4%] with review had alcohol problems compared with 6/279 [2%], not reviewed; difference 2%, [95% CI –1 to 5%], p = 0.2).

4.1.2.6.5. Time of last review and episodes of status epilepticus

A higher proportion of those who had been reviewed had had at least one episode of status (those reviewed 31/327 [9%], those not reviewed 9/279 [3%]; difference = 6%, 95% CI 3 to 10%, p = 0.002).

4.1.2.6.6. Time of last review and seizure status

Those with no review were more likely to be seizure-free, or to have had fewer than five seizures than those with review (those not reviewed 138/150 [92%], those reviewed 99/185 [54%]; difference = 38%, 95% CI 30 to 47%, p < 0.0001) in whom seizure frequency is known.

The seizure status is shown in table 2.

Table 2 Chiltern audit: seizure status, where known, in those who had/had not been reviewed within 15 months of the audit

	Seizure free		< 5 seizures		Yearly or less		Weekly to monthly		Daily		Total
	N	%	N	%	N	%	N	%	N	%	
No review	121	81	17	11	6	4	6	4	0	0	150
Review	84	45	15	8	21	11	59	32	6	3	185
Total	205	61	32	10	27	8	65	19	6	2	335

Chi squared (4df) = 61.36, p <0.0001

Chi squared trend (1df) = 59.71, p < 0.0001

The trend shows that those who had epilepsy review within 15 months of the audit had more frequent seizures than those with no review. In interpreting these figures it should be noted that in 43% of those with review, and 46% of those with no review, the seizure frequency was either not documented or was unclear.

4.1.2.7. No review by a specialist

In all, 122 (20%) patients appear never to have been seen by a specialist. In 30% of these there is no seizure frequency documented and in a further nine percent it was unclear. Almost one third were seizure-free and nine percent had fewer than five lifetime seizures. Only two percent appeared to have a clear history of ongoing seizures.

4.1.2.8. Review by epilepsy specialist nurse

In the practice with an attached epilepsy specialist nurse, all patients (N = 75) had documented review for epilepsy.

Fourteen of these patients (19%) had not had epilepsy review for at least 15 months before the audit. Seven were seizure-free (two on no AEDs, three on monotherapy and two on polytherapy). Three had seizures weekly to yearly (two on monotherapy, one on polytherapy). One had fewer than five seizures (monotherapy) and in three, seizure frequency was not documented (one on no AEDs, two on monotherapy).

4.1.3. Documented history of seizures available

4.1.3.1. Seizure frequency documented

Seizure frequency was documented in 335 (55%), of whom 205 (61%) were seizure-free when this was last recorded. Twenty eight (8%) were experiencing seizures at least weekly. Seizure frequency was documented in 76% of the records in the practice with an epilepsy specialist nurse, compared with 52% in the others (difference 24% [95% CI 13 to 34%], p = 0.0001).

4.1.3.2. Seizure description documented

A seizure description was available in 280 (46%) records. It was available in the records of 42 (47%) of the 90 diagnosed in the five years before the audit. A description

was documented in 71% of records in the practice with an epilepsy specialist nurse compared with 43% in the others (difference 28% [95% CI 17 to 39%], p <0.0001).

4.1.3.3. Classification of seizures possible

The audit nurses were able to classify the epilepsy in 438 (72%) patients. Classification was possible in 87% of the records in the practice with an epilepsy specialist nurse, compared with 70% in the others (difference 17% [95% CI 8 to 25%], p = 0.003).

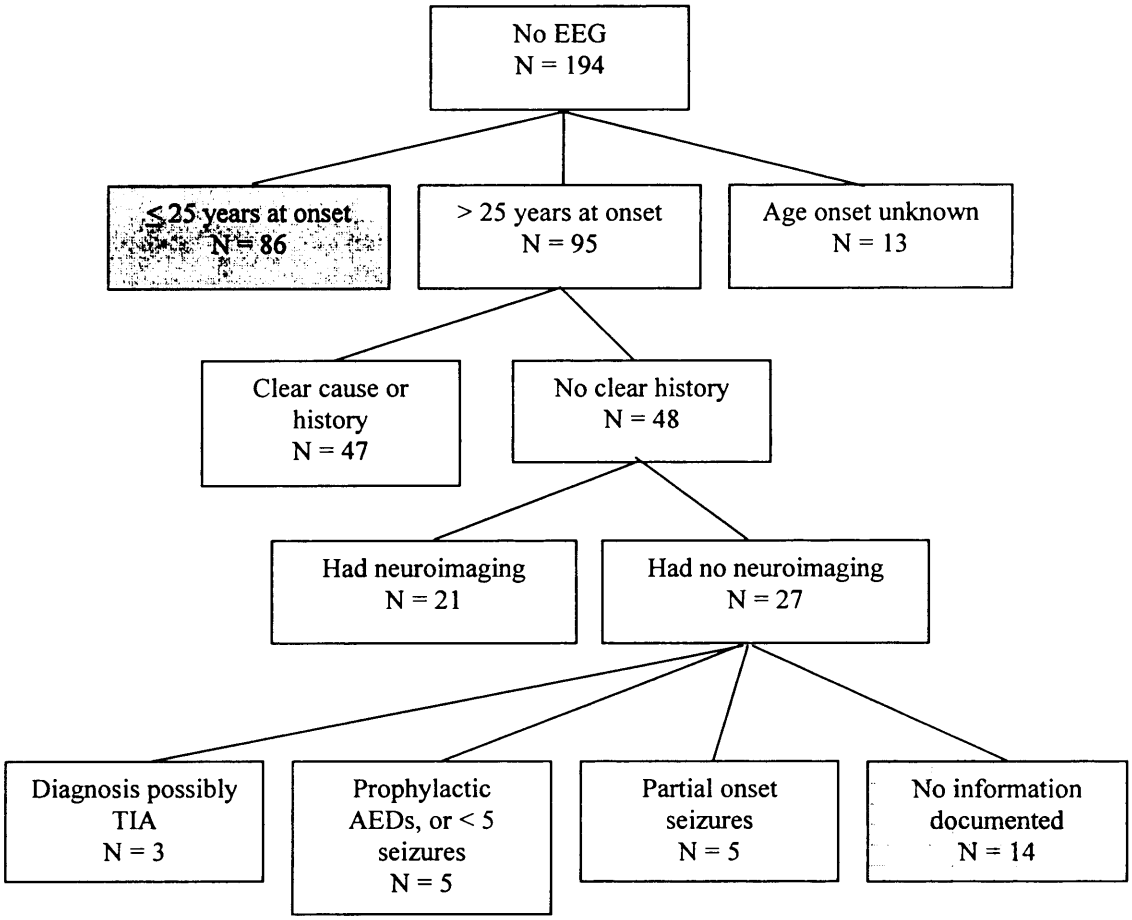
4.1.4 Investigations of epilepsy

4.1.4.1. EEG

Of 348 (57%) patients whose seizures started before 25 years old, 262 (75%) had had an EEG. In seven cases this appears to have predated the first seizure, usually because of other pathology such as skull fracture or cerebral palsy. 52% had had an EEG within 3 years of the first seizure. Altogether 414 (68%) had an EEG and 194 (32%) did not. The situation of those with no EEG is illustrated in figure 2.

Figure 2 Chiltern audit: clinical status of those with no EEG

(Those highlighted required EEG according to guidelines and in those crosshatched the situation is particularly unclear).

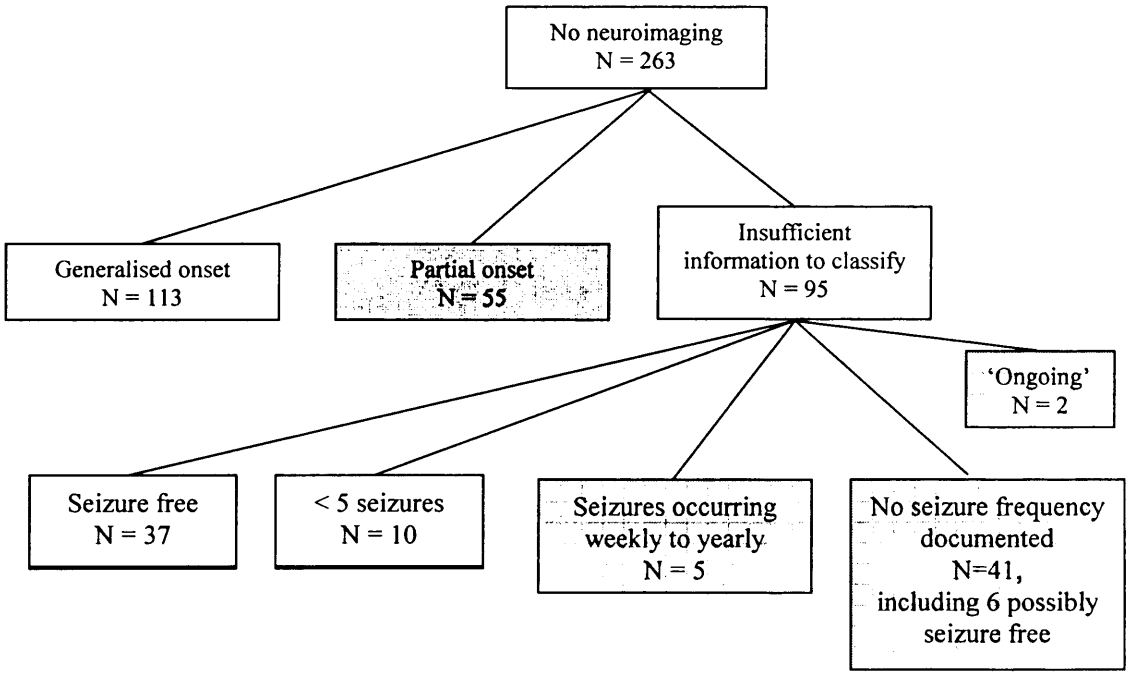


4.1.4.2. Neuroimaging

Of the 608 Chiltern patients 263 (43%) appear to have had no imaging at all. The audit nurses were able to classify the seizures of 168 (64%) of these: 113 had generalised onset and 55 partial onset. Of those with no seizure classification, 61/95 had also had no EEG recording. Thirty seven (39%) were seizure-free and a further six (6%) may have been seizure-free. Ten (11%) had had fewer than five seizures in total. However, one had yearly seizures, three had monthly seizures, one had weekly seizures and in two, seizures were described as 'ongoing'. In 35 people, there was no seizure frequency documented, or it was unclear. This is illustrated in figure 3.

Figure 3 Chiltern audit: clinical status of those with no neuroimaging

(Those highlighted had indications for neuroimaging, according to guidelines and those crosshatched may have required neuroimaging)



There were 103 people who did not have imaging in whom it may have been indicated; 57 (55%) had had an epilepsy review within 15 months of the audit with either a specialist or the GP.

4.1.5. Use of AEDs

In nine patients (1%) it was not possible to establish the number of AEDs taken.

4.1.5.1. Number of AEDs taken

This is shown in table 3.

Table 3 Chiltern audit: AEDs taken

No of AEDs	No of patients	(%)
0	85	14
1	357	60
2	121	20
3	29	5
4	7	1
Total	599	

4.1.5.2. Use of particular AEDs

4.1.5.2.1. Barbiturates (phenobarbital or primidone)

Of 514 patients currently taking AEDs, 54 (11%) were taking phenobarbital and 14 (3%) were taking primidone; two patients were taking both. Thus 66 (13%) patients were taking barbiturates.

A slightly higher percentage of females (35/225, 16%) than males (31/289, 11%) were taking barbiturates (difference 5% [95% CI –1 to 11%], p = 0.1). Fewer people with learning disability (4/58, 7%) were taking barbiturates than those without learning disability (62/456, 14%; difference 7% [95% CI –1 to 14%], p = 0.15), but the difference was not significant. In those in whom it was possible to assess seizure frequency, there was no difference in the proportion who were seizure-free (135 of 239, 56%, not taking barbiturates were seizure-free, compared with 25 of 38, 66% taking barbiturates; difference 9% [95% CI –7 to 26%], p = 0.28). However, those taking

barbiturates were significantly less likely to have had an epilepsy review in the previous 15 months by either the GP or a specialist than those not taking barbiturates (24/66, 36% of those on barbiturates had been reviewed compared with 288/448, 64% of those not taking barbiturates, (difference = 28% [95% CI 15 to 40%], $p < 0.0001$).

Of those taking barbiturates, 48/66 (73%) had ever seen their GP for epilepsy (mean time since last review 4.5 years, median 1.8 years). Of those not taking barbiturates, 364/448 (81%) had ever seen their GP for epilepsy (mean time since last review 2.1 years, median 1 year; difference between groups, Mann Whitney U = 7141, $p = 0.04$). Of those taking barbiturates, 38/66 (58%) had seen a specialist for epilepsy (mean time since last review 14.0 years, median 10.5 years). Of those not taking barbiturates, 376/448 (84%) had seen a specialist for epilepsy (mean time since last review 3.5 years, median 1.0 years; difference between groups, Mann Whitney U = 3543, $p< 0.0001$).

Those taking barbiturates were significantly older than those not taking them (those taking barbiturates mean age 63 years, SD 16, median 65 years, those on no barbiturates mean age 46 years, SD 22, median 44 years; difference between the groups, Mann Whitney U = 7886, $p < 0.0001$). Those taking barbiturates had had epilepsy for mean and median 41 years compared with those not taking them, whose duration was mean 19 years, median 16 years (Mann-Whitney U = 3616, $P < 0.0001$).

4.1.5.2.2. Phenytoin

One hundred and seventy four of 514 (34%) patients were taking phenytoin. Ten of 58 (17%) with learning disability took phenytoin, compared with 164 of 456 (36%) of those without learning disability (difference 19%, 95% CI 8 to 29%, $p = 0.0045$). There was no difference in use of phenytoin between those reported as having a history of problems with alcohol (four of 16, 25%) compared with those without (170 of 498, 34%; difference 9% [95% CI –12 to 31%], $p = 0.447$).

In those in whom it was possible to estimate seizure frequency, 49 of 94 (52%) of those taking phenytoin were seizure-free compared with 111 of 183, (61%) not taking phenytoin, (difference = 9% [95% CI –4 to 21%], $p = 0.17$). However, almost half of

both groups had missing or unclear information on seizure frequency. Side-effects had been reported in 24% of the phenytoin group and in 23% of those not on phenytoin.

Ninety of 174 (52%) on phenytoin had been reviewed in the 15 months before the audit, compared with 222 of 340 (65%) not on phenytoin (difference = 14% [95% CI 5 to 23%], $p = 0.0029$). Those on phenytoin had been reviewed by a specialist less recently than those not on phenytoin (mean 6.1 years, median 2.6 years in those on phenytoin compared with mean 3.8 years, median 0.9 years in those not on phenytoin; Mann Whitney $U = 13560$, $p < 0.0001$). There was no significant difference in the time from the last GP review of epilepsy (mean 2.7 years, median 1.4 years, for those taking phenytoin compared with mean 2.3, median 1.0 years, for those not; Mann Whitney $U = 17658$, $p = 0.27$). Those taking phenytoin were significantly older (mean 59.8 years) than those not on phenytoin (mean 42.5 years; $t = 9.04$, $p < 0.0001$). Those taking phenytoin had had epilepsy for a mean of 26.8 years, median 26 years, compared with mean 20.0 years, median 16 years, for those not taking phenytoin (Mann-Whitney $U = 18974$, $p < 0.0001$).

4.1.5.2.3. Sodium valproate

Of 58 people with learning disability, 20 (34%) took valproate compared with 113 of 456 (25%) without learning disability (difference 10% [95% CI –3 to 23%], $p = 0.11$).

Slightly more females (61 of 225, 27%) than males (72 of 289, 25%) who took AEDs were taking valproate, although the difference is not statistically significant (difference 2% [95% CI –5 to 10%], $p = 0.57$). Twenty-three of the women taking valproate were in the age group 14 to 45 years; two had had a hysterectomy, and in two, information is missing in the audit record. Of the 19 females of childbearing potential, eight were on monotherapy, ten on two AEDs and one (with frequent seizures who had had a recent epilepsy review) on four AEDs. Eight of 19 women of childbearing potential taking valproate had received advice about contraception, six had received preconceptual advice, and eight had had advice about pregnancy. In the six females aged 18 –30 years who had not had a hysterectomy, three had received contraceptive advice, two preconceptual advice and three advice about pregnancy.

4.1.5.2.4. Topiramate

Only 14 (3%) of the 514 patients taking AEDs were on topiramate. Four of 58 (7%) with learning disability took topiramate compared with ten of 456 (2%) without learning disability (Fisher's exact p = 0.12).

Those on topiramate tended to be younger (mean 32 years, median 33 years) than those not on topiramate (mean 49 years, median 48 years; Mann Whitney U = 1887.5, p = 0.003).

4.1.6. Information provision

There were 98 females between 14 and 54 years old who were potentially child-bearing; others had had a hysterectomy, or been sterilised. Approximately one third of these had received any information pertaining to contraception or childbearing. It was noticeable that, with few exceptions, no advice was given to those of childbearing age with learning disabilities. This is illustrated in table 4.

Table 4 Chiltern audit: documented information provision to women with epilepsy

	All women	Those without learning disability	Those with learning disability
Women between 14 and 45 years			
Advice on contraception	35/98	32/85	3/13
Preconceptual advice	28/98	28/85	0/13
Pregnancy advice	27/98	26/85	1/13
Women between 16 and 20 years			
Advice on contraception	0/8	0/6	0/2
Preconceptual advice	0/8	0/6	0/2
Pregnancy advice	1/8	0/6	1/2
Women between 21 and 30 years			
Advice on contraception	12/30	12/25	0/5
Preconceptual advice	13/30	13/25	0/5
Pregnancy advice	11/30	11/25	0/5
Women between 31 and 40 years			
Advice on contraception	14/32	12/28	2/4
Preconceptual advice	10/32	11/28	0/4
Pregnancy advice	10/32	10/28	0/4

Information about driving had been documented in only 243 of 547 (44%) patients aged 16 years and over (47% in those without learning disability and 15% in those with learning disability).

Twenty six percent of patients had received lifestyle advice, and seven percent had been told about receiving free prescriptions, (93% of these were in the practice with an epilepsy specialist nurse attached).

4.1.7. Summary

- Almost half (46%) of patients had had no epilepsy review in the 15 months prior to the audit
    - Those not reviewed took fewer AEDs and were likely to have fewer seizures, where recorded
- Seizure frequency and description were available in around half of records
- Documented information provision was available in a minority of records

4.2. THE PRIMARY CARE SECTION OF THE NATIONAL SENTINEL CLINICAL AUDIT OF EPILEPSY-RELATED DEATH

In the UK during the study period 2412 deaths were recorded in which epilepsy appeared on the certificate. Of these, 298 deaths were audited in the primary care section of the National Sentinel Clinical Audit; 48 of these people do not appear ever to have been referred to specialist care.

4.2.1. Demographic details

4.2.1.1 Those not referred to specialist care

The notes of 48 patients (27 [56%] male) were audited. The mean age at death was 55 years (median 55 years), range 23 to 89 years. Seventeen (35%) had documented problems with alcohol. Six patients (13%) had documented learning disability.

4.2.1.2. Those referred to specialist care

The notes of 250 patients (155 [62%] male) were audited. The mean age at death was 40 years (median 40 years), range two to 86 years. Forty seven (19%) had documented problems with alcohol. Sixty patients (24%) had documented learning disability.

Those dying without being referred were significantly older than those referred (Mann Whitney $U = 2874.5$, $p < 0.0001$).

4.2.2. Access to care

4.2.2.1. People not referred to specialist care

In those whose first seizure was within five years of death, the audit nurses were asked to record any reason why the patient was not referred to a specialist. Of the 14 patients in this category (age range 23-89 years, mean 56 years), in six (43%) no reason was given; four of these were known to have problems with alcohol. Two patients (14%) died immediately after the first seizure, two were in care homes and one was already under the care of psychiatrists. One had multiple other health problems, and the other two never consulted the GP, but attended A&E only.

The audit did not request information on the reason for the lack of referral in those diagnosed over five years before death (N = 34). In many cases, searching the audit record revealed no obvious reason why specialist care was not involved.

Eleven (32%) such patients were under 50 years old at the time of death. Four (36%) of these had learning disability; none had a clear seizure frequency documented. Five (45%) had documented problems with alcohol – two of these (40%) had seizures at least weekly. Of the other two, one was seizure-free.

Nine (26%) such patients were between 50 and 59 years old at death. Two had documented problems with alcohol, but no documented seizure frequency. The other seven had each had epilepsy for at least 19 years; the four with documented seizure frequency all had rare seizures.

Of eight (24%) such patients aged between 60 and 69 years, none had seizure frequency documented clearly. Four (50%) had documented problems with alcohol, one of whom had problems with adherence with medication which had been discussed. In the other four, all with duration of epilepsy of at least seven years, there was no obvious reason for the lack of referral.

Six (18%) such patients were over 70 years old at death. None had documented problems with alcohol or learning disability. Only one, with epilepsy duration in excess of 30 years, had seizure frequency documented (less than yearly). The others had a minimum duration of 30 years, apart from one who also had dementia.

4.2.2.2. Review in all people audited

In the whole primary care section of the Sentinel Audit, the last review was carried out by a specialist in 139 people (47%), by the GP in 95 (32%), and by a specialist nurse in two; in 59 (20%) people no review was recorded. In three audit records the information was not available.

- Last review by specialist: the median time to last review was 24 weeks (mean 64 weeks), and it was carried out within 15 months in 110 (79%)
- Last reviewed by the GP: the median time to last review was 21 weeks (mean 65 weeks) and it was carried out within 15 months in 71 (75%)
- Last review by the epilepsy specialist nurse: last review was six days and eight weeks before death.

Altogether, review was last undertaken more than 15 months before death (by any relevant professional) in 53 (18%) and in under 15 months in 183 (62%).

Of those whose epilepsy had never been reviewed (59 people) 17 (29%) had seen the GP within 28 days of death for another reason. Five of these consultations may have been epilepsy-related. Of those last reviewed more than 15 months before death, (53 people), ten (19%) had seen the GP within 28 days of death, with two being apparently epilepsy-related.

4.2.2.2.1. Use of AEDs according to time of last review

This is shown in table 5.

Table 5 Sentinel Audit (primary care): number of AEDs taken by patients according to time of last review

(AED information missing in 3 patients, review information missing in 3 patients)

	N	No AEDs		Monotherapy		Polytherapy		Mean	Range
		N	%	N	%	N	%		
No review	57	22	39	27	47	8	14	0.8	0-3
Review more than 15 months	53	6	11	35	66	12	23	1.2	0-3
Review 15 months or less	182	5	3	93	51	84	46	1.6	0-5
Total	292	33		155		104			

The number of AEDs taken in the three groups was significantly different (Kruskal Wallis Chi square = 47.9, $p < 0.0001$). Those with no review took significantly fewer AEDs than those reviewed more than 15 months previously (Mann-Whitney U = 1074.5, $p = 0.004$), who in turn took significantly fewer AEDs than those seen within 15 months of death (Mann-Whitney U = 3396.5, $p< 0.0001$).

4.2.2.2.2. Time of last review and duration of epilepsy

Comparing those with review within 15 months of death and those without review in that time, there was little difference in the duration of epilepsy (in those with no review within 15 months of death mean duration was 19.1 years, median 14.3 years and in those with review within 15 months of death, mean duration of epilepsy was 20.4 years, median 19.2 years [Mann Whitney U = 8342, $p = 0.30$]).

4.2.2.2.3. Time of last review and age at death

The age at death was significantly different between the two groups (those with no review within 15 months mean age was 49.1 years, median 47 years, and those with review within 15 months death mean age was 39.4 years, median 39 years (Mann Whitney U = 6823.5, $p< 0.0001$).

4.2.2.2.4. Time of last review and learning disability

Those with documented learning disability were more likely to have been reviewed within 15 months of death (50/66, 76% reviewed) than those without documented learning disability (133/229, 58% reviewed; difference 18% [95% CI 6 to 30%], $p = 0.009$).

4.2.2.2.5. Time of last review and alcohol problems

Those with documented problems with alcohol were significantly less likely to have been reviewed (26/64, 41% reviewed) than those without such problems documented (157/231, 68% reviewed; difference 27% [95% CI 14 to 41%], $p = 0.0001$).

4.2.3. Documented history of seizures available

4.2.3.1. Seizure frequency documented

Seizure frequency was documented in 16 (33%) of people not referred to specialist care. One had a single seizure, one was seizure-free, three had seizures less than yearly, four had seizures between weekly and yearly, two had seizures more frequently than once per week, and in five the seizure frequency was unclear. Seizure frequency was not audited in people referred to specialist care

4.2.3.2. Seizure description documented

This was only audited in people whose first seizure was less than five years before death. In people not referred to specialist care, there was a seizure description in 7/14 (50%). The descriptions were usually vague (such as 'thrashing about in bed' or 'was rigid').

In people referred to specialist care, a seizure description was available in 25 of 40 (63%). In 15 (60%) the seizure was described fairly clearly, in eight (32%) it was stated in terms such as 'fit', 'myoclonic jerk', 'grand mal epilepsy', 'tonic clonic seizures', and in two the description was vague.

4.2.3.3. Cause of epilepsy documented

In people not referred to specialist care there was a presumed cause of epilepsy documented in the notes of ten (21%) people. In six epilepsy was probably due to alcohol in excess or withdrawal, two patients had dementia, in one the cause was a cerebrovascular accident and in one followed a serious head injury. This was not audited in people referred to specialist care

4.2.4. Management plan in the records

This was only audited in those not referred to specialist care. There was a GP management plan in the notes of five (10%).

4.2.5. AED treatment

4.2.5.1 Number of AEDs taken at the time of death

4.2.5.1.1. People not referred to specialist care

Fifteen patients were apparently taking no AEDs. One may have been on valproate and one may have been seizure-free for many years. One visited A&E frequently, but did not apparently see the GP. One elderly patient had multiple other health problems. Seven had problems related to alcohol. Three died within a few days of the first seizure. There was no further information on the other.

Of the 33 patients taking AEDs at the time of death, 28 (85%) were on monotherapy and five (15%) on two AEDs. In 11 patients the GP had checked AED levels in the five years prior to death. In five patients, this was to check phenytoin levels and in three other cases, the levels of different AEDs were checked to monitor adherence to the regimen. In the final three cases, it is not clear why levels were estimated.

4.2.5.1.2. People referred to specialist care

This is shown in table 6. AED information was not available in three people.

Table 6 Sentinel Audit (primary care) AEDs in people referred to specialist care

No of AEDs	No of patients (%)	
0	20	8
1	128	52
2	66	27
3	28	11
4	3	1
5	2	1
Total	247	

4.2.5.2. Use of particular AEDs (in all people taking AEDs)

4.2.5.2.1. Phenobarbital or primidone

Of the 260 people in the Sentinel Audit who were taking AEDs, 20 were taking phenobarbital and four primidone; no-one was taking both, thus 24 (9%) were taking either. Five of 64 (8%) with learning disability were taking barbiturates compared with 19 of 196 (10%) without learning disability (difference = 2%, 95% CI –6 to 10%, p = 0.65). Only one with documented problems with alcohol was taking phenobarbital.

Twelve of 24 (50%) taking barbiturates had been reviewed in the 15 months before death, compared with 165 of 235 (70%) not taking them (difference 20% [95% CI –1 to 41%], p = 0.04). The last epilepsy review had been with a specialist in ten of the 24 on barbiturates (42%), and the GP in six (25%); in eight (33%) no review had been recorded.

Those taking barbiturates were older (mean 50 years, median 49.5 years) than those not on these AEDs (mean and median 41 years; Mann Whitney U = 1890, p = 0.008).

4.2.5.2.2. Phenytoin

Eighty two (32%) were taking phenytoin. Sixteen (25%) of those with learning disability were using phenytoin, compared with 66 (34%) of those without learning disability (difference = 9% [95% CI –4 to 21%], p = 0.19). One third of those with documented alcohol problems were taking phenytoin compared with 31% of those without such problems (difference = 2% [95% CI –13 to 17%], p = 0.77).

Those taking phenytoin were less likely to have been reviewed in the 15 months before death, but the difference is not significant (those taking phenytoin 51 of 81, 63%, reviewed compared with 126 of 178, 71%, not taking phenytoin; difference 8%, 95% CI –5 to 20%, p = 0.21). The last epilepsy review in those taking phenytoin had been by a specialist in almost one half and with the GP in one third; in almost one fifth no review had been recorded.

Those taking phenytoin were significantly older (mean 50 years, median 52 years) than those not taking it (mean 38 years, median 37 years; Mann-Whitney U = 4249, $p < 0.0001$). Those taking phenytoin had a slightly longer duration of epilepsy than those not (mean 24 years, median 22 years, compared with mean 19 years, median 18 years) but the difference is not significant (Mann Whitney U = 5345, $p = 0.07$).

4.2.5.2.3. Sodium valproate

Over 40% of patients (107) took sodium valproate. Males and females were equally likely to be taking valproate (each 41%). Thirty two (30%) were females between 14 and 54 years; in none of these was any provision of information on issues pertaining to contraception or child-bearing documented. Half of all people with learning disability on AEDs were taking valproate, compared with 38% of those without learning disability, but the difference (12% [95% CI –2 to 26%]) is not significant.

In those on valproate, over half last had an epilepsy review with a specialist, 38% with the GP, two with the specialist nurse, and in nine no review was recorded.

4.2.5.2.4. Topiramate

Only eleven (4%) of patients took topiramate, including five (8%) of those with learning disability. Those taking topiramate were significantly younger (mean age 22 years, median 26 years) than the others (mean age 43 years, median 42 years; Mann Whitney U = 486, $p < 0.0001$).

4.2.6. Information provision

4.2.6.1. People not referred to specialist care

Only two people were documented to have received information about epilepsy, one of which was in relation to alcohol withdrawal and the other related to AED use. One was alerted to the hazards of seizures, but in no case was the risk of epilepsy causing death apparently discussed.

4.2.6.2. People referred to specialist care

Ninety-two patients (37%) had any information provision documented. Ten percent had been given information on lifestyle issues, 13% on issues pertaining to AED treatment, 7% about epilepsy itself and 7% of those aged 16 and over on driving. There were 71 women between 14 and 54 years old, of whom only two (3%), aged 26 and 36 years, had received any information pertaining to contraception or childbearing.

4.2.7. Summary

- Epilepsy review occurred within 15 months of the audit in 62%
    - Those with no review within 15 months of the audit took fewer AEDs than those reviewed within 15 months
    - Those with no review within 15 months were older than those reviewed within 15 months
- Documented information provision was available in a minority of records

4.3. THE SPECIALIST CARE SECTION OF THE NATIONAL SENTINEL CLINICAL AUDIT OF EPILEPSY-RELATED DEATH

Extra tables in appendix 3 give further details of results in this section.

4.3.1. Demographic details and classification of death

One hundred and ninety nine cases were assessed initially. Of those, nineteen cases were excluded as having non-epilepsy related deaths. Four had acute symptomatic seizures, four had probable cardiac deaths, in two there was no evidence of epilepsy, one died of the disease causing epilepsy, eight died of unrelated causes.

The remaining 180 cases were included in the analysis (111 [62%] male). Age at death was between two and 82 years (mean 36.7 years, median 36 years). The specialist care section considered both adults and children and people with and without learning disability (see tables 7 and 8).

Table 7 · Sentinel Audit (specialist care): characteristics

	N	%
Adults no learning difficulties	108	60
Adults with learning difficulties	50	28
Children no learning difficulties	7	4
Children with learning difficulties	15	8

Table 8 Sentinel Audit (specialist care): demographics

	Learning disability	No learning disability	
N	65	115	
Male	37 (57%)	74 (64%)	Difference 7% (95% CI −7 to 22%) p = 0.33
Mean (SD) age at death (years)	31.6 (16)	40.5 (16)	t =3.6, p < 0.0001
Mean (SD) age at 1st seizure (years)	9.6 (11)	23.0 (18)	Mann Whitney U = 1586, p < 0.0001

Of 180 cases, 66 (37%) were classified as having adequate care, 98 (54%) as having received care which failed to meet guidelines, four (2%) cases had had one or more large error in their care, and in 12 (7%) the care was unclear. In 66 (37%) cases the death was classified as unavoidable, 59 (33%) as potentially avoidable, 16 (9%) as probably avoidable and 39 (22%) as unclear.

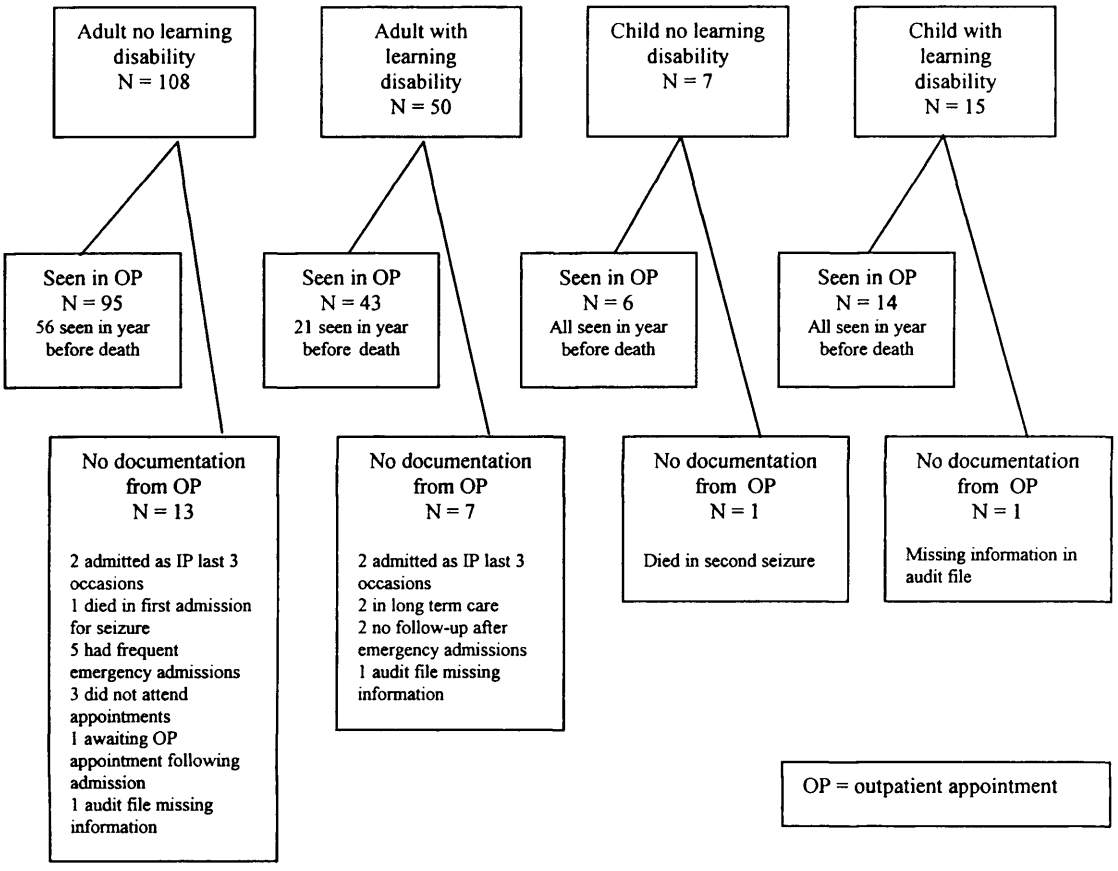
For those with learning disability, the suitability of specialist seen was categorised as:

Good	10 (15%)
Satisfactory	38 (58%)
Not satisfactory	10 (15%)
Unclear	7 (11%).

4.3.2. Access to care

This is illustrated in figure 4, and detailed below.

Figure 4 Sentinel Audit (specialist care); access to specialist care



4.3.2.1. Access to care (those with no learning disability)

Of the 115 people with no learning disability 101 (88%) had documented epilepsy review in outpatients. In fourteen cases it was not possible to calculate the time from the last outpatient visit to death. (In two cases, the last three secondary care episodes were all for inpatient admissions, within six months of death, so the date of the last outpatient appointment is not known. A child died in the second seizure, weeks after the first seizure. One patient was admitted to hospital at the time of the first seizure and died there six months later. Four had had frequent emergency admissions for seizures, three of whom had absconded. A further one who had been seen by neurologists in the past had had two emergency admissions one year and four years before death, with no further outpatient follow-up. Three had failed to attend outpatients on at least two

occasions. One was discharged after a first seizure with a request to be seen by a neurologist; this appointment had not been made several months later. One audit record lacked information.)

Of the 95 adults in whom we were able to calculate the time period from the last appointment until death, 56 had been seen in under a year, including 39 in under six months. Of the 39 who were last seen more than a year before death, in the majority (22) we were unable to account for the loss to follow-up – they appeared to have become 'lost'. Of the other 17, five had failed to attend one or more appointment, and four had been discharged. In one case the consultant had tried assiduously to follow-up the patient, even suggesting domiciliary visits. In one case, only one outpatient appointment was made, and in five cases it is unclear whether the patient may in fact have been seen at another hospital in which the notes were not audited. In one case, a Specialist Registrar had questioned the diagnosis of epilepsy and discharged the patient with advice to stop AEDs.

The six children with outpatient appointments had all been seen within seven months of death.

4.3.2.2. Access to care (those with learning disability)

Of the 65 people with learning disability, 57 had documented outpatient appointments. Those who did not are as follows: one young child, with long-standing epilepsy, died following an admission for status epilepticus, but the audit tool is incomplete regarding outpatient appointments. Two of the seven adults with no outpatient appointments were long-term inpatients, and two had had three inpatient appointments within the nine months before death, so we were unable to ascertain whether they had had outpatient appointments. Two had had at least one admission for seizures with no follow-up arrangements, although one of these may have been seen at another hospital, and the last had significant missing information in the audit tool.

The 14 children with learning disability with documented outpatient appointments had all been seen in the year before death, 13 of these within 6 months of death. Twenty one

(49%) of the 43 adults with documented outpatient appointments had been seen in the year before death. The other 22 had been seen between one and 15 years before death (median 4 years). Of these, in nine cases we were unable to account for the lack of follow-up; they appear to have become 'lost' despite at least four having ongoing seizures when last seen. Three cases appear to have been discharged (one with infrequent seizures, another had no seizure frequency documented when discharged and the other with two to three seizures in the previous six weeks). Two had failed to attend appointments, one with a single seizure had only one appointment, and four cases may have been seen at other hospitals. In three cases it seems probable that the patients may have become 'lost' in the handover from paediatric to adult care.

4.3.2.3. Access to care (those failing to attend appointments)

Of 24 patients (23 adults) in whom there is evidence of having failed to attend outpatient appointments, five appeared to have problems with alcohol. Of the 24, 18 missed one of their last three appointments, five missed two appointments, and one missed all three. In 15 cases (ten of those missing one appointment, four of those missing two, and the one who missed all three) there is evidence that a further appointment was sent. Only four of the non-attending adults and one child had learning disability, but only one adult and the child were sent further appointments.

4.3.3. Surgery

Twenty seven adults (ten with learning disability) and seven children (six with learning disability) were documented to be experiencing at least two seizures per month when last reviewed. Of these, eight adults (two with learning disability) and no children were considered for epilepsy surgery. (In four adults [two with learning disability and two without] specialist opinion was that surgery was not suitable. One declined surgery, one was waiting for referral, one died in the post-operative period and in one no information is available.) In the 19 adults and seven children not considered for surgery, seven adults and three children had probably general onset of seizures and so would probably not be suitable for surgery. Eight adults and two children probably had epilepsy of focal onset which might have benefited from surgery.

4.3.4. Comparing care provided to those with learning disability and those without

4.3.4.1. Overall standard of care

In those with no learning disability care was adequate in 48 of the 110 (44%) in whom this was assessable (ignoring those whose care was classified as unclear). Care was adequate in 18 of 58 (31%) with learning disability (difference 13% [95% CI –3 to 28%], p = 0.11).

4.3.4.2. Death avoidable or not

In those with no learning disability death was unavoidable in 42 of 89 (47%) in those in whom it was assessable, whilst in those with learning disability, death was unavoidable in 24 of 52 (46%) assessable cases (difference 1% [95% CI –16 to 18%], p = 0.91).

4.3.4.3. Documented evidence of having seen a consultant

Of 115 people without learning disability, 81 (70%) had seen a consultant in at least one of the last three outpatient appointments. A further 14 had documented evidence of having seen a consultant at some other time, so 95 (83%) had seen a consultant at some time. Of the 20 who had no documented evidence of having seen a consultant, five were frequent attendees at the A&E department, and three died after one or two seizures.

Of those with learning disability, 40 (62%) saw a consultant in the last three outpatient appointments, and a further eleven saw a consultant at some other time. Thus 78% had seen a consultant at some time. There is no significant difference in the numbers known to have seen a consultant (difference 4% [95% CI –8 to 16%], p = 0.49).

4.3.4.4. Documented history of seizures available

The audit files on one person with learning disability lacked significant amounts of information, and so were excluded from this analysis.

4.3.4.4.1. Seizure frequency noted at last consultation

This was present in the clinical notes of 75% people with no learning disability and 77% people with learning disability (difference 2% [95% CI –11 to 15%], p = 0.79).

4.3.4.4.2. Clear description of seizures recorded

This was present in the clinical records of 86% people without learning disability and in 81% of those with learning disability (difference 6% [95% CI –7 to 16%], p = 0.39).

4.3.4.5. Investigations of epilepsy

4.3.4.5.1. EEG

Two cases with learning disability were excluded from this analysis due to inadequate information in the audit file.

Overall, the proportion of those whose EEG status was satisfactory (those with EEG and those who needed no EEG) was 93/106 (88%) in those without learning disability and 49/62 (79%) in those with learning disability (difference 9% [95% CI –3 to 21%], p = 0.13). Of the 13 people with learning disability who had no EEG but, according to SIGN guidelines should have done, eight had severe learning disability, two sets of audit files were missing information, and the other three people had no obvious reason for the lack of EEG.

4.3.4.5.2. Neuroimaging

Ignoring those in which the need was unclear for reasons other than lack of seizure description, neuroimaging status was satisfactory in 97 of 115 (84%) of those with no learning disability and 39 of 58 (67%) of those with learning disability (difference 7% [95% CI 3 to 31%], p = 0.01).

4.3.4.6. Use of AEDs

In two cases it was not possible to calculate the number or type of AEDs taken; one set of audit files was missing significant amounts of information, and the other patient appears to have been lost to follow-up.

4.3.4.6.1. Number of AEDs taken at the time of death

This is shown in table 9.

Table 9 Sentinel Audit (specialist care): number of AEDs taken by those with and without learning disability

	No learning disability		Learning disability		Total	
	N	%	N	%	N	%
No AEDs	10	9	5	8	15	8
Monotherapy	56	49	19	30	75	42
Polytherapy	49	43	39	62	88	49
Total	115		63		178	

There is a difference between the two groups in the use of no AEDs, monotherapy or polytherapy (Chi squared = 6.41, df = 2, p = 0.04). Further analysis shows that there was no significant difference in the number taking no AEDs (difference 1% [95% CI –8 to 9%], p = 0.86), but that significantly more people with learning disability were on polytherapy (difference in those taking AEDs 21% [95% CI 5 to 36%], p = 0.01).

4.3.4.6.2. New AEDs taken (those taking AEDs)

There was no difference in the proportions of patients taking new AEDs in those without learning disability (37 of 105, 35%) and those with learning disability (27 of 58, 47%; difference 11% [95% CI –4 to 27%], p = 0.16).

4.3.4.6.3. Use of AEDs thought to affect cognition

Five (5%) patients without learning disability took phenobarbital or primidone compared with four (7%) with learning disability, (difference 2% [95% CI –6 to 10%], p = 0.57). Thirty (29%) of those without learning disability took phenytoin compared with 15 (26%) of those with learning disability (difference 3% [95% CI –11 to 17%], p = 0.71). Five (5%) of those without learning disability took topiramate compared with 6 (10%) of those with learning disability (Fisher's exact test, p = 0.30). However, more

with learning disability (31, 53%) took sodium valproate than those without learning disability (36, 34%; difference 20% [95% CI 3 to 35%], p = 0.02).

4.3.4.7. Information provision

This is shown in table 10.

Table 10 Sentinel Audit (specialist care): information provision in those with and without learning disability

Type of information	No learning disability (N=115)		Learning disability (N=65)		Fisher's exact test, p
	N	%	N	%	
Type of epilepsy or syndrome	30	26	17	26	1
Hazards of seizures	10	9	1	2	0.09
Leisure factors	19	17	12	18	0.89
Social factors	28	24	20	31	0.45
Possibility of fatal seizures	3	3	0	0	0.52
Patient support group information	8	7	6	9	0.78
AED information	N=105		N=58		
Importance of AEDs	17	16	3	5	0.06
Side-effects of AEDs	36	34	17	29	0.93

4.3.5. Comparing care provided in those with learning disability according to the suitability of specialist seen

4.3.5.1. Overall standard of care

The standard of care was, to some extent, dependent on the suitability of specialist seen. This analysis was, therefore, not performed.

4.3.5.2. Death avoidable or not

There is no difference in the number of unavoidable deaths between those seen in a satisfactory or good specialty (21 of 40, 53%) and those seen in a specialty classified as not satisfactory (two of nine, 22%; Fisher's exact test, p = 0.20).

4.3.5.3. Documented evidence of having seen a consultant

There is no significant difference between the proportions known to have seen a consultant between those whose specialty was satisfactory or good, (39 of 48, 81% saw a consultant at some time) and in those in whom the specialty was not satisfactory (ten of ten saw a consultant; Fisher's exact test, p = 0.32).

4.3.5.4. Documented history of seizures available

4.3.5.4.1. Seizure frequency noted at last consultation.

(Information was missing in one audit record).

There is no difference in the proportion with seizure frequency noted at the last consultation between those seen in a specialty classified as satisfactory or good (39 of 48, 81%), and in those seen in a specialty classified as not satisfactory (6 of 10, 60%; Fisher's exact test, p = 0.29).

4.3.5.4.2. Clear description of seizures recorded.

(Information was missing in one audit record).

There is no difference in the proportion with a clear description of seizures recorded between those seen in a satisfactory or good specialty (41 of 48, 85%), and in those seen in a specialty which was not satisfactory (7 of 10, 70%; Fisher's exact test, p = 0.46).

4.3.5.5. Investigations of epilepsy

4.3.5.5.1. EEG

(Excluding those with inadequate information in the audit records and the one for whom need for EEG is unclear).

There is no difference in the proportion whose EEG status was satisfactory between those seen in a satisfactory or good specialty (39 of 47, 83%), and in those seen in a specialty which was not satisfactory (7 of 10, 70%; Fisher's exact test, p = 0.59).

4.3.5.5.2. Neuroimaging

There is no difference in the proportion whose neuroimaging status was satisfactory between those seen in a satisfactory or good specialty (30 of 43, 70%), and in those seen in a specialty which was not satisfactory (six of ten; Fisher's exact test, p = 0.81).

4.3.5.6. Use of AEDs

4.3.5.6.1. Number of AEDs taken at the time of death

There was no significant difference in whether or not polytherapy was used between those who received care from a specialty which was not satisfactory (5 of 10, 50%) compared with those who received care from a specialty which was satisfactory or good (31 of 47 on polytherapy, 66%; Fisher's exact test, p = 0.55).

4.3.5.6.2. New AEDs taken (those taking AEDs)

There is no significant difference in whether or not new AEDs were used between those who received care from a specialty which was not satisfactory (5 of 9, 56%) and those who received care from a specialty which was satisfactory or good (19 of 43, 44%; difference 11% [95% CI –24 to 47%], p = 0.53).

4.3.5.6.3. Use of AEDs thought to affect cognition

The analysis was not performed for barbiturates or topiramate due to the small numbers of people with learning disability taking them. Three of nine (33%) people seen in a specialty considered not satisfactory were taking phenytoin, compared with 12 of 43 (28%) seen in a specialty classified as satisfactory or good (difference 5% [95% CI –28 to 39%], p = 0.74). Three of nine seen in a specialty considered not satisfactory were taking sodium valproate compared with 26 of 43 (60%) seen in a specialty classified as satisfactory or good (difference 27%, 95% CI –7 to 61%, p = 0.14).

4.3.5.7. Information provision

This is shown in table 11.

Table 11 Sentinel Audit (specialist care): information provision in those with learning disability according to specialty seen

Type of information	Specialty not satisfactory (N=10)		Specialty satisfactory or good (N=48)		Fisher's exact test, p
	N	%	N	%	
Type of epilepsy or syndrome	2	20	15	31	0.77
Hazards of seizures	1	10	0	0	0.34
Leisure factors	2	20	10	21	1
Social factors	4	40	16	33	0.95
Possibility of fatal seizures	0		0		
Patient support group information	0	0	6	13	0.61
AED information	N=9		N=43		
Importance of AEDs	0	0	3	7	1
Side-effects of AEDs	3	33	14	33	1

4.3.6. Comparing care provided to those with learning disability according to whether or not a consultant was seen

In six audit files it was not possible to establish whether or not the patient had ever seen a consultant.

4.3.6.1. Overall standard of care

The standard of care was, to some extent, dependent on whether a consultant had been seen. This analysis was, therefore, not performed.

4.3.6.2. Death avoidable or not

There is no difference in the proportion with unavoidable death in those who did (19 of 43, 44%) or did not see a consultant (two of six; Fisher's exact p = 0.96)

4.3.6.3. Documented evidence of having seen a consultant

Not applicable

4.3.6.4. Documented history of seizures available

4.3.6.4.1. Seizure frequency noted at last consultation

There was no difference between those who had seen a consultant (38 of 51, 75%) and those who had never seen a consultant (7 of 8, 88%; Fisher's exact test, p = 0.77).

4.3.6.4.2. Clear description of seizures recorded

There was a witness account of the seizures in 45 of 51 (88%) case records of people seen by a consultant compared with three of eight (38%) not seen by a consultant (Fisher's exact test, p = 0.008).

4.3.6.5. Investigations of epilepsy

4.3.6.5.1. EEG

There was no difference between those who had seen a consultant (39/49, 80% with satisfactory status) and those who had never seen a consultant (all 7 had satisfactory EEG status; Fisher's exact test, p = 0.46).

4.3.6.5.2. Neuroimaging

There was no difference between those who had seen a consultant (32 of 46, 70%) and those who had never seen a consultant (satisfactory in four of seven (57%) eligible for analysis; Fisher's exact test, p = 0.80).

4.3.6.6. Use of AEDs

4.3.6.6.1. Number of AEDs taken at the time of death

There was no significant difference in whether or not polytherapy was used between those who had never seen a consultant (six of eight on polytherapy, 75%), and those who had seen a consultant (31 of 50 on polytherapy, 62%; Fisher's exact test, $p = 0.78$).

4.3.6.6.2. New AEDs taken (those taking AEDs)

Five of eight (63%) who had never seen a consultant had used new AEDs, compared with 20 of 46 (43%) who had seen a consultant (Fisher's exact test, $p = 0.54$).

4.3.6.6.3. Use of AEDs thought to affect cognition

This analysis was not performed for barbiturates or topiramate due to the small numbers of people with learning disability taking them. Three of eight (38%) of those who never saw a consultant were taking phenytoin compared with 12 of 46 (26%) who saw a consultant (Fisher's exact test, $p = 0.78$). Five of eight (63%) of those who never saw a consultant were taking sodium valproate compared with 24 of 46 (52%) who never saw a consultant (Fisher's exact test, $p = 0.88$).

4.3.6.7. Information provision

This is shown in table 12.

Table 12 Sentinel Audit (specialist care): information provision in those with learning disability according to whether or not a consultant was seen

Type of information	Consultant never seen (N=8)		Consultant seen (N=51)		Fisher's exact test, p
	N	%	N	%	
Type of epilepsy or syndrome	0	0	17	33	0.11
Hazards of seizures	0	0	1	2	1
Leisure factors	1	13	11	22	0.96
Social factors	2	25	17	33	0.98
Possibility of fatal seizures	0		0		
Patient support group information	0	0	6	12	0.80
AED information	N=8		N=46		
Importance of AEDs	1	13	2	4	0.78
Side-effects of AEDs	0	0	17	37	0.07

4.3.7. Summary

- Care was considered adequate in 44% of those without learning disability and 31% of those with learning disability
- Death was unavoidable in just under half of assessable cases both with and without learning disability
- Seizure frequency and description were available in over three quarters of people both with and without learning disability
- Information provision was documented in a minority of case records

4.4. INVESTIGATION INTO THE USE OF DEATH CERTIFICATES AS CASE ASCERTAINMENT FOR EPILEPSY

There were 246 deaths during the follow-up period. After excluding three because of incomplete information, 181 (74%) deaths occurred in those with definite epilepsy and 62 (26%) in those with possible epilepsy. Epilepsy was mentioned on the death certificates of 16 (7%) altogether; ten (6%) with definite epilepsy and six (10%) with possible epilepsy. Causes of death could be grouped into vascular disease (mostly cerebrovascular disease and ischaemic heart disease) (44%), CNS malignancy (9%), other malignancy (21%), dementia and old age (6%), respiratory disease (5%), congenital disease (3%) and others (including alcohol related, accidents and injuries, other CNS disease, infections) (12%).

In 211 people it was possible to compute the average number of seizures per year either in the five years prior to death or during lifetime prior to death where that was less than five years. Most patients (106, 50%) had no seizures and the mean number of seizures/year was 15 (where seizures occurring more frequently than daily were counted as 365 seizures/year).

Mean age at death was 70 years and median 75 years (range 3 to 98 years).

Factors that appeared to influence mention of epilepsy on the death certificate were seizure frequency, AED treatment, cause of death, and certifying physician (see table 13). Epilepsy was on the death certificate of 23% (3/13) of those on AEDs for ongoing seizures and was on the certificate of 21% (4/19) of those on AEDs who were certified by a coroner.

Subjects with death certificates, those with epilepsy on the death certificates and the results of exploratory logistic regression analysis are shown in Table 13.

Review of clinical and death certificate information suggested that epilepsy should have been on the certificates of 105 (43%) subjects.

Table 13 Exploratory logistic regression of mention of Epilepsy on Death Certificate

	Number with death certificates	Number with epilepsy on death certificate (%)	Odds Ratio (95% CI)
Classification			
Possible epilepsy	62	6 (10)	1
Definite epilepsy	181	10 (6)	0.5 (0.2 to 1.6)
Convulsive seizures			
Yes	175	14 (8)	1
No	59	2 (3)	0.4 (0.1 to 1.8)
Not known	9		
Age at death (years)			
< 65	71	6 (8)	1
65 - 74	48	1 (2)	0.2 (0.0 to 2.0)
75 - 84	76	4 (5)	0.6 (0.2 to 2.2)
85+	48	5 (10)	1.3 (0.4 to 4.4)
Seizures during follow-up			
Yes	129	12 (9)	1
No	82	2 (2)	0.2 (0.1 to 1.1)
Not known	32		
Certifying physician			
Other physician	144	6 (4)	1
Current physician	18	1 (6)	1.4 (0.2 to 12)
Referring physician	47	4 (9)	2.1 (0.6 to 7.9)
Coroner	34	5 (15)	4.0 (1.1 to 14)
Average seizures/year			
None	106	4 (4)	1
1 - 12	87	7 (8)	2.2 (0.6 to 7.9)
More than 12	18	3 (17)	5.1 (1.04 to 25)
Not known	32		
Cause of death			
Malignancy	73	1 (1)	1
Vascular	106	7 (7)	5.1 (0.6 to 42)
Other	64	8 (13)	10.3 (1.3 to 85)
AEDs at last follow-up			
None	97	1 (1)	1
Monotherapy	122	13 (11)	11.4 (1.5 to 89)
Polytherapy	17	2 (12)	12.8 (1.1 to 150)
Not known	7		

4.5. SUICIDE IN PEOPLE WITH EPILEPSY IN ENGLAND AND WALES

Eleven people with epilepsy were identified (age range 28-62 years, mean 40 years) who died probably as a result of suicide. Six deaths were attributed directly to drug overdose and in another five deaths drug poisoning was a contributory factor. Three of the deaths were due to overdose with AEDs, but the verdict was given as suicide in two cases and misadventure in the third. No deaths were recorded in people with epilepsy from hanging. All deaths were investigated and certified by a Coroner, but in only the two cases previously mentioned was the verdict given as suicide. The overall SMR for suicide was significantly reduced at 0.36 (95% CI 0.18 to 0.65), and the SMR was lower in males, despite the fact that more deaths from probable suicide occurred in males (see table). The age at death was similar in males (mean 42 years) and females (mean 37 years) (Mann Whitney U = 9000, p = 0.412).

Table 14 Deaths from suicide with Standardized Mortality Ratios (SMRs)

	Observed number				Expected	SMR (95% CI)
	Sep – Dec 1999	Jan – Apr 2000	May – Aug 2000	Total		
Males	3	1	3	7	23.39	0.30 (0.12 to 0.62)
Females	3	1	0	4	6.98	0.57 (0.16 to 1.47)
Total	6	2	3	11	30.37	0.36 (0.18 to 0.65)

4.6. A META-ANALYSIS OF SUICIDE IN PEOPLE WITH EPILEPSY

4.6.1. Unweighted SMR

The results of the unweighted analysis of SMR are shown in table 15 and illustrated in figure 5. There were 133 suicides reported in the 22 articles, compared with 29.8 expected from national figures, providing an SMR of 4.5 (95% CI 3.7 to 5.3).

4.6.2. Weighted SMR

Further analysis, using national data available for all studies (including Rafnsson and Nilsson) gives an SMR of 5.3 (95% CI 4.5 to 6.3). Using the national data in RevMan software (after rounding the population data) gives an SMR of 5.5 (95% CI 3.8 to 8.0), suggesting that, in this analysis, the weighting of studies according to size of sample does not seriously alter the outcome.

4.6.3. Unweighted SMR by year of publication

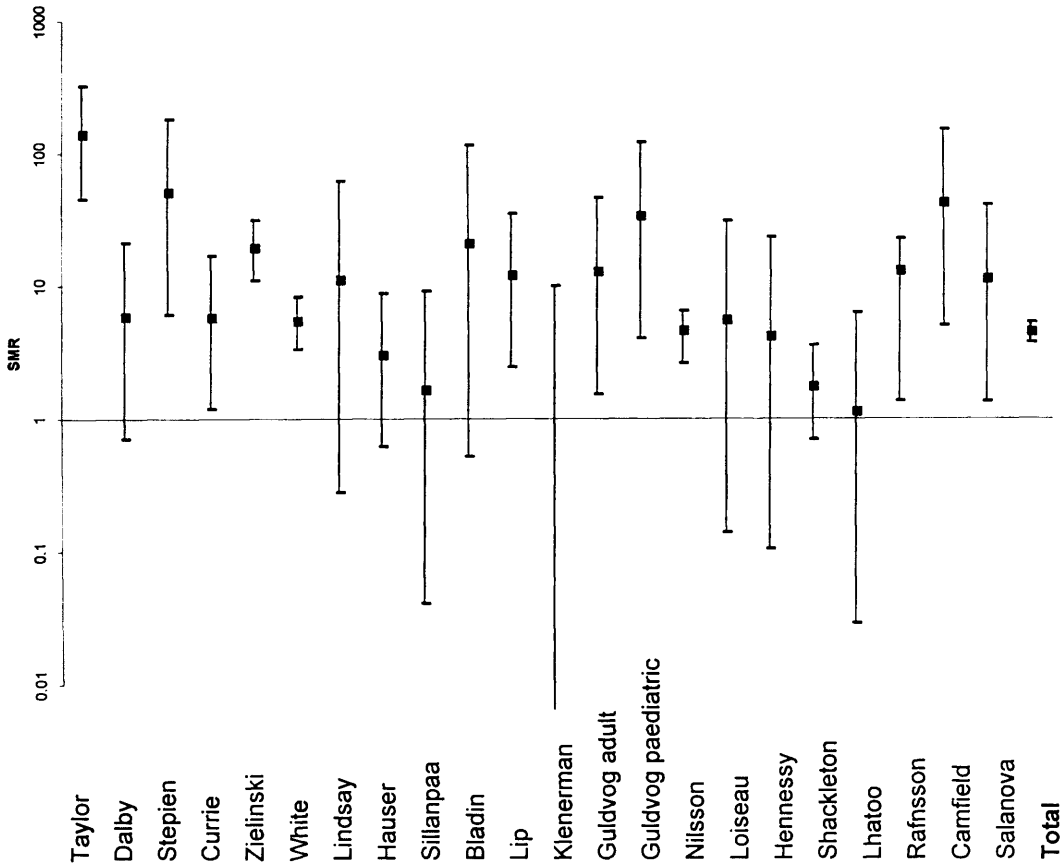
Analysis of the early studies, with 62 observed suicides and 8.22 expected provides an unweighted SMR of 7.5 (95% CI 5.8 to 9.7). Analysis of the more recently published studies with 71 observed suicides compared with 21.6 expected provides an unweighted SMR of 3.3 (95% CI 2.6 to 4.2). The ratio of the SMRs is 2.3 (95% CI 1.6 to 3.3).

Table 15 Meta-analysis: observed and expected suicides in 22 populations of people with epilepsy

(TLE = temporal lobe epilepsy)

Study	Country	Description	No of patients	Patient-years at risk	Deaths from suicide	Expected deaths	SMR	95% CI
Taylor	England	TLE surgery patients	100	566.7	5	0.0358	140	45.4 - 326
Dalby	Denmark	Absence epilepsy	346	3149	2	0.341	5.86	0.71 to 21.2
Stepien	Poland	TLE surgery patients	64	313.5	2	0.0389	51.4	6.11 to 182
Currie	England	TLE patients	666	4662	3	0.521	5.76	1.19 to 16.8
Zielinski	Poland	All people with epilepsy	6710	6710	16	0.832	19.2	11.0 to 31.2
White	England	Epilepsy institution	1980	32873	21	3.87	5.43	3.36 to 8.30
Lindsay	England	Children with TLE	100	1300	1	0.0908	11.0	0.275 to 61.4
Hauser	USA	All people with epilepsy	618	8233	3	0.997	3.01	0.620 to 8.79
Sillanpaa	Finland	Follow-up of children	233	4930	1	0.611	1.64	0.041 to 9.12
Bladin	Australia	TLE surgery patients	110	440	1	0.0486	20.6	0.515 to 115
Lip	Scotland	Clinic patients	1000	2462	3	0.252	11.9	2.46 to 34.8
Klenerman	England	Epilepsy institution		3392	0	0.371	0	0.0 to 9.96
Guldvog (adults)	Norway	Adults post surgery	124	868	2	0.158	12.6	1.53 to 45.6
Guldvog (children)	Norway	Children post surgery	64	1009	2	0.0602	33.2	4.02 to120.0
Nilsson	Sweden	Hospitalised	9061	53520	53	15.2	3.49	2.61 to 4.56
Loiseau	France	First seizure	804	804	1	0.182	5.49	0.137 to 30.6
Hennessy	England	TLE surgery	299	2729	1	0.242	4.14	0.105 to 23.1
Shackleton	Holland	Epilepsy institute	1355	38665	7	4.03	1.73	0.697 to 3.57
Lhatoo	UK	Population incidence	792	11400	1	0.888	1.13	0.029 to 6.28
Rafnsson	Iceland	Population incidence	224	6598	4	0.8	5	1.36 to 12.8
Camfield	Canada	Children new diagnosis	686	8918	2	0.048	41.5	5.02 to 150
Salanova	USA	TLE surgery	215	1514	2	0.180	11.1	1.34 to 40.1
Total					133	29.80	4.46	3.74 to 5.29

Figure 5 Unweighted SMRs for suicide in people with epilepsy



SECTION 5: DISCUSSION

5.1. THE AUDITS

5.1.1. Limitations of the audits

5.1.1.1. Chiltern audit

The Chiltern audit was conducted over a period of almost two years, and inevitably over that time-scale procedures and personnel within the practice change. Nonetheless, the audit provides some indication of the documented care for people with epilepsy in a localised area, and whether it met defined standards.

The area in which the audit took place was not chosen at random, and may not be representative of the care for people with epilepsy as a whole in the UK. The area is relatively affluent, and is close to London, with access to major hospitals.

Case ascertainment was largely through the use of AED prescriptions and should have missed people with epilepsy who were not taking AEDs. The records of some who had taken AEDs in the past were audited.

The audit records covered a large area of clinical activity, but did not involve detailed descriptions. Thus some finer points may have been missed.

5.1.1.2. Sentinel Audit

In the National Sentinel Clinical Audit, 812 of 2412 deaths identified by the use of 'epilepsy' on the death certificate during the study period were considered as probably due to epilepsy and therefore of primary interest to the audit. It was only possible, however, to audit the secondary care of 180, and the primary care of 298, of these. This was largely due to the methodology of the audit. As a result of conducting a Sentinel Audit and not a Confidential Inquiry, the study team was not empowered to require the release of medical records and so was dependent on the cooperation of clinicians. An unknown number of the over 600 deaths whose secondary care was not audited will not have received any secondary care; nevertheless, it is probable that we gained access to the clinical records of less than 50% of people who died an epilepsy-related death during the study period.

It is thus fair to question whether or not the results are valid, or suitable for extrapolation to the people who died an epilepsy-related death but whose clinical records have not been audited. The main criticism would be that the results are biased. This is a possibility, but it would seem intuitive that if any systematic bias occurred it would tend to exclude from the audit those whose care is deemed to be worse. This cannot, however, be assumed.

In the primary care section of the audit, in an attempt to reduce bias caused by using information from specialist care sources in the audit, the officers were instructed not to use any information from letters when gathering information (see section 3.2.4.). It is likely that this reduced the amount of information available to the audit, as information available otherwise is rarely duplicated in primary care records.

Some clinical information was not required in the primary care audit records, as it was felt that this information is more relevant to specialist care. Information regarding seizure frequency was only requested in those not referred to specialist care, and seizure descriptions were only audited in those with onset of seizures within five years of death. It would be relevant to know whether these details are available in all clinical records, whether written by the GP or the specialist, so that another professional unfamiliar with the patient would be able to provide adequate care.

In several cases in the specialist care section of the Sentinel Audit it was not possible to determine whether or not the patient had been seen in the outpatient department; this was in part due to a short-coming in the audit process which required the date of the last three specialist appointments. Four patients (two with learning disability) had had three inpatient episodes in the nine months prior to death and these were documented in the audit record. Three such admissions in a short space of time might lead one to question whether outpatient appointments should have been made in a shorter time-frame. There may be short-comings in follow-up from emergency admissions and A&E visits due to seizures, although those who abscond are difficult to review.

In an audit it is often not possible to determine whether care provided was appropriate or met standards, as many aspects of care for people with epilepsy are dependent on precise clinical details and the acumen and expertise of the clinician. It was not possible, for example, to establish the misdiagnosis rate in either primary or specialist care. Misdiagnosis has important consequences, caused by both the problems associated with a diagnosis of epilepsy and the prolonged use of AEDs, and by missing alternative diagnoses (Scheepers et al., 1998).

5.1.2. Strengths of the audits

5.1.2.1. Chiltern audit

The Chiltern audit was conducted by experienced epilepsy nurses, with good knowledge of the care for people with epilepsy. Only three nurses took part in the data gathering, limiting subjective differences in opinion.

Despite the use of AED prescriptions for case ascertainment in the Chiltern audit, the records of 85 people taking no AEDs were audited. Most people with active epilepsy take AEDs.

5.1.2.2. Sentinel Audit

The main strength of the Sentinel Audit is that it was conducted across all four countries of the United Kingdom and therefore covers a spread of providers of care for people with epilepsy. The audit was designed by a multi-disciplinary team and led by a patient group, thus causing the focus to be on issues relevant to people with epilepsy and their relatives.

5.1.3. Primary care audits

5.1.3.1. Age of sample

The mean age of patients in the Chiltern audit was 47 years, while in the Sentinel Audit the mean age of those not referred to specialist care was 55 years and of those referred to specialist care was 40 years. The difference in age between the two parts of the Sentinel Audit may be due to differences in referral pattern, with those who are older less likely to be referred. The fact that those dying having had specialist care

were younger than those still alive at audit might suggest premature death in those with an epilepsy-related death.

5.1.3.2. Referral of patients

In the Sentinel Audit, it is disquieting that 48 patients were never referred to specialist care for review of their seizures. In some cases the patient was severely ill, and the seizures may well have been the least of the problems experienced. In others, the patient does not appear to have presented to the GP, instead presenting one or more times at the A&E department; it is unknown whether such patients were advised to attend the GP, or whether further arrangements for follow-up were made by the hospital. Of the eleven people aged under 50 years and diagnosed more than five years before death, but without referral, nine had either documented learning disability or documented problems with alcohol; these diagnoses were much less frequently documented in those in the older age groups who were not referred, and the implication that either of these problems makes referral unnecessary is worrying. Overall, however, there was a slightly higher proportion of people with learning disability in the group that was referred than in the group which was not referred. It may be that the patients refused referral or did not attend, or were already under the care of specialist services (although this is unlikely, as they were not known to be receiving specialist care).

In the Chiltern audit twenty percent had apparently never consulted a specialist; almost one third of these were seizure-free, but in many there was no seizure frequency recorded. The figure is similar to that of 19% who had never consulted a specialist found in a questionnaire study to patients in General Practice eleven years ago (Hart and Shorvon, 1995). A recently reported study found that of 55 people with active epilepsy who had not previously been under hospital review, 31% achieved at least one year seizure freedom following consultation with a specialist (Leach et al., 2005). This suggests that all people with epilepsy should be reviewed by the GP to establish current seizure status. Those who are not seizure-free could profitably be offered review with a specialist.

5.1.3.3. Epilepsy review

The analysis of the time to last review was based on a 15 month review period, as this is the time period of interest in the new GP contract. This contract was not, however, in place at the time of either audit, so this may be seen as somewhat arbitrary. Nevertheless, prior to the new contract, many GPs suggested that optimal frequency of review for people with epilepsy would be more often than yearly (Ridsdale et al., 1996). The NICE guidelines, also published since the audits were conducted, recommend that both adults and children with epilepsy should have a regular structured review with a maximum interval between reviews of one year (NICE, 2004c). The Chiltern general practices are located close to specialist epilepsy services. Despite this, almost half had had epilepsy review by neither GP nor specialist within 15 months of the audit, including a substantial minority taking AED polytherapy. Of these, most had consulted a GP for another reason in the previous 15 months. In the Sentinel Audit, just under 40% had not had any epilepsy review in the 15 months before the audit; almost one quarter had consulted the GP for another reason within 28 days of death. This compares unfavourably with the questionnaire study of people with epilepsy in which only nine percent had had no epilepsy consultation in the previous year (Hart and Shorvon, 1995). Although all the patients in that study were taking AEDs for epilepsy, in the two audits reported here the majority of people were on AEDs and should have been reviewed. It seems that, in many cases, patients are not being given care that is relatively easily available; the proximity of the National Society for Epilepsy to the Chiltern practices does not appear to encourage referral, neither do GPs in either audit appear to make the most of opportunistic chances to review epilepsy or assess its impact on patients' lives. The former missed opportunity may be influenced by budgetary constraints, while the latter may have more to do with pressure of time.

Compared with those more recently reviewed, those not reviewed within 15 months in the Chiltern audit seem to have less severe epilepsy, as witnessed by the chances of being seizure-free and of taking fewer AEDs. Nonetheless some of those not reviewed were taking AED polytherapy, and a small number were experiencing seizures at least monthly. In the Sentinel Audit, those with no review within 15 months of death also took significantly fewer AEDs than those who had had epilepsy

review, but again a sizeable minority with either no review at all, or with no review within 15 months of death, were taking AED polytherapy.

5.1.3.4. Seizure information

The Sentinel Audit (those not referred) found seizure frequency had been documented in only one third, and a seizure description in 50% (of those recently diagnosed). The Sentinel Audit (those referred) did not investigate seizure frequency and only considered the seizure description in those recently diagnosed. The rate of over 60% compares favourably with that in the Chiltern audit (under half of those recently diagnosed). It is interesting that the notes appear more full in those for whom the GP does not accept the full responsibility, although the numbers are small, and in a substantial minority there is no description.

5.1.3.5. Use of AEDs

The two audits did not use the same protocol. Specifically, they are not a case-control study. However, some useful preliminary data can be obtained by comparing AEDs taken between the studies. The fact that the patients in the Sentinel Audit who were not referred took fewer AEDs than the others could be due to a variety of reasons, such as that they may have had less severe epilepsy, or that concurrent illnesses made them too ill for either referral or consideration of AEDs. The reasons for the slightly greater number of AEDs taken by those who died having been referred are open to speculation; no firm conclusions can be drawn. Possible reasons could be either that those who died had more severe epilepsy or, perhaps less likely, that the AEDs contributed to the death. This has been suggested for carbamazepine (Timmings, 1998), but not for other AEDs.

5.1.3.5.1. Specific AEDs

Barbiturates (phenobarbital and primidone)

Phenobarbital has been used for seizure control for many years, and is still considered an effective drug for partial onset and generalised tonic-clonic seizures. It is recommended by the WHO as a first line AED in developing countries, and was recently used to good effect in a community-based intervention trial in rural China (Wang et al., 2006). It is rarely used as such in developed countries, however, due to

its side-effects of sedation, other behavioural problems and effects on cognition (Kwan and Brodie, 2004). It is also involved in several drug interactions, largely due to the induction of hepatic enzymes. Primidone is metabolised to phenobarbital and phenylethylmalonamide, and its anti-seizure effects are thought to be largely due to its conversion to phenobarbital. It is rarely recommended.

The results of these audits suggest that some of these patients may have been taking phenobarbital 'by default'; those on barbiturates were significantly less likely to have been reviewed in the 15 months prior to the audit, and were significantly older. It may be, however, that those taking phenobarbital were reluctant to change AEDs because of fear of having further seizures.

Phenytoin

Phenytoin is described as effective treatment for partial onset and tonic-clonic seizures and, although not a first line drug, is still relatively widely used. It may be given once daily. It has, however, a narrow therapeutic index and non-linear relationship between the dose and plasma concentration. Hence toxicity can be a problem. A variety of side-effects including hirsutism and gingival hyperplasia are associated with phenytoin (Joint Formulary Committee, 2005) and it is also a hepatic enzyme inducer.

As with phenobarbital, those in these audits taking phenytoin were older than those not. Although those taking phenytoin had a slightly longer duration of epilepsy than those without, the difference is not clinically important, as the same AEDs were available at the time most patients were diagnosed. The smaller percentage of people reviewed in the groups taking phenytoin may suggest that either clinicians or patients did not wish to review the treatment.

Sodium valproate

Sodium valproate is a broad spectrum AED whose main restriction of use is in women of child-bearing potential, or girls who may become so whilst taking the drug (see section 1.2.2.8.2.). It may also have minor adverse effects in people with learning disability.

Many patients in these audits took sodium valproate. It is somewhat disconcerting that as many women as men were taking this, and particularly that, in the Sentinel Audit, those most likely to be of childbearing potential had no record of information on child-bearing issues; the audit record did not specify issues of child-bearing in the information section, so there is a possibility that this was recorded in the clinical record but missed in the audit. The Chiltern audit found some information provided to relevant women, but even so, this is recorded in minority.

Topiramate

Topiramate is recommended by NICE as treatment for generalised tonic-clonic seizures and focal seizures in people who have not benefited from the older AEDs, or for whom they are unsuitable (NICE, 2004c; NICE, 2004a). Its side-effects include somnolence and difficulties with memory and concentration. In these audits only a small number of patients took topiramate, including some with learning disabilities.

5.1.3.6. Investigations

According to the guidelines current at the time of the Chiltern audit, in almost one sixth of people there was no documented evidence to suggest that EEG was not necessary, but no EEG was documented. A similar proportion in whom neuroimaging may have been indicated appeared to have had none. Whilst investigations of epilepsy are largely in the remit of specialists, it could be argued that the GP could be more proactive in the care of the patient, and perhaps have considered referral for further investigation, particularly as only a minority were known to be seizure-free.

5.1.3.7. Information provision

As noted earlier, documented information provision was generally poor, particularly with regard to issues pertaining to contraception or childbearing. It is noticeable that information provided to people with learning disability seems to be particularly poor.

5.1.4. Specialist care

5.1.4.1. Demographics

Those with learning disability died younger than those without, perhaps because of having more severe epilepsy or due to the compounded risks with comorbidity. This cannot be reliably assessed in a clinical records audit.

5.1.4.2. Epilepsy review

Of 158 patients in whom it was possible to calculate the time period from the last outpatient appointment to death, over one half (97) had been seen in the year before death.

All but two of the children who died had been seen by a specialist within a year of death; one of the other two died in the second seizure, and the other may have been seen. Fewer adults had been seen, including 37% who may have had ongoing seizures (Hanna et al., 2002). The National Sentinel Audit was concerned that one fifth of adults appeared to have been 'lost to follow-up', with a further three people probably lost in the handover from paediatric to adult care (Hanna et al., 2002). Concern was raised by the audit team at the handling of some patients who repeatedly did not attend outpatient appointments; frequently there was no documentation to suggest that effort had been made to establish a reason for non-attendance or to send a further appointment. A study in Northern Ireland of non-attenders at a gastroenterology clinic found that 30% had forgotten to attend or to cancel the appointment, and the authors suggest that no strategy is likely to improve on this (Murdock et al., 2002). However, a small study from New Zealand found that a group who were telephoned 24 hours prior to the appointment had a non-attendance rate of five percent compared with 27% in a control group (Reti, 2003). The Irish study found that, of follow-up patients, 27% had failed to attend at least once previously (Murdock et al., 2002).

An audit of clinical records may not pick up all the options considered by the clinicians. Nevertheless, it is disappointing that surgery was apparently only considered in eight of twenty four patients in whom it may have been indicated.

5.1.4.3. Care in different groups

In virtually all areas of care considered, there was no difference found between those with learning disability and those without, between those whose care had been in a specialty considered satisfactory or not, and between those who had ever seen a consultant or not. Had the care in all settings been excellent, this would suggest that there is no discrimination shown to those with learning disability. Poor record keeping, although better than that found in the primary care audits, hampered the audit. Although three analyses appear to show statistically significant results (fewer people with learning disability than without had a satisfactory neuroimaging status, more of those with learning disability than without were on polytherapy, and, in those with learning disability, more people seen by a consultant had a clear description of the seizures in the clinical records), these results could well have appeared as significant by chance, as so many analyses were performed. Using Bonferoni's correction the p-values found become non-significant.

There was no difference in the overall standard of care, as assessed by the specialist panel, received by those with and without learning disability, but this is no cause for complacency, as the care was only considered adequate in less than half of either group. Death was unavoidable in less than half of assessable cases in each group. The fact that in one fifth of deaths this was not assessable suggests that deaths could be potentially or probably avoidable in even more (or fewer) cases overall. Approximately 80% of patients have documented evidence of having seen a consultant at some time. The implication that one fifth of the patients in this audit, who later died an epilepsy death, may never have seen a consultant is disquieting.

Only fifteen percent of those with learning disability were seen in a specialty classified as 'good' (see Methods 3.3.6.2.). However, over half were seen in a specialty designated as satisfactory.

5.1.4.4. Documented history of seizures

Seizure frequency was noted at the last consultation in around three quarters of people, but in many of these cases, was very unclear (Hanna et al., 2002). The specialist treating the patient may have a good memory for all the salient facts, but

notes are also used to allow another physician caring for the patient to know what has been done (Brook et al., 1996). As seizure freedom is the aim of treatment in epilepsy, it is imperative that seizure status is clearly documented in the clinical records. Similarly, as treatment is often determined by the epilepsy syndrome, this should be clearly stated in the records, along with a seizure description.

5.1.4.5. Investigations

Around four fifths of patients in whom an EEG was indicated had had one. Many of those with learning disability who did not have an EEG had severe learning disability, which may have made the decision to arrange an EEG more difficult; however, in this group diagnosis is often complex, and an EEG may have helped to clarify the diagnosis (Jenkins and Brown, 1992). Similarly, those with learning disability were less likely to have had neuroimaging. This apparently statistically significant difference will no longer be so after correcting for multiple analyses, but the fact remains that in only two thirds of people with learning disability was the neuroimaging status satisfactory.

5.1.4.6. AEDs

The finding that slightly more people with learning disability were using AED polytherapy is not surprising (EUCARE, 2003). It is disappointing, however, that there was no difference in the proportions of people with and without learning disability who were taking drugs which may adversely affect cognition as it could be argued that extra care should be taken in those with learning disability.

5.1.4.7. Information provision

Information provision is perhaps difficult to ascertain accurately from a clinical records audit. However, the case records may be used for medicolegal purposes, and it behoves the clinician to make adequate records about information provision. The Sentinel Audit did not specifically audit information concerning fertility issues in specialist care, but overall, documented information provision was small; the highest documented information was on side-effects of AEDs, which was documented in the records of just under one third of those on AEDs. Even if patients recall more than is documented, this clearly leaves much room for improvement.

5.2. CAUSE OF DEATH IN PEOPLE WITH EPILEPSY

5.2.1. Use of death certificates as case ascertainment

Epilepsy was mentioned on the death certificates of a minority of patients even when there was a history of relatively recent seizures, which could be taken as a surrogate for seizure severity. Those with more than 12 seizures per year were more likely to have epilepsy on the certificate than those with no seizures, but epilepsy was only recorded in three of 18 with such frequent seizures. Those on AEDs were more likely to have epilepsy recorded than those not on AEDs, but again in a small minority (15/139). There was no increased rate of reporting epilepsy by physicians who had completed the most recent follow-up form and should therefore be aware of the diagnosis of epilepsy; indeed the coroner was the most likely to report epilepsy. Neither the presence of convulsive seizures, nor younger age at death appeared to influence mention of epilepsy on the certificate. Cause of death influenced the mention of epilepsy, as those dying from malignancy were less likely to have epilepsy on the death certificate than those certified as dying from causes other than malignancy or vascular disease.

Many studies have been based on information found on death certificates (Antoniuk et al., 2001; Senanayake and Peiris, 1995), but it has long been known that they are an inaccurate record of cause of death (Coyle et al., 1994; Medical Services Study Group, 1978). Death certificates have been found to be a poor source of estimating mortality in diabetes (Morgan et al., 2000), asthma (Hunt et al., 1993; Reid et al., 1998; Wright et al., 1994), and cancer (Rigdon, 1981). In investigations into deaths related to epilepsy, it has been found that, in many cases, epilepsy has not been mentioned on the death certificate. For example, in a paediatric study of deaths in children, where cases were identified by both direct and indirect means, in only 55% of deaths attributable to epilepsy was the diagnosis of epilepsy on the death certificate (Harvey et al., 1993). Similarly, a study of older patients with known seizures included 11 patients who died suddenly and unexpectedly of unknown cause, and were found dead under circumstances compatible with death occurring during a seizure. In only one case was epilepsy mentioned on the death certificate (Luhdorf et al., 1987). It has been suggested that in over 90% of people with epilepsy, it is not mentioned on the

certificate (Morgan and Kerr, 2002). Even in those cases where epilepsy is mentioned, many patients certified as dying from status epilepticus were more likely to have died from SUDEP (Langan et al., 2002).

There are several reasons why epilepsy may not be recorded on death certificates. Death certification is not primarily intended for epidemiological research, but in the UK was instigated in 1837 as an important legal and social requirement. The Home Office, the government department responsible for internal affairs in England and Wales, initiated a review into death certification in 2001, in response to the conviction of a GP for the murder of 15 patients. This review lists nine items as being the most essential elements of death certification. As well as confirming that death has occurred, establishing the identity of the deceased person and ensuring that unnatural deaths are properly investigated, this list includes the provision of an indication of the likely cause of death, and provision of statistical information about the cause and circumstances of the death (The Home Office, 2001).

In 1978, it was suggested that in a fifth of deaths there was a major discrepancy between the cause of death certified and that determined by the consultant and the case notes (Medical Services Study Group, 1978). The highest proportion of major discrepancies occurred among deaths certified by the coroner, but it was noted that most other death certificates are completed by the most junior member of the hospital team. However, it has been argued that the errors were not as serious as appeared (Adelstein, 1978). Furthermore, in a more recent study senior hospital doctors were found to make more errors than their juniors (James and Bull, 1995). The Home Office review suggested that the quality of death certification by doctors was uneven due to lack of training and to the low priority given to this duty (The Home Office, 2001). The error rate in deaths certified by coroners may be exacerbated by the fact that the primary purpose of post-mortem examinations performed is legal, and any history available to the pathologist is more likely to come from the police than from clinicians (Devis and Rooney, 1999).

Under the current system of death certification in the UK it is likely that, in many cases, the diagnosis of epilepsy is correctly absent from the certificate. This is

because the information required is that of conditions leading to death, and of other conditions contributing to death. Our results are in keeping with this, as those dying with malignancy were significantly less likely to have epilepsy on the certificate than those with other pathologies, excluding vascular. However, SMRs for malignancy are increased in many studies of mortality in epilepsy (Lhatoo et al., 2001; Nilsson et al., 1997). Although the malignancy could be the cause of the seizures this is not necessarily always the case, particularly as SMRs for non-CNS tumours are often raised in people with epilepsy. The Home Office review suggested that, as well as recording the fact and circumstances of the death, and thus assisting the prevention and investigation of crime, the collection of mortality data was of considerable epidemiological importance (The Home Office, 2001). The review suggested that any study of death certification should take account of its current uses and also consider how these might change in the future. The Baker Report, also set up in response to the above conviction, suggested that in a revised certification system, brief information about the circumstances of death and the patient's clinical history should be recorded (Baker, 2001). However, the Report of the Fundamental Review of death certification and coroner services did not appear to include this recommendation (Home Office, 2003). The Shipman Inquiry (The Shipman Inquiry Third Report, 2003) suggested a dual system of forms, the second of which provides space for a 'brief chronological account of the deceased's medical history before death...'. The government is reviewing the coroners' service, based on the above reports (without following all the recommendations), and this will probably change the way in which deaths are certificated. The certificate would still record the medical cause of death, however, and so may not record clinical details which are not pertinent to the death (Department for Constitutional Affairs, 2006). Unless this sort of information is provided for registration purposes, death certificates used in isolation will continue to be a poor source of information about mortality in epilepsy or other chronic diseases.

The current situation complicates efforts to conduct research into the epidemiology and causes of SUDEP, as this can only be diagnosed with any degree of certainty after a postmortem examination has not revealed a toxicological or anatomical cause for death. Unless the coroner or clinician requesting the post-mortem is both aware that the subject had epilepsy and aware of the existence of SUDEP, this diagnosis might

not be reached. Furthermore, it suggests that the case ascertainment of the Sentinel Audit may have missed some epilepsy-related deaths, although it is not possible to quantify the proportion missed.

This study seems to indicate that in the UK a minority of people with epilepsy would be picked up by a study of death certificates alone. Although a high seizure frequency, the use of AEDs and the absence of malignancy appear to influence the likelihood of epilepsy being on the death certificate, it is still recorded in only a small minority of patients.

The present system of death certificates in the UK is not an effective way to look at mortality in epilepsy, and only large general population-based studies, with 'flagging' of records by the NHSCR can hope to investigate the causes of death in people with epilepsy.

5.2.2. Suicide in people with epilepsy in England and Wales

The SMR of 0.36 appears to indicate a protective effect of epilepsy on death by suicide. No previous study has reported an SMR for suicide in epilepsy of less than one, and there is no evidence that epilepsy protects people from suicide, as the low SMR implies. If epilepsy were not recorded in all death certificates of people with epilepsy who died during the study period, then the number of deaths from suicide in people with epilepsy would be underestimated.

It is interesting that none of the deaths in people with epilepsy in this study was due to hanging, despite the fact that over 40% of deaths from suicide in England and Wales in 2000 were due to hanging (Office for National Statistics, 2003). Suicide by hanging is more common in males in the general population, and this may be reflected in the lower SMRs for suicide in males in this cohort. The case control study in Sweden, using different case ascertainment, also found the method of suicide was more often intoxication and less often hanging and shooting compared with the general population of Sweden (Nilsson et al., 2002).

In that study the SMR for suicide was 3.5 (95% CI 2.6 to 4.6) (Nilsson et al., 1997). This study, however, was amongst adults (>15 years) and was not a population-based study. People who attend hospitals have higher morbidity and mortality than those in community cohorts.

Calculations in the current study are based on the assumption that the information is accurate and representative of the general and epilepsy populations. In England and Wales a coroner investigates deaths that may have been suicide and it is therefore unlikely that any such deaths have been missed. Deaths where coroners recorded open verdicts were specifically sought but no further deaths that could be suicide were identified. Sometimes the attribution of cause of death is difficult, and there is a risk that deaths due to suicidal intent are not considered or not registered as such. This situation may not necessarily introduce bias, as information on the cause of death was obtained in the same way for the epilepsy and the general population cohorts. The low SMR found suggests that, although deaths from suicide may not have been missed, some of the deaths from suicide have been attributed to people in the general population (without epilepsy). This is consistent with the conclusion (see 5.2.1.) that death certificates are unreliable as a source of case ascertainment for studies of death in people with epilepsy.

It is important that the risk factors, prognosis and causes of death in epilepsy are understood fully, to reduce any avoidable morbidity and mortality from epilepsy. In the interim, adequate seizure control and taking of precautions should be established for all patients in order to avoid more deaths.

5.2.3. Meta-analysis of suicide in people with epilepsy

The SMR for suicide in people with epilepsy is estimated as 4.5, clearly higher than that suggested by the previous study (section 5.2.2.). Anecdotal evidence suggests that the rate of suicide in people with epilepsy may be falling, and the ratio of the SMR of the earlier published studies to the later ones suggests that this may indeed be the case. This work needs to be validated, taking into account the timing of the deaths and using weighting of the SMRs.

There are several limitations for the study. A new literature search was not done, and studies may have been missed; a further follow-up of the Sillanpaa papers has been published. It was not always possible to obtain national data for the midpoint time of the study to calculate expected deaths. Where possible these were taken from the papers themselves. No account was taken of the age at death of the patients, although the overall age of the cohort was considered when choosing the age group used from national datasets. The readily available software to produce weighted SMRs did not allow for numbers as large as the total country populations, and so the weighted SMR is only an approximation.

There are many problems inherent in performing a meta-analysis. The first is in performing the literature search to extract all appropriate studies, including studies in other languages and those unpublished. On this occasion a new literature search was not done, and a search done by others, several years ago, was relied on. This does not appear to have included unpublished or other language literature.

Other authors have attempted to produce an overall figure for suicide in epilepsy. One published in 1997 produced a figure for the percentage of deaths in epilepsy due to suicide, but averaged the rates (Robertson, 1997). This provided a figure of 13.2% of all deaths in people with epilepsy compared with 1.4% in the general population. Finding the ratio of the total number of deaths by suicide to the total number of deaths in epilepsy provides a more accurate figure of 4.1%. The inappropriate calculation was repeated including more studies in 2003 (Jones et al., 2003), this time suggesting that suicides constitute 11.5% of epilepsy deaths, whereas the more accurate ratio of all deaths by suicide to all deaths in epilepsy is 3.8%. The ratio of total deaths by suicide to total deaths still does not take fully into account the size of the study populations, and weighting should ideally be applied.

A review of the mortality risk in epilepsy found that the overall mortality rate was influenced by the source population and, to a smaller degree, by whether an incident or a prevalent population was considered (Shackleton et al., 2002). This was not considered in the current study. SMRs have also been shown to be influenced by the type of epilepsy and the population studied. An unweighted meta-analysis published

in 1997 found the overall SMR to be 5.1 (95% CI 3.9 to 6.6), but that it was 8.0 in people with temporal lobe epilepsy, 87.5 in surgically treated patients, 4.9 in institutionalised patients but only 4.1 in outpatients (Harris and Barraclough, 1997).

5.2.4. Cause of death in people with epilepsy

These results together show that death certificates are not a reliable method of case ascertainment for studying death in people with epilepsy as a whole, or for investigating deaths in people with epilepsy from suicide. They do not, however, show that death certificates are not useful for investigating deaths due to epilepsy. It seems probable that deaths related to epilepsy are more likely to be identified in this way than deaths unrelated to epilepsy; the present studies cannot quantify this.

5.3. Use of clinical guidelines

Guidelines can be defined as 'systematically developed statements to assist practitioner decisions about appropriate healthcare for specific clinical circumstances' (Field, quoted in Grimshaw and Russell, 1993). As described in the section on provision of clinical services for people with epilepsy in the UK in this thesis, there is no shortage of guidelines and government recommendations on the care of people with epilepsy. The main purpose of clinical guidelines is to improve the quality of care for patients (Feder et al., 1999), but in practice they may do little to change behaviour (Woolf et al., 1999). They may, however, draw attention to previously unrecognised health problems. Guidelines which are firmly evidence-based can clarify which interventions work, and which do not; however scientific evidence is often lacking (Woolf et al., 1999). Guidelines are considered valid if 'when followed, they lead to the health gains and costs predicted for them' (Institute of Medicine, quoted in Eccles et al., 1996). They should also be reproducible and reliable (Littlejohns and Cluzeau, 2000).

Guideline recommendations may be wrong or, even if good for patients in general, may be inappropriate for individuals or ignore their preferences (Woolf et al., 1999). They may also need to be adapted for use within the local healthcare setting (Feder et al., 1999). It has been shown that clinical guidelines can improve the quality of care

(Grimshaw and Russell, 1993), but they may not always do so; in part this may be because they are not put into practice (Woolf et al., 1999).

A systematic review in the early 1990s looked at 59 evaluations of the effect of guidelines. All but four studies detected significant improvements in the care process following the use of the relevant guidelines. The review found that guidelines were more likely to be followed when the physicians had been involved in their development than when they were developed by others (Grimshaw and Russell, 1993). Eleven of the studies involved the outcome of care, and all but two of these found significant improvements in outcome.

The attitudes towards the use of guidelines has been investigated in a questionnaire study of randomly selected GPs in the west of England. GPs were asked to complete the sentence 'The one thing most likely to make me turn to a guideline is...', and the key factors identified were brevity, simplicity, ease of retrievability, reputable source and quality, and the complexity of the presenting problem. Almost all GPs said that they adapted guidelines to the needs of particular patients (Watkins et al., 1999).

Dissemination of guidelines may be a significant factor in their use. In the Netherlands, a systematic implementation programme follows guideline development. In France guidelines are disseminated through GP networks, and their effectiveness evaluated through local audit. In the USA guidelines are commonly used for both quality improvement and cost control (Woolf et al., 1999). Reviews have shown that relatively passive methods of dissemination (for example, with publication in professional journals or by mail) infrequently leads to changes in practice. Methods suggested to improve on this include seminars and workshops, audit and feedback, and reminders (Feder et al., 1999).

Following the publication of the 1997 SIGN guidelines for the diagnosis and treatment of adults with epilepsy, a study (The TIGER trial, [Tayside Implementation of Guidelines in Epilepsy Randomized trial]) aimed to determine the effectiveness of dissemination strategies (Davis et al., 2004). All general practices (except those in the pilot study) in the local area were invited to take part in the study, and GPs responding

were grouped by practice location. Sixty eight practices in 53 locations were randomised. The practices in the control group (24 practices in 18 locations) were sent a copy of the guideline by post. The intermediate intervention group (22 practices in 18 locations) received the guideline, an invitation to interactive workshops, and two structured protocol documents to use with the guideline. The intensive intervention group, as well as being offered the same interventions as the intermediate group, were also offered the services of a specialist epilepsy nurse, to promote the use of the guideline, to help establish epilepsy review programmes and to provide epilepsy information for both GPs and patients. Adult patients receiving AEDs on the list of participating GPs were sent questionnaires including questions measuring eight dimensions of health-related quality of life (the SF-36 general health-related quality of life instrument [the SF-36 scale]) before and after the interventions. The numbers of prearranged review consultations for epilepsy and the numbers of consultations in which epilepsy counselling was given were also determined in the practices. Analysis was conducted by intention to treat. Fifty six percent of eligible patients returned the first questionnaire, and 72% of those returned the second.

Of 238 primary care staff invited to a workshop, less than ten percent attended (including no practice managers), and only two practices routinely used the protocols provided. Only six of 22 practices in the intensive intervention group took up the offer of help from the epilepsy specialist nurse. There were no significant differences among the patients of the three groups in SF-36 scale either before or after the intervention. The number of planned reviews per patient did not change after the intervention, while the number of sessions at which counselling was given increased marginally. There was no difference in these data in the three arms of the study. After the intervention the mean number of reviews per patient per year was 0.14 (compared with the recommendation of at least one). The authors speculate that the problem may be related to a lack of perceived need for change in practice rather than lack of time or resources. They also suggest that many primary care practitioners do not see epilepsy care as their responsibility, but rather that of secondary care (Davis et al., 2004).

A more recent study from Norway investigated adherence to guidelines on the management of women with epilepsy by neurologists, and also sent a questionnaire to

assess the knowledge of these issues to some of the patients (Kampman et al., 2005). The study consisted of two periods: in the first two years guidelines were not actively disseminated, but were available in publications. In the second period a condensed local recommendation was developed and this was presented at an interactive meeting, made available on the internet and in print; patient education handouts were also placed in waiting rooms. The case notes of patients seen by the neurologists were investigated for documentation that issues relevant to women with epilepsy had been discussed, during both time periods. Sixty percent of women had been seen during both periods. Fertility-related issues had been discussed at least once in one third of cases (but a higher proportion during the earlier period of passive dissemination). Five oral contraceptive failures were documented in 62 women taking carbamazepine. Pregnancy-related issues had been discussed with 65% of (28) women prior to conception. Questionnaires sent to women who had consulted a neurologist in the first time period were returned by 71%. Seventy one percent of women needing contraception and taking enzyme-inducing AEDs were aware of potential conflicts with the oral contraceptive pill; under half remembered hearing this from the neurologist. Over 60% of women had heard from their neurologist that they should contact the neurologist when planning pregnancy, and 56% of women knew from the neurologist that folate was recommended in women of child-bearing potential. It seemed that patients completing the questionnaire remembered hearing more information from the neurologists than was documented in the medical records, although approximately one quarter of relevant women did not remember having received the information at all (Kampman et al., 2005).

5.4. Use of audit

One problem inherent in a clinical records audit is that it is reliant on data recorded in the clinical records. The Chiltern and Sentinel audits have confirmed that record keeping is poor, particularly in primary care. Whilst clinical record keeping is of importance to clinical audit, it is also of vital use in patient management and care. It is possible that some care was better than found in the audit, but good care should not reduce the need for good clinical records. It has, however, been suggested that 'the weakness of such a system of audit... is that excellent humane medical care can be given by a doctor who writes appalling records' and that 'complaints may be made by

patients that "he never even looked at me, he was too busy writing"' (Hopkins, 1990). Nevertheless, it has been hypothesised that the process of making and documenting a complete assessment, and of developing and documenting a clear plan would be associated with improved clinical outcomes and patient satisfaction (Solomon et al., 2000).

Quality of care is generally considered in three dimensions: structure, process and outcome (Hopkins, 1990). Whilst the structure (the availability of buildings, equipment and suitably trained staff, for example) is relatively easy to audit, it is unlikely to be a good guide to the quality of care; 'bad care can occur in well equipped hospitals' (Hopkins, 1990). The process (the activities of medical care) is the subject of these audits. Auditing the outcome seems at first sight to be a more useful measure of quality of care – the end result is what is probably most important to patients and their relatives. However, outcomes as an endpoint are only useful if they relate to the quality of care – many people get better despite their treatment. For some chronic conditions like epilepsy the time interval between the care provided and the outcome can be long, and poor care does not always relate to bad outcome (Kampman et al., 2005). Mortality rates in the UK have improved vastly over the past 100 years, and the initial improvements were due in large part to improvements in housing and hygiene, and to improved understanding of infectious diseases. Avoidable mortality should be a more useful parameter to measure, and this was attempted in the Sentinel Audit. The expert panel identified that specialist care had been inadequate in over half of adults. However, as found by others, difficulties arise in identifying deaths which were avoidable and those which are dependent on other factors such severity of the illness, comorbidities and age. The panel felt that death was probably avoidable in nine percent, although potentially avoidable in 30%. In almost one quarter they were unable to make a judgment (Hanna et al., 2002). Many forms of epilepsy-related death, particularly SUDEP, but to a lesser extent death from status epilepticus and from accidents, occur unexpectedly, and so it is even more difficult to distinguish those which are due to deficiencies in care. The Sentinel Audit considered such areas as inadequate control of seizures (known to be a risk factor for SUDEP), insufficient follow-up or premature discharge from secondary care, inadequate investigations to make a safe diagnosis, and inappropriate or inadequate AEDs used.

The Sentinel Audit considered the main outcome of interest as death, particularly epilepsy-related death. Improved seizure control could also be regarded as a positive outcome; in the audits presented here documentation of seizure control was taken as evidence of quality of care. There was insufficient data in the clinical records to investigate seizure control as such. Achieving monotherapy with AEDs whilst controlling seizures may also be a positive outcome as side-effects are likely to be reduced. Again, this was regarded as evidence of quality of care in these audits. Information provision may also aid the patient in coping with a long-term condition. Patients may regard improvements in quality of life as being of equal importance as reduction of premature mortality.

5.5. AUDITS OF EPILEPSY SERVICES

Many guidelines suggest that audit should be an integral part of epilepsy care (CSAG, 2000; SIGN, 2003) and over the years many audits have been carried out. An audit in the 1970s of care in 17 general practices for adults with epilepsy found that 95% of patients had been referred to hospital at some stage, although a small minority had been referred to a hospital without a neurologist. At that time most patients were on phenobarbital or phenytoin, but the authors found that half of those with generalised convulsive seizures were probably undertreated. A further finding was that follow-up seemed disorganised; two of three patients with daily generalised seizures had last seen the GP several months previously. Of the 11% of subjects currently supervised in hospitals, half were having generalised seizures less frequently than yearly, while three subjects had been discharged from hospital follow-up whilst experiencing weekly seizures. Two thirds of the subjects were ineligible to drive under the regulations current at that time, but almost one fifth of these were driving. A small minority were driving against advice, but larger numbers had either been told they could drive or felt that they had received such consent (Hopkins and Scambler, 1977).

Another study, published only two years later, of care of people with epilepsy in one general practice found a slightly different picture (Zander et al., 1979). Twenty one of 29 patients who had either had seizures or had taken AEDs in the previous two years were reviewed; 13 (62%) had had no seizures within two years and only four had had

a seizure within one year. A further four subjects were not reviewed, as they were under regular hospital follow-up; three of these had seizures which were very difficult to control. Six subjects (29%) had possible side-effects of AEDs.

An audit of the care for adults with active epilepsy (taking AEDs or having had a seizure within two years) in six general practices in the south-east of England in the 1990s used three sources of information; a questionnaire sent to GPs, a medical records audit and a questionnaire sent to patients (Ridsdale et al., 1996). Ninety percent of 283 patients selected to receive questionnaires returned them completed; 32% of these reported having seizures in the previous six months. GPs estimated that the patients would have seen a specialist within 24 months (the records audit estimated median 39 months) and would have consulted a GP in 12 months (the records audit estimated 14 months). Most GPs felt that ideal epilepsy monitoring by GPs would take place at least six monthly. GPs estimated that 73% of patients would have received advice on driving; the medical records audit found documented evidence in 46%, and 59% of patients reported having received such advice. GPs estimated that 30% patients would have received advice on side-effects of AEDs; medical records found documented evidence in only nine percent, while 51% of patients recalled receiving such advice.

A general practice records audit of care for people with epilepsy also published in the 1990s sought more documented information on the process of care (Jacoby et al., 1996). Whilst more than four fifths recorded the date of the first seizure, less than half had recorded the seizure frequency in the previous year. The seizure type was documented in two thirds, and there was a witness description of the seizure in half. Three quarters had had an EEG, and one third CT scanning. Of those on AEDs, 31% were on polytherapy, and in one quarter AED side-effects had been discussed. Less than a quarter of women had documented information provision on interactions between AEDs and the oral contraceptive pill. A similar finding to the two audits of primary care described in this thesis was that, although over half had not had any epilepsy review in the year before the audit, only eight percent had not seen the GP at all during that time.

A recently published audit of epilepsy care in general practice from the north of England, conducted at a similar time to the Chiltern audit (December 2001 to March 2003 compared with January 2001 to November 2002) showed similar conclusions (Minshall and Smith, 2006). The authors found that it was not possible to collect reliable information on seizure frequency, side-effects of AEDs or lifestyle issues. Only 41% of people with epilepsy had been seen for epilepsy by the GP in the previous year (compared with 38% in 15 months in the Chiltern audit) and 49% had seen no doctor for an epilepsy review in one year (compared with 46% in 15 months in the Chilten Audit). These results suggest that our findings are not anomalous.

One specialised epilepsy clinic, whose origin predated the recommendations of the Winterton report, audited the first one thousand patients referred to it (Tobias et al., 1994). Patients were referred for rationalisation of their AED therapy or for clarification of the diagnosis in up to one third of patients each. One fifth had recurrent seizures despite treatment, and 15% were referred from the A&E department. Over 90% had EEG recording, of which over 80% were reported as abnormal. One third had CT scanning, of which one third demonstrated abnormalities. On referral, 38% of patients were taking monotherapy and 27% polytherapy; 35% were taking no AEDs. By the time of the audit, over half the patients were taking monotherapy and one quarter were taking polytherapy; one quarter were not treated. In those patients whose pre-referral and pre-audit seizure data were both available, seizure frequency had improved in three quarters, and half were seizure-free. Interestingly, one third of patients were lost to follow-up, of whom 40% had a history of alcohol abuse. This audit demonstrates some of the problems observed in attempting to audit outcome in specialist care clinics; the outcome figures are likely to be less favourable due to the number of patients with intractable epilepsy referred, together with those with alcohol-related epilepsy, and epilepsy associated with other morbidities, such as learning disabilities and neurodevelopmental disorders.

Another audit of a specialist clinic also published in the 1990s illustrates the same problem (Martin and Millac, 1994). The records were audited of 55 patients with refractory epilepsy seen at a specialist clinic, who had data available for two three month periods nine months apart. In 40% of patients seizure frequency actually

increased substantially, while in only 11% was there a substantial reduction in seizures. Use of AED monotherapy was similarly disappointing, with fewer people taking monotherapy in the second time period.

SECTION 6. CONCLUSIONS

CONCLUSIONS

This work describes six different studies with a common purpose of investigating standards of care for people with epilepsy in the UK and the ways in which this may affect the mortality rate in people with epilepsy.

The thesis confirms previous suggestions that care for many people with epilepsy is substandard. It has not, however, been able to confirm or refute the implication that substandard care may contribute to premature mortality in epilepsy. The Sentinel Audit found that of those seen in hospitals, care was substandard and death probably avoidable in many. In most cases, however, the audit did not have access to reliable data on the details of the death, and it is not possible to be sure that the deaths were related to epilepsy. Even if the cause of death is known for certain, it is rare that this can be blamed directly on medical services or lack of them. Unlike diabetes or asthma, for example, where death may be a direct result of poor control, death in epilepsy is not an inevitable consequence of poor seizure control. Other important outcomes for patients, such as improved seizure frequency and reduced side-effects of AEDs may be more directly related to quality of care.

The use of audit to quantify the process of care is problematic while record keeping remains poor. The new GP contract may well be instrumental in improving record keeping, as GPs are paid according to set standards. Data from the first completed year of the Quality and Outcomes Framework shows that almost all practices have set up a register of people with epilepsy (NHS Health and Social Care Information Centre, 2005). Over 90% of adult patients registered by general practices have a record of seizure frequency and of epilepsy medication review in the previous 15 months and over 60% are said to be seizure-free. It will be of great interest to see whether this results in any changes in care. Will people with frequent seizures or disabling AED side-effects be referred to a GP with a special interest in epilepsy or to specialist care? Will people who have been seizure-free for many years be asked to consider AED reduction? Will women of child-bearing potential with epilepsy be encouraged to take AEDs suitable for their situation? Will all people with epilepsy be provided with the information they need?

The Sentinel Audit alerted many people to the risks inherent in epilepsy, and particularly to the existence of SUDEP, and led to many government and non-governmental initiatives. It is hoped that the combined effect of these will lead to improvements in care of people with epilepsy.

Randomised clinical trials of care for people with epilepsy are not an option. It would not be ethical to randomise any patient to substandard care and, even if a group were randomised to 'usual care' it is likely that the existence of the trial would alter the management of any patient in the trial. Audit assesses the situation as it is, and takes into account the realities of real life. If record keeping is generally improved, then this is likely to be the best way of monitoring patient care.

This thesis has shown that case ascertainment is problematic. Death certificates may identify a proportion of people whose death was related to epilepsy, but only if they are completed by someone who knows that the person had epilepsy and who is aware of the risks of SUDEP and of suicide in people with epilepsy. The Sentinel Audit may have increased the awareness of SUDEP by pathologists. It seems likely that the only reliable way to ensure complete case ascertainment of epilepsy-related death will be to use large-scale prospective studies of people with epilepsy, with timely reporting of death to the study, so that contemporaneous enquiries can be made about the manner and cause of death. Whether this would be feasible is open to doubt.

Epilepsy care in some countries is generally considered to be superior to that in the UK. Comparing death rates from epilepsy (even if they were reliably available) between countries with different models of care would suffer from many confounding issues. It is possible, however, that simultaneous audits of care of people dying from epilepsy-related causes in different (but geographically, culturally and economically similar) countries may be useful. In this thesis it was not possible to find a direct link between standards of care, and death. Were more reliable data available on cause of death and standards of care, however, correlations could be sought between quality of care and mortality rates from epilepsy in different regions of the world.

It is important that the risk factors for both SUDEP and suicide in epilepsy are firmly established so that efforts can be made to reduce those that are avoidable. Further research is needed to determine the cause(s) of SUDEP.

SUGGESTIONS FOR FUTURE WORK

1. A further audit of the Chiltern practices following the Quality and Outcomes Framework to see whether the presumed improvement in record keeping is matched by appropriate care for people with epilepsy.
2. Further audit of epilepsy-related death following the publication of the previous audit. This would ideally be a Confidential Inquiry, which would ease access to the records but also, and more importantly, would eliminate some bias in case ascertainment.
3. A concurrent audit of epilepsy-related death in another European country to see if any link can be found between epilepsy-related death and service provision.
4. Further research into the cause of SUDEP. Large epidemiological studies could improve our knowledge of the risk factors for SUDEP, and identify predictors for death. Identifying the cause or causes of SUDEP would clearly provide the most satisfactory information, and then risk factors could be identified much more clearly and eliminated or reduced where possible.

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APPENDICES

APPENDIX 1. EXAMPLES OF RECOMMENDATIONS AND GUIDELINES FOR CARE PUBLISHED RECENTLY IN THE UK

Non-government publications

- 1998. The Joint Epilepsy Council, 'Service Development Kit' (Epilepsy Task Force., 1998)
    - Provided specifications for epilepsy services
    - Provided examples of good practice from all over the country
    - Recommended that there should be equity of access to epilepsy services in response to needs assessment
- 1999. British Epilepsy Association 'Epilepsy Care: Making it Happen' (British Epilepsy Association, 1998)
    - Recommended a service vision of high quality services which are accessible, appropriate and well informed
    - Recommended a service which offers early diagnosis, treatment and ongoing support
    - Recommended that services should be cost and clinically effective
    - Recommended that primary care-based patient management should be closely integrated with epilepsy specialists in secondary care,
    - Recommended the appointment of clinical nurse specialists,
    - Recommended increased liaison between primary, secondary and tertiary care
    - Provided minimum standards for all levels of care, as well as for health authorities
- 2002. Joint Epilepsy Council 'National Statement of Good Practice for the treatment and care of people who have epilepsy' (Frost S et al., 2003) aimed to:
    - Improve the clinical management of epilepsy
    - Improve the quality of life for those with epilepsy, whether seizure-free or not
    - Increase the number of people who successfully withdraw from therapy
    - Describe how general practice should contribute to quality epilepsy care, as part of integrated care

- Primary Care Guidelines for the management of females with epilepsy (Epilepsy Guidelines Group, 2004).
    - This gives guidance to help the non-specialist address the specific needs of women with epilepsy

Government and national publications

- 2000. Clinical Standards Advisory Group report 'Services for Patients with Epilepsy' (CSAG, 2000)
    - Based on an assessment of service provision and on the views of over 2000 patients and clinicians
    - Found clear advances in the previous decade in the provision of specialist services for epilepsy, but these were usually on an *ad hoc* basis
    - Found an enthusiasm to develop high quality local services
    - Made various recommendations to provide services equitably across the country.
- 2002. National Sentinel Clinical Audit into epilepsy-related death (Hanna NJ et al., 2002) (commissioned by NICE and managed by the charity 'Epilepsy Bereaved') found that:
    - 54% of adults and 77% of children had inadequate secondary care
    - 39% deaths in adults and 59% in children were potentially or probably avoidable
    - Primary care showed lack of access to specialists and little evidence of structured management plans
- 2003. Improving Services for people with Epilepsy. Department of Health Action Plan in response to the National Clinical Audit of Epilepsy-related death (Department of Health, 2003b)
    - Asked NHS and primary care trusts and strategic Health Authorities to review local epilepsy services and address any shortfall as part of their local delivery plans
    - Included some funding to enable the National Society for Epilepsy to develop further the information outreach services

  - Included funding to be spent in developing neurological services through the work of the Modernisation Agency
  - Suggested more general practitioners and nurses with a special interest (GpwSI) in neurology
- 2003 Guidelines for the appointment of General Practitioners with special interest in epilepsy were published (Department of Health, 2003a).
- 2003 (Scotland). Scottish Intercollegiate Guidelines Network 'Diagnosis and Management of Epilepsy in adults' (SIGN, 2003). This:
  - Provided guidance about diagnosis, treatment and management of epilepsy
  - Made recommendations relating to models of care
  - Made recommendations relating to audit of epilepsy care and provision of information
- 2004. NICE guidelines 'The diagnosis and management of the epilepsies in adults and children in primary and secondary care' (NICE, 2004c)
- 2004. NICE technology appraisals 'Newer drugs for epilepsy in adults' and 'Newer drugs for epilepsy in children' (NICE, 2004a; NICE, 2004b).
- The National Primary and Care Trust Development Programme suggested competencies for primary care (NatPact, 2005). Included in these is quality in clinical care, including epilepsy. PCTs should:
  - Work with the voluntary sector
  - Have an epilepsy register
  - Undertake regular check ups to assess progress and adherence to drug regimes
  - Have developed effective links with secondary care providers
  - Commission services to provide timely access to consultants
- The National Service Framework (NSF) into long-term conditions was published in March 2005, with implementation over a ten-year period. NSFs aim to:
  - Provide blueprints for care
  - Raise standards
  - Reduce variations in services

- Address particular issues including the provision of a 'seamless service' with continuity of care, including guidance on the transition from paediatric to aduit services.

The NSF into long-term conditions (Department of Health, 2005b) does not address individual neurological conditions in detail, but Quality Requirements relevant for people with epilepsy included:

- Integrated assessment to prevent unnecessary reassessment and repetition of basic information
- Developing a personalised care plan, including reviewing information provision
- Each person having a named point of contact for advice and information
- Provision of prompt access to ongoing neurological advice and treatment
- Access to appropriate vocational assessment and vocational rehabilitation
- The offer of appropriate respite care

- As part of 'Standards for Better Health', health care organisations will need to ensure that care given conforms to nationally agreed best practice; NICE technology appraisals form part of the core standards to which health care organisations must conform, and NICE guidance and NSFs are part of the developmental standards, to which progress is expected to be made (Department of Health, 2005c). The Healthcare Commission, covering work formerly done by the Commission for Health Improvement, will undertake an annual review of the provision of health care by each NHS body in England, and will aim to determine that all trusts are meeting core standards and achieving developmental standards.
- 'Our health, our care, our say' is a recent white paper concerned with reforming health and social care (Department of Health, 2006). It aims to give people access to the GP of their choice at a suitable time. It also aims to tackle inequalities in access to community services and to support people with long-term needs.

APPENDIX 2. ADDITIONAL FIGURES FROM SECTION 4.1

Figure A1. People with epilepsy with no epilepsy review by GP or specialist

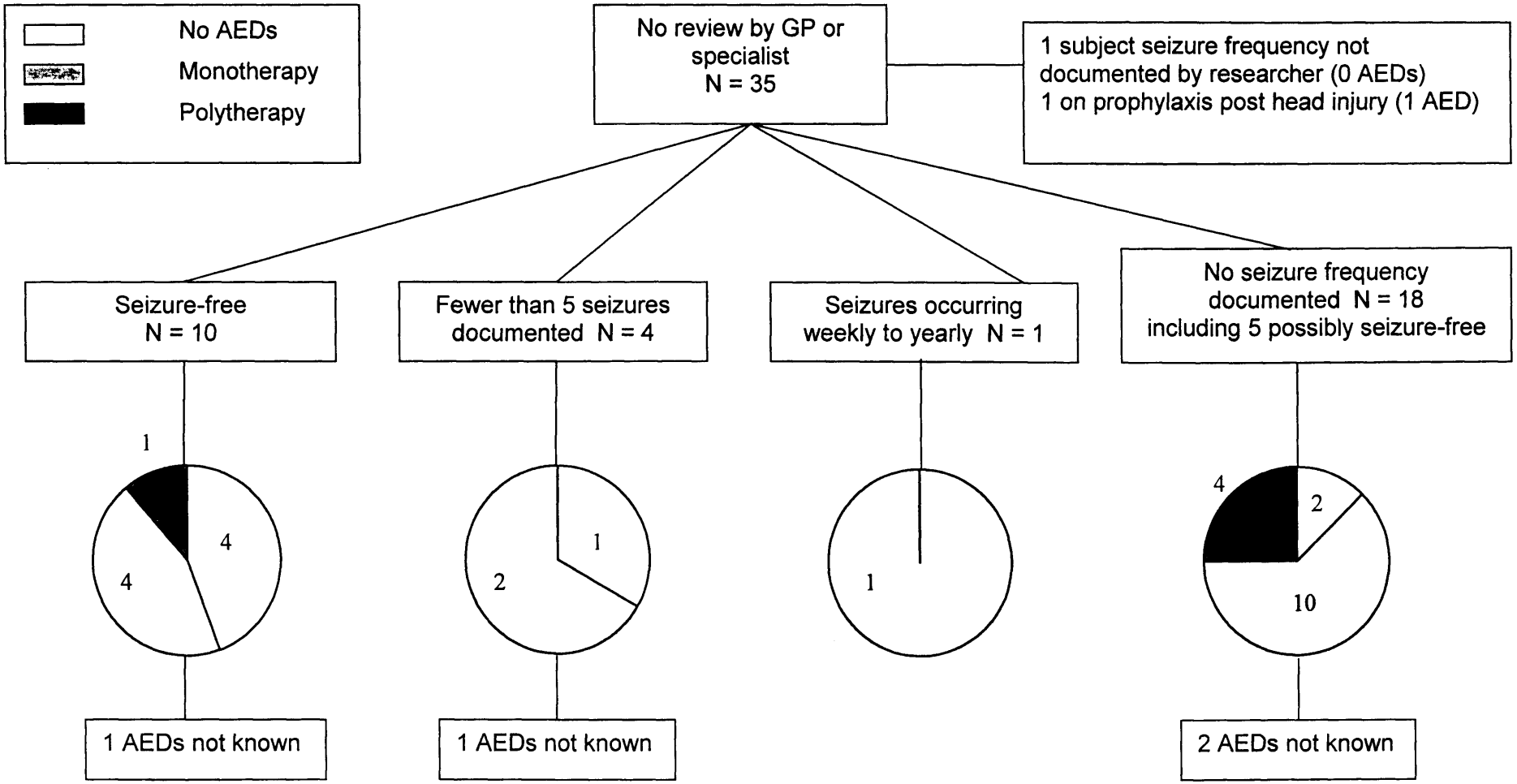
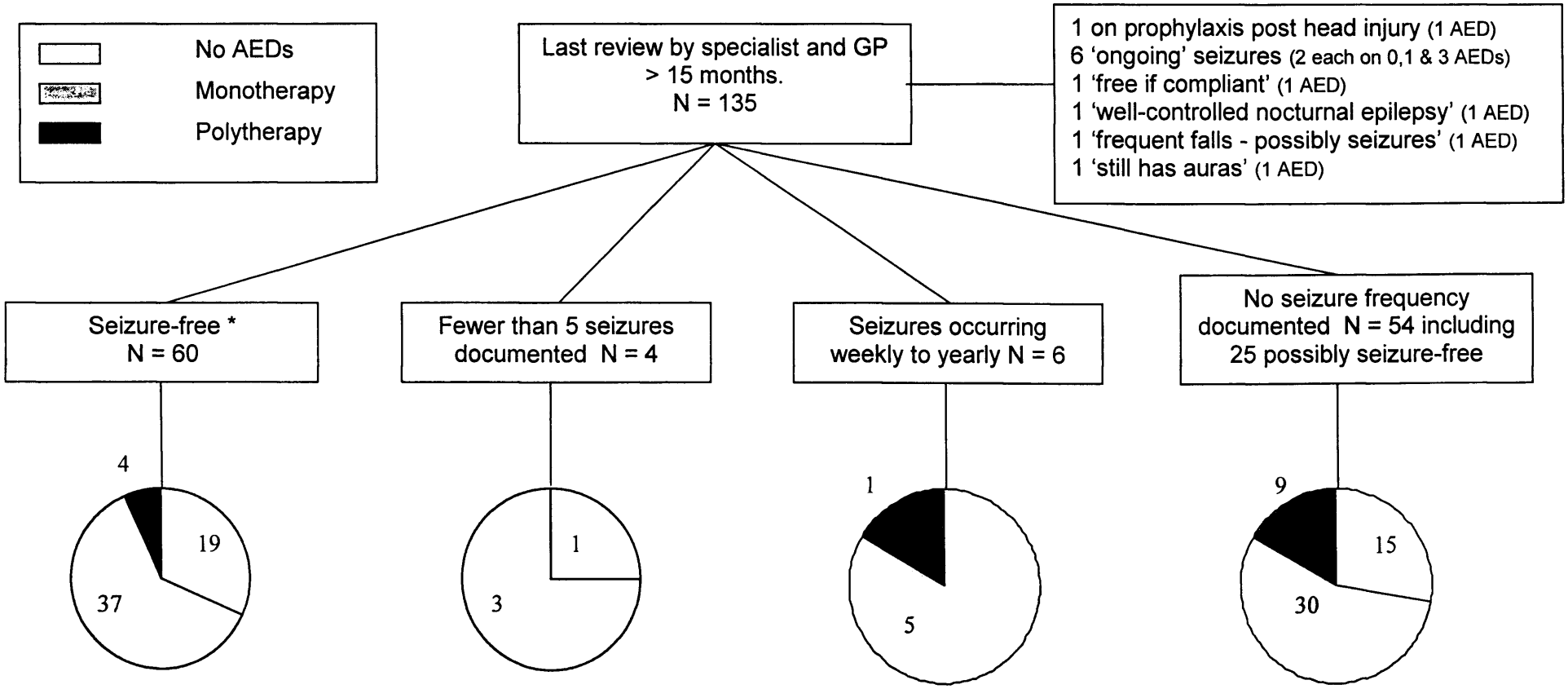


Figure A2: people with epilepsy without recent review by GP or specialist



* In 2 cases, 'epilepsy specialist' was epilepsy specialist nurse

Figure A3: people with epilepsy with no review by specialist and no recent review by GP

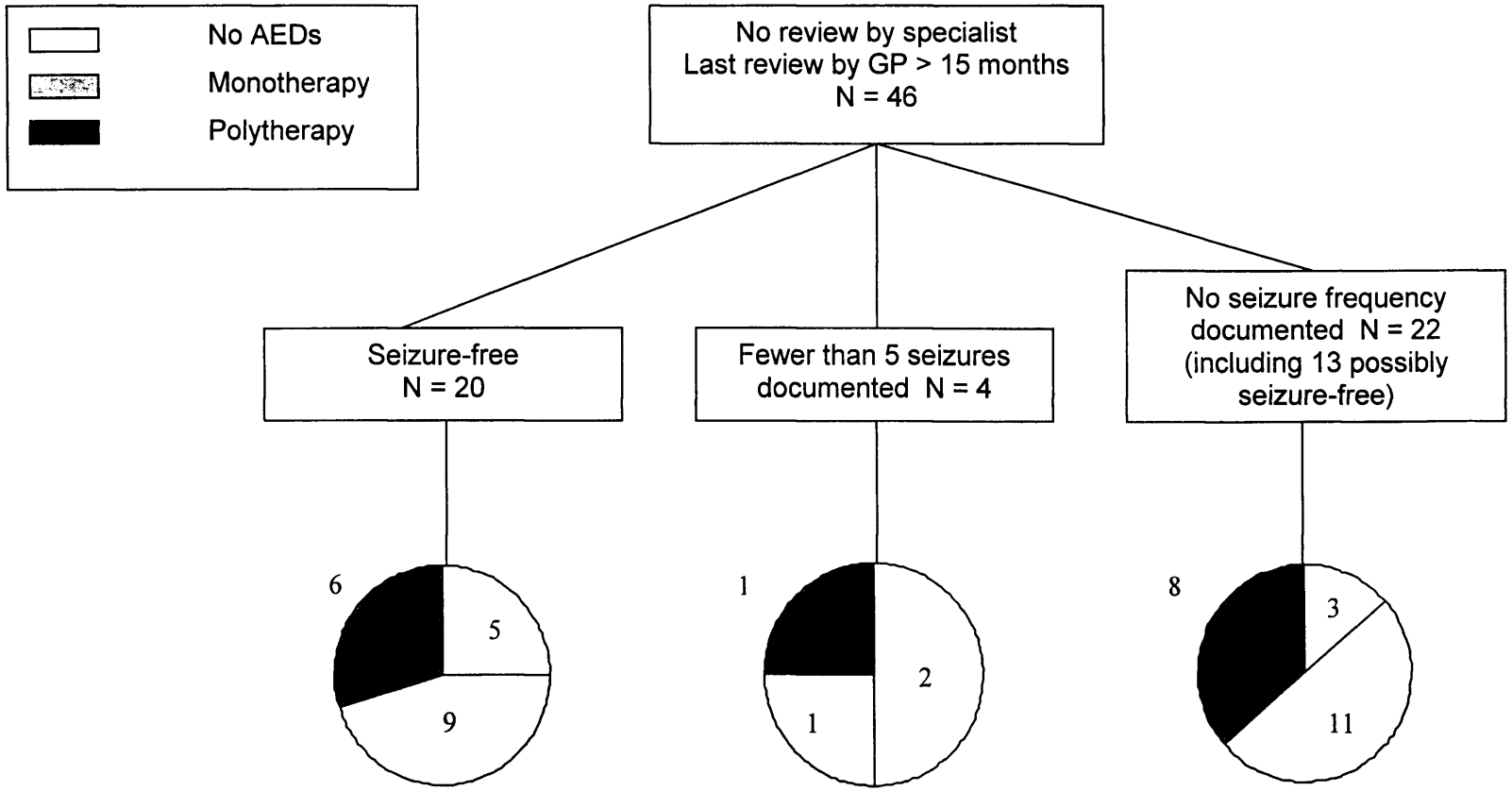
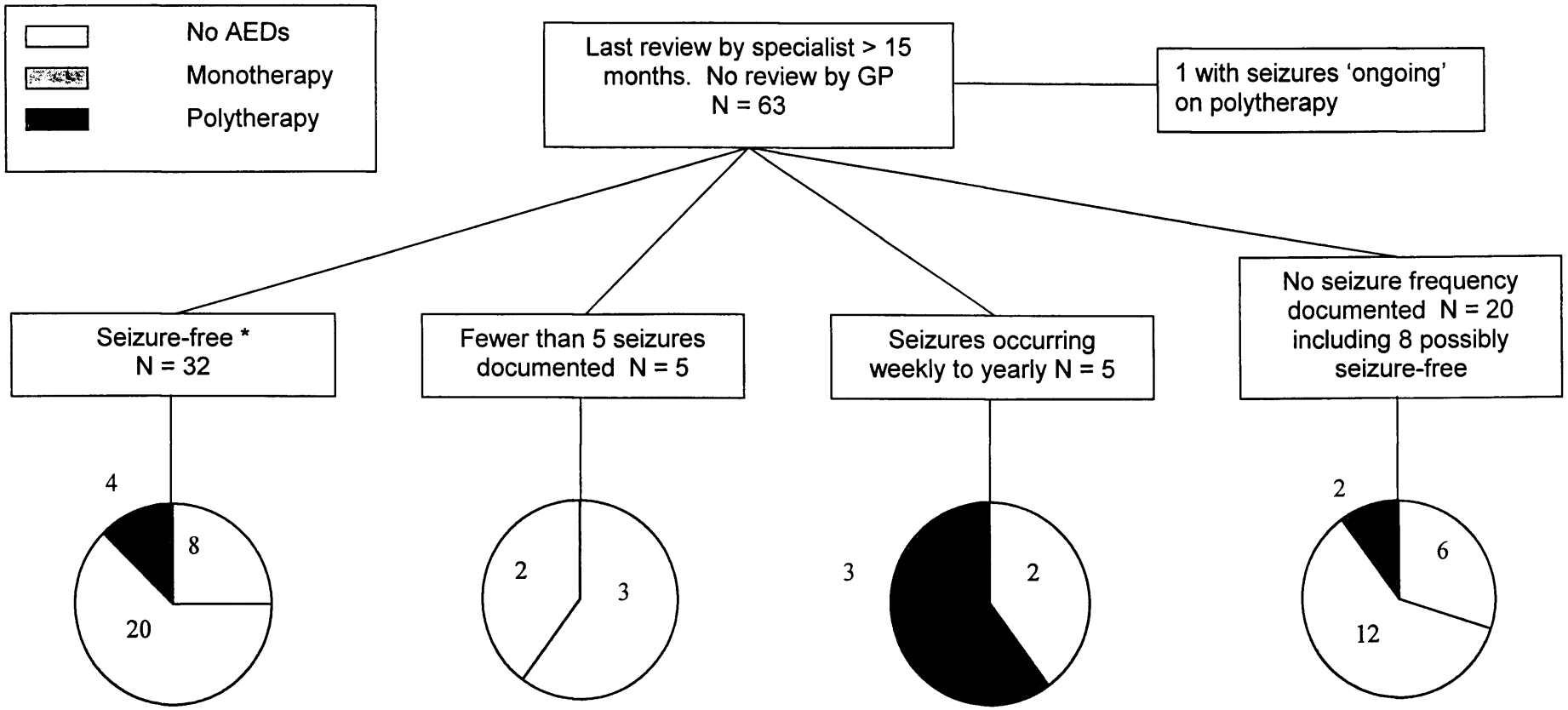


Figure A4: people with epilepsy with no review by GP and no recent review by specialist



* In one case 'epilepsy specialist' was an epilepsy specialist nurse

APPENDIX 3. ADDITIONAL TABLES FROM SECTION 4.3: THE SPECIALIST CARE SECTION OF THE NATIONAL SENTINEL CLINICAL AUDIT OF EPILEPSY-RELATED DEATH

Comparing care provided to those with learning disability and those not

Audit records with significant missing information are usually omitted from the relevant tables.

Table A1 Sentinel Audit (specialist care): overall standard of care in people with and without learning disability

	No learning disability		Learning disability		Total	
	N	%	N	%	N	%
Care adequate	48	41.7	18	27.7	66	36.7
Care inadequate	59	51.3	39	60.0	98	54.4
Major error in care	3	2.6	1	1.5	4	2.2
Care unclear	5	4.3	7	10.8	12	6.7
Total	115		65		180	

Table A2 Sentinel Audit (specialist care): death avoidable or not in people with and without learning disability

	No learning disability		Learning disability		Total	
	N	%	N	%	N	%
Death unavoidable	42	36.5	24	36.9	66	36.7
Death potentially avoidable	35	30.4	24	36.9	59	32.8
Death probably avoidable	12	10.4	4	6.2	16	8.9
Circumstances unclear	26	22.6	13	20.0	39	21.7
Total	115		65		180	

Documented history of seizures available

Table A3 Sentinel Audit (specialist care): seizure frequency noted at last consultation in people with and without learning disability

	No learning disability		Learning disability		Total	
	N	%	N	%	N	%
Seizure frequency documented	86	74.8	49	76.6	135	75.4
Not documented	29	25.2	15	23.4	44	24.6
Total	115		64		179	

Table A4 Sentinel Audit (specialist care): clear description of seizures recorded in people with and without learning disability

	No learning disability		Learning disability		Total	
	N	%	N	%	N	%
Clear description documented	99	86.1	52	81.3	151	84.4
Not documented	16	13.9	12	18.8	28	15.6
Total	115		64		179	

Investigations of epilepsy

Table A5 Sentinel Audit (specialist care): EEG in people with and without learning disability

	No learning disability		Learning disability		Total	
	N	%	N	%	N	%
Had EEG	80	69.6	47	74.6	127	71.3
OK for no EEG	13	11.3	2	3.2	15	8.4
No EEG, but needed	13	11.3	13	20.6	26	14.6
Need for EEG unclear	9	7.8	1	1.6	10	5.6
Total	115		63		178	

Table A6 Sentinel Audit (specialist care): neuroimaging in people with and without learning disability

	No learning disability		Learning disability		Total	
	N	%	N	%	N	%
Neuroimaging status satisfactory	97	84.3	39	60.0	136	75.6
Unclear – no clear description of seizure	4	3.5	9	13.8	13	7.2
Neuroimaging status not satisfactory	14	12.2	10	15.4	24	13.3
Need for neuroimaging unclear	0	0	7	10.8	7	3.9
Total	115		65		180	

Use of AEDs

Table A7 Sentinel Audit (specialist care): number of AEDs taken at the time of death in people with and without learning disability

Number of current AEDs	No learning disability		Learning disability		Total	
	N	%	N	%	N	%
0	10	8.7	5	7.9	15	8.4
1	56	48.7	19	30.2	75	42.1
2	33	28.7	26	41.3	59	33.1
3	15	13.0	9	14.3	24	13.5
4	1	0.9	1	1.6	2	1.1
5	0		3	4.8	3	1.7
Total	115		63		178	

Table A8 Sentinel Audit (specialist care): new AEDs taken by people with and without learning disability (in those taking AEDs)

	No learning disability		Learning disability		Total	
	N	%	N	%	N	%
No new AEDs	68	64.8	31	53.4	99	60.7
New AEDs	37	35.2	27	46.6	64	39.3
Total	105		58		163	

Comparing care provided in those with learning disability according to the suitability of specialist seen

Table A9 Sentinel Audit (specialist care): avoidability of death according to specialist seen

	Not satisfactory	Satisfactory	Good	Unclear	Total
Unavoidable	2	18	3	1	24
Potentially avoidable	6	13	3	2	24
Probably avoidable	1	2	1	0	4
Unclear	1	5	3	4	13
Total	10	38	10	7	65

Table A10 Sentinel Audit (specialist care): documented evidence of having seen a consultant according to specialist seen

	Not satisfactory	Satisfactory	Good	Unclear	Total
Yes, in last 3 appointments	8	26	5	1	40
Yes, at some stage	2	6	2	1	11
No consultant seen	0	6	3	5	14
Total	10	38	10	7	65

Documented history of seizures available

Table A11 Sentinel Audit (specialist care): seizure frequency noted at last consultation according to specialist seen

	Not satisfactory	Satisfactory	Good	Unclear	Total
Yes	6	31	8	4	49
No	4	7	2	2	15
Total	10	38	10	6	64

Table A12 Sentinel Audit (specialist care): clear description of seizures recorded according to specialist seen

	Not satisfactory	Satisfactory	Good	Unclear	Total
Yes	7	33	8	4	52
No	3	5	2	2	12
Total	10	38	10	6	64

Investigations of epilepsy

Table A13 EEG status according to specialist seen

	Not satisfactory	Satisfactory	Good	Unclear	Total
EEG status satisfactory	7	30	9	3	49
EEG status not satisfactory	3	7	1	3	14
Total	10	37	10	6	63

Table A14 Sentinel Audit (specialist care): neuroimaging status according to specialist seen

	Not satisfactory	Satisfactory	Good	Unclear	Total
Neuroimaging status satisfactory	6	26	4	3	39
Unclear – no clear description of seizure	2	3	2	2	9
Neuroimaging status not satisfactory	2	6	2	0	10
Need for neuroimaging unclear	0	3	2	2	7
Total	10	38	10	7	65

Use of AEDs

Table A15 Sentinel Audit (specialist care): number of AEDs taken at the time of death according to specialist seen

	Not satisfactory	Satisfactory	Good	Unclear	Total
0	1	3	1	0	5
1	4	9	3	3	19
2	4	18	2	2	26
3	1	5	3	0	9
4	0	1	0	0	1
5	0	1	1	1	3
Total	10	37	10	6	63

Table A16 Sentinel Audit (specialist care): use of new AEDs according to specialist seen (in those taking AEDs)

	Not satisfactory	Satisfactory	Good	Unclear	Total
No new AEDs	4	21	3	3	31
New AEDs	5	13	6	3	27
Total	9	34	9	6	58

Comparing care provided in those with learning disability according to whether or not a consultant was seen. (In six audit files it was not possible to establish whether or not the patient had ever seen a consultant.)

Table A17 Sentinel Audit (specialist care): death avoidable or not, according to whether a consultant was seen.

	No consultant seen	Consultant seen	Total
Unavoidable	2	19	21
Potentially avoidable	3	21	24
Probably avoidable	1	3	4
Unclear	2	8	10
Total	8	51	59

Table A18 Sentinel Audit (specialist care): use of AEDs according to whether a consultant was seen

	No consultant seen	Consultant seen	Total
0	0	4	4
1	2	15	17
2	4	21	25
3	1	8	9
4	0	0	0
5	1	2	3
Total	8	50	58