The Measurement of Outcome in the Treatment of Epilepsy

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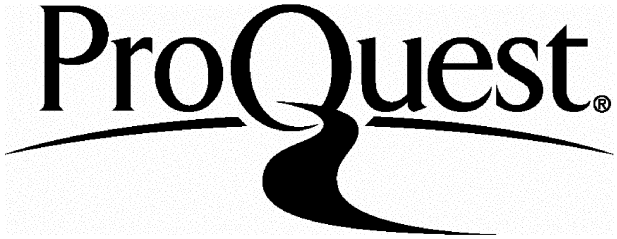

Abstract

Seizure frequency has until recently been the usual measure of efficacy of epilepsy treatment. The aims of this thesis were to develop and implement two new outcome measures of epilepsy therapy. A new seizure severity scale and a measure of the handicap associated with epilepsy were designed and evaluated. The psychosocial burden of epilepsy was assessed in an unselected population using the new measure of handicap. The benefits of epilepsy surgery and programs of comprehensive epilepsy assessment were investigated in patients with intractable seizures.

The new seizure severity scale was found to be reliable and to have construct validity. It is now in use in international antiepileptic drug trials. The Subjective Handicap of Epilepsy scale (SHE) was found to be a reliable and valid measure of the impact of epilepsy on the life of an individual with epilepsy.

In a unselected community-based sample of persons with epilepsy, the severity of subjective handicap was related to seizure frequency and to the duration of remission of epilepsy. A third of persons with active epilepsy were found to be significantly handicapped by their condition. Between a third and a half of subjects had psychiatric symptoms. Scores on a measure of general health indicated that active seizures and drug treatment both had detrimental effects on well-being.

In a longitudinal observational study, significant improvements in seizure control, subjective handicap, quality of life and psychiatric status were seen in 42 surgically treated patients compared with 82 subjects assessed for surgery but not operated upon. Compared with control groups, 67 patients who underwent a program of comprehensive assessment improved on some measures of quality of life and handicap. Remission of seizures had a primary role in achieving a major reduction in handicap and gains in quality of life.

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Author's contribution

The author conducted all the interviews and performed all of the developmental studies that resulted in the two scales described in this thesis. The author designed the new questionnaires and all the studies described herein. The conduct, recruitment, clinical data recording, follow-up and data entry for all the studies was done by the author. The author carried out all analyses using SPSS for Macintosh and a "4th Dimension" relational database (designed by the author using ACIUS, Inc. software).

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Section 1

Introduction and

Critical Review of the Literature

Introduction

Epilepsy is a common neurological disorder. For many patients the prognosis for ultimate seizure control is good with modern methods of treatment. For about 25% of patients, however, seizure control is not obtained. For these individuals, the condition may be associated with enduring social, psychological and vocational consequences. Until recently, methods of assessing the outcome of therapy have not considered the broader implications of chronic epilepsy. The primary aim of this thesis is to develop and implement novel outcome measures sensitive to these consequences of epilepsy.

A critical review of the literature concerning the natural history of epilepsy, the social and psychological consequences of the disorder and the available methods of outcome assessment was carried out. Having identified weaknesses in our understanding of outcome measurement, two new measures were developed. One of these was then used to assess the social burden of epilepsy in the community. A longitudinal study was also undertaken of two methods of treating severe chronic epilepsy: (i) epilepsy surgery and (ii) comprehensive epilepsy assessment at a residential epilepsy centre.

Critical Review of the Literature

1.1.0 Introduction

The literature will be reviewed with particular reference to the natural history of epilepsy, its social consequences and the outcome of the available forms of treatment. Special emphasis will be placed on the methods that have been developed to systematically measure the psychological and social impact of the condition. The review will be divided into two sections. The first starts with a brief historical account of ideas about epilepsy and its treatment. Epilepsy will then be defined and classified. A short account will be given of the causes and natural history of the disorder. The psychological and social effects of epilepsy will then be discussed in detail. The effect of medical, surgical and rehabilitative treatment will be described, focusing on how treatment affects seizures and social outcome. In the second section the principles of outcome measurement will be surveyed, and a detailed account will be given of the available methods relevant to epilepsy. The section will conclude by highlighting the deficiencies in our understanding of outcome measurement in epilepsy.

1.1.1 A historical review of ideas about epilepsy

Epilepsy has been recognised since antiquity. Accounts of seizures have been found in ancient Akkadian, Egyptian, Chinese and Babylonian sources (Temkin, 1971; Goldensohn, 1997). The first monograph on the condition appeared in the Hippocratic collection of medical writings entitled "On the Sacred Disease" (400 BC). The author anticipated by some 2000 years the idea that epilepsy was a disorder of the brain when he wrote:

> "the disease called Sacred is not, in my opinion, any more divine or more sacred than other diseases, but has a natural cause, and its supposed divine origin is due to men's inexperience, and to their wonder at its peculiar character" (Hippocrates, 1923).

The writer also understood the social effects of the disorder;

> "Such as are habituated to their disease have a presentiment when an attack is imminent, and run away from men, home, if their house be near, if not to the most deserted spot, where the fewest people will see the fall, and immediately hide their heads. This is the result of shame at their malady..."

The Romans, who called the disease the "morbus comitialis", had a superstitious view of epilepsy. Temkin quotes Pliny saying "epileptics drink the blood of gladiators, a thing horrible to see... they think it most efficacious to suck it as it foams from the man himself" (Temkin, 1971). Galen writing in the second century AD recognised that epilepsy was a disease of the brain, and that the brain could be affected primarily ("idiopathic') or secondarily ("sympathetic" epilepsy) (Temkin, 1971). He developed a theory in which a thick humour (phlegm or black bile) obstructed the outflow of the ventricles. He believed that convulsions possibly had a beneficial effect by expelling the noxious material. Treatment involved purgation, moderate exercise and attention to diet.

Medieval theories of epilepsy encompassed possession, lunacy, madness and contagion. The idea that epilepsy may be contagious may have accounted for the popular fear and stigmatisation of the "epileptic". Treatment included medicinal methods and the use of religious relics. The late eighteenth and early nineteenth century saw a more careful study of epilepsy under hospital conditions, chiefly in France, and the terms, Grand Mal, Petit Mal, absence, and etat de mal (status epilepticus) were introduced (Temkin, 1971). The second half of the nineteenth century saw rapid advances in both physiology and clinical observation. Jackson in 1873 defined epileptic seizures, as "the name for occasional, sudden, excessive, rapid and local discharges of grey matter", a

definition that is not out of place today. This period also saw an rise in interest in the medical and social treatment of people with epilepsy, particularly in specialized hospitals (The National Hospital for the Paralysed and Epileptic, Queen square, London, opened in 1860) and colonies (Bethel in Germany, founded in 1867, and The Chalfont Colony in Buckinghamshire, UK opened in 1894) (Holmes, 1954; Sander *et al.*, 1993) .

The twentieth century has seen an explosion in our understanding of the causes and mechanisms of epilepsy, great advances in its treatment, but many of the social consequences persist. It is only in the last twenty years that any systematic attempt has been made to assess the effects of treatment, and only in the last decade has this has included social and psychological outcomes (Trimble and Dodson, 1994).

1.1.2 Definitions and classifications

An epileptic seizure can be defined as "a clinical manifestation presumed to result from an abnormal and excessive discharge of a set of neurones in the brain". Epilepsy may be defined as a "a condition characterised by recurrent (two or more) epileptic seizures, unprovoked by any immediate identified cause..." (Commission on epidemiology and prognosis of the International League Against Epilepsy, 1993).

Epilepsy is very heterogeneous both in its clinical manifestations, the seizure types, and in its causes, the epilepsies and epileptic syndromes. Classificatory schemes for both seizure types and epileptic syndromes attempt to bring order to this complexity. Seizures are classified according seizure phenomenology (principally based on whether onset is focal or not, and whether consciousness is affected) as well on EEG criteria (Appendix 1). Epileptic seizures are a symptom of an underlying disturbance of the brain and as yet there is no classification based on a complete understanding of the aetiology of all types of epilepsy. Epilepsy syndromes that share common

features are classified using "The Classification of Epilepsies and Epileptic Syndromes" (Appendix 2). The main divisions are between the generalized syndromes, in which the initial epileptic manifestation involves both hemispheres, and the localization-related syndromes in which the seizures are of focal (partial) origin. The syndromes are subdivided into idiopathic epilepsies (age-related onset and a presumed genetic aetiology), symptomatic epilepsy (the consequence of a known brain disorder) and the cryptogenic epilepsies (whose cause is occult but presumed to be symptomatic) (Wolf, 1997).

1.1.3 The epidemiology and prognosis of epilepsy

Epilepsy is very common. The estimated annual incidence (the rate of occurrence of new cases) in developed countries is 24 to 53 per 100,000 (Hauser, 1997). If single seizures are included this figure is 86 per 100,000 (Hauser and Kurland 1975). The cumulative incidence rate of a diagnosis of epilepsy by the age of 75 is 2-4% (Hauser *et al.*, 1993). The age-specific incidence rate is greatest in the first year of life and in old age. Most studies have reported a slightly higher incidence in males. Several studies have found higher incidence rates in the developing world, though prevalence rates may not be different (Shorvon and Farmer, 1988). The prevalence (the number of established cases at any one time) is between 4-10 per 1000.

The risk of recurrence after a single seizure is estimated to be 78% at three years (Hart *et al.*, 1990). The risk is highest in the first 3 months after the first seizure, if the seizure is partial and in the symptomatic epilepsies. However, in general, the prognosis for remission of epilepsy is good, particularly in those without underlying neurological impairment. The chance of entering a period of five year remission within 9 years after an first seizure is 71% (Cockerell *et al.*, 1995). Over half of patients have less than 10 attacks in total (Goodridge and Shorvon, 1983). The influence of antiepileptic (AED) treatment on prognosis is controversial. Studies in populations never exposed to any AED treatment have suggested that about 50% of

persons enter remission spontaneously (Zhou, 1989; Keranen and Riekkinen, 1993; Mani *et al.*, 1993). The response to treatment also does not seem to be substantially prejudiced if treatment is delayed (Feksi *et al.*, 1991). The main determinant of prognosis for remission is the underlying aetiology (Sander and Sillanpää, 1997).

Epilepsy is associated with a two to three fold increase in age-standardized death rate, with accidents, suicide and epilepsy related deaths being particularly important causes of death (Nashef *et al.*, 1995). Sudden unexpected death in epilepsy occurs at a rate of 1/200 in those with intractable epilepsy (O'Donoghue and Sander, 1997).

1.1.4 The aetiology of epilepsy

Epilepsy has many different underlying aetiologies and the spectrum differs considerably from infancy to adulthood. In infancy and childhood the major causes are the idiopathic epilepsies of age-related onset and the symptomatic epilepsies (epilepsy secondary to congenital abnormalities, metabolic, infective and neuronal migration disorders) (Aicardi, 1994). In epilepsies of adult onset the commonest causes are cerebrovascular disease, tumours, alcohol, trauma and cerebral infection (Sander *et al.*, 1990). In many cases the cause remains unclear despite investigation, though with high resolution MRI imaging this is likely to decline. In the developing world infective causes are much more common (Bharucha and Shorvon, 1997).

In patients with intractable epilepsy who are considered for surgical treatment the commonest causes are hippocampal sclerosis, developmental lesions (such as dysembryoplastic neuroepitheliomas), low grade gliomas, arteriovenous malformations and cavernomas (Kim *et al.*, 1995).

1.1.5 The psychiatric associations of epilepsy

A number of issues have been discussed in the literature concerning epilepsy and mental health; the prevalence of psychiatric disorders in people with epilepsy, the

phenomenology of these disorders, non-epileptic attack disorder, the psychoses of epilepsy, personality disorder and the potential neurobiological links between epilepsy and psychiatric disorder. The first three of these will be discussed.

There are few reliable estimates of the prevalence of psychiatric disorder in people with epilepsy. Methodological problems abound in the literature, including the diagnostic criteria for epilepsy and "psychiatric caseness", selection bias and controlling for treatment and comorbidity. Methods of case finding have involved the use of validated questionnaires (Jacoby *et al.*, 1996; Ridsdale *et al.*, 1996), informal clinical assessment (Pond and Bidwell, 1960), and structured psychiatric interviews (Rutter *et al.*, 1970; Edeh and Toone, 1987). Many studies have used highly selected samples (Currie *et al.*, 1971; Kogeorgos *et al.*, 1982).

A number of population based studies have been carried out in the United Kingdom, using general practitioners' records for identifying cases of epilepsy. In 1960 Pond and Bidwell, in a study of adults and children, using a non-standardized interview, found an overall prevalence of 29% of any psychological disorder, and 50% in those with temporal lobe epilepsy (Pond and Bidwell, 1960). In 1987, Edeh and Toone, using a standardized psychiatric interview in adults on AED treatment (70% with active epilepsy) found 48% to have a psychiatric disorder, focal epilepsy again being associated with a higher rate (Edeh and Toone, 1987). Using the Hospital Anxiety and Depression scale (Zigmond and Snaith, 1983) for case identification, in a survey of treated adults (half with active epilepsy) Jacoby found 9% to be depressed and 25% anxious, the proportions doubling if seizures occurred more than once per month (Jacoby *et al.*, 1996). With similar methods, Ridsdale found 15% to be depressed and 30% anxious (Ridsdale *et al.*, 1996). Neither study included for comparison patients who had ceased AED treatment. Hospital based studies have found that about half of the patients had a psychiatric disorder (Currie *et al.*, 1971; Kogeorgos *et al.*, 1982). In children with epilepsy, Rutter found that 34% had a

psychiatric disorder, a rate five times that of the general population and three times that of children with other chronic disorders (Rutter *et al.*, 1970).

In a study of the phenomenology of depression in epilepsy, Robertson found about half the patients to have an endogenous depression, the severity of which was not related to seizure frequency. Treatment with phenobarbitone was a risk factor (Robertson *et al.*, 1987). Blumer has postulated that there may be a specific interictal dysphoric disorder which must be distinguished from ictal depression (Blumer and Altschuler, 1997).

Non-epileptic attacks (NEA - also known as psychogenic non-epileptic seizures or pseudoseizures) are commonly mistaken for epileptic seizures (Lesser, 1996). A population based study estimated the prevalence to be 5% of epilepsy cases (Scheepers *et al.*, 1998). About a quarter of referrals to a specialized epilepsy centre were found to have NEA (Riaz *et al.*, 1998). The attacks are frequently associated with anxiety, depression, family stress, and a history of sexual abuse (Lesser, 1996; Moore and Baker, 1997). Diagnosis and treatment is multi-disciplinary and requires an index of suspicion given the history of the attacks, prolonged observation with video of the attacks, post-attack prolactin measurement, EEG monitoring, and once the diagnosis is secure, psychotherapeutic intervention. There have been no controlled studies of outcome, but anecdotal evidence has suggested that about half become seizure free (Lesser, 1996; Aboukasm *et al.*, 1998).

1.1.6 Quality of life for people with epilepsy

There are a large number of studies exploring the impact epilepsy may have on the quality of life of the individual (Whitman and Hermann, 1986; Hermann, 1992; Trimble and Dodson, 1994). Four themes have dominated the literature: (i) surveys of selected, or unselected, populations of people with epilepsy to ascertain the prevalence of vocational, social and "quality of life" problems (Dodrill *et al.*, 1984;

Trostle *et al.*, 1989; Collings, 1990; Chaplin *et al.*, 1992; Jacoby, 1992; British Epilepsy Association, 1995) (ii) studies undertaken to reveal the cause of the psychosocial problems in epilepsy (for example medical versus social causes) (Whitman and Hermann, 1986; Collings, 1990) (iii) sociological studies of stigma and identity in epilepsy (Ryan, 1980; Schneider and Conrad, 1980; Dell, 1986; Scambler and Hopkins, 1990) and (iv) the measurement of quality of life outcomes of epilepsy treatment. The fourth topic has until recently received the least attention.

Surveys of people with epilepsy have revealed a number of core problems (Table 1.1). The frequency and severity of problems reported in studies has depended to a great extent on the population selected. Population based studies (Trostle *et al.*, 1989) and studies of people with well controlled epilepsy have revealed a low incidence of problems, with only minimal effect on employment and social disability (Jacoby, 1992; Jacoby, 1995). This is not the case for those with active epilepsy. A recent study of 4449 members of the British Epilepsy Association, of whom about 70% had active epilepsy, revealed that over 50% of respondents felt epilepsy affected their energy and drive, ability to concentrate, general health, sleeping habits, and that it limited work, physical and social activities (British Epilepsy Association, 1995). A similar "epilepsy self-help group" study in the USA demonstrated that emotional problems, worry and lack of confidence, job-related problems and lifestyle restrictions were felt to be "the greatest problem experienced because of epilepsy" (Arntson *et al.*, 1986). Jacoby has examined how the severity of epilepsy influences psychosocial well-being in a large community study using sound methodology (Jacoby *et al.*, 1996). The principle finding was that seizure frequency was the best predictor of self-reported quality of life. Once remission had been achieved, there was little evidence that duration of remission further affected quality of life, apart from an increased likelihood of being married or employed. Duration of epilepsy, however, was related to the incidence of depression and anxiety. Other clinical variables had little impact on quality of life. It should be noted that psychosocial

problems are common in the developing world as well, though this not been systematically studied (Shorvon and Farmer, 1988; Kleinman *et al.*, 1995).

Table 1.1 A summary of the major factors that have been reported as having a negative impact on the quality of life of people with epilepsy

Physical
Seizure frequency
Seizure severity
Tiredness and lack of energy
Sleep disturbance
Side-effects of medication
Seizure related injuries and incontinence
Impairments because of associated neurological disorder
Psychological
Anxiety and depression
Loss of self-esteem
Reduced self-confidence
Impaired concentration and cognition
Memory impairment
Fear of seizures or death in seizures
Unpredictability of seizures
Sexual difficulties
Social and vocational
Unemployment and underemployment
Loss of educational possibilities (secondary to illness)
Financial consequences of treatment, unemployment and insurance problems
Driving and travelling
Reduced rates of marriage
Limitation of leisure pursuits
Limitation of social activities
Stigma and embarrassment
Alterations in social development, family dynamics and over-protection

A population based investigation of people newly diagnosed as having epilepsy has demonstrated that many patients experienced "mild or moderate" problems soon after the diagnosis in several aspects of daily living (in particular fear of seizures, acceptance of the diagnosis, and worry about employment), but "severe" problems were found in less than 15% (Chaplin *et al.*, 1992). The best predictor of psychosocial problems was seizure frequency.

Studies of groups of people with particularly severe epilepsy have revealed a striking degree of social isolation and unemployment, many having few close friends and the majority having had no experience of paid employment (Thompson and Oxley, 1988). Sexual dysfunction, a neglected area of investigation, may be particularly common in intractable temporal lobe epilepsy (Morrell, 1991).

A number of studies have specifically explored the problems persons with epilepsy face with regard to employment. The main issues are: whether epilepsy causes unemployment and under-employment, whether it is associated with greater sickness and accident rates and whether there are specific factors that are associated with employment problems. Selection bias, the background unemployment rate and the effect of disorders associated with epilepsy all complicate the interpretation of studies of employment in epilepsy. In samples of well controlled epilepsy, employment is generally not a problem (Jacoby, 1995). In recent population-based studies in the United Kingdom of patients of employable age 50-75% were employed, which is lower then that expected (Elwes *et al.*, 1991; Hart and Shorvon, 1995; Jacoby *et al.*, 1996). A study in an area of high unemployment, found that people with epilepsy had disproportionately greater difficulty finding work, that unemployment was long-term, and that additional neurological or psychiatric impairments (progressive disorders excluded) increased the unemployment rate to 79% (Elwes *et al.*, 1991). Accurate information on underemployment is hard to come by. A number of reports, some rather dated, have suggested that it exists, both

in industry and in the service sector (Jones, 1965; MacIntyre, 1976; Dasgupta *et al.*, 1982; Lisle and Waldron, 1986). Accident and sickness rates have not been found to be increased amongst people with epilepsy (MacIntyre, 1976; Dasgupta *et al.*, 1982). Nevertheless, surveys have found employers to be reluctant to take on people with epilepsy (John and McLellan, 1988) and anecdotal evidence has suggested that disablement employment advisers find it hard to place people with epilepsy (MacIntyre, 1976). The factors predictive of success in finding employment include educational qualifications, previous work experience, intelligence and seizure control (Hauser and Hersdorffer, 1990). Longitudinal studies of unselected populations of children followed until adulthood have shown that epilepsy in childhood may lead to higher levels of unemployment, more low-status employment, and a lesser sense of well-being compared to children without epilepsy even after the disorder has remitted and treatment ceased (Harrison and Taylor, 1976; Britten *et al.*, 1986; Sillanpää, 1990).

Comparison of people with epilepsy and other chronic diseases with respect to quality of life are few, but one study has shown that epilepsy may affect quality of life more than hypertension or diabetes, but less than depression (Vickrey *et al.*, 1994).

1.1.7 Children and quality of life

The onset of epilepsy in a child can be traumatic for both the child and its family. The effect of this event on relationships within the family, in particular mother-child interactions, has been the focus of many studies (Hoare, 1988; Ferrari, 1989). The parental reactions to the diagnosis are varied, but include: anxiety, fear, denial, anger, and grief at the loss of "the perfect child". These concerns may affect the way parents subsequently treat their child with epilepsy. It is commonly held that this can result in over-protection and reduced expectations on the part of the parents and lead to dependency in the child (Hoare, 1984).

Chronic childhood epilepsy is associated with an increased risk of psychological morbidity. Studies have shown that up to 50% of children show evidence of disturbance usually in the form of neurotic or conduct difficulties (Rutter *et al.*, 1970; Hoare and Kerley, 1991). In the "Isle of Wight study", Rutter found a prevalence of psychiatric disorder of 11% in children with chronic physical disorders not involving the central nervous system, 30% in children with uncomplicated epilepsy, and 58% if a brain lesion and epilepsy was evident. A more recent Canadian community based study of children with epilepsy and normal intelligence, found that over a 7 years 23% had been referred to psychiatric services, and this was felt, on indirect evidence, to be twice that expected (Camfield *et al.*, 1993). Hoare, in a small study using a parent-completed questionnaire found evidence that children with epilepsy, compared to children with diabetes, had greater emotional dependency (Hoare, 1984). Similarly, Austin, using standardised rating scales, compared children with asthma to those with epilepsy, and found that those with epilepsy had more anxiety, more behaviour problems and worse school achievement (Austin *et al.*, 1994). Bagley has observed an interaction between the behaviour disturbance shown by the child (perhaps as a results of "organic factors") and the social and environmental pressures in the family (Bagley, 1971). Some investigators have found that epilepsy in a child can also have an adverse effect on the psychological health of the mother and siblings (Rutter *et al.*, 1970; Hoare, 1984), though this was not as marked in another study (Hoare and Kerley, 1991). Studies of parents of young adults with severe epilepsy have revealed that anxiety, depression and dissatisfaction with their social situation are common (Thompson and Upton, 1992).

It is evident from many studies that both biologic and family factors are important in causing psychosocial and behavioural difficulties (Hermann *et al.*, 1988; Hermann *et al.*, 1989). Biological factors include the degree of seizure control (Hermann *et al.*, 1988) and underlying cerebral damage (Rutter *et al.*, 1970). Antiepileptic

polypharmacy and, in particular, the use of phenobarbitone is well known to cause cognitive impairment, emotional and behavioural problems (Vining *et al.*, 1987; Hermann *et al.*, 1989) though this may improve on drug withdrawal (Cull *et al.*, 1992).

1.1.8 Other psychosocial issues

Many other areas of social research have been undertaken in epilepsy, of which only two will be mentioned in passing due to lack of space. Chief amongst these is stigma. Research has included the reasons for it, whether it is "felt" or enacted (i.e. actually experienced) and how stigma is managed by the patient (Schneider and Conrad, 1980; Britten *et al.*, 1984; Dell, 1986; Scambler and Hopkins, 1990). The second field of inquiry explores the opinions of people with epilepsy about their disorder and its treatment. These studies have revealed that coming to terms with epilepsy is an active process of rationalization which may not use a "medical" model (Scambler, 1994). Both these areas of research have underlined that patients are not passive recipients of "problems" but are usually actively engaged in coming to terms with their disorder.

1.1.9 The treatment of epilepsy

Once a secure diagnosis of epilepsy has been achieved the management of a patient will typically include; explaining the diagnosis, the cause and prognosis; and counselling about the legal, social and occupational implications of the diagnosis. The need for antiepileptic drug (AED) treatment must be assessed and the most efficacious and least toxic drug for a given patient selected. The patient also requires information on the potential side-effects (including those specific to conception and contraception) and seizure precipitant factors. Associated psychiatric or neuropsychological disorder may have to be evaluated and treated. For those who continue to have disabling seizures despite AED treatment an assessment of suitability for definitive or palliative surgery for epilepsy may be carried out.

1.1.9.1 Antiepileptic drug treatment

The decision to advise starting AED treatment requires both an awareness of the risk of recurring seizures for an individual patient (taking into account aetiology, frequency of seizures and other factors) and of the personal circumstances of the patient. The choice of antiepileptic drug traditionally has been dictated by the epilepsy syndrome, though the evidence for many of the recommendations is not robust.

1.1.9.2 The outcome of drug treatment

Recent studies have suggested that when newly diagnosed epilepsy is treated with one of the standard AED (carbamazepine, sodium valproate, phenytoin and phenobarbitone) the one year remission rate is 65-80% (Sander, 1993). Randomized controlled trials have shown that carbamazepine, valproate, and phenytoin are equally effective in controlling tonic-clonic seizures, whether primarily or secondarily generalized, in adults (Callaghan *et al.*, 1985; Mattson *et al.*, 1985; Turnball *et al.*, 1985; Mattson *et al.*, 1992; Richens *et al.*, 1994; Heller *et al.*, 1995) and in children (Verity *et al.*, 1995; de Silva *et al.*, 1996). One trial has found carbamazepine to be modestly superior to valproate in the control of complex partial seizures (Mattson *et al.*, 1992), whereas others have not (Richens *et al.*, 1994; Heller *et al.*, 1995; Verity *et al.*, 1995; de Silva *et al.*, 1996). Carbamazepine and lamotrigine are equally effective in monotherapy for newly diagnosed generalized seizures(Brodie *et al.*, 1995). Open observational studies have shown that valproate to be preferable in idiopathic generalized syndromes, especially in patients with juvenile myoclonic epilepsy (Covanis *et al.*, 1982; Collaborative study group: Bourgeois *et al.*, 1987; Panayiotopoulos *et al.*, 1994). Carbamazepine may worsen seizure control in patients with absences and myoclonic seizures (Shields and Saslow, 1983; Snead and Hosey, 1985). Ethosuximide and valproate have been found to be equally effective for absence seizures (Sato *et al.*, 1982). In an Italian

cohort, starting an AED after the first seizure (rather than the second) reduced from 40% to 20% the chance of further seizures, but had no effect on the ultimate prognosis (Musicco *et al.*, 1997).

1.1.9.3 Patients failing first line AED treatment

If first line AED therapy fails, adding a second drug is associated with complete seizure freedom in at most 10% of patients (Mattson *et al.*, 1985). A review of add-on therapy in patients with refractory epilepsy participating in recent trials of novel AEDs revealed that only 2% achieved seizure freedom (Walker and Sander, 1996). A meta-analysis of novel AED (gabapentin, lamotrigine, tiagabine, topiramate and zonisamide) used in an add-on setting and using a 50% seizure frequency reduction as a mark of success, has shown no conclusive difference in terms of efficacy or tolerability between the drugs with a typical responder rate of 25-50% (Marson *et al.*, 1996). The clinical relevance of a 50% reduction in seizure frequency is discussed in section 1.3.3.1.

1.1.9.4 Antiepileptic drug withdrawal

Once epilepsy has gone into remission the question arises whether treatment can be withdrawn. A randomized trial of withdrawal of treatment in patients free of seizures for 2 years, found that 78% of those remaining on treatment and 59% in whom it was withdrawn remained seizure free at 2 years (Medical Research Council, 1991). Jacoby examined the effect on quality of life of drug withdrawal (Jacoby *et al.*, 1992). The decision to randomise to AED withdrawal after 2 years seizure freedom had little effect on psychosocial outcomes, but relapse of seizures led patients rating themselves worse off on a few of the scales. Remaining on AED treatment also had a small detrimental effect.

1.2. The role of epilepsy surgery

1.2.1 Introduction

A significant fraction of patients continue having seizures despite AED therapy. In some of these, particularly those with well-circumscribed lesions, seizures may cease following surgical treatment. The major syndromes that are amenable to definitive surgical therapy are mesial temporal lobe epilepsy associated with hippocampal sclerosis and the lesional partial epilepsies, particularly when the pathology is dysembryoplastic neuroepithelial tumour, ganglioglioma, low grade glioma and cavernous angioma (Wieser *et al.*, 1993). Rasmussen's encephalitis, hemimegancephaly and childhood vascular insults can be successfully treated by hemispherectomy. A number procedures also exist when the pathology is diffuse (multilobar resection and corpus callosotomy), or when the pathology arises in eloquent cortex (multiple subpial transection). These techniques have been found to have a lower success rate (Engel *et al.*, 1993).

1.2.2 The prognosis of intractable epilepsy

In broad terms, the factors associated with a poor prognosis for seizure control are well known. These include epilepsy associated with gross structural or developmental pathology, progressive neurological syndromes and severe childhood epilepsy syndromes (e.g. Lennox Gastaut syndrome) (Sander, 1993). On a population basis, the prognosis for generalized as opposed to partial seizures and idiopathic as opposed to remote symptomatic epilepsy, in fact, have not been found to differ substantially (Annegers *et al.*, 1979; Cockerell *et al.*, 1997). It is likely that the broad classificatory scheme used in these studies hide important prognostic differences. The risk for intractability, given an initial period of poor seizure control, for individual epilepsy syndromes, defined by aetiology, is still incompletely understood.

1.2.3 Prognosis of temporal lobe epilepsy

There have been remarkably few prospective, population based, studies of the prognosis of typical mesial temporal lobe epilepsy. A follow-up study of 100 unselected prospectively collected (1948-1964) children with temporal lobe epilepsy (on clinical and EEG criteria) revealed that 32% entered long-term remission off medication without surgical treatment. If remission occurred, it always did so by the age of 16 years. A review of studies documenting prognosis in temporal lobe epilepsy has found a 30-50% remission rate (Hauser, 1991). An prospective population based study using modern definitions and MRI imaging has not yet been performed.

1.2.4 Syndromes amenable to epilepsy surgery

The commonest syndrome amenable to surgery is mesial temporal lobe epilepsy associated with hippocampal sclerosis. Characteristically it is associated with complicated febrile convulsions in childhood (Duncan and Sagar, 1987; French *et al.*, 1993), intractable complex partial seizures of temporal type (Engel *et al.*, 1997), a unilaterally small hippocampus on MRI (Williamson *et al.*, 1993) and a typical interictal EEG pattern (Williamson *et al.*, 1993). Characteristic surface ictal EEG (Risinger *et al.*, 1989; Ebersole and Pacia, 1996) and depth EEG findings have also been described (King *et al.*, 1997). There are material specific lateralized neuropsychological deficits (especially memory dysfunction) (Sass *et al.*, 1990; Rausch and Babb, 1993). The outcome after epilepsy surgery is usually good (Engel *et al.*, 1997). The particular clinical characteristics of the other lesional syndromes depend on the site and nature of the pathology and are beyond the scope of this introduction.

1.2.5 Selection of surgical candidates

A detailed discussion of process of selection of candidates for surgery will not be made. Typically, however, it involves the selection of patients that are refractory to

medical treatment, currently disabled by their seizures, have definite pathology on MRI imaging, have concordant EEG and neuropsychological findings and have the ability to withstand the surgery (medically and psychologically). In addition, the patient must have a realistic understanding how quality of life will be changed by becoming seizure free and must comprehend the risks of failure. The possible adverse effects, both neurological and neuropsychological, must also be understood. The standard forms of definitive temporal lobe surgery include; en-bloc anterior temporal lobectomy (Falconer *et al.*, 1955), selective amygdalo-hippocampectomy (a procedure that preserves lateral structures) (Wieser, 1988), lateral temporal lobe resections (Keogan *et al.*, 1992), and lesional surgery in the temporal lobe (with or without resection of mesial structures).

1.2.6 Outcome of epilepsy surgery with respect to seizure frequency

When interpreting studies reporting the outcome of temporal lobe surgery it must be borne in mind that they often vary with respect to outcome classification, duration of follow-up, patient selection and operative techniques. A widely used classification scheme is shown in Table 1.2. The scheme incorporates both seizure frequency as well as an implicit, though poorly specified, "quality of life" assessment. A large number of other classificatory schemes exist whose relationship to broader outcomes has been discussed by Vickrey (Vickrey *et al.*, 1995).

A survey of major centres performing epilepsy surgery (reported at the Palm Desert conference in 1991) provided an overview of the success of various types of procedure (Table 1.3). Studies at single centres have reported that 60-70% of patients with temporal lobe resections are seizure free at five years follow-up (Rougier *et al.*, 1992; Sperling *et al.*, 1996). Similar results were found after selective amygdalo-hippocampectomy (Wieser, 1998).

Table 1.2 Classification of post-operative outcome

Class 1	Free of disabling seizures (excludes postoperative seizures in the first few weeks)
	A. Completely seizure free since surgery
	B. Non-disabling simple partial seizures only
	C. Some disabling seizures after surgery, but seizure free for at least two years
	D. Generalised convulsions with antiepileptic drug withdrawal only
Class 2	Rare disabling seizures ("almost seizure free")
	A. Initially free of disabling seizures, but has rare seizures now
	B. Rare disabling seizures since surgery
	C. More than rare disabling seizures after surgery, but rare seizures for at least 2 years
	D. Nocturnal seizures only
Class 3	A. Worthwhile seizure reduction[a]
	B. Prolonged seizure free intervals, amounting to greater than half the follow up period, but less than 2 years
Class 4	No worthwhile improvement
	A. Significant seizure reduction
	B. No appreciable change
	C. Seizures worse

[a] Determination of "worthwhile improvement" will require analyses of additional data such as percentage seizure reduction, cognitive function, and quality of life.

from (Engel *et al.*, 1993)

Table 1.3 Outcome (percentage seizure free) for Temporal lobe and Neocortical resections (1986-1990) reported at the Palm Desert Conference, 1991; adapted from (Engel *et al.*, 1993).

	Temporal Lobe resections		Cortical Resections	
Outcome	Anterior Temporal Lobectomy	Amygdalo-Hippocamp-ectomy	Extra-Temporal Resections	Lesionectomy
Seizure free %	67.9	68.8	45.1	66.6
Improved %	24	22.3	35.2	21.5
Not improved %	8.1	9.0	19.8	11.9
Number of Operations	3579	413	805	293

Table 1.4 Outcome (percentage seizure free) for Hemisphere removals and corpus callosotomy (1986-1990) reported at the Palm Desert Conference, 1991; adapted from (Engel *et al.*, 1993).

Outcome	Hemispherectomy	Multilobar resection	Corpus Callosotomy
Seizure free %	67.4	45.2	7.3
Improved %	21.1	35.5	60.9
Not improved %	11.6	19.3	31.4
Number of Operations	190	166	563

Engel has emphasized that considerable change in seizure status may occur in the first post-operative years and that with prolonged follow-up approximately 20-30% may relapse (Engel, 1987). Patients who have occasional seizures during the first post-operative year have been found to have a 40% chance of remission at 5 years (Elwes *et al.*, 1991; Sperling *et al.*, 1996). Patients who have frequent seizures in the first year rarely become seizure free later (Elwes *et al.*, 1991). The outcome at 2 years is thus a very strong predictor of status at 5 years (Elwes *et al.*, 1991). Once a patient is seizure free for 2 years, relapses are said to be occasional seizures rather than intractable epilepsy (Elwes *et al.*, 1991). Patients with hippocampal sclerosis may be those at highest for late recurrence (Berkovic *et al.*, 1995).

The predictors of a good result after temporal lobe surgery have been the subject of many studies and include; finding a pathological lesion in the resected specimen (Duncan and Sagar, 1987; Berkovic *et al.*, 1995), a history of complicated febrile convulsion (Duncan and Sagar, 1987), a resectable abnormality on the MRI (Berkovic *et al.*, 1995), the extent of resection (Bengzon *et al.*, 1968; Nayal *et al.*, 1991; Wyler *et al.*, 1995) and the absence of frequent generalized seizures (Williamson *et al.*, 1993). Studies that have used multivariate models to predict the success of temporal lobe surgery have emphasised the role of unilateral hippocampal sclerosis on MRI, finding pathology in the resected specimen, unilateral interictal EEG abnormalities and the absence of frequent generalized seizures (Berg *et al.*, 1998; Radhakrishnan *et al.*, 1998).

A review of schemes classifying the outcome of epilepsy surgery has found wide variation in methodology (Vickrey *et al.*, 1995). Some schemes have used absolute seizure frequency, some percentage seizure frequency reduction, some a mixture of both and others have incorporated subjective outcomes. Simple partial seizures have been handled inconsistently. Vickrey evaluated how the schemes performed against a quality of life measure in a group of 133 adults after epilepsy surgery. The seizure

classification (over the last 12 months) that most closely reflected quality of life was: (1) completely seizure free (2) auras or 1 seizure with loss of consciousness (3) 2-12 seizures (4) more than 12 seizures.

No randomized controlled trial of epilepsy surgery versus medical therapy has ever taken place. Attempted trials have foundered due to poor recruitment (Dashieff *et al.*, 1994). Uncontrolled studies using medically treated historical controls have suggested that surgery is more effective in relieving seizures than medical therapy alone (Guldvog *et al.*, 1991; Vickrey *et al.*, 1995). Of 248 patients who were evaluated for epilepsy surgery in one North American centre, 60% of the operated and 11% of the non-operated medical controls had a good outcome at 5 years (seizure free or only auras post-operatively)(Vickrey *et al.*, 1995). Similar results were found in a retrospective comparison of 185 medically treated patients and 201 patients operated in Norway 1949-1988 (Guldvog *et al.*, 1991). Given the consensus that temporal lobe resections are highly effective in appropriate patients, it is unlikely that a randomized study will now ever be performed.

1.2.7 Neurological complications

The operative mortality rate after temporal lobectomy has been estimated to be about 1% (Jensen, 1975). In more recent series the rate was lower (Pilcher *et al.*, 1993). Mortality long after epilepsy surgery is usually due to epilepsy-related death or suicide (Jensen, 1975; Sperling *et al.*, 1996). Sudden unexpected death has been estimated to occur at a rate of 1-2/100 per year in patients whose seizures do not remit (O'Donoghue and Sander, 1997). Late mortality is, however, still lower than that expected for patients with intractable epilepsy (Jensen, 1975; Vickrey, 1997). A number of neurological deficits are recognised to occur after temporal lobe surgery (Table 1.5). The complications of extratemporal surgery are specific to the operative site. Hemispherectomy and corpus callosotomy have specific complications

(hydrocephalus or haemosiderosis and disconnection syndromes respectively) (Pilcher *et al.*, 1993).

Table 1.5 Complications of temporal lobe epilepsy surgery

Hemiparesis (permanent)	2%
Hemiparesis (transient)	4%
Minor visual field defect	50%
Quadrantanopia	2-4%
Hemianopia	2-4%
Aphasia (permanent)	1-3%
Aphasia (transient)	30%
Global amnesia	<1%
Infections	<1%
Cranial nerve palsies	1-3%

adapted from (Jensen, 1975; Pilcher *et al.*, 1993)

1.2.8 Psychiatric outcome

The psychiatric outcome of epilepsy surgery is largely determined by pre-operative psychiatric status and seizure outcome (Taylor, 1987). The major psychiatric complications after temporal lobe surgery include a short lived episode of depressive and anxiety, psychosis and suicide. Early studies have remarked on the beneficial effect of surgery on aggressive personality disorder (Taylor, 1972). Hyposexuality has been noted both before and after surgery (Taylor and Falconer, 1968; Jensen and Larsen, 1979).

1.2.8.1 Depression, anxiety and suicide

Depression and anxiety occurred in the first few months after temporal lobe surgery in 40-50% of patients in two prospective studies, but these were usually transient and

amenable to treatment (Blumer *et al.*, 1998; Ring *et al.*, 1998). Later episodes of depression have been said to relate to seizure relapse (Blumer *et al.*, 1998). Non-epileptic seizures have been reported to occur after surgery (Parra *et al.*, 1998). Suicide occurred after temporal lobe surgery in 9 of 193 patients of the Maudsley series (Taylor and Marsh, 1977), and 6 of 74 of the Danish series attempted suicide (Jensen and Larsen, 1979).

1.2.8.2 Psychosis

Two principal issues exist in connection with psychosis and surgery. The first is whether surgery influences the course of psychosis. In the Maudsley series, 16 of 100 were psychotic pre-operatively, and only 2 of them (not of schizophreniform type) improved (Taylor, 1972). In the Danish series only 1 of 11 became normal, though 5 "improved" (Jensen and Larsen, 1979). The second issue is whether psychosis develops de novo after surgery. This occurred in 7 of 84 of the Maudsley series and in 9 of 63 non-psychotic patients in Jensen's series, six of whom were seizure free. Other smaller series have also noted cases of de novo psychosis (Polkey, 1983; Stevens, 1990; Mace and Trimble, 1991). Trimble has suggested that patients with right sided operations are at greatest risk for new-onset psychosis (Trimble, 1992). Most centres have now stopped operating on actively psychotic patients, though not all, some arguing that seizure freedom remains a benefit (Reutens *et al.*, 1997). Paranoid psychosis has been reported after selective amygdalo-hippocampectomy in one study (Khan and Wieser, 1992), but not another (Naylor *et al.*, 1994). Psychosis may occur less often in patients operated on in adolescence (Fenwick, 1994).

1.2.9 Neuropsychological outcome

The literature on the neuropsychological effects of epilepsy surgery, in particular temporal lobectomy, is large and will not be reviewed in detail. Interpretation of the studies of cognitive outcome, however, requires consideration of the pre-surgical neuropsychological ability, the nature of tissue resected, the side and type of surgical procedure, the outcome in terms of seizures, the methods of assessment and the length of follow-up. Scores several months after temporal lobectomy on tests of general intelligence are not affected greatly (Saykin *et al.*, 1992). Declines in verbal and non-verbal memory have been often been noted after left and right temporal lobectomy respectively (Jones-Gotman, 1991). The greatest memory decline has occurred in those with high pre-operative scores and an intact hippocampus (Rausch *et al.*, 1997). Memory supported by the side opposite the operation has been noted to sometimes improve (Saykin *et al.*, 1992). Global amnesia has been recorded if there was bilateral hippocampal damage (Baxendale, 1998). A decline in naming ability has followed left temporal lobectomy, but this was seldom profound (Saykin *et al.*, 1992).

1.2.10 The social outcome of epilepsy surgery

1.2.10.1 Early studies

A land-mark series of studies was reported by Taylor and Falconer in 1968 on the psychosocial outcome of 100 consecutive patients submitted to temporal lobectomy (Taylor and Falconer, 1968). Though their sociological methods may now be criticised, their conclusions still hold true today. Surgery offered the best hope for a good social outcome, if the patient had been rendered seizure free and if the seizures themselves had been responsible for the preoperative social problems.

The multi-factorial nature of the outcome of surgery was revealed by a detailed analysis of the correlations between the biological and social data. The "social adjustment score", devised by the authors, was applied to the 100 patients before and

after surgery. The preoperative data was retrospectively culled from the patients' case-record and the postoperative scores were determined by personal interview. The social score rated 7 items: (1) domicile (2) the quality of family relationships (3) non-family relationships (4) the use of leisure (5) sexual adjustment (6) working ability and capacity (7) history of living in an institution. In each of these categories the patient was rated according to the opinion of Taylor. Inter-rater reliability was said to be satisfactory in a subsample of 10. Data on the validity of the method was limited. Total seizure relief occurred in 42% of patients and a further 20% had only occasional seizures. "Social adjustment scores" improved to some extent in 51%, with 17% moving from the abnormal to the normal range. Of those patients who showed some improvement 60% had been completely relieved of seizures and 24% were having occasional seizures. In the group as a whole, social status worsened in 12%. Seizure relief was a necessary factor to achieve improvement in psychosocial status, but for some patients it was not sufficient.

Preoperatively the correlates of poor social status were; an early onset of epilepsy, a low IQ, a family history of psychiatric disorder, a history of psychosis or psychopathy, and previous institutionalization. This suggested that a combination of more severe brain damage (low IQ and a greater duration of epilepsy) was interacting with other psychiatric factors to impede social adjustment. The best postoperative social adjustment was obtained by those patients with complete seizure relief, with evidence of mesial temporal sclerosis in the resection specimen and with an absence of psychiatric disorder.

The biggest improvements in social outcome occurred in working capacity and non-family relationships, with lesser or no improvement in use of leisure and sexual adjustment. This was interpreted as demonstrating that seizure relief can alter life in those situations in which seizures have a direct impact (the work place or with non-intimate relationships), but less so where internal drives were more important (sex

and intimate relationships). Psychiatric disorder was also associated with aetiologies of epilepsy that were less likely to respond to surgery. Patients with pathologies not restricted to a single focus, therefore at risk of intellectual and behaviour disorders, were also more likely to have encountered inadequate schooling and hence have had limited opportunities to develop social skills. Multi-focal damage therefore, had its impact through many pathways.

A number of other case series published before 1980 have documented the psychosocial outcome after temporal lobectomy. Jensen in a study of 74 patients found only 3 gained employment after surgery, 11 became dependent on disablement benefits and there were few gains in marital status (Jensen, 1976). The prospects for employment were much better in those operated before the age of 17 years. Two other small series have underlined that not everyone benefits from becoming seizure free (Ferguson and Rayport, 1965; Horowitz and Cohen, 1968).

1.2.10.2 Recent studies

The literature since 1980 turns on a number of themes: occupational outcome, psychosocial outcome, the determinants of outcome, surveys of patient satisfaction, the role of patient expectation, adjustment difficulties and formal studies using validated outcome measures. These will be reviewed.

1.2.10.3 Occupational outcome

A number of methodological issues need to be considered when reviewing the available studies. Unemployment and under-employment, "post-operative improvement" are variously defined and it can be difficult to disentangle preoperative work ability from outcome. Differences in employment and financial benefits between study countries also exist. Nevertheless most centres have reported some improvement in vocational status post-operatively (Augustine *et al.*, 1984; Khan and Wieser, 1992; Mihara *et al.*, 1994; Williams *et al.*, 1994; Sperling *et*

al., 1995; Kellett *et al.*, 1997; Lendt *et al.*, 1997; Reeves *et al.*, 1997), though not all (Guldvog *et al.*, 1991). All studies have found that seizure freedom and good preoperative educational and employment experience are important in maintaining employment post-operatively.

1.2.10.4 Psychosocial outcome

The definition of "psychosocial" outcome of epilepsy surgery has been even more problematical. The outcomes are often assessed by measures used by a single investigator (Guldvog *et al.*, 1991; Rausch, 1991; Khan and Wieser, 1992; Mihara *et al.*, 1994; Williams *et al.*, 1994; Kellett *et al.*, 1997; Lendt *et al.*, 1997). "Psychosocial outcome" has usually incorporated elements of behaviour, psychiatric symptoms, social functioning, employment, independence and life satisfaction. Generally, however, psychosocial functioning has improved after successful surgery (Hermann *et al.*, 1989; Hermann, 1990; Dodrill *et al.*, 1991; Rausch, 1991; Khan and Wieser, 1992; Chovaz *et al.*, 1994; Williams *et al.*, 1994). All studies have emphasized the role of seizure freedom in determining outcome. A multivariate analysis of factors associated with a good outcome has replicated Taylor's study that preoperative status and surgical success are both important (Hermann *et al.*, 1992). Benefits may, however, be delayed, as Bladin has found that one third patients have difficulties adjusting to successful surgery, mainly in the domains of family dynamics and the "burden of normality" (Bladin, 1993). Data on the psychosocial outcome of surgery on children is scarce but it may be particularly good (Hermann, 1990).

Studies of patient satisfaction have found 75% of patients believe they benefited from surgery (Passingham *et al.*, 1993; Guldvog, 1994). A number of investigators have reported that patients may have unrealistic expectations of the benefits of epilepsy surgery, particularly in the sphere of social and personal life and that this can be associated with subsequent dissatisfaction (Baxendale and Thompson, 1998;

Wheelock, 1998; Wheelock *et al.*, 1998; Wilson *et al.*, 1998). Patients who have practical and realistic expectations were more likely to consider surgery successful (Wilson *et al.*, 1998).

1.2.10.5 Studies using validated methods

Vickrey has developed a outcome measure for epilepsy surgery (ESI-55) (Vickrey *et al.*, 1992), based on the well established generic health status scale, the SF-36 (Ware, 1992). Using this it was found retrospectively that seizure free patients had a better quality of life than patients with auras, who in turn scored higher than those with residual seizures. Only one study has used the ESI-55 prospectively and compared the outcome of medically and surgically treated patients (McLachlan *et al.*, 1997). McLachlan studied 51 patients treated with temporal lobectomy and 21 patients treated medically because they were unsuitable for surgery. At 24 months patients who were seizure free and those with a 90% seizure reduction showed improvements on 5 of 10 scales of the ESI-55. Patients whose surgery was not successful had a decline in quality of life. The authors also noted that only 2 scales ("Health perceptions" and "Quality of Life") detected a treatment effect at 12 months post surgery, whereas at 2 years improvements in self-rated cognition, energy and social function became apparent. In addition, it was observed that young patients benefited the most.

1.2.11 Rehabilitation and intensive medical therapy

There is very little data on the impact of comprehensive medical assessment and rehabilitation despite the wide spread development of epilepsy centres. One uncontrolled study of prolonged in-patient treatment at an epilepsy unit has revealed improved seizure control and reduced drug side-effects (Theodore *et al.*, 1983). A study comparing outpatient treatment at an epilepsy centre with treatment at a university hospital found a higher incidence of side-effects at the epilepsy centre, but no conclusion about the broader impact of therapy could be drawn as no quality of

life assessments were made (Lammers *et al.*, 1994). A randomized controlled trial of epilepsy care carried out at an epilepsy clinic compared with a general neurology clinic reported no difference in seizure frequency at 12 months, but found in favour of the epilepsy clinic in terms of drug toxicity (Morrow, 1990).

Thompson has described the profound psychosocial effects that occur in patients with severe intractable epilepsy (and their carers) and made recommendations for its alleviation, chiefly with the use of residential multi-disciplinary assessment and rehabilitation (Thompson and Oxley, 1989; Thompson and Upton, 1992; Thompson and Shorvon, 1993). However, very little is known about the outcome of such interventions. A number of descriptive studies of varied types of rehabilitation have been performed, which claim that benefits do arise following treatment (Freeman and Gayle, 1978; Fraser *et al.*, 1983; Beran *et al.*, 1987). None have involved validated outcome measures or a control group and so no reliable conclusion can be drawn.

1.2.12 The role of general practice in epilepsy care

The majority of people with epilepsy receive their care in general practice, with about 50% of patients seeing their general practitioner at least once a year for this purpose (Buck *et al.*, 1996). In a population based sample, 81% of patients with epilepsy had been seen in an hospital clinic at some time, but only 28% were under active follow-up and only 6% attended a specialist epilepsy clinic (Hart and Shorvon, 1995). A number of Government reports have highlighted deficiencies in epilepsy care and made recommendations for improving the situation (Central Health Services Council, 1956; Central Health Services Council, 1969; Department of Health and Social Security, 1986). Chiefly, these are; the central role of the general practitioner in continuing care, the role of the specialist in diagnosis and initial management, the need for specialist clinics for patients with difficult to control epilepsy, greater attention to social issues and fostering of better links between primary and secondary care. Audits of care in general practice have often revealed that in reality both the

process and outcome of care is not optimal (Jones, 1980; Cooper and Huitson, 1986; Hall and Ross, 1986; Buck *et al.*, 1996; Jacoby *et al.*, 1996; Redhead *et al.*, 1996; Ridsdale *et al.*, 1996). The deficiencies noted have included poor recording of epilepsy data that affect management (Jacoby *et al.*, 1996; Ridsdale *et al.*, 1996), insufficient information given to patients about epilepsy (Jones, 1980; Cooper and Huitson, 1986; Buck *et al.*, 1996) and a lack attention to social and psychological issues (Jones, 1980; Cooper and Huitson, 1986; Buck *et al.*, 1996; Ridsdale *et al.*, 1996). Only one study has examined the impact of social problems in general practice with validated methods (Buck *et al.*, 1996; Jacoby *et al.*, 1996). The authors noted that patients particularly valued more information about epilepsy. More optimistically it has been found that repeated audit cycles can improve both the process and outcome of general practice care (Taylor, 1987; Redhead *et al.*, 1996). Prospective studies using validated methods have, however, not been performed.

1.3 Outcome measurement in medicine

1.3.1 Introduction

The last 40 years has seen an explosion of interest in improving the methods of assessing the outcome of medical care. Reasons for this include the increasing incidence of chronic conditions, the realisation that the side-effects of therapy may be as much a burden to the patient as the disease itself and the rise of "evidence-based" medicine. Health status scales have become integral to outcome measurement. They can be specific to one disease, or suitable for any disease (generic scales). Most scales generate a multidimensional profile, covering physical, emotional and social of aspects of disease. Some scales produce a single number that summarises the health state. Health economists have used single index scales and subjected them to "valuations" by panels of experts and lay people to derive "utilities". These can then be used in cost-utility analyses of medical interventions. The validity of quality of life measurement and the ethics of using these techniques for resource allocation, has been the subject of considerable philosophical discussion (Griffin, 1986; Carr-Hill and Morris, 1991; Nussbaum and Sen, 1993; Nordenfelt, 1994). A detailed account of these important theoretical issues is beyond the scope of this introduction, but four topics will be mentioned. First, what constitutes a good "quality of life" and how should this inform the content of scales? Three broad approaches exist: (1) that it consists of certain conscious experiences: pleasure, happiness and the absence of pain - the "hedonist" theory (2) that it consists of the fulfilment of one's desires (which may or may not be well informed) (3) that it consists of the realization of certain objective values (Brock, 1996). Second, are quality of life scales objective or subjective measures ? At first glance they appear to be subjective. Indeed, they are, but they must also be related to objective facts for the judgements to be intelligible (Griffin, 1986). Third, is quality of life actually measurable and can interpersonal comparisons be made? Griffin has argued affirmatively to both as long as a purely hedonist theory of quality of life is rejected (Griffin, 1986). Finally, even if quality of life can be measured, how are these

measurements to be "valued" and how is this information to be used in an ethical allocation of health care resources ? There is no acceptable answer at present, though the pressure to make such judgements is rising.

1.3.2 Methodology

Considerable methodological care needs to be taken when assessing complex outcomes such as disability and personal well-being. The technical literature on this is now very large (McDowell and Newell, 1987; Bowling, 1991; Wilkin *et al.*, 1993; Streiner and Norman, 1995). Whether health status questionnaires form an "ordinal" or an "interval" scale is much debated and has implications for both statistical analysis and interpretation (Streiner and Norman, 1995). The traditional view, based on Stevens's theory of levels of measurement, was that scales were at best ordinal and that parametric statistics were not permissible. Current thinking, derived from operational theory, maintains that the numbers derived from scales are not in a direct empirical relation with an "objective" entity. They are measurements because the numbers result, relatively consistently, from a set of precisely defined operations (i.e. applying the scale). Applying scales at different times and to groups of people under different conditions therefore generates quantitative relationships. As long as the relationships are monotonic and the distributional assumptions are met, then parametric statistics are permissible (Mitchell, 1986; Davison and Sharma, 1988).

For a scale to be useful the extent of measurement error should be known and small compared to the phenomenon under observation. In the context of health measurement scales this is known as reliability. Internal consistency and test-retest reliability are two forms of reliability that are typically reported for a scale. Internal consistency is a measure of the degree to which the items in the scale measure a single underlying concept. The procedure examines whether all the individual questions (items) selected for use in the scale are a reliable estimate of all the items that could hypothetically be chosen. The idea is derived from the "domain-sampling" model of reliability theory, which states that there a large number of

questions that could be asked about any given topic and that the items selected in a scale are merely a random sample from this "domain". The correlation between a total score obtained using the actual scale and a hypothetical true score is the reliability index of the scale. The "true score" is never known, but can be estimated using the average correlation amongst the items. Cronbach's coefficient alpha is the statistical technique for measuring internal consistency, and an alpha of 0.7-0.9 is often recommended (values exceeding 0.9 suggest redundancy of items).

Test-retest reliability examines the stability of measurement over a short period of time, typically a few days, during which no change should have occurred to the attribute. The results are expressed using an intraclass-correlation coefficient (ICC) (Shrout and Fliess, 1979) or the method of Bland and Altman (Bland and Altman, 1986). A Pearson correlation coefficient is not infrequently used in the literature, though this is incorrect as it is insensitive to systematic differences in scores (bias). The required reliability depends on what is considered acceptable for a particular study, an ICC of 0.8-0.9 being a typical value. Greater reliability is required when the score is applied to an individual than in a group study. Unfortunately, reliability data has often been presented as though it applied to the scale independent of the conditions of use.

An obvious requirement of a scale is that it should measure what it claims to measure. This is referred to as validity. Validity can also be thought of as the type of conclusions the scale correctly allows one to make about the object under study. The same scale can lead to correct predictions in one context and erroneous ones under different conditions. The three major forms of validity are: content validity (the coverage of the important aspects under investigation), criterion validity (performance against a "gold standard") and construct validity (how successfully the results predict or explain hypotheses derived from theory) (Nunnally and Bernstein, 1994). Other forms of validity include convergent validity (the correlation with a

scale measuring a similar attribute) and divergent validity (the failure to correlate with a scale measuring an unrelated health concept). Any scale should also be acceptable to the subjects on whom it is to be used, particularly with regard to ease of completion. Finally, the scale needs to be responsive to those changes in health status that medical interventions are likely to produce.

1.3.3 Outcome measurement and epilepsy treatment

Until recently, seizure frequency has been the standard end-point in epilepsy surgery and trials of new AED. However, seizure severity, anti-epileptic drug side-effects and health related-quality of life are now increasingly recognised as important aspects of epilepsy (Trimble and Dodson, 1994).

1.3.3.1 Seizure frequency

There are several problems with using seizure frequency as the only outcome measure in epilepsy. Firstly, the error that occurs in counting seizures, particularly with frequent brief partial seizures, during AED trials has never been formally examined. Secondly, the benefit to a patient of a 50% reduction in seizures, the usual criterion of effectiveness in clinical trials, is unclear. There is no evidence from the available literature that a 50% reduction in seizures is related to broader health gains. Some have advocated using seizure freedom as the key index in AED trials (Walker and Sander, 1996). However, as seizure freedom currently occurs in less than 5% of patients in add-on trials of the new AED, this is an insensitive measure. Some investigators have used survival anaysis (e.g. time to first seizure) instead of seizure frequency as an outcome measure, though without any evidence as to how the two are related. A third issue is the validity of comparing changes in seizure frequency for seizures of differing severity (to be discussed further in section 1.3.3.2). A fourth issue is the appropriateness of the statistical models typically used in the analysis of seizure data. Seizure counts are assumed to be random events, however, there is evidence that they deviate from a random Poisson distribution.

Clustering, time-trends and regression to the mean have all been reported to be important effects (Spilker and Segreti, 1984; Hopkins *et al.*, 1985; Albert, 1991; Balish *et al.*, 1991). Two implications are that sample sizes calculations currently in use may be underestimates and that baseline observation periods may be too short.

1.3.3.2 Seizure severity

The concept of seizure severity arose from the observation that patients sometimes report changes in the severity of their habitual seizures independent of changes in seizure frequency. This change in severity may be reflected, for instance, in quicker recovery from seizures, fewer falls or injuries, or less disruptive automatisms. The first attempt to incorporate seizure severity in evaluations of AEDs arbitrarily weighted generalised tonic clonic seizures with a fixed score twice that of partial seizures (Gruber Jr *et al.*, 1957; Cereghino *et al.*, 1974). In 1978 the Department of Veterans Affairs (VA) co-operative study of antiepileptic drugs developed a composite scale in order to provide standardised end-points for use in multi-centre trials of new antiepileptic drugs (Cramer *et al.*, 1983). The scale used values, chosen by an expert panel, for seizure frequency, seizure severity and drug side-effects and them combined them into a single score. Recently, three scales have been developed specifically to measure seizure severity: the Liverpool seizure severity scale (Baker *et al.*, 1991), the Hague seizure severity scale (Carpay *et al.*, 1996) (a version for children derived from the Liverpool scale) and the Chalfont seizure severity scale (Duncan and Sander, 1991).

1.3.3.2a The Liverpool scale

The Liverpool seizure severity scale (LS) scale is a patient-administered questionnaire of 16 items (Baker *et al.*, 1991) consisting of 2 subscales, a 10 question scale ("ictal" scale) measuring ictal and post-ictal phenomena and a 6 question scale ("percept" scale) related to the predictability and impact of seizures. The items, which were chosen by an expert panel, include objective seizure related events and

the subjectively perceived severity of each seizure. A revised scale, with additional items has been developed after it was observed that patients confused their seizure types (Baker *et al.*, 1998). Further developmental work is underway, including a scale to be completed by parents for trials involving children and translations of the scale into other languages (Smith *et al.*, 1995).

Reliability data have been presented in the form of a test-retest Pearson correlation coefficient of 0.8 for both subscales and a Cronbach's alpha of 0.85 for the ictal scale and 0.69 for the percept scale (Baker *et al.*, 1991). The more appropriate intraclass correlation coefficient and Bland-Altman method were not reported. Validity of the scale has been explored by demonstrating that the scores on the LS "ictal scale" of simple partial, complex partial and generalised seizures were all significantly different from one another. This did not apply to the percept scale. A further study has shown that the percept subscale has low internal consistency and failed tests of item discriminant validity (Wagner *et al.*, 1995). The revised LS has been found to be reliable and the scale discriminated between different seizure types (Baker *et al.*, 1998).

1.3.3.2b The Hague scale

The Hague scale (HS), developed by Carpay and colleagues in the Netherlands, is a 13 item scale which is completed by a parent about their child (Carpay *et al.*, 1996). It is based very closely on the Liverpool scale, but contains 4 new items. Responses are on a four point Likert scale and all questions are a subjective evaluation of the frequency or severity of certain seizure related events. The scale is completed as an overall assessment of the seizures, rather than for each seizure type independently. This is likely to lead to confusion if changes occur to one type of seizure and not another. The scale was found to be internally consistent and test-retest data on 18 respondents suggested the scale was adequately reliable, but a larger sample would be needed to confirm this.

1.3.3.2c The Chalfont scale

The original Chalfont seizure severity scale (CS) was a 11 item scale focusing solely on the objective clinical events of a seizure. It was administered by interviewing a patient and a witness to the seizures (Duncan and Sander, 1991). Like the LS, the scale was applied to different seizure types separately, but unlike the LS the differentiation was made on the basis of clinically classifying the seizures into distinct types. The scale's content was derived from open interviews with people with epilepsy. Most items had a 5 point Likert scale scoring system based on the frequency of occurrence of that item. The scoring of the scale was derived using a combination of patient and expert opinion in order to create an acceptable ranking of scores for different seizure types. The scale has been reported as sufficiently reliable in both inter-observer and test-retest settings (Duncan and Sander, 1991). The CS has face and content validity but no independent construct validity has been published. The scoring system is rather complex.

1.3.3.2d Comparing the scales

The LS and HS differ from the CS in one important respect. The LS and HS include items which are entirely subjective (e.g. "my seizures have mostly been: very severe, severe, mild, very mild...). The CS scale however focuses only on objectively determinable events. The reason for this difference is that the developers of the CS scale believed it better to separate subjective and objective issues into separate scales. The validity of subjective questions about events for which the person is unaware is very questionable. A formal comparison of the two scales has not yet been undertaken. The CS requires further validatory evidence and a simplification of the scoring method.

1.3.3.2e Outcome studies using seizure severity

Seizure severity, as measured by the LS, has been shown to be associated with aspects of psychological well-being (as measured by anxiety and self-esteem scales) (Smith *et al.*, 1991). The LS "ictal subscale" has been shown to be responsive to change in an add-on placebo controlled trial of Lamotrigine (Smith *et al.*, 1993). It remains to be determined whether the small reduction in seizure severity observed (about 5%) in favour of Lamotrigine was of material benefit to the patients, although the fact that some patients chose to continue with Lamotrigine despite a lack of reduction in seizure frequency suggested that seizure severity may have played a role. Other AED trials using the LS are currently underway.

1.3.3.3 Measuring the side-effects of antiepileptic drugs

Two scales have been published to measure the impact of antiepileptic drug side-effects (Gillham *et al.*, 1996; Aldenkamp and Baker, 1997) and a further unpublished scale is in use as part of the Liverpool quality of life model. The Side-effects and life satisfaction scale (SEALS) is a 50 item scale (Gillham *et al.*, 1996), from which 5 factors were extracted by factor analysis (accounting for about half the variance). These factors were: cognition, dysphoria, temper, tiredness and worry. It has been shown to have adequate test-retest reliability and to be sensitive to side-effects of anti-epileptic drugs. Used in a prospective controlled comparison of lamotrigine and carbamazepine, the SEALS scale found lamotrigine to be the better tolerated drug (Gillham *et al.*, 1996). The Neurotoxicity scale, developed in the Netherlands, is a 24 item scale with a 5 factor structure (explaining 66% of the variance) (Aldenkamp and Baker, 1997). Fatigue and cognitive slowing were the major factors. The scale has a number of flaws: the wording of the questions is poor (e.g. "It costs more time for me to get started"), the test-retest reliability is unknown and the scale was not able to discriminate between patients on polytherapy and monotherapy. The scale can not be recommended.

1.3.4 The measurement of quality of life in epilepsy:

A number of instruments exist that measure the psychological, social and vocational impact of epilepsy. More recent scales have been developed explicitly within a framework of "quality of life measurement". These will now be reviewed in detail.

1.3.4.1 Washington Psychosocial Seizure Inventory

The first instrument designed to investigate the broader psychological and social consequences of epilepsy was the Washington Psychosocial Seizure Inventory (WPSI)(Dodrill *et al.*, 1980). The scale was intended to be "*...a systematic and objective evaluation* of the extent of psychosocial problems in areas important for epileptics".

1.3.4.1a Content, reliability and validity

The content of the measure was determined by a panel of experts in epilepsy. The scale includes eight domains as shown in Table 1.6. A review of studies using it is available (Dodrill and Batzel, 1994). An assumption underlying the scale is that scores on the WPSI subscales should correlate highly with an expert's opinion about an individual. Dodrill applied the self-rated scale to 127 patients with epilepsy and then determined the correlation of a professional rating of the individual. The items were placed in their respective subscales in order to maximise agreement with the expert rating. Test-retest reliability (over 30 days) and internal consistency were found to be acceptable, though the former was carried out on only 21 subjects and was not reported with an ICC. A version for use in adolescents has also been produced (Batzel *et al.*, 1991). The assumption that the scale items must correlate with an observers opinion can be challenged, as there is clear evidence that patients and observers disagree in health status evaluation (Slevin *et al.*, 1988; Sprangers and Aaronson, 1992; Hays *et al.*, 1995). The rejection of items because they correlated poorly with an observer has threatened the validity of a scale. The yes/no response format of the WPSI has limited sensitivity of the scale. About 10% of the items on

the scale relate to problems in the past (e.g. were you usually happy as a child ?). These are unlikely to change and hence are not useful as an outcome measure.

1.3.4.1b Studies using the WPSI

Dodrill has investigated the psychosocial problems of adults with epilepsy at five centres across the USA (Dodrill *et al.*, 1984). The groups were a selected sample of 315 people seeking assistance from specialised epilepsy centres or epilepsy societies, and one group of patients attending private neurologists in Mississippi. Overall, 50% of people were classified as having "definite" or "severe" emotional, interpersonal, or vocational difficulties in daily life. The "problem profiles" from the five centres were all very similar, except that patients of private neurologists reported fewer financial problems. A community-based USA sample (in which 69% of patients had not had a seizure within 12 months) found that only 19% had major difficulties (Trostle *et al.*, 1989). In an examination of the impact of the severity of epilepsy on psychosocial functioning, a non-significant trend in WPSI scores by seizure frequency was found. This relationship was confirmed in another study in which a particularly high incidence of psychosocial difficulties occurred in people with more than 100 life-time tonic-clonic seizures (Dodrill, 1986). A comparison of psychosocial difficulties in the USA, Canada, Finland and Germany established that emotional and social problems were common to all countries, but the impact of vocational and financial problems related to the degree of support provided by government agencies (Dodrill *et al.*, 1984).

Table 1.6 The Washington Psychosocial Inventory

Subscale	Underlying constructs
Family background	Problems during childhood, such as lack of security within the family circle or school may lead to psychological difficulties in adult life.
Emotional adjustment	Problems with anxiety, depression, and poor self image may occur in people with epilepsy.
Interpersonal adjustment	Lack of friends, discomfort in social situations and difficulties with the opposite sex are key psychosocial difficulties for people with epilepsy.
Vocational adjustment	People with epilepsy are at risk of employment difficulties and may request vocational counselling.
Financial status	Financial insecurity is a problem for some people with epilepsy.
Adjustment to seizures	People with epilepsy may bear feelings of resentment and embarrassment towards their seizures.
Medicine and medical management	The concern expressed by physician's towards patients and patient compliance are important in regard to optimum treatment.
Overall psychosocial functioning	An index of adjustment and need for psychological help

Table 1.7 The ESI-55 indicating the source of the items

ESI subscales	SF-36 items	New items
Health perceptions	5	4
Energy and fatigue	4	0
Overall quality of life	0	2
Social function	2	0
Emotional well-being (Mental Health)	5	0
Cognitive function	0	5
Physical function	10	0
Pain	2	0
Role limitation (physical health)	4	1
Role limitations (emotional health)	3	2
Role limitations (cognition / memory)	0	5
Global change	1	0

1.3.4.2 Epilepsy Surgery Inventory (ESI-55)

Vickrey developed the ESI-55 to assess the outcome after epilepsy surgery (Vickrey *et al.*, 1992). In order to allow comparisons between epilepsy and other diseases, Vickrey combined a widely used generic health status measure known as the SF-36 (Ware, 1992) with 19 new items, chosen by a group of "experts" as being relevant to epilepsy. Particular emphasis was placed on a rigorous statistical and psychometric evaluation of the items.

1.3.4.2a Content

The 55 items in the scale make up 11 subscales and one global change item as shown in Table 1.7. In addition the results can be reported with 3 summary scales: "physical", "mental" and "role-functioning". The scale makes use of the concept of "role", which refers to the ability to carry out the type of everyday activity that would be usual for a given individual (work, study, housework etc.). The scale asks whether physical, emotional or cognitive difficulties affect "role-functioning". The principal addition in the ESI-55 to the SF-36 are 10 items tapping cognitive functioning. There are no questions that relate specifically to the social, occupational or stigmatising effects of epilepsy. Indeed, it has been pointed out that the scale has a strong emphasis on "functioning" and does not appear to be derived from a "patient-based account" of quality of life (Hunt and McKenna, 1995). Only two of the ESI-55 questions can be considered as specific to epilepsy.

1.3.4.2b Reliability and validity

The scale has been validated and tested for reliability in a population of epilepsy surgery patients (Vickrey *et al.*, 1992). Internal consistency was found to be acceptable for all but one of the scales. Test-retest reliability has subsequently been reported to be adequate for some of the subscales (Wagner *et al.*, 1995). Six of the subscales had more than 50% of subjects on the maximum score possible. Similar findings occurred in a sample of people with more severe epilepsy (Wagner *et al.*,

1995). The scores on the ESI-55 were found to be related to different seizure outcomes after epilepsy surgery. A comparison of the WPSI and ESI-55 has showed the latter to be more responsive to change (Wiebe *et al.*, 1997).

1.3.4.2c Studies using the ESI-55

Using only the SF-36 component of the ESI-55 Vickrey has shown that patients who were seizure free after surgery had a better quality of life than did a sample of patients with diabetes, hypertension or heart disease (Vickrey *et al.*, 1994). Patients with recurrent seizures scored worse in several areas than these "medical" groups except for the depressed patients, who were even worse. The SF-36 was sensitive to seizure frequency and to the side-effects of anti-epileptic drugs ("social functioning" and "mental health" scales) (Wagner *et al.*, 1995).

1.3.4.3 Quality of Life in Epilepsy Inventory (QOLIE)

Having noted the weaknesses of the ESI-55, the QOLIE development group set out to produce a more comprehensive instrument to measure the quality of life in people with epilepsy. The instrument was designed to be both a research and a clinical tool. A major role for the scale was envisaged to be the evaluation of new antiepileptic drugs, epilepsy surgery and other therapeutic interventions (Devinsky *et al.*, 1995).

1.3.4.3a Content

Three QOLIE scales of different lengths have been developed, one of 89 items, one of 31 and one of 10 items. The later was intended as a screening tool for use in a doctor's office before a consultation (Cramer *et al.*, 1996). The QOLIE-31 has been translated into several languages and scores on the QOLIE-31 have been found to be related to various measures of severity of epilepsy, to AED toxicity and to mood (Cramer *et al.*, 1998). The contents of the QOLIE-89 is shown in Table 1.8. All the scales are scored from 0 to 100, with 100 representing a higher quality of life. An overall score consisting of a weighted sum of all the items was also created.

Although the QOLIE-89 is an advance on the ESI-55, it is still heavily weighted towards "functioning". Less than 20% of the items are concerned with occupational and social life difficulties, loss of self-esteem and stigmatisation. Most of the "social" questions are about *how often* the individual can not work or visit friends, rather about how he/she *"feels"* about their work or social life.

1.3.4.3b Reliability and validity

The original QOLIE questionnaire contained 99 items, but this was reduced to 86 items plus 3 single questions after further testing. The performance of the QOLIE underwent extensive testing in a sample of 304 people drawn from 25 epilepsy centres around the USA (Devinsky *et al.*, 1995). The internal consistency of the 17 QOLIE subscales varied between 0.79 and 0.89. The authors ensured the items were placed in the correct subscales by performing multi-trait scaling analysis (Hays and Hayashi, 1990). The test-retest reliability, performed on 230 people, produced an intra-class correlation coefficient of 0.58 to 0.85. The authors felt that 3 scales did not meet reliability criteria. For the best subscales, 68% of retest values will lie +/- 10 scale points around the first score, and for the least reliable subscales +/- 30 points.

A factor analysis of the QOLIE-89 revealed 4 factors: (1) epilepsy related items, (2) cognition, (3) mental health and (4) physical health. The authors proceeded to validate the scale by testing the correlation of the QOLIE subscales with scores on other well established tests (Perrine *et al.*, 1995). Mood, as assessed by the "profile of mood states" (POMS) questionnaire (McNair *et al.*, 1992) was the best predictor of score on every subscale of the QOLIE-89. The correlation of POMS scores with self-assessed cognitive functioning exceeded even that of objective standardised tests. The cognitive subscales of the QOLIE did however, continue to correlate with the relevant psychometric tests if the mood component was removed. Construct validity was demonstrated by showing that patients with few or no seizures in the

preceding year demonstrated a better quality of life on the QOLIE-89, than patients with frequent seizures. The epilepsy related items differentiated best in this regard. Open-ended questions accompanying the questionnaire suggested that no major quality of life domains were omitted. The authors have gone on to examine the correlation between how a close relative assesses a patient using the questionnaire and a patient's own view (Hays *et al.*, 1995). The correlations varied from 0.29 (poor) to 0.57 (moderate). This lack of agreement neither supports nor invalidates the scale, as it is well established that relatives and patients disagree about quality of life (Sprangers and Aaronson, 1992). Disagreement was more common in the poorly educated and proxy respondents systematically reported better cognitive functioning then did the patients themselves. The authors recommended caution in using proxies in assessing quality of life.

Table 1.8 QOLIE scale content

QOLIE 89 subscale	Items based on SF-36 and ESI-55	New items or from other sources
Physical function	10	0
Role-limitations (physical)	5	0
Role-limitations (emotional)	5	0
Emotional well-being	5	0
Overall quality of life	2	0
Energy/fatigue	4	0
Health perceptions	6	0
Pain	2	0
Language	0	5
Attention	0	9
Memory	1	5
Social isolation	0	2
Social support	0	4
Work/driving/social	0	11
Health discouragement	0	2
Seizure worry	0	4
Medication effects	0	3
Single questions		
Sexual relations	0	1
Overall Health	0	1
Change in Health	1	0

1.3.4.4 The Liverpool model

Baker and Jacoby have developed the "patient-based health related quality of life model" (HRQL) in which "global health" was divided into physical, psychological and social domains (Baker *et al.*, 1993). Since 1991 they have published a series of measures based on this model. These have included the Seizure Severity Scale (Baker *et al.*, 1991), a "Health-Related Quality of Life Model" (Baker *et al.*, 1993), an "Impact of Epilepsy Scale" (Jacoby *et al.*, 1993) and a "Life-fulfilment Scale" (Baker *et al.*, 1994) .

1.3.4.4a Content

There are three main domains: physical, psychological and social health. At a second level, physical health was considered to consist of seizure frequency, seizure severity, activities of daily living and general health as measured by the Nottingham Health Profile (NHP) (Hunt and McEwen, 1985). Psychological health was subdivided into anxiety and depression (Zigmond and Snaith, 1983) and "positive well-being" (Bradburn and Caplovitz, 1969; McNair *et al.*, 1992). The authors also included measures of self-esteem (Rosenberg, 1965) and a "mastery" scale (the extent of control over the direction of one's life) (Pearlin and Schooler, 1978). To assess the impact on social life the "Social Problems Questionnaire"(SPQ) was used (Corney and Clare, 1985). All of the measures except seizure severity were originally designed for contexts other than epilepsy. Later additions to the model included the "Impact of Epilepsy Scale" (Jacoby *et al.*, 1993) and the "Life-fulfilment Scale" (Baker *et al.*, 1994). The Impact of Epilepsy Scale is a 7 item scale asking how epilepsy affects work, relationships, health and feelings about self. The Life-fulfilment Scale is a 12 item scale based on the method of Krupinski (Krupinski, 1980). "Life-fulfilment" is calculated by subtracting the score of the subject's present situation from their ideal score.

1.3.4.4b Reliability and validity

The scales were validated in the context of a double blind add-on trial of lamotrigine in 79 subjects with chronic epilepsy. Adequate internal consistency was found for most of the scales except the SPQ and the percept subscale. The fact that the stability of most of the measures is unknown is an important draw back. The seizure severity scale, the affect balance scale and mastery scales were used longitudinally in the lamotrigine trial and were able to detect a significant benefit of lamotrigine. The SPQ, NHP and mood scales proved unsuitable as outcome measures. The Impact of Epilepsy Scale was tested in 75 patients with chronic epilepsy. The internal consistency was satisfactory and subsequently test-retest reliability has been subsequently reported to be adequate (Wagner *et al.*, 1995). Factor analysis revealed a single underlying construct called "impact of epilepsy". The impact score correlated highly with measures of mood and well-being. In a subsequent community based study the scale discriminated well between people with different seizure frequencies (Jacoby *et al.*, 1996). The Life-fulfilment Scale was validated in a sample of 75 people with chronic epilepsy. The internal consistency was adequate, but no test-retest reliability has been reported. Factor analysis of the scale revealed two factors. Significant correlations existed between "Personal-fulfilment" score and other measures of psychological health. The material-fulfilment scale appeared a less valid measure. In a subsequent large community based study the measure was insensitive to quality of life issues (Jacoby *et al.*, 1996).

1.3.4.5 Other methods under development

A number of questionnaires have been developed but only used by the developing author (Chaplin *et al.*, 1990; Collings, 1990). A innovative but complex approach is being developed by Selai and Trimble to allow serial individualised assessments of quality of life (Kendrick and Trimble, 1994; Selai, 1995). The method overcomes the objection that "questionnaire" based methods address only quality of life issues

chosen by the investigator. During an interview, a psychologist defines the impact of a disorder on the quality of life of an individual patient. The discrepancy between the present situation and a patient-chosen ideal is then calculated. More work however is required before this method is practical for comparing large groups of people.

1.3.4.6 Problems with the quality of life model

A number of methodological difficulties arise when quality of life models are applied as outcome measures in epilepsy. The first problem is defining the scope of "quality of life". As many factors potentially affect a person's quality of life, the content of scales has typically been restricted to "health-related quality of life". However, defining the boundaries of "health-related" remains problematic. For example; is "under-employment" in someone with controlled epilepsy, a health problem? The term "health-related" would seem unhelpful without a detailed understanding of the typical social consequences of epilepsy. Secondly, if a quality of life model were to be chosen as a main outcome measure, difficult decisions may arise over what adjustment is made for co-morbidity or life-events, which may themselves have a profound influence on quality of life. These issues are particularly pertinent if generic quality of life scales (as opposed to disease specific scales) are used as they are generally less sensitive to change in interventions on special groups (Patrick and Deyo, 1989) and intuitively they would seem to be more sensitive to non-specific effects. Thirdly, quality of life models typically consist of a mixture of physical symptoms (e.g. pain or fatigue), assessments of emotional state (e.g. "happiness", "anxiety", and "depression" scales) and aspects of occupational or social functioning. Treating these disparate consequences of disease within a single framework may cause difficulties. The time course over which different consequences are likely to improve are very different. The causal mechanisms and, more importantly, the appropriate interventions at the various levels of disease consequence are quite different (Wade, 1992). In a review of health status

measurement McDowell and Newell have argued that "health indices should measure a specific aspect of health, generally defined in terms of a specific concept or theory" (McDowell and Newell, 1987). Thus, although the notion of "health related quality of life" is a helpful organizing concept for bringing together the physical, psychological, functional and social effects of disease, its very complexity suggests that it may be helpful, when trying to understand the impact of therapeutic interventions, to focus on different "levels" separately.

1.3.4.7 Impairment, disability and handicap

Before the recent rise in interest in quality of life, the World Health Organisation had already developed a framework for the consequences of a disease on an individual in its "International Classification of Impairment, Disability and Handicap" (ICIDH) (World Health Organisation, 1980). Impairments are defined as the effects of disease at an organ or system level (typically symptoms and signs). Disabilities are the impact on the ability to carry out normal "activities" (such as walking). Handicap is the disadvantage, as a consequence of ill health, that prevents an individual from living out a role in society (e.g. to work or be a parent) that most people would consider normal or desirable. An abbreviated classification of Impairments, Disabilities and Handicaps is shown on Tables 1.9 - 1.12. The ICIDH is, however, a classification and not a measuring instrument. In the current version it defines six dimensions of handicap; mobility, orientation, physical independence, occupation, social integration and economic self-sufficiency and for each 9 levels of severity. A 6 item generic scale, which closely follows this structure, the London handicap scale, has recently been developed (Harwood *et al.*, 1994).

Handicap can, theoretically, be further divided into "objective" and "subjective" handicaps. Although the WHO classification does not make this distinction, recent critiques of the ICIDH have proposed that this would be a useful perspective (Peters, 1995). Objective handicaps are limitations in those roles that society regards as "the

norm" (e.g. holding down a job, driving, having a spouse and having leisure pursuits). As such, the presence or absence of an objective handicap is easy to measure, but does not take into account a patient's perspective and imposes a societal standard. Subjective handicap is the patient's own assessment of whether they feel handicapped in these domains.

To date, little use has been made of the ICIDH scheme in describing the consequences of epilepsy. At the level of impairment, seizures are obviously identified as the key variable (Table 1.9). The scheme however focuses on the frequency of seizures. Absences are separated from other seizures, but seizure severity is not explicitly discussed. Disability has no obvious place in the scheme as the inability to perform a task is always transient. However, associated neurological impairments (due to cerebral damage) may result in motor, sensory or cognitive disabilities. Most of the consequences of epilepsy operate at the level of handicap, many of these being directly imposed on the patient by society (e.g. occupational and driving restrictions, and stigmatisation). The advantage of thinking about the consequences of epilepsy as a handicap, is that it recognises that therapeutic interventions can either help at the level of impairment (by relieving the seizures) or at the level of handicap by changing the reaction of the person and his/her environment to the seizures. It has been noted earlier that a significant fraction of patients with epilepsy remain intractable despite current medical and surgical treatment. The main hope for improving the quality of life for these patients may be to consider how to lessen the negative impact of recurrent seizures, rather than a relentless pursuit of improved seizure control.

In its current state, however, the ICIDH classification of Handicap (Table 1.12) is not particularly well adapted to developing an outcome measure for people with epilepsy. One aim of this thesis will be redress this deficiency.

Table 1.9 Classification of Impairments

1	Intellectual impairments
10-14	Impairments of intelligence
15-16	Impairments of memory
17-18	Impairments of thinking
19	Other intellectual impairments
2	Other psychological impairments
20-22	Impairments of consciousness
23-24	Impairments of perception and attention
25-28	Impairments of emotive and volitional function
29	Behaviour pattern impairments
3	Language impairments
4	Aural impairments
5	Ocular impairments
6	Visceral impairments
7	Skeletal impairments
8	Disfiguring impairments
9	Generalized, sensory, & other impairments

Table 1.10 Impairments of consciousness

20	Impairment of clarity and quality of consciousness
21	Intermittent impairment of consciousness
	includes: intermittent ictal disturbances characterised by a total or partial loss of consciousness or by states of altered awareness, and a variety of local cerebral signs and symptoms
21.0	Profound intermittent interruption of consciousness
	includes: epilepsy with a frequency of seizures of once per day or greater
21.1	Severe intermittent interruption of consciousness
	includes: epilepsy with a frequency of seizures of once per week or greater
21.2	Moderate intermittent interruption of consciousness
	includes: epilepsy with a frequency of seizures of once per month or greater
21.3	Mild intermittent interruption of consciousness
	includes: epilepsy with a frequency of seizures of less than once per month
21.4	Intermittent disturbance of consciousness
	includes: psychomotor epilepsy
21.5	Other seizures
	includes: petit mal
21.6	Other intermittent interruption of consciousness
	includes: syncope and drop attacks
21.7	Fugue states
21.8	Other
21.9	Unspecified
22	Other impairment of consciousness and wakefulness
	includes: disturbances of the sleep/wakefulness

Table 1.11 Classification of Disabilities

10-19	Behaviour disabilities
20-29	Communication disabilities
30-39	Personal care disabilities
40-49	Locomotor disabilities
50-59	Body disposition disabilities
60-69	Dexterity disabilities
70-79	Situational disabilities
80	Particular skill disabilities
90	Other activity disabilities

Table 1.12 Classification of Handicaps

1. Orientation handicap
2. Physical independence handicap
3. Mobility handicap
4. Occupation handicap
5. Social integration handicap
6. Economic handicap
7. Other handicaps

1.4 Summary and conclusions to literature review

1. The natural history of epilepsy is largely determined by its aetiology. For the majority of patients, epilepsy is a condition that remits and is relatively easily treated. However, for about 25%, seizures will continue despite medical therapy. An important additional treatment is epilepsy surgery. When applied to appropriately selected patients, surgery relieves seizures in about two thirds.

2. Recurrent seizures have a major impact on psychological, social and vocational aspects of life.

3. Outcome measurement in epilepsy has, to date, placed undue reliance on seizure frequency. Seizure severity, psychological symptoms, quality of life and handicap are important additional components in the evaluation of the success of epilepsy therapy.

3. The burden of epilepsy in patients in community based samples, particularly in respect of psychiatric symptoms and quality of life, is poorly understood. There is a need for studies of the prevalence of psychiatric symptoms in patients with active epilepsy compared with patients gone into remission and have stopped treatment. Similarly, the prevalence of people "significantly handicapped" by epilepsy is unknown.

4. Our understanding of the benefits of epilepsy surgery on quality of life is based largely on uncontrolled retrospective studies. There is a need for prospective longitudinal studies using control groups to investigate the effectiveness of epilepsy surgery.

5. Patients disabled by intractable epilepsy are sometimes referred to epilepsy centres for comprehensive assessment with the aim of intensive treatment including psychological and social interventions. This effectiveness of this approach remains unevaluated.

6. As a result of the review of the literature the following problems were selected for investigation in this thesis:

(1) The development of instruments to measure the broader consequences of epilepsy. In particular, to design and validate scales to measure seizure severity and the handicap associated with epilepsy.

(2) To assess the impact of epilepsy on psychiatric symptoms and handicap in an unselected population.

(3) To assess the effect of epilepsy surgery on quality of life and handicap in a prospective controlled investigation.

(4) To assess the impact of a period comprehensive assessment and treatment at an epilepsy centre on quality of life and subjective handicap.

Section 2

The Development and Evaluation of

The National Hospital Seizure Severity Scale

The development and evaluation of a new seizure severity scale

2.0 Introduction

In Section 1.3.3.2 it was discussed how seizure severity has become an important additional measure of treatment outcome in epilepsy. The studies in this section present an evaluation and further development of the Chalfont Seizure Severity Scale (CS). The material in this chapter has been published in part as:

O'Donoghue MF, Duncan JS, Sander JWAS. The National Hospital Seizure Severity Scale; a further development of the Chalfont Seizure Severity Scale. Epilepsia 1996; 37:563-571.

2.0.1 Aims

The aim of the studies in this section were:

(1) To determine which factors were the most appropriate to include in a revised seizure severity scale.

(2) To assess the value of the item weighting in the Chalfont Seizure Severity Scale.

(3) In the light of the results of (1) and (2) to produce a refined version of the Chalfont Seizure Severity Scale.

(4) To evaluate the inter-rater and test-retest reliability of the new scale.

(5) To provide construct validity for the new seizure severity scale.

A reassessment of the content and weighting system of the Chalfont scale

2.1.1 Background

It will be recalled that the Chalfont seizure severity scale (CS) was a 11 item scale focusing solely on the objective clinical events of a seizure, and was administered by interviewing a patient and a witness to the seizures (for the factors see Table 2.1). The items had been derived from open interviews with people with epilepsy and the scoring used a combination of patient and expert opinion to create an acceptable ranking of scores for different seizure types. This led to a rather complex scoring system (Table 2.1). The following study was designed to see if all the factors and the weighting system were necessary. The aspects of seizure severity that were of most interest were the objective characteristics of seizure events rather than the impact, subjectively, of the seizures on the life of a patient.

2.1.2 Methods

2.1.2.1 Subjects

Twenty five subjects (15 female and 10 male, median age of 27 years) attending the epilepsy clinic of the National Hospital for Neurology and Neurosurgery (NHNN) were recruited for an initial pilot study. Following their normal appointment with one of the clinic's consultants, the subjects were interviewed by the author, in a quiet room set aside for the purpose. All subjects had active epilepsy despite antiepileptic medication and were clinically of normal intelligence.

2.1.2.2 Eliciting and weighting the seizure severity factors

There were two phases to the interview. First, an open ended question, designed to elicit severity factors was posed to the subjects: "You are probably aware that there are several different types of seizure, or that seizures can vary in severity. What sort of things happen in a seizure, or immediately afterwards, that make a seizure severe ?". The responses were recorded verbatim.

In the second phase, patients were presented with 6 factors from the Chalfont seizure severity scale, with two additional factors ("embarrassment" and "aftermath of a seizure"). The subjects were asked to weight the items, in terms of seizure severity, on a scale of 0 to 10, with 10 representing very severe. The subjects were asked to do this with a standard question, paraphrasing if required, "How important is this factor [e.g. incontinence] on a scale of 1 to 10, when considering how severe a seizure is?" They were asked to consider either their own seizure or a hypothetical seizure incorporating the factor under consideration. The median weighting score (and range) were then calculated for each factor.

2.1.3 Results

2.1.3.1 Qualitative observations

Four of the 11 factors included in the Chalfont scale were mentioned by patients as important (Table 2.2), but seven items were not (lack of warning, dropping objects, automatisms, convulsions, duration of seizure, falls and seizures while asleep). Many patients found it difficult to grasp the concept of a group of factors contributing to seizure severity. Subjects tended to respond in terms of the effect that epilepsy in general had on them. Several patients felt unable to comment as they said they said were unconscious during the seizure, and so "couldn't tell what is severe". When the patients were prompted to think of the kind of events that occur in seizures, most could produce 2 or 3 ways in which a seizure could be regarded as severe. The responses referred either to ictal or postictal symptoms or to consequences of a seizure on daily life (Table 2.2). Embarrassment, however, emerged as a important subjective seizure severity factor. Only one subject revealed a seizure symptom (unpleasant auras) not mentioned in the Chalfont scale.

Considerable difficulties were encountered during the weighting exercise. Patients found it counter-intuitive to attach relative importance to the factors. The commonest response was that the factors were all important. Some subjects were unable to provide

weights for every factor. The choices were particularly problematic if the individual had not experienced that factor.

Table 2.1 Items and item weighting in the Chalfont seizure severity scale.

Item	Weighting of item (by frequency)
Loss of awareness	0/1
Warning before seizure	0/1
Dropping or spilling object	0/4
Fall to the ground	0/4
Injury	0/20
Incontinence	0/8
Automatism	0/4/12
Convulsion	0/12
Duration of seizure	0/1/4/16
Duration of recovery phase	0/5/20/30/50/100
Seizure confined to sleep	divide by 2

Table 2.2 Severity factors generated by 25 subjects.

Factors revealed by subjects	Number of subjects
Events during a seizure	
Incontinence of urine	3
Injuries	2
"When I lose consciousness in a seizure"	2
"It is horrible if I remain conscious"	1
"When I bite my tongue"	1
"When I have the unpleasant aura"	1
Consequences of a seizure	
Embarrassment	7
"Muscle aches after seizures"	1
"When it leaves you tired next day"	1
"When it disrupts work"	1
"Depression afterwards.."here we go again" feeling"	1
"Headaches afterwards"	1
"Confusion afterwards"	1
Other responses	
"Everything about a seizure"	2
"I feel helpless in a seizure"	1
"Severity depends on where I have it"	1
"When it makes me afraid to go shopping"	1
"Stigma associated with seizures"	1
"When my wife worries"	1
"The effect on other people"	1

Table 2.3 Median and range of weighting scores for each severity factor

Factor	median score	range of scores
Loss of awareness	3.0	0-9
Injuries	6.5	0-10
Falls	7.0	0-10
Aftermath of seizure	7.5	2-10
Time taken to recover	7.5	0-10
Embarrassment	8.0	0-10
Incontinence	9.5	0-10
No warning before seizure	9.5	1-10

2.1.3.2 Weighting the severity factors

Table 2.3 shows the median and range of weighting for the selected seizure severity factors. The range in weightings for all 6 factors was at least 8 out of maximum of 10. There was also a ceiling effect, with subjects weighting most factors 8-10. Incontinence and lack of warning were given the highest ratings and loss of awareness the lowest.

2.1.4 Discussion

The experiments established two results. Firstly, the weighting system used in the original CS could not be replicated. Most of the factors were weighted by the subjects as equally important. Secondly, no symptom emerged as an additional severity factor, though the embarrassment experienced by subjects was highlighted as an important subjective factor. It was observed that many patients had difficulty generating severity factors, and found it even harder to weight them in order of importance. What could account for the difficulty ? Cognitive factors are unlikely to have played a major role as subjects with clinically apparent cognitive deficits were not enrolled. Patients typically

responded to the questions in terms of the impact of a seizure on daily life, rather than having a view as to the importance of the relative components of a seizure. It likely that *subjectively* it is the whole experience of a seizure that is relevant to the patient. The technique used in this study to weight the items (direct magnitude estimation of each factor using a visual analogue scale), differed from that used by the developers of the CS who used a comparison of the total score of eight example seizures to infer the weights of the items according to expert opinion.

Why were all the CS factors not mentioned by the subjects ? First the factor "convulsion" is a seizure type in itself, and therefore it is not surprising that this was not referred to as a separate severity factor. Automatism may not have been mentioned as it is a technical description of a seizure. No subject in this sample experienced seizures only in sleep, suggesting this is rarely an important factor. When patients were presented with the factors from the Chalfont scale that they had not mentioned as important, they nevertheless indicated during the weighting procedure that they were relevant. This suggested that the CS had content validity.

2.1.5 Conclusions

Several conclusions were drawn from the pilot study. First, that the Chalfont scale had content validity. Second, that patients' subjective view of seizure severity consisted of more than seizure symptomatology and included the personal consequences of the seizure. The subjective severity of the seizures therefore is likely to vary greatly according to personal circumstances. Thus, any scale designed to measure the objective severity of a seizure needs to focus on narrowly definable events (chiefly symptoms). Third, that a weighting system for items was not a helpful refinement, because it appeared that all items were of approximately equal importance. Finally, it was concluded that, given the concordance between the severity factors elicited in this study with those obtained by the developers of the CS and the Liverpool scale, a further survey of a larger sample was unlikely to yield important new factors.

Development of the National Hospital Seizure Severity Scale (NHS3)

2.2.1 Development of the new scale

Following the observations made in section 2.1, the CS scale was simplified and refined. Four items were eliminated, a change in the wording of two items was made and the scoring system was simplified. The item on dropping objects was removed as it was judged to parallel the item on falls. The item on seizures occurring only in sleep was eliminated as it was found to occur too rarely to warrant inclusion. A single item on total time to complete functional recovery after a seizure replaced separate items on seizure duration and recovery phase as patients usually can not provide accurate timings for the two separate phases. The item on loss of consciousness was incorporated into the question on auras. The instructions for the item on automatisms were changed to emphasise the concept of embarrassment. The item on injuries was changed to reflect severity of injury rather than frequency because some patients in section 2.1 reported this as more relevant.

A simpler scoring system was introduced so that all items except the question on lack of warning of a seizure had equal weight. This adjustment was made so that a brief typical absence and a brief complex partial (CPS) seizure with aura and mild automatism (judged by the author to be of equivalent severity) both scored 3 points. If this had not been done, a typical absence would have scored higher than a brief CPS by two points. One point is added to each seizure type to avoid assigning a seizure with a score of zero severity. A minimum of one point is scored by a simple partial sensory seizure lasting less than one minute. The maximum score of 27 is achieved by a severe complex partial seizure leading onto a secondarily generalised tonic clonic seizure with falling, injury, incontinence and recovery taking longer than 3 hours.

The design and layout of the scale underwent a number of revisions until the final version was produced. The final layout of the scale contained a revised set of brief instructions for use, and a more detailed series of instructions accompanied the scale. The instructions emphasized that when a patient has two or more seizure types, each

seizure type is scored separately. It also underlined the importance of specifying a fixed time frame for the assessment. At follow up visits each seizure type is again scored separately. The scale has been renamed "The National Hospital Seizure Severity Scale" (NHS3) and is presented in Figure 2.1 and Appendix 3 with the additional notes to facilitate its standardized administration. The scale has now been published (O'Donoghue *et al.*, 1996).

2.2.2 Assessing the reliability and validity of the NHS3

2.2.2.1 Methods for assessing reliability

Internal consistency of the scale was assessed with Cronbach's coefficient alpha. The scale was tested for both inter-observer and test-retest reliability. The subjects were a consecutive sample of 87 adult patients accompanied by a witness to their seizures, attending an epilepsy follow-up clinic at the NHNN. Inter-observer reliability was assessed by two neurologists who administered the scale to the 87 patients, who had 129 seizure types between them. The ratings were made 15 to 30 minutes apart. For test-retest reliability, 18 patients (from the above sample) with 57 seizure types were tested on two occasions 1 to 8 weeks apart (24 observations were made by observer 1 and 33 by observer 2). The patients confirmed that there had been no subjective change in seizure severity in the intervening period. Inter-observer and test-retest reliability is reported using an intraclass correlation coefficient (ICC), based on a two way random effects analysis of variance model with the assumptions that the observers used in this analysis were a sample of all potential users of the scale. The ICC is the ratio of variance of scores between subjects to the sum of components of variance from all sources (subjects, observers and error) (Streiner and Norman, 1995). The ICC is calculated using the formula:

$$ICC = (MS_{bms} - MS_{ems}) / ((MS_{bms}) + (k-1)(MS_{ems}) + (k(MS_{jms} - MS_{ems})/N))$$

where N is the number of subjects, K is number of raters, MS_{bms} is the mean square between subjects, MS_{jms} is the mean square between raters and MS_{ems} is the mean square residual (error).

The ICC reports the reliability of a single observation, and ranges from 0 (no agreement) to 1 (perfect agreement). From this can be derived a standard error of measurement (SEM), which than can be used to express the reliability of a single score (with 95% confidence) in terms of scale points (Nunnally and Bernstein, 1994). Because the ICC reported here is the result of only a single sample, a lower confidence interval was calculated for the ICC using the approximation developed by Fleiss and Shrout (Fleiss and Shrout, 1978). In addition, because the ICC is dependent on the range and variability of scores in the subject population the reliability also estimated using the method of bias and limits of agreement as recommended by Bland and Altman (Bland and Altman, 1986). This method derives the mean difference between raters (bias) and the limits (in scale points) between which 95% of the differences between two raters can be expected to lie. Confidence limits were calculated for the mean difference between raters (bias) and the upper and lower limits of agreement between raters (two standard deviations of difference between raters), using the formulae of Bland and Altman. These confidence limits are presented because the calculated bias and the limits of agreement in our study arise from a single sample of two raters from a population of potential raters.

2.2.2.2 Methods for assessing the validity of NHS3

Construct validity of the scale was sought by demonstrating that patients were in agreement (subjectively) with the severity scores of certain types of seizure. In "experiment 1" 5 "prototype" seizures (called Seizures A, B, C, D, E) were created as written descriptions on pieces of card (Figure 2.1). The cards were presented, unlabelled and in random order, to 80 patients (from the 87 in the above sample) who then ranked them in severity. The "prototype" seizures were not systematically related to the seizure types experienced by the subjects. The rankings given by the 80 patients for each of the "prototype" seizures were compared with the rank derived from the NHS3 scale. Agreement between "patient ranking" and "NHS3 ranking" was tested for with a weighted kappa statistic, with values greater than 0.8 indicating very close agreement. In "experiment 2" 50 patients (from the 87 patients in the above sample)

were asked to rate the severity of each of the "prototype" seizures on a visual analogue scale (VAS) marked from 0 to 100 (and labelled: 0 = the least severe seizure imaginable, 100 = the most severe seizure imaginable). The mean VAS score for each of the "prototype" seizure was then transformed to the 1 to 27 scale of the NHS3. From this, the "VAS predicted score" was calculated for each prototype seizure. The "VAS predicted score" was compared with the NHS3 score.

2.2.4 Results

2.2.4.1 Scores for five seizure types

The subjects (45 male) had a median age of 31 years (inter-quartile range 27-44). Fifty two subjects had one seizure type only, 37 had two types, and one had three types. For the 129 seizures the median seizure severity was 8.0, mean 9.1, standard deviation 6.1, and range 1 to 25. Five seizure types, classified in the standard way had significantly different mean seizure severity scores (Table 2.3) (Kruskal Wallis $p<0.001$) and pair-wise comparisons of severity for all seizure types were significantly different except for comparisons of absences, simple partial seizures and myoclonic jerks (Mann-Whitney $P<0.001$). When the scale was administered during a follow up consultation (when the seizure types had already been established) it took 2-3 minutes per seizure type to complete.

Table 2.4 Median NHS3 scores (and ranges) for different seizure types

Seizure type	Number observed	Median score	Range
Myoclonic	3	1	0
Typical absence	7	3	0
Simple partial	18	2	1-7
Complex partial	56	7.5	3-15
Tonic clonic	45	15	5-24
Total	129	8	1-24

2.2.4.2 Internal consistency

Internal consistency of the scale, as measured by Cronbach's alpha, was 0.77. Table 2.5 displays the effect of deletion of each item in turn on the alpha coefficient. Deletion of no item led a significant increase in alpha.

Table 2.5 Cronbach's alpha for the scale with each item deleted

Scale Item	Alpha if item deleted
Convulsion	0.72
Fall	0.69
Injury	0.72
Incontinence	0.76
Warning	0.76
Automatism	0.79
Recovery	0.71

2.2.4.3 Inter-rater reliability

An intraclass correlation coefficient of 0.90 was determined for inter-observer testing. The standard error of measurement for a single observation was thus 2.0 scale points, predicting that 95% of observations would be within plus or minus 4 scale points. The 99% lower confidence interval for the ICC was 0.86. The mean difference between the two observers was 0.15 scale points with a standard deviation of 2.08 scale points. The limits of agreement therefore between two observers for an individual observation were {-4.0,4.3} scale points. The score differences were approximately normally distributed around zero. The confidence intervals for the estimation of mean differences (bias) were {-0.2,+0.5}. The confidence intervals for the upper limit of agreement were {3.7,4.9} and for the lower limit of agreement were {-4.6,-3.4}. The magnitude of the inter-observer differences was not related to the mean score of the two observers (Figure 2.2).

2.2.4.4 Test-retest reliability

An ICC of 0.90 was found for test-retest observations. The standard error of measurement was 2.0 scale points. The 99% lower confidence interval for the ICC was 0.85. The mean difference between the first and second application of the scale was +0.5 (s.d. 2.8). The limits of agreement were {-5.1,+6.1}. The confidence intervals for the mean difference were {-0.24,+1.24}. The confidence intervals for the upper level of agreement were {+4.8,+7.4} and for the lower level of agreement {-6.4,-3.8}. There was no systematic effect of the magnitude of the severity score on the test-retest reliability (Figure 2.3). Differences were approximately normally distributed around zero.

2.2.4.5 Validity

2.2.4.5a Experiment 1

The rankings given by 80 subjects to the 5 prototype seizures were compared to the rankings derived from the NHS3 scores (Table 2.5). Close agreement is indicated by the figures in the left-right downward diagonal squares (outlined). The weighted kappa was 0.82, indicating very good agreement between patients' ranking and the scale score. Disagreement only occurred over seizures C and D, which were those with the closest score using the NHS3 (see experiment 2).

2.2.4.5b Experiment 2

The mean VAS score matched the NHS3 score closely for each prototype seizure (Table 2.7). This indicated that the relative severity of the 5 types of seizure as judged by the 50 patients was reflected in the scores produced for each seizure by the scale.

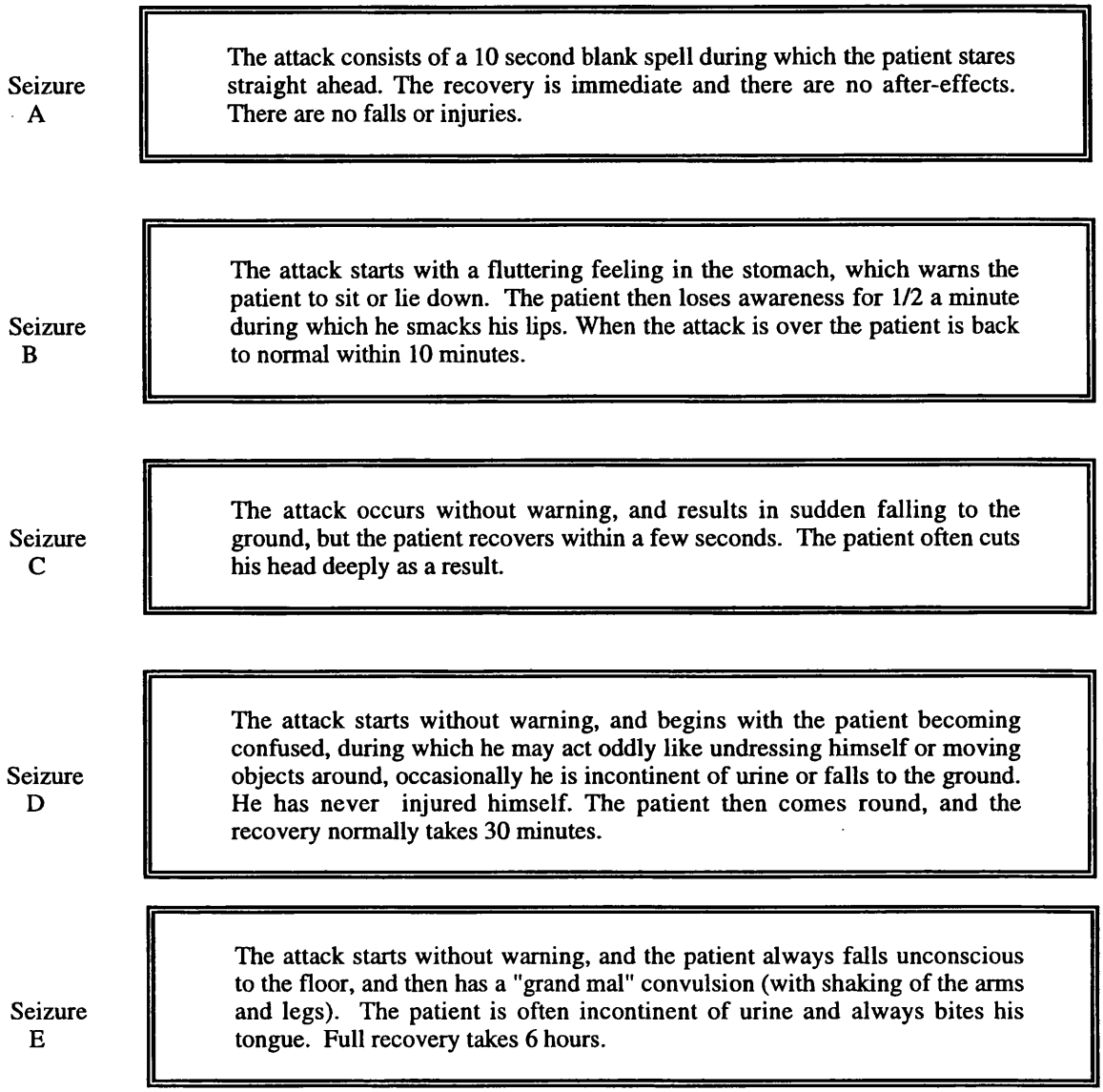


Figure 2.1 The 5 prototype seizures as presented to the patients in experiments 1 and 2.

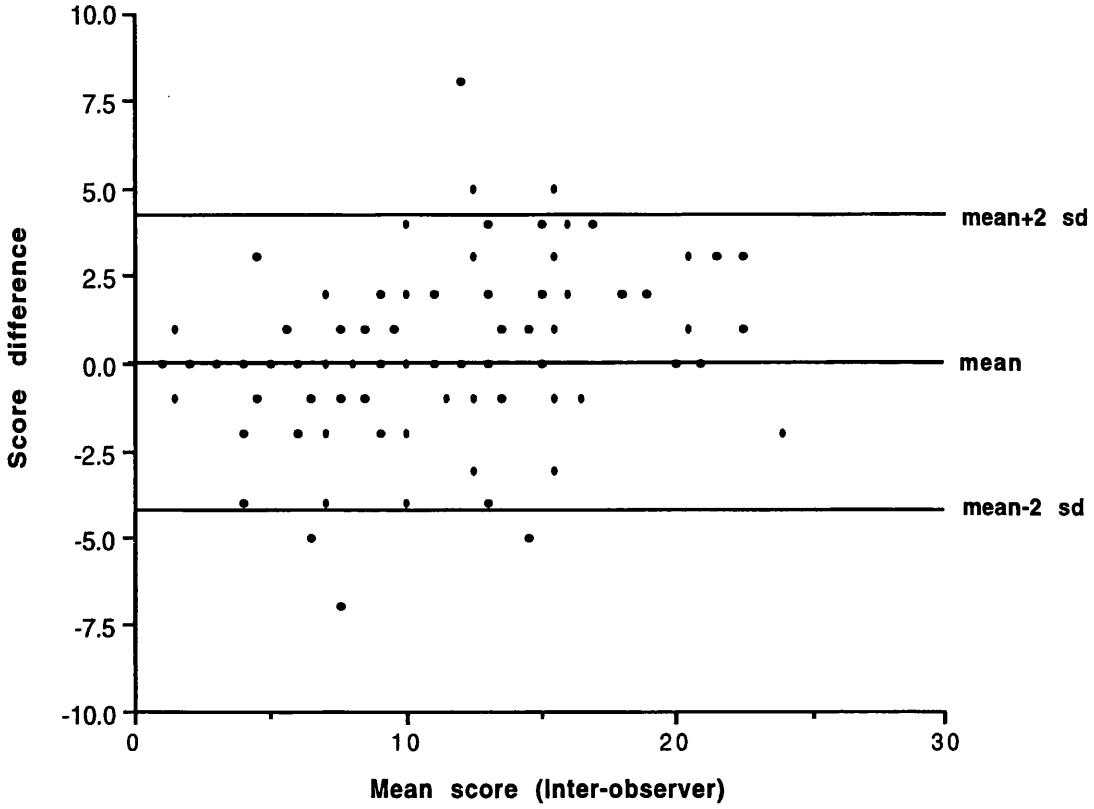


Figure 2.2 Inter-observer score differences plotted against the mean seizure severity score of the two observers. Each dot represents one or more patients. The mean difference and 2 standard deviations (s.d.) above and below the mean are indicated by the horizontal lines.

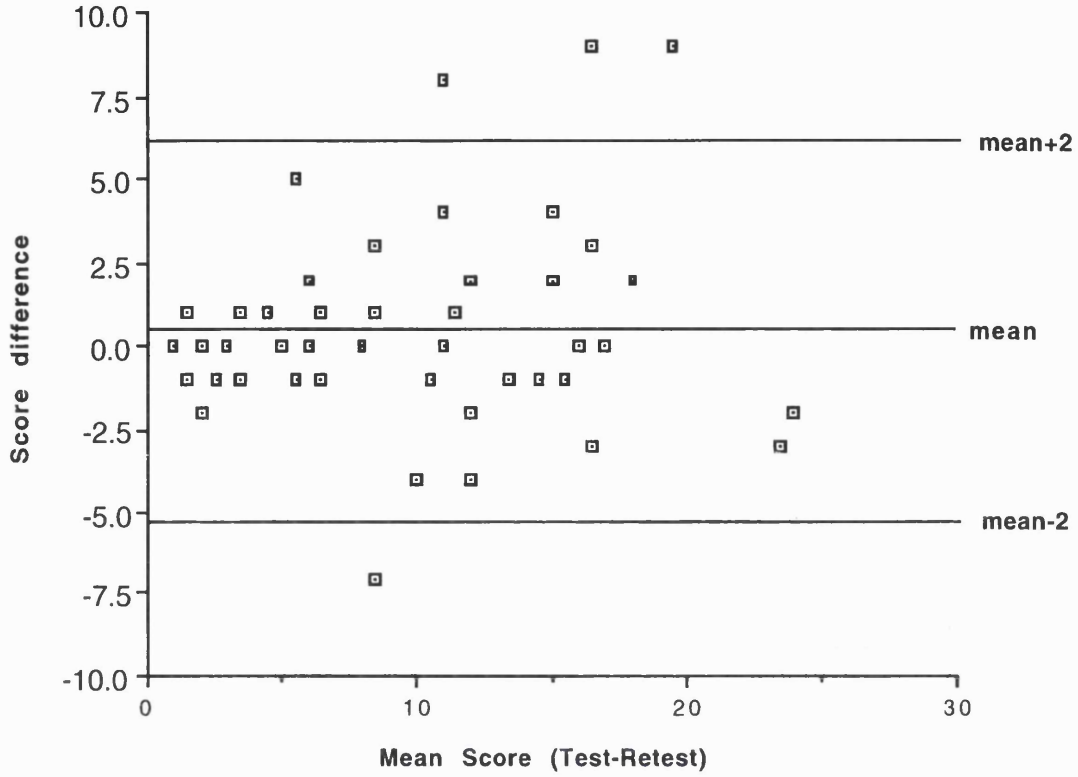


Figure 2.3 Test-retest score differences plotted against the mean seizure severity score for the two measurements. The mean difference and 2 standard deviations (s.d.) above and below the mean are indicated by the horizontal lines.

Table 2.6 How the 80 patients ranked the 5 "prototype" seizures. The number in each cell indicates the number of patients for a given pair of rankings.

	Prototype seizures as ranked by NHS3 score				
Prototype Seizures as ranked by patients	**A (least severe)**	**B**	**C**	**D**	**E (most severe)**
1 (least severe)	**72**	8	0	0	0
2	7	**67**	5	1	0
3	1	5	**45**	26	3
4	0	0	20	**48**	12
5 (most severe)	0	0	10	5	**65**

NHS3 = National Hospital Seizure Severity Scale

Table 2.7 The scores (for prototype seizures A,B,C,D and E) as derived by the National Hospital Seizure Severity Scale (NHS3) compared with the scores derived from 50 patients using a visual analogue technique.

	Seizure A	Seizure B	Seizure C	Seizure D	Seizure E
seizure type:	absence	complex partial	atonic	complex partial	tonic-clonic
NHS3 Score	3	4	11	13	21
Score derived from VAS rating	3	5	14	16	23

NHS3 = National Hospital Seizure severity scale, VAS = Visual analogue scale.

2.2.5 Discussion

The principal results were that the NHS3 was reliable and had construct validity. The interpretation of these findings will now be discussed.

The alpha coefficient of 0.77 in our study indicated that the scale has adequate internal consistency. The alpha would rise slightly with the elimination of the item on automatisms, but at the cost of a reduction in the ability to assess complex partial seizures. This item has been retained.

For the scale to be useful in AED trial settings it is critical that it is adequately reliable (especially between different raters). The ICC of 0.90 for both the inter-observer and retest condition indicated adequate reliability. When the reliability data was expressed using the method of Bland and Altman no systematic bias between observers or between the first and second administration of the scale was found. In addition, there was no systematic relation between size of measurement error and score on the scale. However, the limits of agreement (plus or minus two standard deviations of the differences) were quite wide, particularly for the test-retest condition. These limits of

agreement, which were similar to those found in earlier work on the Chalfont scale, are a significant proportion of the maximum score on the scale (about 30%), and may be equivalent to the median magnitude of an NHS3 score for a typical complex partial seizure. The standard error of measurement for a single observation (derived from the ICC) was equivalently wide. These considerations suggest that the scale will be adequately reliable for use in AED trials when data are analysed by groups, but that when assessing an individual seizure type, in a single patient, over time, the level of precision reported here should to be taken into account. It is likely that the scale is not able to measure small changes (2-3 scale points) reliably in individual patients. The cause of the imprecision is most probably related to reliance on the memory of both the subject and the witness to score the scale. Ideally, the reliability study should be repeated by observers not involved in its development and in a new sample of patients. A replication of the findings would increase confidence in the generalizability of the reliability estimates.

The scores from our sample of subjects were not normally distributed, being skewed towards lower values, reflecting a considerable number of patients in the sample with absences or brief complex partial seizures. The scores in Table 2.4 indicated that the scale discriminated (on a group basis) between different clinical seizure types for all comparisons except between absences, simple partial seizures and myoclonic jerks.

The meaning of score changes on the scale requires further explanation. An example of a 4-5 point change would be the cessation of injuries, or quicker recovery plus a reduction in the frequency of urinary incontinence. The minimum change that is significant for an individual patient has yet to be determined, but is likely to be approximately 2-3 points, as the validation experiment suggested that most people ranked "seizure D" above "seizure C" (2 points difference).

Experiments 1 and 2 have provided evidence for construct validity for the NHS3. The NHS3 scores for absences, mild complex partial seizures, atonic attacks, severe

complex partial seizures, and generalised tonic clonic seizures were almost exactly the same as those predicted using the visual analogue technique (Table 2.7). Thus, the scaling of the NHS3, though reliant on only objective criteria, is in accord with the subjective assessment of the relative severity of different seizure types by patients with epilepsy.

The responsiveness of the NHS3 remains to be determined. This is currently taking place in two trials with the new antiepileptic drug, Topiramate (Personal communication, Dr H.Coles, Cilag-Janssen, UK) and in a trial of the experimental drug, ucb LO59 (Personal communication, Dr U. Falter, ucb Pharma, Belgium).

2.2.6 Conclusions

1. The National Hospital Seizure Severity Scale is sufficiently reliable for group studies.

2. The scale is simpler to complete and score than the Chalfont scale.

3. The scale is valid from the subjective point of view of a person with epilepsy.

4. The scale is a valuable additional outcome measure in trials of novel antiepileptic drugs. A number of international multicentre antiepileptic drug trials using the measure are taking place.

Section 3

The Development and Validation of the Subjective Handicap of Epilepsy Scale

Introduction

The outcome measures sensitive to the psychosocial effects of epilepsy were reviewed in section 1.3.4. It was concluded that there remained a need for scales that assessed the long-term social and vocational handicapping effects of chronic epilepsy. This chapter describes the development of such a measure: "The subjective handicap of epilepsy scale". The material in this chapter has been published as:

O'Donoghue MF, Duncan JS, Sander JWAS. The Subjective Handicap of Epilepsy: a new approach to measuring treatment outcome. Brain 1998; 121:317-343.

3.1 Methods

3.1.1 Development and piloting of the scale

The content of the proposed scale was determined using a number of methods. A review of the psychosocial literature on epilepsy was carried out to identify the key problems that affect the lives of people with epilepsy. Open unstructured interviews were held with approximately 100 people attending a tertiary referral clinic to define the areas of handicap. In addition, "expert opinion" was sought of specialists (at the Institute of Neurology, London) in neuropsychology, social work and health status measurement to highlight potential areas of interest. The available quality of life scales for epilepsy (Dodrill *et al.*, 1980; Vickrey *et al.*, 1992; Baker *et al.*, 1993; Jacoby *et al.*, 1993; Baker *et al.*, 1994; Devinsky *et al.*, 1995) were also reviewed.

It was decided not to subject the pilot versions of the proposed scale to formal statistical methods of item selection (e.g. correlation with established scales). This was done as there was no "criterion" scale against which to validate the scale. The process of design and evaluation of the scale, therefore, involved an initial purely qualitative stage, followed by a formal series of investigations of reliability, scaling and validity.

It was decided that the scale should consist of a series of subscales with each item scored using the Likert method (Streiner and Norman, 1995). Subscale totals were simple sums of the component items. Potential items were created by the author and then presented to people attending an epilepsy clinic for assessment of relevance and intelligibility. Questions were adapted, added and deleted on the qualitative evidence of these interviews. A pilot version was administered to 30 members of an epilepsy self-help group, and a revised pilot version to 30 post-surgical patients for a preliminary assessment of reliability, data quality, and content validity. The pilot investigations will not be presented, instead the formal analysis of the properties of the scale forms the content of this chapter.

3.1.2 Plan of the investigations

The scale was administered to approximately 500 people attending the National Hospital for Neurology and Neurosurgery (NHNN) (sample described further in section 3.1.3). The scale was assessed for reliability (test-retest and internal consistency as described in section 3.1.4.2), acceptability (time needed to complete and measures of data quality) and scaling properties (as described in section 3.1.4.1). The scale was then subjected to a series of tests of validity and hypothesis testing further described in section 3.1.4.3.

3.1.3 Sampling and questionnaire administration

The scale was administered to two populations; (1) "Group A"; patients attending the epilepsy clinics at the NHNN and (2) "Group B" a cohort of consecutive patients who had undergone surgical treatment for epilepsy in the last 10 years at the NHNN. Group A was drawn from two sources. Firstly, a consecutive sample of 183 patients with definite epilepsy (2 or more seizures), without learning disability, who had attended the epilepsy follow up clinic of two specialists in epilepsy. The index visit had been at least one year before the questionnaire administration so that newly diagnosed cases were not enrolled. Group A also included 191 consecutive patients referred for Video-EEG telemetry for assessment for epilepsy surgery. Patients with learning disability (IQ <70) were not enrolled.

Group B was derived from a cohort of 129 consecutive patients who had undergone surgical treatment for epilepsy 1986-1993 at NHNN. One patient had died of a seizure related-death 6 months post-surgery and 3 had moved abroad, leaving 125 available for the study with at least 6 months follow-up. Clinical details for all subjects were reviewed from the hospital case records to confirm demographic details, diagnosis, seizure classification and recent seizure frequency.

A booklet containing the final version of the SHE scale, the Hospital Anxiety and Depression scale (Zigmond and Snaith, 1983), the General Health Questionnaire (Goldberg, 1978), demographic and seizure related questions, open ended "quality of life" items and ESI-55 (in that order) was mailed to all subjects. A single reminder was sent approximately 6 weeks after the first mailing. Missing values for scale items were interpolated if 75% or more of any scale had been completed, otherwise the subscale was described as "missing". The only exception to this rule were items on the change scale which were defaulted to the value of "the same" if missing. The following demographic and seizure related information was also requested; years of schooling, educational achievements, employment details, marital status, age of onset of epilepsy, seizure types, seizure frequency, additional disability and co-morbidity. Current seizure frequency was determined using information from the questionnaire, which requested seizure frequency data for tonic-clonic seizures (GTC), absences (AS), simple partial seizures (SPS) and complex partial (CPS) seizures. Each item was accompanied by a vignette of a typical seizure. The case records were also examined to corroborate the approximate seizure frequency. If the self-reported classification was correct, the self-reported frequency of each type was used. If there was a conflict in reported types, AS and CPS were collapsed into CPS for those with localization related epilepsies, and AS and CPS to AS in those with idiopathic generalized epilepsies. Myoclonic seizures were coded as SPS. A number of open-ended quality of life questions were also included in the questionnaire.

3.1.4 Plan of analysis

3.1.4.1 Scaling properties of SHE scale

The response rate was calculated as the percentage of replies with analysable data on the SHE scale. Data quality was assessed as the percentage of missing values for each item (whether eventually interpolated or not). Respondent burden was assessed by timing 40 patients while they completed the scale in front of the investigator (during the test-retest studies) without assistance or time pressure. "Debriefing" after SHE scale completion was used in these patients to identify items that consistently caused problems. Means and distributions of the subscales were examined for normality and for ceiling and floor effects. The means and standard deviations of the individual items were inspected to ensure approximate equivalence allowing the subscale totals to be derived from unweighted item scores. The acceptability of placement of individual items in their hypothesised subscales was assessed by ensuring that the "corrected item - total correlation" (the correlation of an item with the subscale total with the direct effect of the item removed (Norusis, 1990)) was at least 0.4 for each item. Furthermore, multitrait scaling analysis was performed to assess whether each item was correlated more highly with its own subscale than with all other subscales. This was examined by comparing the median "corrected item-total correlation" of all items within one subscale with the median correlation of an item with all other scales. The former should exceed the latter if the items are correctly scaled. Finally, "Scaling success" was calculated, using the method adopted by Wagner (Wagner *et al.*, 1995). The percentage of corrected-item total correlations that exceed, by 2 standard errors, derived from a Fisher's z-transformation, (Altman and Gardner, 1989), "item-other total correlations" indicates whether all items are correctly placed. The optimum value is 100%.

3.1.4.2 Reliability of the SHE scale

Internal consistency of the subscales, using Cronbach's alpha (Cronbach, 1951), was evaluated for all subscales in the entire population, and a subsidiary analysis was carried out for respondents on the 3 alternative versions of the "Work & Activity" subscales (in

work, in education, and not in work), to ensure that the different versions of this subscale were equivalently reliable.

The test-retest reliability of the SHE subscales was examined in 110 subjects. Three test-retest intervals were used. Twenty-three respondents were retested at 24 hours (both times in the presence of the investigator), twenty four subjects at one week (once in the presence of the investigator and once by mail, and 63 subjects at 4-8 weeks interval (both by mail). Use of the three intervals, allowed the hypothesis that the reliability would not differ by time interval to be tested. If it is assumed that the longest interval would be most prone to the effect of a recent change in seizure frequency, the sensitivity to minor changes in health status can also be examined. In addition, an item asking whether there had been a "recent worsening of epilepsy or general health" was given to the 63 respondents at the longest retest interval, to assess the sensitivity to recent minor changes in health status. The reliability analysis was performed using an intra-class correlation coefficient, assuming a two-way random effects analysis of variance model. For the rare occasions when a two way model led to negative variance estimates, "time" (the effect of retest) was dropped from the model, and a one way analysis performed. An estimate of the lower confidence interval for the ICC was calculated using the approximation developed by Fleiss and Shrout (Fleiss and Shrout, 1978). The reliability was also expressed, following the work of Bland and Altman (Bland and Altman, 1986), as the mean test-retest score difference (time 2 - time 1) to estimate the "bias" and the repeatability coefficient (1.96 times the standard deviation of the differences). This coefficient, used by the British Standards Institute (British Standards Institution, 1979) as a measure of the reliability of scientific measurements, indicates between which values (in scale points) 95% of repeat values should lie.

3.1.4.3 Construct validity of the SHE scale

Evidence for construct validity of the scale was obtained through four investigations. Firstly, an examination of the mean scores on the SHE scale in subgroups of the cross-sectional clinic attendees group (group A) when divided by factors such as seizure

frequency and employment status. Secondly, the sensitivity, retrospectively, of the SHE scale to differences in seizure outcome after epilepsy surgery (group B) was investigated. Thirdly, a correlation analysis of scores on the SHE scale and the ESI-55 in the entire dataset was performed. Fourthly, a factor analysis was used to provide evidence for the proposed dimensionality of the scale.

3.1.4.3a The effect of seizure frequency

The first test of validity of the SHE scale was done using the "known groups technique". With this method, the mean scale scores are compared for groups of subjects who are hypothesised to differ in the attribute under investigation (on the basis of theory or prior investigations). If score distributions are in accord with predictions, the investigation can be said to provide validatory evidence for the instrument. In this case it was hypothesised, on the basis of many previous studies (Trostle *et al.*, 1989; Jacoby, 1992; Jacoby *et al.*, 1993; Jacoby, 1995), that the degree of handicap would be related to current seizure frequency for both groups A and B. For the cross-sectional clinic population (group A), the overall seizure frequency was split into four groups: (1) seizure free for one or more years (2) less than 1 seizure per month (CPS, GTC or AS) or only SPS (3) 1-4 seizures per month (CPS, GTC or AS) (4) more than 1 seizure per week (CPS, GTC or AS). For the post-surgical population (group B) the seizure outcome was classified into (1) seizure free for one year (or seizure free since the operation if the post-operative duration was between 6 months and 1 year). (2) SPS only (3) CPS or GTC seizures less than 1 seizure per month (4) One or more seizures per month. The latter classification was used so that the specific effect of SPS could be examined.

The statistical analysis was performed using planned comparisons, followed by post-hoc analyses controlling the accepted significance level for multiple comparisons. The planned comparisons, in the cross-sectional population, were the mean scale scores of those (1) seizure free versus not seizure free, (2) auras or rare seizures versus a greater number of seizures and (3) l-4 seizure per month versus more frequent seizures. These three comparisons were carried out using the Helmert system of orthogonal contrasts

(Hand and Taylor, 1987), which allows for a complete partition of the variance and does not require adjustment of the significance level. For the post-surgical population, the comparisons were (1) seizure free versus not seizure free, (2) auras v all other seizures and (3) rare seizures (less than 12 per year) v regular seizures. The sample size of the aura and rare seizure groups were relatively small, however, tests of homogeneity of variance were not significant and therefore an ANOVA was appropriate. Next, trend analyses of scale scores were performed using polynomial contrasts (Hand and Taylor, 1987) to see if scores were linearly related to seizure frequency category. For each of these analyses the scores on the ESI-55 scales were also examined. Finally, the data was explored using post-hoc analyses with the Student-Newman-Keuls procedure (Norusis, 1990). Because anxiety and depression may cause subjects to indicate poor health across multiple domains, a second analysis was carried out using an analysis of covariance with the total HAD scores as a covariate to adjust for anxiety and depression.

3.1.4.3b The effect of employment and other factors

A second test of validity was a planned analysis of subscale scores on responses to three additional questions that were postulated to relate to handicap. Firstly, the effect of employment status was examined. This was categorised into; full-time/part-time compared with those subjects either unemployed or on disability benefit (students, homemakers and those retired were not analysed as there was no a priori hypothesis as to their "average subjective handicap"). Secondly, the scores according to the response to the question whether "epilepsy had affected your choice of education , training, job or career". Finally, scores were compared by response to an additional single item that asked "in the last year what has affected your quality of life more overall; 'epilepsy' or 'other changes' ". It was hypothesised that "subjective handicap of epilepsy" would be higher in those people who perceived their quality of life was primarily determined by epilepsy and in those who felt that epilepsy had affected their choice of main activity. It was hypothesised that these two questions would pick out subjects whose lives had specifically been affected by the consequences of epilepsy rather than other life events, and hence be helpful in demonstrating that the scale measured disease specific handicap.

3.1.4.3c Correlational and factor analysis

Scores on the SHE scales and the ESI-55 subscales in the entire dataset were correlated. It was postulated that the SHE scales would correlate best with the scale in the ESI-55 that measured a related construct (i.e. "ESI-55 role scales" and the SHE "Work & Activity" scale). The dimensionality of the scale was explored using factor analysis. The suitability of the dataset for factor analysis was first checked by inspecting the correlation matrix for the percentage of correlations greater than 0.3, checking the approximate normality of the variables, and ensuring the presence of at least 10 times the number of cases compared to items. Finally, sampling adequacy was tested with the Kaiser-Meyer-Olkin statistic (Norusis, 1990). The entire dataset was then subjected to a principle components analysis, selecting the number of factors with Catell's scree test, (Cattell, 1966) followed by orthogonal (varimax) and an oblique (oblimin)(Norusis, 1990) rotations to extract factors underlying the scale.

3.2 Results

3.2.1 SHE Questionnaire content

The interview process suggested a number of core problems that "handicap" people with epilepsy; (1) work related handicaps, which applies also to people in education and training, as well as the effect of epilepsy on other "daily activities" (2) Social and personal life difficulties (3) Feelings about oneself with epilepsy (4) the subjective physical consequences of epilepsy. These concepts were further broken down to more specific handicaps, and these were then used to derive potential questions (Table 3.1).

Two other scales were added to enhance the usefulness of the SHE scale if it was to be used in isolation. First, a "satisfaction" dimension indicating how happy a person is with various aspects of his/her life. Second, a change scale was created to measure self perceived improvement or worsening across handicap dimensions. The time frame for the scale items was "the last six months", apart from the "change" scale which was with respect to "the last year' (because it was envisaged that the scale would be used 1 year after an intervention).

The "Work & Activity" scale comprised three, mutually exclusive, related, alternative subscales. The respondent was asked to complete the scale appropriate to their main activity. This was done as it had been observed, during the early development of the measure that subjects had difficulty completing the ESI-55 "role" items, in which "work or activities" are treated as one concept, and this problem led to missing values or "guessing" responses. Accordingly, the three "Work & Activity" scales, for those in employment, for those in education or training and for those not in work, differ slightly in question phrasing and item content to make them specifically relevant to the main activity.

3.2.2 SHE Scale scoring

The scale contained 32 items in 6 subscales; (1) "Work & Activity" (8 items), (2) "Social and Personal" (4 items), (3) "Physical" (4 items), (4) "Self-Perception" (5 items), "Life-Satisfaction" (4 items), and (6) "Change" (7 items - one item on "control of epilepsy" was not included in the study on post-surgical patients). Scoring was on a Likert scale (1 to 5 for each item). Item scores were summed, and the subscale score was linearly transformed onto a 0-100 scale, with 0 indicating worst handicap and 100 least handicap (or most satisfaction). This scoring was chosen so that improvement on all scales would be in a similar direction, and that the metric was comparable with the SF-36 (Ware, 1992), ESI-55 and the QOLIE scales (Devinsky *et al.*, 1995). On the change scale, 50 equalled no change, 0 indicated "much worse" and 100 "much better".

3.2.3 Characteristics of the study population

The response rate in the cross-sectional clinic sample (group A) was 77%, and in the post-surgical sample (group B) was 84%. The clinical characteristics of responders and non-responders are shown for group A in Table 3.3 and for group B in Table 3.4. There were no significant differences in age, sex, duration of epilepsy, or seizure frequency between responders and non-responders for group A. In the post-surgical sample males were more common amongst the non-responders, but otherwise no differences were noted.

3.2.4 Data Quality

One item was dropped ("Does your epilepsy ever create problems getting on with your partner ?") as it was answered with an unscored response option by 35% of respondents. Apart from this item, only 0.3% of item responses were coded as missing. Only four questions had more than 1% missing values; Q.28 2.5%; Q.8. 2%; Q.2 and Q.7. 1%. The median time to complete the questionnaire for forty respondents was 8 minutes (range 4 to 21 minutes). No item caused frequent comprehension problems and no important additional areas of concern to people with epilepsy was revealed in debriefing.

Table 3.1. Domains and constructs of the Subjective Handicap of Epilepsy scale.

Domains of handicap	Specific constructs within each domain
Work and Activities	Difficulties in obtaining and maintaining employment
	Being in employment which is not one's first choice
	Problems at work due to seizures and medication
	Travelling and driving
	Alterations to daily routine due to seizures or medication
	Effect of epilepsy on leisure and recreation.
Social and Personal Life	Difficulties secondary to "revealing" epilepsy
	Alteration in the development of socialisation due to childhood epilepsy.
	Alteration in relationship with partner and friends due to epilepsy
	Social limitations due to travelling and economic constraints
	Sexual life
Feelings about oneself	Stigmatization
	Feeling of not being in control of one's future,
	Fear of seizures
	Fear of seizures in public
Physical	Seizure related injuries and symptoms
	Subjective effect of medication on well-being
Life-Satisfaction	Happiness with one's work, leisure, and social life.
Change	Self-reported change across all domains

3.2.5 Descriptive statistics and scaling properties

Graphical analyses of the subscales scores revealed that all scales were approximately normally distributed, apart from the "Social & Personal" which was moderately negatively skewed. The percentage of respondents scoring at floor values (minimum) and at ceiling (maximum) on each scale were less than 5% for all scales except "Social and Personal" which had an 18% ceiling effect (Table 3.4). This indicated that the scale measured a broad range of subjective handicap. For no single scale item did more than 50% of respondents achieve a similar score, except for the change scale items in which 50-60% of respondents indicated no change. The individual item means were within 1 scale point and standard deviations within 0.5 scale points, indicating that item weighting was unnecessary.

The median corrected correlation of each item with its own scale total always exceeded the correlation of that item with other scale totals (Table 3.4). The percentage of items in each scale in which the "corrected item-total correlation" exceeded by two standard errors "item-other total" correlations are indicated by the "scaling success statistic" in Table 3.4. The results demonstrated that all scales were appropriately constructed, although 2 items in the "physical" scale were also closely related to the "Work & Activity" scale.

Table 3.2 Clinical characteristics of responders and non-responders in group A (Clinic and EEG telemetry samples).

	Responders (77%, n = 287)	Non-responders (23%, n = 87)
Median age (years)	34	32
% Male	46	54
Median duration of epilepsy (years)	22	22
Syndromic classification		
(% of persons in each syndrome category)		
Localization related - known aetiology	59	47
Localization related - cryptogenic	21	22
Idiopathic generalized epilepsy	14	11
Generalized (cryptogenic / symptomatic)	2	5
Unclassified	4	15
Seizure frequency		
(% of persons in each seizure category)		
Seizure free more than 1 year	14	25
SPS only or < 1 seizure per month	16	9
1-4 Seizures per month	19	21
More than 4 seizures per month	51	45

SPS = Simple Partial Seizure

Table 3.3. Clinical characteristics of responders and non-responders in Group B (Post-surgical group)

	Responders (84%, n = 105)	Non-responders (16%, n = 20)
Median age (years)	31	33.5
% Male	45	70
Median duration post-operation (months)	28	32.5
Seizure frequency		
(% of persons in each seizure category)		
Seizure free in the last 12 months	48	44
Simple partial seizures	11	6
Rare seizures (less than 1 per month)	11	6
More than 1 seizure per month	30	44

Table 3.4. Descriptive statistics, scaling successes and internal consistency of SHE scale in 392 Patients.

Subscale	Score at Minimum %	Score at Maximum %	Median corrected item-total correlation	Median "item-other scale" correlation	Scaling success %	Cronbach's alpha
Work & Activity	1	5	0.69	0.48	83	0.88
Social & Personal	1	18	0.72	0.50	100	0.86
Physical	2	1	0.49	0.41	66	0.72
Self-Perception	5	4	0.69	0.49	90	0.87
Life-Satisfaction	1	2	0.60	0.39	96	0.79
Change	0	3	0.74	0.39	100	0.88

3.2.6 Reliability

Cronbach's alpha for each scale indicated very satisfactory internal consistency (Table 3.4). Deletion of no item would have led to a significant increase in alpha. Alpha for the alternative versions of the "Work and Activities" scale were: (1) In employment (n=189) alpha = 0.85; (2) In education (n=36) alpha = 0.87; (3) Not in work (n=163) alpha = 0.90. This confirmed that the alternative versions were equally reliable. Test-retest reliability was carried out on 110 subjects. The overall intraclass correlations (ICC) for each scale ranged from 0.83-0.89 indicating highly satisfactory reliability (Table 3.5). The lower 95% confidence intervals for the ICC were in the range 0.76-0.84. The test-retest reliability was examined at three time intervals; 24 hours, 1 week and 4-8 weeks (see Table 3.6). The ICC was in very close agreement for each interval and indicated that the scales are equally stable over these intervals. The only subscale for which any difference was noted was the "Social and Personal" in which it may be noted that the ICC is slightly lower at the 1 week interval. This was accounted for by 4 outliers that were retained in the analysis. Of the 63 subjects who were retested at 4-8 weeks, twenty indicated a recent worsening in seizures or general health (usually the occurrence of a tonic clonic seizure). Analysis of variance indicated no effect of recent seizures, demonstrating that the scale is not sensitive to minor fluctuations in health. The test-retest reliability was examined by calculating the mean difference between the first and second rating (bias). There was no bias (Tables 3.5 and 3.6), either for all 110 subjects, or when analysed at the three different time intervals. The size of the test-retest differences were plotted against scale scores and this demonstrated that the reliability was equivalent across the range of score values. The repeatability coefficients for each scale indicated that 95% of repeated values for an individual respondent lay within approximately 25 points on the subscale (Table 3.5).

Table 3.5 Reliability statistics for the 6 subscales for all 110 subjects (mean test - retest difference, repeatability coefficient and intra-class correlation coefficient).

Subscale	Mean test-retest difference (in scale points)	Repeatability coefficient (in scale points)	Intra-class correlation coefficient
Work & Activity	0.6	24.8	0.89
Social & Personal	-1.9	27.6	0.86
Physical	1.8	24.2	0.87
Self-Perception	3.2	26.7	0.88
Life-Satisfaction	-0.2	23.0	0.86
Change	4.0	20.0	0.83

Table 3.6 Reliability statistics for the 6 subscales at 3 test-retest time intervals (mean test-retest difference, repeatability coefficient and intra-class correlation coefficient).

Retest interval/ SHE scale	Mean test-retest difference (in scale points)	Repeatability coefficient (in scale points)	Intra-class correlation coefficient
Retest at 24 Hours(n=23)			
Work & Activity	3.6	20.0	0.88
Social & Personal	-0.6	30.6	0.80
Physical	-1.7	22.6	0.84
Self-Perception	2.6	29.9	0.84
Life-Satisfaction	-0.2	20.4	0.89
Change	4.0	25.9	0.81
Retest at 1 Week (n=24)			
Work & Activity	0.2	18.6	0.92
Social & Personal	-8.3	31.6	0.69
Physical	-0.3	21.8	0.89
Self-Perception	-1.8	17.2	0.96
Life-Satisfaction	-1.3	18.1	0.91
Change	-1.7	18.5	0.87
Retest at 4-8 weeks(n=63)			
Work & Activity	0.48	28.2	0.83
Social & Personal	0.05	23.5	0.80
Physical	3.85	25.5	0.84
Self-Perception	5.2	27.9	0.85
Life-Satisfaction	0.21	25.6	0.79
Change	1.65	18.2	0.76

3.2.7 Validation studies

3.2.7.1 Clinic and EEG Telemetry sample (Group A)

3.2.7.1a Effect of seizure frequency on SHE scale scores

The first validatory hypothesis to be tested was that subjective handicap, as measured by the scale, would be related to seizure frequency over the last year. Subjects who were seizure free had the highest scores (least handicap) (Table 3.7). A series of univariate analyses of variance (ANOVA), using planned contrasts were carried out examining scale scores by seizure category. The first contrast (subjects seizure free v those not seizure free) revealed highly significant differences for all scales ($P<0.0001$, Table 3.7) except for the Life-satisfaction scale for which the difference was smaller ($P<0.05$,. Table 3.7). For the second comparison (those with less than one seizure per month versus those with more frequent seizures), significant differences on all scales were evident ($P<0.001$, Table 3.7). The final contrast was between those subjects with 1-4 seizures per month with those with more frequent seizures, on which the "Physical" scale demonstrated a significant difference ($P<0.05$, Table 3.7). A linear trend of decreasing mean SHE scale score (worsening handicap) across increasing seizure frequency was confirmed using an ANOVA with polynomial contrast for linear trend ($P<0.0001$, Table 3.7). Lastly, post-hoc analysis using the Student-Newman-Keuls procedure for multiple comparisons (at $P<0.05$) revealed that for three scales ("Work & Activity", "Physical" and "Self-Perception") it was possible to achieve a clear distinction for all, or all but one, of the potential category comparisons. The least discrimination was found in the "Life-Satisfaction" and the "Change" scales. The mean "Change" score of approximately 50 for all groups, except for those seizure free, indicated no self-perceived change over the last 12 months. This suggested that subjective handicap was a relatively stable trait.

The analyses were repeated controlling for psychiatric morbidity (using total HAD score, anxiety plus depression, as a covariate) because of the possibility that psychiatric symptoms were an important influence on the SHE scores. The linear trend for all mean SHE scales scores against seizure frequency category remained highly significant (Table 3.7). On the first contrast (seizure free versus not) the "Life-Satisfaction scale" and

'Social Life" no longer differed significantly, but the other scales continued to do so ($P<0.0001$, data not shown). On the second contrast (auras or infrequent seizures versus more frequent seizures) all scales detected a significant difference ($P<0.04$ to $P<0.001$), whilst on the final contrast (more or less than 4 seizures per month) the "Physical" and the "Work and Activity" scales detected a difference ($P<0.01$ and $P<0.05$, data not shown). The pattern of significant differences were thus very similar to the analysis without HAD total score as a covariate. In summary, psychiatric status did not account for the differences in SHE scores at different seizure frequencies.

3.2.7.1b Effect of seizure frequency on HAD and GHQ scores

The direct comparison of psychiatric morbidity by seizure frequency revealed a small but significant difference for mean HAD anxiety and total GHQ scores for the comparison of frequent seizures versus no or rare seizures (Table 3.8). The proportion of persons who scored above cut-off for "caseness" on the HAD anxiety scale with no seizures, rare seizures, 1-4 seizures or more than 4 seizures per month was 18%, 21%, 29% and 36% respectively. The proportions for HAD depression scale were 5%, 5%, 5%, 7%, and for "caseness" on GHQ 30 scale were 28%, 41%, 45%, 53%.

3.2.7.1c Effect of seizure frequency on ESI-55 scores

The mean ESI-55 scores (and 95% C.I.) for 6 of the 11 subscales and the three summary scales in the cross-sectional population with differing seizure frequencies are shown in Tables 3.9a and b. The 4 subscales for which there were only small or no significant differences between the groups (Physical function, Pain, Energy and fatigue, and Emotional well-being) are not shown. Significant differences in the seizure free v not seizure free comparison were found for all the ESI-55 subscales shown in Tables 3.9a and b, but for only 5 subscales were these also found in the second comparison (less than 1 seizure per month v more frequent seizures). None of the final comparisons (1-4 seizures per month v more than 1 per week) reached significance. A linear trend in ESI-55 score was found for all subscales shown ($P<0.01$, Tables 3.9a and b).

Table 3.7 Mean SHE scale scores (and 95% confidence interval) according to seizure frequency for group A (Clinic and EEG telemetry).

Seizure frequency (n)	Mean SHE scale score and (95% confidence interval)					
	Work	Social	Physical	Self-P.	Life-S.	Change
Seizure free (38)	81††† (76,86)	78†† (71,85)	68††† (63,73)	68††† (60,75)	66† (61,72)	64††† (59,68)
SPS or <1 Sz/M (47)	67$^{\$\$\$}$ (62,73)	77$^{\$\$\$}$ (70,84)	57$^{\$\$\$}$ (52,62)	56$^{\$\$\$}$ (50,63)	65$^{\$\$}$ (59,71)	55$^{\$\$}$ (51,59)
1 - 4 Sz / M (54)	51 (46,56)	63 (56,69)	48^{+} (43,53)	43 (37,49)	55 (49,61)	49 (45,52)
More than 4 Sz / M. (147)	45 (42,49)	62 (57,66)	40 (37,44)	39 (35,43)	56 (53,59)	48 (46,51)
F ratio for Linear trend across seizure outcome categories	109.4***	19.2***	65.8***	50.1***	14.0***	39.2***
F ratio for Linear trend across seizure outcome categories controlling for total HAD score	87.6***	10.1**	50.7***	36.3***	4.3*	27.8***

1. Significant mean SHE scale score differences for contrast:

seizure free v not seizure free; $^{\dagger\dagger\dagger}P < 0.0001$, $^{\dagger\dagger}P < 0.01$, $^{\dagger}P < 0.05$.

2. Significant mean SHE scale score differences for contrast:

Less than 1 seizure per month v more frequent seizures; $^{\$\$\$}P < 0.0001$, $^{\$\$}P < 0.01$.

3. Significant mean SHE scale score differences for contrast:

1-4 seizures per month v more than 4 per month; $^{+}P < 0.05$.

4. F ratio for linear trend in SHE scale score across seizure frequency:

$^{***}P < 0.0001$, $^{**}P < 0.002$, $^{*}P < 0.04$.

Abbreviations: Work = Work and Activity, Self P. = Self-Perception, Life-S. = Life-Satisfaction., HAD = Hospital anxiety and depression scale, SPS = simple partial seizures, Sz = seizure, M = Month.

Table 3.8 Mean HAD and GHQ scale scores (95% CI) according to seizure frequency for group A (Clinic and EEG telemetry sample)

Seizure frequency (n)	HAD Anxiety score (Max. 21)	HAD Depression score (Max. 21)	GHQ score (Max. 90)
Seizure free (38)	6.5 (5.0,8.1) †	3.7 (2.6,4.9)	25.8 (22,30) *
SPS or <1 Seizure /M (44)	7.3 (6.2,8.4)	3.6 (2.6,4.5)	27.7 (24,31)
1 - 4 Seizures / M (55)	8.1 (6.9,9.2)	4.6 (3.6,5.6)	30.4 (27,34)
More than 4 Sz / M. (143)	9.3 (8.5,10.0)	5.0 (4.4,5.6)	33.0 (31,35)

1. Significant mean HAD anxiety scale score differences for contrast:

seizure free v not seizure free; $^{\dagger}P < 0.03$.

2. Significant mean GHQ scale score differences for contrast:

seizure free v not seizure free; $^{*}P < 0.05$.

Table 3.9a Mean ESI-55 subscale scores (and 95% confidence interval) according to seizure frequency for Group A (Clinic and EEG telemetry).

Seizure frequency (n)	Mean ESI-55 Scale scores and (95% confidence interval)				
	Role P	Role E	Health P.	Social F.	Cognition
Seizure free (38)	85††† (78,91)	82†† (74,90)	72† (66,77)	87††† (81,94)	76††† (68,83)
SPS or <1 Sz/M (47)	73$^{\$}$ (64,83)	68 (57,79)	68 (63,72)	77 (69,85)	69$^{\$\$}$ (63,76)
1 - 4 Seizures / M (54)	59 (48,69)	66 (56,76)	64 (59,69)	69 (62,76)	61 (55,67)
More than 4 Sz / M. (147)	59 (53,66)	64 (57,70)	60 (57,63)	70 (65,75)	56 (52,60)
F ratio for linear trend across seizure frequency categories	18.8***	6.6*	13.4***	15.2***	25.4***

1. Significant mean scale score differences for contrast:

seizure free v not seizure free; ††† ($P < 0.001$), †† ($P < 0.01$); † ($P < 0.05$).

2. Significant mean scale score differences for contrast:

less than 1 seizure per month or SPS only v more frequent seizures: $^{\$\$}$($P < 0.01$), $^{\$}$($P < 0.05$).

3. No significant differences for contrast:

1-4 seizures per month v more than 4 seizures per month.

4. F ratio for linear trend in ESI-55 scale score by seizure frequency

***($P < 0.0001$), **($P < 0.001$), *($P < 0.01$).

Abbreviations: Role P = Role-Physical, Role E = Role-emotional, Health P = Health Perceptions, Social F = Social Function, SPS = simple partial seizures, Sz = seizure, M = Month.

Table 3.9b. Mean ESI-55 subscale and summary scores (and 95% confidence interval) according to seizure frequency for Group A (Clinic and EEG telemetry sample)

Seizure frequency (n)	Mean ESI-55 Scale scores and (95% confidence interval)				
	Role M.	QOL	S.Mental H	S.Physical H	S.Role F
Seizure free (38)	87†† (79,94)	69†† (64,74)	70†† (65,75)	81†† (77,85)	84††† (77,89)
SPS or <1 Sz /M (47)	73 (64,82)	67$$$ (62,71)	66$$ (62,71)	75$ (69,80)	72$ (65,79)
1 - 4 Seizures / M (54)	67 (57,76)	59 (54,63)	60 (56,65)	70 (65,76)	65 (57,72)
More than 4 Sz / M. (147)	62 (56,68)	55 (53,58)	58 (55,60)	67 (63,70)	62 (58,67)
F ratio for linear trend across seizure frequency categories	16.5***	25.3***	20.6***	17.6**	22.5**

1. Significant mean scale score differences for contrast:

seizure free v not seizure free; ††† ($P < 0.001$), †† ($P < 0.01$); † ($P < 0.05$).

2. Significant mean scale score differences for contrast:

less than 1 seizure per month or SPS only v more frequent seizures; $$$($P < 0.0001$),$$($P < 0.01$), $($P < 0.05$).

3. No significant differences for contrast:

1-4 seizures per month v more than 4 seizures per month.

4. F ratio for linear trend in ESI-55 scale score by seizure frequency: ***($P < 0.0001$), **($P <$ 0.001).

Abbreviations: Role M = Role memory, QOL = Quality of life, S.Mental H = Summary Mental Health, S.Physical H = Summary Physical Health, S.Role F = Summary Role Function, SPS = simple partial seizures, Sz = seizure, M = Month.

3.2.7.1d Effect other factors (SHE scale)

The second set of validatory hypotheses that were tested were the relationship between scale scores and (1) employment status and (2) the effect of epilepsy on career or job choice and (3) what factor the subject perceived as the main determinant of their quality of life. It was postulated that most scales should indicate that those in work would feel less handicapped. The mean SHE score was significantly greater (i.e. less handicapped) for those in employment for 5 scales ($P< 0.0001$, Table 3.10a) and also for the satisfaction scale ($P<0.005$). Higher scores were also seen on the "Change" scale for the "less handicapped" groups, but the size of this difference was less than on the other 5 scales, suggesting that the overall differences were not simply accounted for by recent change.

In the second analysis, actual employment status was ignored, but subjects were asked whether their epilepsy had made a difference to job or career choice. This analysis avoided the assumption that current employment status represented the person's ideal choice of main activity, as it was noted that 59% of those in work responded that job choice had been affected. In addition, subjects currently not in work could be analysed. Ninety one percent of subjects responded to this item, and 66% indicated that epilepsy had affected their career or job. Those subjects whose job choice had been affected by epilepsy were more handicapped all on scales ($P<0.00001$, Table 3.10b).

Table 3.10a Mean SHE scale scores (and 95% confidence interval) for Group A (effect of employment status)

Groups	Mean SHE scale score and (95% confidence interval)					
	Work	Social	Physical	Self-P	Life-S	Change
Employment status						
Employed (138)	62 (58,65)	73 (69,76)	54 (51,57)	51^{++} (47,55)	64 (61,67)	56 (53,58)
Unemployed (88)	44 (39,49)	58 (52,64)	39 (34,44)	39 (34,45)	50 (45,54)	46 (42,49)

Significant mean SHE scale score difference: Employed v Unemployed
all comparisons P <0.0001, except $^{++}$ P < 0.001.

Table 3.10b Mean SHE scale scores (and 95% confidence interval) for Group A (effect of epilepsy on career)

Groups	Mean SHE scale score and (95% confidence interval)					
	Work	Social	Physical	Self-P	Life-S	Change
Has epilepsy affected choice of education, job, or career ?						
No (87)	69 (65,74)	80 (76,84)	57 (53,61)	59 (53,64)	69 (66,73)	56 (53,60)
Yes (174)	48 (45,51)	61 (58,65)	45 (41,48)	41 (37,44)	54 (51,57)	50 (47,52)

Significant mean SHE scale score difference: Yes v No

all comparisons P <0.0001.

Abbreviations: Work = Work and Activity, Self P. = Self-Perception, Life-S. = Life-Satisfaction., SPS = simple partial seizures, Sz = seizure, M = Month.

Table 3.10c Mean SHE scale scores (and 95% confidence interval) for Group A (effect of main factor determining quality of life)

Groups	Mean SHE scale score and (95% confidence interval)					
	Work	Social	Physical	Self-P	Life-S	Change
What has most affected your quality of life in the last year ?						
Other changes(87)	69 (65,74)	75 (70,79)	57 (53,61)	60 (55,65)	62+ (58,66)	56 (53,59)
Epilepsy (168)	44 (41,47)	59 (55,63)	41 (38,44)	36 (32,39)	55 (52,58)	48 (46,50)

1. Significant mean SHE scale score difference: Epilepsy v Other changes

all comparisons $P < 0.0001$, except $^{+}$ $P < 0.005$.

Abbreviations: Work = Work and Activity, Self P. = Self-Perception, Life-S. = Life-Satisfaction., SPS = simple partial seizures, Sz = seizure, M = Month.

In the third analysis subjects were asked "What in the last year has affected your quality of life more overall": "epilepsy" or "other changes in my life". The hypothesis was that subjects who felt that epilepsy was the dominant quality of life factor, would also be those who felt most "handicapped" by epilepsy. Eighty nine percent of subjects responded to this item, and 66% indicated that epilepsy had been the dominant factor. The responses were not identical to the career question, in that only 74% of subjects who felt epilepsy had affected job choice, indicated that epilepsy had been the dominant factor in quality of life, and that 48% of subjects who felt epilepsy had not affected their job, still believed that epilepsy was the determining factor in quality of life. Patients who felt that epilepsy was the dominant factor scored significantly lower on 5 scales ($P<0.0001$, and "Life-Satisfaction" scale; $P<0.005$; Table 3.10c).

3.2.7.2 Post-surgical population

3.2.7.2a Effect of seizure frequency on SHE scale score

The first validation hypothesis to be tested in the post-surgical population was that "subjective handicap", as measured by the SHE would be related to seizure outcome. The highest score (lowest handicap) was obtained by those subjects rendered seizure free by surgery (Table 3.11). There was also a trend of decreasing score by increasing seizure frequency and severity. The planned comparisons revealed significant differences for those subjects seizure free compared with those not seizure free for all subscales (Table 3.11). The comparison of auras v all other seizures was significant for the "Self-Perception" ($P<0.01$) scale and just failed to reach significance for the "Work & Activity" scale. The comparison of rare seizures (less than 1 per month) versus more frequent seizures was significant for the "Work & Activity" and "Social & Personal" scale and just failed to achieve significance for the "Self-Perception" and "Change" scales. The relatively wide confidence intervals, due to small sample size, for the two middle outcome categories may preclude the detection of differences between these groups. A linear trend of scale scores by outcome category was also found for all scales (Table 3.11).

3.2.7.2b Effect of seizure frequency (ESI-55)

Eight scales showed a significant difference in the primary comparison of seizure free v not seizure free (only four of which P <0.01, Table 3.12a and b). Only one ESI-55 scale (Health perceptions) detected a difference on the second comparisons. A linear trend was found for 6 of the scales.

Table 3.11 Mean SHE scale scores (and 95% confidence interval) according to seizure outcome for post-surgical group

Seizure outcome (n)	Mean SHE scale score and (95% confidence interval)					
	Work	Social	Physical	Self-P	Life-S	Change
Seizure free (48)	$84^{\dagger\dagger\dagger}$ (79,89)	$84^{\dagger}$ (79,89)	$72^{\dagger\dagger\dagger}$ (67,77)	$78^{\dagger\dagger}$ (72,84)	$71^{\dagger}$ (66,76)	$78^{\dagger\dagger}$ (72,84)
SPS (12)	75 (61,89)	80 (62,98)	63 (49,77)	$81^{\$\$}$ (68,94)	66 (55,76)	69 (54,85)
Less than 1 Sz/ M (12)	71^{++} (56,86)	78^{+} (63,92)	57 (47,66)	66^{+} (51,81)	65 (50,80)	66 (50,82)
More than (31) 1 Sz per month	50 (40,59)	60 (50,70)	50 (42,59)	51 (41,61)	54 (45,64)	59 (53,65)
F ratio for linear trend	34.6^{***}	16.1^{**}	21.2^{***}	26.7^{***}	9.4^{*}	12.5^{**}

1. Significant mean SHE scale score differences for contrast:

seizure free v not seizure free: $^{\dagger\dagger\dagger}P < 0.0001$, $^{\dagger\dagger}P < 0.01$, $^{\dagger}P < 0.05$.

2. Significant mean SHE scale score differences for contrast:

auras v all other seizures: $^{\$\$}P < 0.01$.

3. Significant mean SHE scale score differences for contrast:

Less than 1 seizure per month v more than 1 seizure per month; $^{++}P < 0.01$, $^{+}P < 0.05$.

4. F ratio for linear trend: in SHE scale score across seizure frequency

$^{***}P < 0.00001$, $^{**}P < 0.0001$, $^{*}P < 0.001$.

Abbreviations: Work = Work and Activity, Self P. = Self-Perception, Life-S. = Life-Satisfaction, SPS = simple partial seizures, Sz = seizure, M = Month.

Table 3.12a Mean ESI-55 scale (and 95% confidence interval) according to seizure outcome for post-surgical group

Seizure Outcome(n)	Mean ESI-55 scale scores and (95% confidence interval)				
	Role P	Role E	HP	SF	Cog
Seizure free (48)	84† (76,92)	81†† (73,90)	82†† (78,86)	87†† (81,92)	74 (68,80)
SPS (12)	78 (56,100)	65 (45,85)	86$^{\$\$}$ (78,94)	81 (72,89)	75 (59,91)
Less than 1 Sz / M (12)	62 (39,85)	48 (22,75)	72 (58,87)	76 (64,88)	78 (71,85)
More than 1 Sz / M (31)	69 (54,84)	65 (51,80)	61 (53,69)	65 (54,76)	66 (56,76)
F-ratio for linear trend across seizure outcome	5.1	5.4	30.2***	15.1**	1.2

1. Significant mean score differences for contrast:

seizure free v not seizure free: †† ($P < 0.01$); † ($P < 0.05$).

2. Significant mean score differences for contrast:

less than 1 seizure per month or SPS v more frequent seizures $^{\$\$}$($P < 0.001$).

3. No significant differences for contrast:

less than 1 seizure per month v more than 1 seizure per month .

4. F ratio for linear trend in ESI-55 scores across seizure outcome

***($P < 0.0001$), **($P < 0.001$).

Abbreviations: Role P.= Role-Physical, Role E. = Role-Emotional, HP = Health Perceptions, SF = Social Function, Cog = Cognition, SPS = simple partial seizures, Sz = seizure, M = Month.

Table 3.12b Mean ESI-55 scale and summary scores (and 95% confidence interval) according to seizure outcome for post-surgical group

Seizure Outcome(n)	Mean ESI-55 scale scores and (95% confidence interval)				
	ROLE M	QOL	S.MH	S.PH	S.RF
Seizure free (48)	83 (75,91)	72†† (67,77)	73† (69,78)	82† (77,87)	82† (76,87)
SPS (12)	87 (75,98)	65 (52,77)	72 (64,80)	80 (70,90)	77 (66,88)
Less than 1 Sz / M (12)	67 (47,86)	60 (44,76)	66 (54,77)	73 (60,85)	65 (49,80)
More than 1 Sz / M (31)	74 (61,86)	57 (49,65)	61 (54,67)	71 (64,78)	68 (59,78)
F-ratio for linear trend across seizure outcome	4.1	9.1*	12.3**	8.4*	8.4*

1. Significant mean score differences for contrast:

seizure free v not seizure free: †† ($P < 0.01$); † ($P < 0.05$).

2. No significant mean score differences for contrast:

less than 1 seizure per month or SPS v more frequent seizures.

3. No significant differences for contrast:

less than 1 seizure per month v more than 1 seizure per month.

4. F ratio for linear trend in ESI-55 scores across seizure outcome: **($P < 0.001$), *($P < 0.01$).

Abbreviations: Role M = Role memory, QOL = Quality of life, S.MH = Summary Mental Health, S.PH = Summary Physical Health, S.RF = Summary Role Function, SPS = simple partial seizures, Sz = seizure, M = Month.

3.2.7.2c Effect of other factors (SHE scale)

As in the cross-sectional population a second set of validatory investigations were carried out on the post-surgical group based on the response to the three additional questions on (1) employment status, (2) the effect of epilepsy on career or job choice and (3) the major determinant of quality of life (epilepsy v "other changes"). Those subjects who were employed had higher scores (less handicap) than those not in work for all scales ($P<0.001$) (Table 3.13a). Those subjects who felt their career or job choice (post-operatively) had *not* been affected scored more highly on all but the "Change" scale ($P<0.001$, Table 13.3b). Finally, those subjects who felt that epilepsy was *not* the dominant factor in their quality of life scored more highly on all scales except the "Change" scale ($P<0.001$, Table 13.3c).

3.2.8 Correlations of SHE scale with the ESI-55

For all 392 subjects in the study the correlation of the SHE scale scores with ESI-55 scales are shown in Table 3.14. Correlations for the SHE scales with the ESI-55 summary scales (not shown) were all 0.5-0.6. The SHE "Work & Activity" scale was strongly correlated with ESI-55 "Role-physical, Health-perception and Social functioning scales". The SHE "Physical" scale was related to the ESI-55 "Energy and fatigue, Cognition, and Role memory scales". The SHE "Social & Personal" scale was correlated with the ESI-55 "Social functioning". The SHE "Self-perception" was best correlated with ESI-55 "Health Perceptions". The SHE "Life Satisfaction" was best correlated with the ESI-55 "Quality of life" visual analogue scales. The SHE change scale was highly correlated with the ESI-55 "Change" scale. These results strongly suggest that relationships that one would predict to exist between the ESI-55 and the SHE scaled are indeed confirmed.

3.2.9 Factor analysis

The dataset met all criteria required for an adequate factor analysis. Factor extraction by principle components (PC) followed by orthogonal or oblique rotation gave

comparable results. The 6 factor model accounted for 65% of the variance. Table 3.15 displays the rotated factor matrix, with the loading of the 6 factors on each item, if the loading is greater than 0.4. Also shown are the subscales in which each subscale was placed, a priori, on the grounds of content validity. Inspection of the matrix revealed that the postulated dimensionality of the SHE scale was largely confirmed by the factor analysis. The only significant deviation of the factor model, from the proposed scale structure, was that two items in the "physical scale" would appear to be closely related to the "Work & Activity" scale. The original SHE scale structure has been retained as the content of this scale had greater face validity.

Table 3.13a Mean SHE scale scores (and 95% confidence interval) according to post-operative employment status

Groups (n)	Mean SHE scale scores and (95% confidence interval)					
	Work	Social	Physical	Self-P	Life-S	Change
Employment status post-surgery						
Employed (45)	83***	86***	71***	77**	73***	77**
	(76,89)	(80,92)	(66,76)	(71,83)	(68,79)	(72,83)
Unemployed (34)	56	64	50	61	53	60
	(47,65)	(55,73)	(42,59)	(51,70)	(45,60)	(52,67)

1. Significant mean SHE scale score difference: Employed v Unemployed

***$P < 0.0001$, ** $P < 0.001$.

Abbreviations: Work = Work and Activity, Self P. = Self-Perception, Life-S. = Life-Satisfaction.

Table 3.13b Mean SHE scale scores (and 95% confidence interval) according to effect of epilepsy on career choice for post surgical group

Groups (n)	Mean SHE scale scores and (95% confidence interval)					
	Work	Social	Physical	Self-P	Life-S	Change
Has epilepsy affected choice of education, job or career(post-surgery) ?						
No (54)	83*** (78,88)	84* (79,89)	72*** (68,77)	79** (74,85)	71* (66,76)	74 (68,79)
Yes (34)	58 (48,67)	69 (59,78)	51 (44,59)	60 (51.69)	57 (49,65)	66 (58,74)

1. Significant mean SHE scale score difference: Yes v No

***P < 0.0001, ** P < 0.001, * P < 0.005.

Abbreviations: Work = Work and Activity, Self P. = Self-Perception, Life-S. = Life-Satisfaction.

Table 3.13c Mean SHE scale scores (and 95% confidence interval) according to dominant factor determining quality of life for post surgical group

Groups (n)	Mean SHE scale scores and (95% confidence interval)					
	Work	Social	Physical	Self-P	Life-S	Change
What has most affected your quality of life in the last year ?						
Other changes (52)	80 *** (74,86)	84*** (79,90)	69*** (64,73)	76*** (71,82)	68* (63,73)	71 (65,77)
Epilepsy (34)	54 (45,64)	61 (51,70)	51 (42,59)	53 (44,63)	55 (47,63)	65 (59,71)

1. Significant mean SHE scale score difference: Epilepsy v Other Changes

$^{***}P < 0.0001$, $^{*}P < 0.005$.

Abbreviations: Work = Work and Activity, Self P. = Self-Perception, Life-S. = Life-Satisfaction

Table 3.14. Correlation matrix of SHE scale and ESI-55 scales (n=392)

ESI-55 Scale	SHE Scale					
	Work	Social	Physical	Self-P.	Life-S.	Change
Physical Function	0.37	0.32	0.36	0.29	0.29	0.27
Role-Physical	**0.5**	0.38	0.5	0.41	0.38	0.39
Role-Emotional	0.37	0.33	0.39	0.35	0.38	0.3
Vitality	0.38	0.32	0.54	0.43	0.46	0.4
Health Perception	**0.56**	0.49	0.56	**0.63**	0.46	0.41
Social Function	**0.57**	**0.56**	0.54	**0.56**	0.51	0.42
Mental Health	0.37	0.46	0.43	**0.53**	0.54	0.42
Cognition	**0.55**	0.49	**0.64**	**0.59**	0.40	0.41
Pain	0.32	0.35	0.46	0.33	0.29	0.23
Role Memory	**0.5**	0.4	0.5	0.48	0.37	0.37
Change	0.37	0.21	0.4	0.35	0.26	**0.59**
Quality of Life	**0.54**	0.47	0.54	0.55	**0.68**	**0.58**

All correlations significant ($P<0.01$). Strongest correlations shown in **bold.**

Abbreviations: Work = Work and Activity, Self P. = Self-Perception, Life-S. = Life-Satisfaction.

Table 3.15 Factor loading of the rotated factor matrix. Shown are the item number, the subscale in which it has been placed and the 6 extracted factors. Underneath each factor is the postulated meaning of the factor.

		Factors 1 to 6 (and postulated meaning)					
Item	SHE Scale	1 Work	2 Change	3 Self-P.	4 Social	5 Life-S.	6 Phys
1	Work	.69					
2	Work	.78					
3	Work	.57					
14	Work	.65					
15	Work	.55					
17	Phys	.66					
18	Phys	.71					
26	Change		.76				
27	Change		.74				
28	Change		.63				
30	Change		.78				
31	Change		.80				
32	Change		.79				
19	Work	.45		.57			
20	Work			.63			
21	Self-P.			.68			
22	Self-P.			.60			
23	Self-P.			.70			
24	Self-P.			.65			
25	Self-P.			.61			
8	Social				.66		
9	Social				.77		
10	Social				.73		
11	Social				.67		
12	Life-S.				.52	.48	
6	Work	.40				.52	
7	Life-S.					.78	
13	Life-S.					.58	
16	Life-S.					.52	
5	Phys						.66
4	Phys						.52

Scale abbreviations: Work = Work & Activity, Self P. = Self-Perception, Phys = Physical, Social = Social and Personal, Life-S. = Life Satisfaction. Q29 (not used in the surgical sample) was not included in this factor analysis.

3.3 Discussion

3.3.1 Development of the SHE scale

The scale was developed because there was no outcome measure sensitive to the common long-term psychosocial consequences of epilepsy. The Washington Psychosocial Inventory (WPSI) was considered inadequate because it focused on objective criteria and its response format (all yes/no) was insensitive (Dodrill *et al.*, 1980). The Epilepsy Surgery Inventory, covered generic health well but had few items relevant to psychosocial handicap (Vickrey *et al.*, 1992). The author had access to pre-publication versions of the Liverpool Quality of Life Model, (courtesy of Professor David Chadwick) an important advance at the time, but the scales used (Affect balance (Bradburn and Caplovitz, 1969), Profile of Mood states (McNair *et al.*, 1992), Self-esteem (Rosenberg, 1965), and Mastery (Pearlin and Schooler, 1978) were generic scales (focusing on mood state) that were developed in contexts other than epilepsy. A concern existed that they may not transfer well to patients with epilepsy, and that social and vocational problems were still not well covered. The "Impact of Epilepsy" scale did address these issues but it was considered too brief (factor analysis revealed only a single dimension) (Jacoby *et al.*, 1993). Therefore a scale was constructed to measure the key areas in which people epilepsy are most commonly handicapped.

3.3.2 Content

Following a review of the literature and interviews with people with epilepsy the key content areas had been defined and subsequent item selection occurred along qualitative rather than statistical lines. It may be a criticism that the items were not selected using statistical criteria (i.e. high correlations with known epilepsy scales). The development plan however was to select the best items following in-depth interviews and then subject the scale to rigorous evaluation of reliability and validity in a large sample of people with epilepsy.

The Work and Activities scale covered occupational and vocational handicap, as well the impact on "daily activities" for those not in work. The scale tapped

"underemployment", difficulties at work and insecurity of employment. The "Social and Personal" scale dealt with relationships within and beyond the family. The "Self-Perception" scale measured "felt stigma", worry due to seizures, locus of control (whether the subject feels in control of his/her life) and item on overall impact of epilepsy. The "Physical" scale was a mixture of symptoms (pain, "unwell" and tiredness), disabilities ("memory"). The consistency with which complaints of this nature were reported to create difficulties with daily activities (especially work) suggested it would be appropriate to handle these within the scale, though it did not meet the strict definition of a handicap.

3.3.3 Reliability

The internal consistency and test-retest reliability, were high, in that both Cronbach's alpha and the intraclass-correlation coefficient exceeded, or nearly did so, the value of 0.8 recommended for scales used in group comparisons (Nunnally and Bernstein, 1994). Furthermore, the scale was not affected by minor fluctuations in seizure control that may occur within a time frame of a few weeks. This was an important property, because if the scale scores had been sensitive to transient changes in physical health (insufficient to affect handicap), this would have confounded the ability to measure the postulated long-term underlying trait "subjective handicap". Using the method of Bland and Altman, 95% of repeated values on all the subscales were within approximately 25 scale points. This was equivalent to an effect size of 1 (change in score / standard deviation of baseline scores). For an individual, therefore, a change of 1 effect size is reliable, though for studies with a control group much smaller differences should be reliably detectable. The Cronbach's alpha of the alternate versions of the "Work & Activity" scales were equivalent, which suggested that the wording differences had not affected the internal consistency of the scales. As with any scale, it will be valuable to repeat the reliability estimates in a population outside the developer's institution.

3.3.4 Scaling characteristics and ease of use

Validity for the grouping of the SHE items into the various scales was provided by the correlation of each item with its own scale total (Table 3.4). This showed that each item (corrected for the effect of the item itself) was more closely related to its own scale, than to the other scales. The approximate equivalence of means and standard deviations of the items meant that a complex weighting system was not necessary. The scales demonstrated a good range of scores, which indicated that the SHE was sensitive across the spectrum of severity of handicap.

The investigations suggested that the SHE scale is practicable and acceptable to patients, in that an unselected clinic population (apart from those with obvious learning disabilities) were able to complete the scales, on average, in less than 10 minutes with good data quality.

3.3.5 Validity

The content validity of the SHE is supported by the method of its construction. The review of the literature and available quality of life scales, together with the unstructured interviews and expert opinion used to select the items provided a consistent set of themes. Free text responses to an item requesting "Is there anything more you would like to tell us about how epilepsy has affected your quality of life in general ?" produced more details on the concepts used in the SHE scale but no new core "handicaps". An additional two item scale on sexual functioning was used in the post-surgical group, but not in the cross-sectional population, and it is not part of the scale. Piloting of these two sexual items revealed a 10-20% non-response rate and "debriefing" of some respondents suggested it may too intrusive in contexts in which sexual functioning was not "on the agenda".

Construct validity was obtained from several sources. Firstly, the level of handicap was clearly related to the frequency of seizures. This in keeping with findings in other studies (Jacoby *et al.*, 1993; Jacoby *et al.*, 1996). All scales detected differences in

handicap between subjects who were seizure free and those not seizure free, as did all scales in the comparison between subjects with less than or more than one seizure per month. One scale ("Physical") detected a difference in the comparison of patients with less than one seizure per week with more than one per week, and another scale ("Work & Activities") just failed to reach significance. When psychiatric symptoms were controlled for, the scale remained sensitive to seizure frequency. This suggested that the scales were highly sensitive to the handicapping effect of increasing seizure frequency, in spite of the fact that seizure frequency is not explicitly part of the content of the scales.

One method of expressing the sensitivity of health scales to differences between patient groups (if the groups have an intuitive gradation) is "relative efficiency analysis" (Liang *et al.*, 1985), in which the F-ratio for linear trends across the groups on different scales are compared, the higher the F ratio the more sensitive the scale. For the SHE scale, the F-ratios (see Table 3.7) ranged from 109 ("Work and Activities") to 14.0 (Life-Satisfaction). Comparison of F ratios for linear trend of the SHE scales with the ESI-55 scales (Table 3.9) for the "Work & Activity" related handicaps revealed that the ESI-55 scales were only 25% as sensitive. For social functioning they were comparable. The SHE "Physical" and "Self-Perception" did not have direct counterparts in the ESI-55, but were more sensitive than all ESI-55 scales. The scales that focused on handicap were more sensitive than the more conventionally oriented "Life-Satisfaction" scale. This supported the contention that focusing on specific aspects of outcome is more sensitive than global satisfaction assessments. Two explanations for this are possible. Firstly, patients may adapt over time to limitations in their lives and come to accept, cognitively, as "satisfactory" what previously was unacceptable, though if asked specifically about symptoms or feelings, reduced well-being is revealed (de Haes *et al.*, 1992). Secondly, non-health related events influence quality of life and hence may limit the sensitivity of the "Life satisfaction" scales.

Further evidence for construct validity was that the SHE scales were sensitive, retrospectively, to the kind of changes in handicap one expects after a major intervention such as successful epilepsy surgery. All scales detected differences according to seizure outcome. The SHE scales were more sensitive in detecting differences post-surgery than the ESI-55, in that F ratios for linear trends for the ESI-55 scales (Table 3.12a and b) are lower than of those SHE scale (Table 3.11), with the exception of the "Health perceptions" scale which performed well. Interestingly, the ESI-55 "Health perceptions" scale was also found to be the most sensitive in Vickrey's original publication (Vickrey *et al.*, 1992). The incremental validity of the SHE scales over the ESI-55 scales was probably because all the SHE scales were focused on the specific effects of epilepsy, whereas many of the ESI-55 items are based on a generic instrument. These findings, taken together, suggest that the SHE scales are more sensitive to the handicapping consequences of epilepsy than the ESI-55 scales.

Assuming that people who were seizure free were less handicapped was a reasonable first hypothesis. However, it was felt to be more persuasive if it could be shown that the SHE scores were related to handicap-related constructs. Therefore, the scores on a number of other criteria were examined. People who were objectively handicapped (e.g. unemployed) scored much lower on all of the scales. In addition, people who considered that they are not following their first choice of main activity, even if employed, also scored lower on the SHE scales. Finally, subjects who rated epilepsy as the main determinant of the quality of their life scored significantly lower on all scales. These lines of evidence suggested that the SHE scales are sensitive to the long-term, disease specific, consequences of epilepsy.

Further construct validity was sought by correlating the ESI-55 scales and the SHE scales. There were clear relationships between ESI-55 and the SHE scale. The activity related items (called "Role" in the ESI-55) and social function in both scales correlated highly. The SHE "Physical" (which dealt with physical symptoms not mobility) was correlated with the ESI-55 "Energy and fatigue". The SHE "Self Perception" had no

direct counterpart in the ESI-55, but did appear to be related to the ESI-55 "Health perceptions" and to mental and social concepts. Though the item content of the 2 "perception" scales were different, it appeared that both tapped into people's perception of themselves. The SHE "Life-Satisfaction" was more highly correlated with the ESI-55 "Quality of Life" scale than any other scale. Though the format of the scales was different (Likert and visual analogue respectively) they clearly had a similar content. The SHE and ESI-55 "change" scales were also highly correlated.

The SF-36, which forms the core of the ESI-55, now has a large body of evidence supporting its validity as measure of aspects of health (Ware, 1992; Jenkinson *et al.*, 1993; McHorney *et al.*, 1993; Jenkinson *et al.*, 1994; Ruta *et al.*, 1994). That several SHE scales were correlated with appropriate ESI-55 scales further suggested the scale is measuring valid constructs.

The factor analysis demonstrated that the dimensions of the SHE scale that had been postulated at the outset were largely confirmed. Two physical items ("injuries" and "feeling unwell" were closely associated with the "Work & Activity" scale. It may have been that these two items were sensitive to an underlying "severity of epilepsy" dimension which is also strongly related to the overall effect of epilepsy on activities. The original structure was maintained as the face validity of this grouping was superior.

It may be asked whether the SHE really measured "handicap" rather than another related construct. In health services research this type of distinction is usually demonstrated by establishing convergent and discriminant construct validity, that is to say, that the scale correlated highly with measures related to "handicap" but poorly with unrelated constructs. At present no other handicap scale exists in the field of epilepsy with which to provide convergent validity. However, the performance of the SHE against indices of objective handicap, such as employment status and career choice (Tables 3.10a-b and 3.13a-b) suggested that the SHE was highly related to handicap. Evidence of discriminant validity was provided by the pattern of the correlations of

SHE subscales with ESI-55 subscales (Table 3.14). For instance, the SHE "Social and Personal" was most closely related to the ESI-55 social functioning scale and least to physical mobility (ESI-55 "Physical function"), and the SHE "Self-Perception" to ESI-55 mental health and social constructs rather than mobility. Other relationships appeared more complex as the "Work and Activity" scale is related to "Role-Physical", "Social Functioning" and "Cognition". This was not surprising as handicaps in occupational and social life may have shared causes. Because of the complex interactions between the many consequences of epilepsy, sole reliance, for the purposes of validation, on the relative strengths of correlations (convergent and discriminatory), between constructs was not justified.

It is not uncommon for health status scales to be dominated by the effect of psychological symptoms. Therefore, it was important that when mood disorder was controlled for, differences in SHE score according to seizure frequency remained. Anxiety appeared to be more common than depression, as has been shown before (Jacoby *et al.*, 1996; Ridsdale *et al.*, 1996). A prevalence of 50% caseness on the GHQ30 is similar to a previous hospital based study (Kogeorgos *et al.*, 1982).

Some investigators have pointed out that questionnaires using a standardised set of items do not allow patients to express their own priorities for the outcome of treatment (Kendrick and Trimble, 1994; Selai, 1995). Some measures have been developed to allow patients to chose the domains to be examined (Guyatt *et al.*, 1987; O'Boyle *et al.*, 1992; Ruta *et al.*, 1996). However, such methods remain complex and usually require the presence of a trained investigator. One study, using a self-completed "individualized" scale, reported that only 63% of subjects returned a correctly completed questionnaire (Ruta *et al.*, 1996). It is also unclear how to analyse data from subjects who report that their priorities have changed at follow-up from the baseline.

3.3.6 Potential uses

Some explanation of the role of SHE scale in the context of the other available scales is required. The ESI-55 has the advantage that it contains the SF-36, and hence comparisons across disease categories can be made, if this is thought to be an essential part of an investigation. The recently developed QOLIE-89 instrument shares many of its items with the ESI-55, but has a broader coverage of the social and occupational issues (Devinsky *et al.*, 1995). As no prospective studies with the scale are available, the sensitivity to change remains to be determined. The performance of the new items in the QOLIE scale, compared to the SHE scale, also remains to be examined. The Liverpool impact scale (Jacoby *et al.*, 1993), is an 8 item instrument, which shares the measurement aims of the SHE scale. Concern about its brevity, and hence sensitivity to the relevant issues, suggested a more extensive scale was required. The final SHE scale contains 4 scales that measure, from a patient's perspective, the handicap associated with epilepsy. It is postulated that subjective handicap is a medium-term to long-term trait, and that only therapies that have a major impact on impairment (seizures) or rehabilitative interventions directed specifically at modifying the causes of handicap will affect this attribute. In addition, one scale measuring life satisfaction in a manner more akin to current quality of life scales, and a 7 item global change scale are included. The latter, "non-handicap" scales, are included so as to maximise the validity of the SHE as a measure of change when used in isolation. If "subjective handicap", "Life-satisfaction" and self-perceived "change" all improve after an intervention, one can be more confident that benefit has arisen.

Another desirable characteristic of any outcome measure that has not been addressed is responsiveness. This will be considered in section 5.

3.4 Conclusions

(1) The SHE scale has been shown to have good internal consistency and test-retest reliability.

(2) The SHE scale can be completed quickly and easily with good data accuracy by patients attending hospital clinics.

(3) Evidence has been presented that the SHE scale is responsive to the specific handicap associated with epilepsy.

(4) The scale was demonstrated to be sensitive retrospectively to different seizure outcomes after epilepsy surgery.

(5) Factor analysis of the SHE has supported the proposed scale structure.

(6) The SHE scale is a useful additional outcome measure of epilepsy treatment.

Section 4

The Psychosocial Consequences of Epilepsy: a Community Study

4.0 Introduction

The literature review highlighted the psychosocial consequences of chronic epilepsy (sections 1.1.5-8). It was concluded that the prevalence of handicap due to epilepsy, in an unselected population, remained unknown. It was noted that the prevalence of "psychiatric caseness" of people with treated epilepsy (compared with those no longer on treatment) was also uncertain. The medical care of people with epilepsy in general practice was noted to be deficient, particularly with respect to attention to social factors (section 1.2.12). The evidence regarding the validity of the SHE scale presented in section 3 was derived from a highly selected sample of subjects (those attending a specialist centre). The validity of the SHE scale would be strengthened if the findings could be replicated in an unselected sample. The studies in this section will address these problems. The prevalence of significant handicap due to epilepsy will be investigated using the SHE. The rate of psychiatric symptoms will be assessed in subjects with active and remitted epilepsy (on and off therapy). It will be seen if the SHE scores achieved by subjects in long-term remission can be used as a potential "target" for interventions for epilepsy. The broader impact of epilepsy, and antiepileptic drug treatment, on health status will also be assessed using a generic health scale, and a comparison will be made with scores obtained in United Kingdom population based samples. The material in this chapter has been published as:

O'Donoghue MF, Goodridge DMG, Redhead K, Sander JWAS, Duncan JS. Assessing the psychosocial consequences of epilepsy: a community-based study. Br J Gen Pract 1999: 49;211-214.

4.1 Aims

The study was carried out in an unselected and community based sample of people with active and remitted epilepsy in order to assess the psychosocial consequences of epilepsy. Specific aims were to:

(1) To investigate the subjective handicap associated with epilepsy (using the SHE scale) and to study the relationship of handicap to seizure frequency, duration of remission, and treatment status.

(2) To determine the proportion of people with epilepsy, in an unselected sample, that could be considered to be "handicapped" by epilepsy.

(3) To investigate objective indices of handicap, such as unemployment.

(4) To provide further evidence of validity of the SHE scale as an outcome measure, particularly to determine SHE scores in persons with epilepsy in prolonged remission.

(5) To measure levels of self-reported general health using the SF-36, and how this related to seizure frequency and antiepileptic drug treatment.

(6) To assess self reported mental health using the Hospital Anxiety and Depression scale (HAD) and the Mental Health Inventory (MHI-5) and compare this with UK normative data.

4.2 Methods

4.2.1 Identification of persons with epilepsy

The survey was conducted in two large group general practices in the United Kingdom (Warders Medical Centre, Tonbridge, Kent and the St. James' House Surgery, King's Lynn, Norfolk). Both medical centres had a long-standing interest in the treatment and audit of epilepsy. Computerised medical records, with an epilepsy patient database, had been installed some years earlier at each centre (Goodridge and Shorvon, 1983; Redhead *et al.*, 1996). The Tonbridge site had a list size of 13,300 patients and King's Lynn 22,500.

The disease and drug treatment registers were searched to identify persons having at least one non-febrile epileptic seizure (excluding seizures confined to the first year of life). This was supplemented by a manual search of all the medical records for mention of epilepsy in a subset of 6000 inhabitants at the Tonbridge site practice (this had taken place 2 years earlier as part of an epidemiological study). Use of this group maximised ascertainment of cases of epilepsy in remission. The records of identified cases were reviewed to determine seizure type, epilepsy syndrome, age at onset, date of most recent seizure, and current treatment status. Active epilepsy was defined as a seizure within the two years preceding 1 January 1996. "On treatment" was defined as taking regular antiepileptic drugs on 1 January 1996. Co-morbidity was defined as any major illness or disabling condition present within the last 2 years. Consultations recorded by the general practitioner's (GP) for depression, anxiety, psychosis, attempted self-harm, other psychiatric symptoms were noted, as were the use of anti-depressant or anti-psychotic medication. The psychiatric diagnosis was derived from the GP's record, or a psychiatrist's report.

4.2.2 Survey methods

All persons, aged 15 or over, with a history of at least one epileptic seizure were eligible for the survey, except for subjects with known severe learning disability, or other severe physical disabilities which would preclude completion of the questionnaire. The survey booklet included the Subjective Handicap of Epilepsy Scale (SHE), the SF-36 (derived from the ESI-55) (Ware, 1993) and the Hospital Anxiety and Depression scale (Zigmond and Snaith, 1983). The administration and scoring of the SHE was performed as detailed in section 3.2.2. The SF 36 scales covered physical health, role functioning (daily activity), pain, energy, social functioning, mental health (the Mental Health Inventory - MHI-5) and health perception. All scales were scored from 0 to 100, with 100 representing optimum health. The questionnaire was mailed to subjects and one reminder letter was sent after six weeks.

4.2.3 Seizure data

Seizure frequency for respondents was divided into: (1) more than 1 seizure per month; (2) less than 1 seizure per month but at least one in the last 12 months; and no seizures for : (3) 12-24 months (4) 2-5 years (5) 5-10 years (6) 10-20 years and (7) more than 20 years. For non-respondents, seizures were classified (from GP notes) into: (1) at least one seizure in the last 2 years (2) no seizure in the last 2 years but on antiepileptic drug (AED) therapy and (3) no seizures in the last 2 years and no AED therapy.

4.2.4 Identification of psychiatric cases and subjective handicap

The Hospital Anxiety and Depression scale (HAD) was used as a measure of anxiety and depression, with cut-off scores of 10/11 for a definite, and 7/8 for a borderline case, as in previous studies (Lewis and Wessely, 1990; Jacoby *et al.*, 1996; Ridsdale *et al.*, 1996). The Mental Health Inventory (MHI-5) consisted of 5 items scored on a 6 point Likert scale (Ware, 1993). In other studies with the MHI-5, respondents who have scored on the lowest 3 points of each scale item (resulting in a MHI-5 of less than 40) have a 70-80% chance of scoring above the cut-off for depression on the Centre for

Epidemiological Studies Depression scale (Radloff, 1977) or a 30-50% chance of a DSM-III diagnosis of major depression (Ware, 1993). For subjective handicap no criterion existed for "severe handicap". The median SHE score of 157 patients undergoing video EEG telemetry for consideration of epilepsy surgery was used as the cut-off point (section 3.2.7). Patients who were prepared to undergo epilepsy surgery were assumed to be significantly handicapped by their condition. As a measure of the awareness of psychiatric morbidity, the GP's notes were searched for any record of psychiatric symptoms. As a proxy measure of the GP's awareness of the severity of handicap, the proportion receiving specialist epilepsy help was noted.

4.2.5 Analysis

The clinical characteristics of responders and non-responders were compared. A planned comparison of mean SHE and SF 36 scores of all persons with active epilepsy versus cases in remission was carried out. The scores on the SHE were compared for persons with differing seizure frequencies and lengths of remission. The impact of antiepileptic drug treatment on SHE and SF 36 scores was assessed by a comparison of patients (in remission) on and off treatment. The UK norms for the SF-36 were used for comparison with the epilepsy sample (Jenkinson *et al.*, 1993). All comparisons were performed with non-parametric statistics because the distributions were often skewed (by the patients in remission).

4.3 Results

4.3.1 Clinical characteristics

Three hundred and sixty nine persons with epilepsy, active or remitted, were identified (Table 4.1). Forty four percent were male and the median age was 44 years. The prevalence of active epilepsy in the combined population was 3.7/1000. For those on antiepileptic drug treatment, whether active or remitted, the prevalence was 7/1000. Forty one subjects were not sent a questionnaire because they were under 15 years and 19 because of severe physical and learning disabilities.

Table 4.1 Clinical characteristics of all ascertained cases of epilepsy N (%).

Source	Tonbridge - 6000 subset	112 (30)
	Tonbridge - All other cases	91 (25)
	King's Lynn	166 (45)
Gender	Male N. (%)	162 (44)
	Female N. (%)	207 (56)
Epilepsy	Active epilepsy	134 (36)
	Remitted on treatment	119 (32)
	Remitted off treatment	116 (32)
Psychiatric history*	Yes	64 (18)
	No	282 (82)
Comorbidity†	Yes	151 (57)
	No	200 (43)

Missing clinical data: *22 subjects †18 subjects.

In 109 (30%) of subjects eligible for a questionnaire the seizures could be classified from the GPs' records. Generalized tonic-clonic seizures occurred in 77% of subjects, complex partial seizures 19%, simple partial seizures 8%, absences 9% and myoclonic jerks 2%. Epilepsy syndromes were frequently hard to classify. Responders were more likely to have active epilepsy, be female and to have had a longer duration of epilepsy (Table 4.2).

Table 4.2 Clinical characteristics of Responders and Non-responders

	Responder N (%)	Non-responder N (%)
Male N. (%)	65 (49)	69 (51)
Female N. (%)	110 (63)*	65 (37)
Age (median years)	45.5	43.5
Duration of epilepsy (median years)	11	6†
Tonbridge N. (%)	105 (60)	70 (40)
King's Lynn N. (%)	67 (50)	67 (40)
Comorbidity present %	43	40
Psychiatric consultation in last 2 years %	17	18
Response rate according to seizures N. %:		
Active epilepsy	69 (70)¶	29 (30)
Remitted on treatment	53 (47)	59 (53)
Remitted off treatment	53 (54)	46 (46)

* More female responders ($\chi^2 = 6.4$, $P = 0.011$).

† Shorter duration of epilepsy in non-responders ($P<0.01$)

¶ More responders with active epilepsy ($\chi^2 = 11.9$, $P = 0.003$).

Amongst the respondents, 69 had active epilepsy, 53 epilepsy in remission on AED treatment and 53 were in remission off therapy. Twenty eight persons (16.5%) had more than 1 seizure per month, 26 (15.3%) had less than 1 seizure per month but more than 1 per year, 15 (8.8%) had their last seizure between 12 -24 months ago, 22 (12.9%) were in a 2-5 year remission, 19 (11.2%) in a 5-10 year remission, 37 (21.8%) in a 10-20 year remission, 23 (13.5%) in greater than a 20 year remission and in 5 the date was unknown.

4.3.2 Objective handicap

Of respondents of working age with active epilepsy, 34% were unemployed or off work due to disability, compared to 11% of those whose epilepsy was in remission (Table 4.3). A third thought they had been turned down for a job because of their epilepsy and a quarter felt that they had been dismissed from a job because of it. Social security benefit was the main source of income for 40% of those with active epilepsy, compared with 12% of those with remitted epilepsy (Table 4.4). Of the 64 subjects who had seizures while of school age, 40 percent stated that epilepsy had adversely affected their academic progress.

Table 4.3 Employment status of persons of working age (M < 65, F < 60 years).

	Active Epilepsy N (%)	Epilepsy In Remission N (%)
Employed full-time	9 (18)	41 (53)
Employed part-time	8 (16)	13 (17)
Housewife	9 (18)	11 (14)
Education or training	4 (8)	3(4)
Unemployed or Disabled	17 (34)	9 (11)
Retired	3 (6)	1 (1)

Base=128. Employment status missing on 4 subjects

Table 4.4 Main source of income for respondents (all ages).

	Active epilepsy (n=67)	Epilepsy In Remission (n=98)
Subject's own salary	9 (13%)	35 (36%)
Partner or Parent	16 (24%)	26 (27%)
Disability / Unemployment Benefits	27 (40%)	12 (12%)
Retirement Pension	15 (22%)	25 (25%)

Base=165. Income data missing on 10 subjects

4.3.3 Subjective Handicap and General Health

The Subjective Handicap of Epilepsy scores revealed decreasing handicap (or better "functioning") as seizure frequency decreased and the length of remission increased (Table 4.5). Beyond 5-10 years the scores reached a plateau. A comparison of active versus remitted epilepsy was significant for all scales except "Change" (Mann Whitney $P<0.0001$). A comparison of subjects with more than versus less than one seizure per month was significant for 4 of the scales (Table 4.5). The mean score on the "Change" scale did not vary between groups. This suggested that the SHE measured a stable trait. There was a significant difference on scores on the "Life-Satisfaction" (Mann Whitney, $P<0.007$) and "Physical" (Mann Whitney, $P<0.03$) scales when comparing remitted persons on and off AED treatment. This suggested that AED treatment had a deleterious effect on well-being. Ten years after remission 10% of subjects still reported worrying "often or very often" about having a seizure.

Table 4.5a Median (inter-quartile range) SHE scores (Work and activity, Social Life, Physical) according to seizure frequency or years in remission.

Seizure Category	Work & activity	Social Life	Physical
> 1 Seizure per month	44 (28,69)*aa	72 (44, 88)*	38 (19, 62)*a
< 1 Seizure per month	69 (53, 91)b	88 (62, 100)	56 (38, 75)
1-2 Years remission	100 (72,100)	88 (88, 100)	69 (50, 88)
2-5 Years remission	97 (86, 100)	100 (94, 100)	75 (62, 85)
5-10 Years remission	100 (97,100)	100 (100, 100)	81 (69, 88)
10-20 Years remission	100 (100, 100)	100 (100, 100)	88 (75, 94)
> 20 Years remission	100 (100,100)	100 (100, 100)	88 (75, 94)

Table 4.5b Median (inter-quartile range) SHE scores (Self Perception, Life-Satisfaction, Change) according to seizure frequency or years in remission.

Seizure Category	Self-Perception	Life-Satisfaction	Change
> 1 Seizure per month	33 (20, 68)*a	53 (41, 69)*	46 (36, 52)a
< 1 Seizure per month	60 (45, 90)	59 (44, 75)	50 (50, 61)
1-2 Years remission	75 (40, 90)	75 (56, 88)	57 (50, 64)
2-5 Years remission	75 (65, 90)	75 (50, 81)	54 (50, 68)
5-10 Years remission	90 (80, 100)	75 (56, 94)	52 (50, 64)
10-20 Years remission	95 (85, 100)	81 (69, 94)	50 (50, 61)
> 20 Years remission	100 (95, 100)	88 (75, 100)	50 (50, 50)

For both tables:

1. Significant difference in SHE score for contrast:

Active versus remitted epilepsy: * (P<0.0001).

2. Significant difference in SHE score for contrast;

>1 per month versus <1 per month: aa (P<0.01); a (P<0.03).

3. Significant difference in SHE score for contrast:

<1 per month versus 1-2 Year remission: b(P<0.003).

Abbreviations: > greater than, < less than.

A third of all cases of active epilepsy were found to be subjectively handicapped on four SHE scales (Table 4.6). The proportion rose to one half, if seizures occurred more than monthly. In the 6000 inhabitants in which the ascertainment of epilepsy (active *or* in remission) was complete, about 10% were classified as handicapped because of epilepsy. Scores on the Life-Satisfaction and Change scales are not shown as it was inappropriate to classify someone as a "case" on these scales.

Table 4.6 Percentage of subjects scoring as cases of subjective handicap according to seizure and treatment status.

SHE scale:	Active epilepsy		Remitted Epilepsy	
	All active epilepsy (n=68)	More than 1 seizure per month (n=28)	On AED Treatment (n=50)	Off AED Treatment (n=50)
Work & Activity scale	32 (21,43)	56 (38,74)	0	0
Social scale	29 (19,39)	46 (28,64)	8	0
Physical scale	37 (26,48)	54 (36,72)	4	0
Self-perception scale	34 (23,45)	54 (36,72)	2	2

"Subjective Handicap" defined by a SHE scale score below median score of 157 epilepsy surgery candidates (section 3.2.2). Base varies slightly due to subjects with missing responses. AED=antiepileptic drug.

The SF 36 scale scores for persons in remission were higher than for those with active epilepsy (indicating better health) for all 8 scales (Table 4.7a,b). Scores on the "Vitality" and "General health" scales indicated better health in those who had discontinued AEDs compared with those on treatment but in remission (Table 4.7a,b). The mean SF-36 score for those with active epilepsy was lower on all scales compared with UK norms (mean scores) (Tables 4.8a-b). The effect on Role-functioning scales

and Vitality was particularly marked. Vitality and General health scores were also lower in those in remission but on treatment compared with normal values.

Table 4.7a Median and (inter-quartile range) SF-36 scale (Physical function, Role-Physical, Role -Emotional, Vitality) scores for 3 seizure activity categories.

Seizure Status (n)	Median SF-36 scale score and (inter-quartile range)			
	Physical Function	Role Physical	Role Emotional	Vitality
Active epilepsy (65)	90 (58,100)†	75 (0,100)†††	67 (0,100)†††	40 (30,70)††
Remission on AEDs (50)	95 (80,100)	100 (75,100)	100 (100,100)	55 (35,75)
Remission off AEDs (50)	100 (90,100)	100 (100,100)	100 (100,100)	65 (55,80)¶

Table 4.7b Median and (inter-quartile range) SF-36 scale scores (General Health, Pain, Social Function, Mental Health) for 3 seizure activity categories.

Seizure Status (n)	Median SF-36 scale score and (inter-quartile range)			
	General Health	Pain	Social Function	Mental Health
Active epilepsy (65)	62 (40,82)†	78 (44,100)†	78 (44,100)††	64 (40,80)††
Remission on AEDs (50)	67 (52,77)	89 (67,100)	100 (67,100)	74 (56,88)
Remission off AEDs (50)	82 (67,95)¶¶	100 (78,100)	100 (89,100)	80 (64,88)

For both tables :

Significant difference in SF-36 score for comparison (Mann-Whitney test):

1. Active epilepsy versus all remitted epilepsy: ††† (P<0.0001); †† (P<0.001), † (P<0.01).

2. On versus off AED treatment *(All persons in remission)*: ¶¶ (P<0.003), ¶ (P<0.01).

Table 4.8a Mean, Median and (95% confidence intervals for the mean) SF-36 scale (Physical function, Role-Physical, Role -Emotional, Vitality) scores for 3 seizure activity categories compared with UK normative data.

Seizure Status (n)	Mean, Median SF-36 scale score and inter-quartile range			
	Physical Function	Role Physical	Role Emotional	Vitality
Active epilepsy (65)	73,90 (64,81)	58,75 (46,67)	59,67 (47,70)	48,40 (42,54)
Remission on AEDs (50)	83, 95 (77,90)	80,100 (70,90)	85,100 (75,95)	55,55 (48,61)
Remission off AEDs (50)	92,100 (87,96)	89,100 (81,96)	88,100 (80,96)	66,65 (60,71)
UK mean 20-24 years (1008)†	91.6	90.4	80.4	62.2
UK mean 60-64 years (525)†	76.2	75.9	84.8	61.8

† data from (Jenkinson *et al.*, 1993)

Table 4.8b Mean, Median and (95% confidence interval for the mean) SF-36 scale scores (General Health, Pain, Social Function, Mental Health) for 3 seizure activity categories compared with UK normative data (means).

Seizure Status (n)	Median SF-36 scale score and (inter-quartile range)			
	General Health	Pain	Social Function	Mental Health
Active epilepsy (65)	61,62 (55,67)	70,78 (62,78)	70,78 (62,78)	61,64 (55,67)
Remission on AEDs (50)	66,67 (61,72)	80,89 (73,87)	85,100 (78,91)	69,74 (63,76)
Remission off AEDs (50)	78,82 (74,83)	86,100 (80,92)	92,100 (87,96)	75,80 (70,79)
UK norms 20-24 years (1008)†	74.5	84.3	87.8	72.0
UK norms 60-64 years (525)†	68.1	76.9	86.2	76.4

† data from (Jenkinson *et al.*, 1993)

4.3.4 The prevalence of psychiatric symptoms

One hundred and twenty four subjects (34%) had consulted their GP at some point for psychiatric symptoms, and 64 (17%) had done so in the previous 2 years. Depression (23%), anxiety (6.5%), and overdose (6%) were the commonest reasons. Thirty three patients (9%) were taking antidepressant medication. The prevalence of recorded psychiatric symptoms in the last 2 years in those with active epilepsy was 20%, in those with remitted epilepsy on AED treatment 18%, and remitted off treatment 17%. The percentages of subjects scoring as definite cases of anxiety and/or depression on the HAD scale and the MHI-5 are shown in Table 4.9. More cases of anxiety than depression were detected for all seizure categories, and there was a clear effect of seizure frequency. More cases scored positively on the HAD than the MHI-5. The level of agreement between scales was moderate (kappa = 0.47, Table 4.10). Only a third of those who were classified as a definite "case" on the HAD (and half those who scores positively on both scales) had a record of psychological symptoms in their medical notes in the last 2 years (Table 4.11). The relationship with employment status was also of note, as 48% of those unemployed or on disability benefits scored as cases, compared with 16 % of those in work, an odds ratio of 4.6 (95% C.I. 1.7, 12.6).

Table 4.9 Percentage of cases of anxiety and depression by treatment and seizure status (and 95% confidence interval).

	Active Epilepsy		Epilepsy in remission	
	More than 1 Seizure / month (n=27) %(95%C.I.)	Less than 1 Seizure / month (n=36) %(95%C.I.)	On AED Treatment (n=49) %(95%C.I.)	Off AED Treatment (n=43) %(95%C.I.)
Case on MHI-5	29 (12,46)	23 (9,37)	14 (4, 24)	2 (0,13)
HAD Anxiety	48 (29,67)	33 (18,48)	20 (9,31)	19 (7,31)
HAD Depression	33 (15,50)	11 (1,21)	6 (0,13)	0
HAD Anxiety or Depression	55 (36,74)	38 (22,54)	20 (9,31)	19 (7,31)

Abbreviations: AED= antiepileptic drug, HAD Hospital anxiety and depression scale, MHI-5 = Mental Health Inventory.
Base = 155 due to missing HAD responses on 20 subjects.

Table 4.10 Agreement (number of cases) between HAD scale and MHI-5 for psychiatric caseness

	MHI-5 Positive	MHI Negative
HAD Positive	20	25
HAD negative	4	103

Kappa = 0.47

Table 4.11 The number of persons who were classified as psychiatric cases using the HAD and MHI-5 according to whether they had a consultation in the last two years for psychological symptoms.

	Psychiatric symptoms noted by GP in the last 2 years
HAD case	33%
MHI-5 case	42%
MHI-5 and HAD case	47%

4.4 Discussion

Scores on the SHE and SF 36 scales showed a clear relationship with the severity of epilepsy. The largest difference was between active and remitted epilepsy. The scores were seen to plateau with longer remission (5-10 years). This may have reflected increasing confidence that epilepsy had finally "resolved". Scores of 90-100 on the SHE scales would thus seem a good target for interventions. The SHE "Life-Satisfaction" and "Physical" scales, and the SF 36 "Vitality" and "General Health" scales revealed a beneficial effect of not being on AED treatment for those in remission.

The subjective handicap associated with epilepsy appeared to be under-recognised. Half of the subjects with more than one seizure per month were as severely handicapped as patients drawn from an epilepsy surgery program. Given the degree of self perceived handicap, the proportion of patients that were receiving specialist treatment was not high. Only 16 (24%) of the active epilepsy patients surveyed were under on-going neurological follow-up.

The prevalence of objective handicap (e.g. unemployment) in the sample mirrored that of subjective handicap. Several studies have confirmed that unemployment is a very significant problem with epilepsy, and that seizure frequency is the most important factor. However, co-existent psychiatric symptoms and academic under-achievement have been found to pose an additional disadvantages. It is uncertain whether the high prevalence of psychiatric caseness in the unemployed group in this sample was a cause or consequence of unemployment.

The high prevalence of caseness on the HAD is comparable to previous studies (Jacoby *et al.*, 1996; Ridsdale *et al.*, 1996). The community prevalence of psychiatric disorder diagnosable by ICD-9 criteria is of the order 10% (Goldberg, 1994), though this rises to 13-18% if screening questionnaires are employed (Finlay-Jones and Burvill, 1977; Meltzer *et al.*, 1988). The prevalence of mood disorder in our sample of people with

remitted epilepsy off treatment was comparable to the population average figure. Although the persons identified as psychiatric "cases" were not subsequently assessed using research diagnostic criteria, the convergent evidence from the two mental health scales used suggested that a significant fraction of patients had a mood disorder. These symptoms were often not recognised by (or had not been recorded by) the GP. An alternative explanation is that the subjects had not presented to the GP with mood symptoms.

It is well known that psychiatric illness may go unnoticed in general practice (Freeling *et al.*, 1985). Psychiatric illness detected using survey questionnaires are not necessarily less severe than those already known to health services (Brown *et al.*, 1985). Previous studies have suggested that concurrent physical illness is associated with a lack of recognition of depression by GPs (Freeling *et al.*, 1985). In the case of epilepsy it is possible that attention was focused, by the patient and the general practitioner, on recurrent seizures and that psychological aspects remained hidden or attributed to the seizures.

The comparison of SF-36 scores in this sample with UK normative data, suggested that active epilepsy had a major effect on self-rated well being, especially in relation to ability to carry out daily activities and sense of energy and fatigue. Antiepileptic medication also had adverse effects even if seizures had ceased. The benefits of AED withdrawal if seizures have ceased remains uncertain. Jacoby has examined this issue as part of the MRC antiepileptic drug withdrawal study (Jacoby *et al.*, 1992). Randomization to drug withdrawal was not associated with major improvements in well-being. It appeared that successful drug withdrawal could be highly beneficial, but relapse due to withdrawal was quite detrimental. However, it is clear that relapse and treatment at follow-up were confounded variables. The data suggest that a policy of drug withdrawal is the best approach as long as relapse would not be socially deleterious (e.g loss of employment).

A number of methodological limitations apply to the study. First, the sample size is modest. Second, the overall response rate of 57% is somewhat low, though the response rate for people with active epilepsy (70%) is comparable to similar studies. It is likely that the group who were excluded due to learning disability were particularly handicapped by epilepsy and associated neurological impairments and further research on these subjects would be valuable. Children were also excluded as the SHE is not yet validated persons under 16 years. The accuracy of information in general practice records is also open to question. However, this data was restricted to information which had been shown by audit (at one of the practices) to be accurate (Redhead *et al.*, 1996).

The SHE scales were completed by the respondents with good data accuracy and the response rate in the active epilepsy group was acceptable. In the future, this could probably be increased if the forms were introduced personally by the patients' GP or practice nurse.

A number of further applications of these scales could be explored. The SHE, SF-36 or HAD scales could provide useful clinical information to the GP by identifying patients in particular need of support. In addition, it could serve as a method of audit of care in general practice. Population-based application of the SHE and SF-36 could assist in needs-based service planning.

4.5 Conclusions

(1) The severity of subjective handicap was related to seizure frequency and to the duration of remission of seizures. The consequences of epilepsy disappeared 5-10 years into remission. Scores of 90-100 on the SHE scale represent a valid target for interventions designed to alleviate the handicap of epilepsy.

(2) A third of persons with active epilepsy were significantly handicapped by their condition. The proportion rose to one half in those with more than one seizure per month.

(3) Between a third and a half of subjects scored as "cases" on the HAD scale and the mental health subscale of the SF-36. Only one third of the psychiatric morbidity revealed by the questionnaires had been recorded by the general practitioner. The prevalence of psychiatric caseness in patients on treatment was two to three times that of those who had ceased treatment.

(4) Scores on the SF-36 indicated that people with active seizures perceived themselves as significantly less healthy than those in remission. Drug treatment had a detrimental effect on certain aspects of well-being.

(5) The occurrence of seizures, even at low frequencies, is associated with psychosocial handicap and this may remain covert in general practice.

Section 5

A Longitudinal Study of the Impact of Epilepsy Surgery and a Program of Comprehensive Epilepsy Assessment

5.0 Introduction

Most studies of the treatment of epilepsy have reported change in seizure frequency as the primary outcome measure. This been noted to be problematic for several reasons. The literature review concluded that studies of the outcome of the treatment of chronic epilepsy should be multidimensional and long-term. As a consequence, a method for measuring the handicapping consequences of epilepsy was developed and validated (Section 3).

Retrospective studies of epilepsy surgery have concluded that becoming seizure free, or nearly seizure free, usually results in significant improvements on a variety of indicators of psychosocial functioning. However, the reliability and validity of the available measures for epilepsy surgery is open to question. The review of the literature concluded that there remained scope for further investigations of the impact of epilepsy surgery. It was also noted that despite the widespread development of epilepsy centres, there was little data on the effectiveness of comprehensive multi-disciplinary medical assessment. In particular, programs that included psychosocial interventions, have remained entirely unevaluated.

It was decided to investigate the outcome of both epilepsy surgery and programs of comprehensive epilepsy assessment. The newly developed subjective handicap of epilepsy scale, together with other established quality of life and mental health scales, were chosen as the main outcome measures.

5.1 Aims

1. To investigate, in a consecutively recruited cohort of patients with intractable epilepsy, the effectiveness of epilepsy surgery. The main outcome measures were: seizure frequency, mental health, quality of life and the subjective handicap of epilepsy. Assessments were made at baseline and at a follow-up of one year.

2. To investigate, in a consecutively recruited cohort of patients with intractable epilepsy (not suitable for epilepsy surgery), the effectiveness of a program of multi-disciplinary epilepsy assessment. The program included medical, psychological and social interventions. The main outcome measures were : seizure frequency, mental health, quality of life and the subjective handicap of epilepsy. Assessments were made at baseline and at a follow-up of one year.

5.2 Methods

5.2.1 Study design

A randomized placebo controlled investigation of either surgery or comprehensive assessment was considered impracticable and unethical. Patients, and referring primary care physicians, were known to see an advantage of surgery over "no surgery", and to prefer referral to a specialist epilepsy centre over "no referral". Blinding was also impossible as outcome was to be measured with self-completed scales. However, control groups were considered essential in order to attribute the outcomes in the treated subjects to the interventions, rather than to spontaneous change or the effect of group membership. In the absence of a group randomized to "no treatment", groups were selected to model the effect of no treatment. For the surgically treated patients, a control group of subjects was chosen who underwent evaluation for epilepsy surgery during the study period, but who had not been operated on one year after initial assessment. Patients did not proceed to surgery either because their epilepsy was not amenable to surgery, or because the subjects had chosen not to proceed, or because the subjects had not yet undergone surgery. Two control groups were employed to model the spectrum of severity of epilepsy for the comprehensive assessment group. First, a cohort of patients attending a epilepsy follow-up clinic. Second, the non-operated surgical patients were used to control for the more severe end of the spectrum. The two investigations were run in parallel so that the size of the change in the surgery group, which was anticipated from previous studies to be quite large, could be used to help interpret changes observed in the comprehensive assessment group.

5.2.2 Selection of subjects

Four groups of subjects were enrolled from the epilepsy clinics of the National Hospital for Neurology and Neurosurgery, London, UK (NHNN).

(1) "Surgery": patients who underwent surgical treatment for intractable epilepsy between December 1994 and January 1996.

(2) "Non-operated": potential surgical candidates assessed during the study with MRI and video-EEG telemetry who were found to be unsuitable, declined or had not undergone a surgical procedure one year after baseline assessment.

(3) "Clinic": patients with epilepsy undergoing long-term follow-up at NHNN who were not part of the surgery program.

(4) "Chalfont": Non-surgical patients with intractable epilepsy referred for comprehensive assessment at the Chalfont Centre for Epilepsy (affiliated with the NHNN, the Institute of Neurology, London and the National Society for Epilepsy).

The Surgical subjects were derived from a consecutively recruited cohort of 190 patients referred to the NHNN video-EEG telemetry unit for pre-surgical assessment between mid 1994 and January 1996. Subjects with an IQ below 70 or who could not read English were excluded. The Surgical cohort was later divided into two subgroups ("Surgery" and "Non-operated") depending on whether a surgical procedure had been carried by January 1996. Sixteen subjects were assessed at baseline but have not followed-up beyond 1 year post-operatively and are not reported here. All respondents to baseline assessments were followed up either 1 year after surgery or 1 year after their first assessment if they belonged to the Non-operated group.

The "Clinic" sample was derived from a consecutive sample of 184 patients with definite epilepsy (2 or more seizures) who attended the epilepsy follow-up clinic of two specialists in epilepsy at NHNN. The index visit had been at least one year before the baseline questionnaire administration so that newly diagnosed cases of

epilepsy were not enrolled. Subjects with an IQ below 70 were excluded, as were patients who were in the surgery program. All respondents to the baseline assessment (130) were then followed up at 1 year.

The "Chalfont" sample were a consecutively enrolled cohort of 154 patients referred to the centre for detailed assessment between January and November 1995. Exclusion criteria included; estimated IQ below 70 (36 subjects), declined to participate (2), surgical candidates (7), and sudden death during admission (1). Four subjects failed to complete the baseline assessments, leaving a cohort of 104 subjects who were assessed at baseline and 1 year after discharge from the unit.

5.2.3 Procedures common to all subject groups

5.2.3.1 Clinical data

At baseline, and at follow-up, the following information was abstracted from the hospital case records and recorded on specially designed forms: aetiology, seizure classification, epilepsy syndrome classification, approximate seizure frequency, MRI data, EEG data, antiepileptic drugs taken, and neuropsychological scores. The notes were also searched for record of psychiatric symptoms (depression, anxiety, psychosis, self-harm, and other).

5.2.3.2 Seizure data

Seizure frequency data was collected at baseline, and at follow-up, using questionnaires. Respondents were presented with vignettes of 4 types of seizure; "tonic-clonic", "simple partial", "complex partial" and "absences". These vignettes approximated the International classification of seizure types, though subtle distinctions between typical and atypical absences were not used. Subjects were asked to estimate how frequently they had experienced each type of seizure in the last 12 months using 6 response options (never, 1 in 1 year, less than 1 per month, 1-4 per month, more than 1 per week, daily). The self reported seizure classification

was compared with case record seizure classification. If there was agreement, the self-reported frequency of each seizure type was used. If there was a conflict in reported seizure types, the seizures were recoded in the following way to simplify the analysis. Patients reporting absences and complex partial seizures were coded as having purely complex partial seizures if they were known to have localization related epilepsy. Similarly, patients known to have generalized epilepsies (idiopathic, cryptogenic or symptomatic), who reported both "complex partial seizures" and "absences" were coded as having "absences". Myoclonic seizures were coded as simple partial seizures. Subjects with localization-related epilepsies, who claimed to have both complex partial seizures and absences 1-4 per month, were coded as having complex partial seizures more than 1 per week (assuming that complex partial seizures of different intensity were being referred to by the subjects). A similar procedure was adopted for those with generalized epilepsies, except that the seizures were coded as absences. Subjects who reported they were seizure free had this verified using the case record, otherwise adjustments were not made to the estimated frequency. A additional 7 point Likert scale question was included to measure subjective change in seizure frequency from "1- much more often" to "7 -much less often" with a separate scoring point for no seizures at all. The points scoring 1-2 and 6-7 on the Likert scale were subsequently coded as worse and better respectively, and 3-5 points coded as unchanged.

5.2.3.3 Health status questionnaires

Booklets were sent to subjects containing the following questionnaires: Subjective Handicap of Epilepsy scale (see Appendix 2), the Hospital Anxiety and Depression scale (as used in section 4.2.4) (Zigmond and Snaith, 1983), and the General Health Questionnaire (Goldberg, 1978), ESI-55 scale (Vickrey *et al.*, 1992) . A summary of the content of the scales is shown on Table 5.1. Also included in the questionnaire were demographic questions: years of schooling, educational achievements, employment, welfare benefits received, marital status, and open ended

questions about quality of life. Questionnaires were mailed to all subjects and a single reminder was sent approximately 6 weeks after the first mailing. Missing values for scale items were interpolated if 75% or more of any scale had been completed, otherwise the subscale was coded as "missing".

The General Health Questionnaire was used at baseline as a secondary measure of psychiatric caseness. It is one of the most widely used psychiatric rating scales, with a lot of evidence concerning its reliability and validity (Goldberg, 1978). It was dropped from the follow-up assessment, because of its length (30 questions) in order to minimise respondent burden. The usual cut-offs (4-5) for identifying a case of psychiatric disorder were applied.

5.2.4 Group specific procedures

5.2.4.1 Surgical group

The baseline questionnaire assessments were made some weeks before the Surgical subjects were admitted for Video-EEG telemetry, so as to avoid the discomfort and unusual setting of the telemetry unit influencing the assessments. The Surgical group had the following additional data collected; histology if operated and the reason for not proceeding to surgery when applicable.

5.2.4.2 Chalfont group

The Epilepsy assessment unit, at the Chalfont centre, is a multi-disciplinary unit led by a consultant neurologist with special expertise in epileptology. Staff also include: neurophysiologists, neuroradiologists, neuropsychiatrists, neuropsychologists, medical social workers, nurse specialists in epilepsy and other ancillary therapists. The centre has epilepsy-dedicated MRI, EEG and pharmacology laboratories. Patients are referred primarily by neurologists, and general practitioners, from throughout the United Kingdom. In the main, patients have intractable and disabling

epilepsy and are admitted for an extended period of evaluation (lasting 1-4 months). Therapy includes medical, psychological and social interventions. The Chalfont subjects were assessed during their first week at the centre. A small number of subjects with poor literacy skills or visual impairment were assisted with the completion of the forms. In addition the following "process" data was collected: whether or not MRI, EEG, ambulatory EEG, video-EEG telemetry or neuropsychological testing had been performed. Medical social worker assessments, use of psychotherapy and antiepileptic drug (AED) changes were also noted. The neurologist in charge of the assessment unit (Professor John S. Duncan) recorded the aims of the admission on a specially designed form at a multi-disciplinary meeting approximately one week after admission. Specific information on "diagnostic aim", "realistic seizure frequency reduction", and "the main objective for AED treatment" was recorded. At discharge the author determined, from the hospital case notes, whether a *new* seizure classification, epilepsy syndrome classification, or aetiology had resulted from the period of assessment.

5.2.5 Analysis

5.2.5.1 Baseline

Clinical data, demographic data and scores on the SHE, ESI-55, HAD, and GHQ scales were compared for subjects who completed assessments at both time points with those who responded only at baseline. In addition, clinical data were compared for subjects who did not respond at baseline (and hence did not enter the study) with responders at baseline. Significant differences in categorical data were tested for using Chi-square test, and for scale means with analysis of variance (ANOVA). The baseline differences in clinical, demographic and health status scores were then compared for the four treatment groups again using chi-square and ANOVA as appropriate.

5.2.5.2 Outcome

The principal outcome measures were subjective handicap (SHE scale score), quality of life (ESI-55 scale score), psychiatric status (HAD score) and seizure frequency. A multiple univariate analysis of covariance (ANCOVA) (with baseline scores as covariate) with planned comparisons ("contrasts") was the main method of analysis for the SHE scale data. The dataset was first subjected to a test of the important assumptions for ANCOVA. This included testing for multivariate normality of sampling distributions, homogeneity of variance, reliability of the covariate, linearity of regression, and homogeneity of regression of the covariate on the outcome variable. The sample sizes were sufficiently large and distributed to meet the first two assumptions. The reliability of the SHE scales was in excess of 0.8 (see section 3.2.6) and therefore could be used as a covariate. The SHE scale scores at baseline (the covariate) were plotted against follow-up (figure 5.1) to demonstrate that the regression slopes were all approximately the same. The SHE social scale did have one group (surgical group, Figure 1b) for which the regression line differed significantly, however, because the size of the effect was not large, it was ignored. For the SHE change scale (Figure 5.1f) there was a major departure from the assumption of homogeneity of regression, therefore, a difference score (follow-up - baseline) was calculated and an ANOVA performed on the mean change scores. The sample sizes of the four treatment groups were not equal therefore a regression approach for the ANCOVA was used (Tabachnick and Fidell, 1996). The planned ANCOVA contrasts on the SHE scale were:

(1) Surgical versus Non-operated group

(2) Chalfont versus Clinic and Non-operated group

(3) Chalfont versus Clinic group only.

ESI-55 scores were not all normally distributed (due to marked ceiling effects for some scales), homogeneity of variance was not always present, and the assumption

of homogeneity of regression was sometimes not met. This implied a group by covariate interaction (examples of some of the diagnostic plots are shown in Figure 5.2). The ESI-55 data were transformed to a change score (follow-up - baseline), with zero indicating no change and a positive score an improvement. This resulted in a dataset which met criteria for analysis of variance.

In order to assist interpretation of the meaning of score changes, the proportion of subjects who improved or worsened by more than 1 effect size (change / standard deviation of the scale) was reported for each group and for each scale. Changes of 1 effect size or more can be considered large statistically and clinically.

The sample sizes needed were determined by choosing the SHE scale score as the principal outcome measure. The standard deviation of each of the SHE scales in samples used in the validation and community studies was in the range 20-30 scale points, therefore, 25 was chosen as a representative value. A change of 25 points on a SHE scale also represented a reliable change for an individual during the reliability studies. A much smaller difference is reliable when comparing groups. A change in score of 12.5 was chosen as the minimum clinically relevant difference (effect size 0.5) and 25 points as a major change (effect size = 1). For an ANCOVA sample size calculation Norman and Streiner have suggested using the main comparison of interest and performing the calculation as for a paired t-test (Norman and Streiner, 1994). In this case, for an alpha of 0.05 and 90% chance of detecting an effect size of 0.5, a sample size of 42 in each group was sufficent. The estimate is conservative as the ANCOVA is a more powerful test.

5.2.5.3 Qualitative observations

Standardized questionnaires can only assess outcomes that are considered of interest at the outset. Therefore, a number of additional questions (with free text responses) were posed to explore the subjects' perception of the benefits and adverse effects of either epilepsy surgery or comprehensive assessment. The responses were searched for common themes, but were not subjected to a formal coding procedure, because the volume of material was too small for this to be worthwhile.

To explore the impact of epilepsy surgery, responses of subjects in the longitudinal and the validatory study (section 3.5) were analysed. The following questions were posed:

- What have been the benefits (on health and quality of life) of the operation?
- What have been the negative effects of the operation ?
- Have there been difficulties for you since the operation ?
- Have there been difficulties for others close to you since the operation ?
- Is there anything more you would like to tell us about how epilepsy has affected your quality of life in general ? (work, personal life, how you feel about yourself.... or anything you think is important).

The Chalfont subjects were posed the following questions:

- What have been the benefits (on your epilepsy, health and quality of life) of coming to the Chalfont Centre ?
- What have been the negative effects of coming to the centre ?
- Are you glad you came to the centre ?

Table 5.1 Contents of the outcome measures used in the study

Scale	Content
SHE	
Work and Activities	Employment, daily activities, travelling, leisure
Social and Personal	Difficulties with relationships and making friends
Physical	Seizure and medication related effects on well-being
Self-Perception	Stigma, being in control, fear, confidence
Life-Satisfaction	Happiness with one's work, leisure, and social life
Change	Self-reported change across all domains
ESI-55	
Physical function	Physical disabilities (largely mobility)
Role- physical health	Activities limited by physical health
Role - emotional health	Activities limited by mental health
Cognitive function	Memory and thinking
Role - memory	Activities limited by memory problems
Social function	Limitations in social functioning
Emotional well-being	Anxiety and depression items
Energy and fatigue	Energy and fatigue
Pain	Pain
Health perceptions	Perception of one's own health
Overall quality of life	2 Visual analogue scales
Global change	Single global change item
HAD	Anxiety and Depression
GHQ 30	Anxiety and Depression

5.3 Results

5.3.1 Response rates and responder characteristics

Four hundred and eighty two subjects were eligible for the study. The number of respondents at baseline and at follow-up are shown in Table 5.2.

Table 5.2 Number of respondents at each stage of the study

Responder status	Surgery	Non-Operated	Chalfont	Clinic
Eligible for questionnaire	49	141	108	184
Responded at baseline	45	113 *	104	130
Responded at follow-up	43	82	68	95
Responder rate (%)	98	85	65	73

*Includes 16 subjects who have not taken part in the study as follow-up is less than 1 year post surgery.

The overall response rate to the first questionnaire was 81.3%. Of those who were enrolled into the follow-up study, 77% responded at follow-up. The subjects that did not respond at baseline were significantly more likely to be seizure free (Table 5.3 χ^2=43.1, P=0.00001). There were no significant differences in gender, age, duration of epilepsy, type of epilepsy, and AED treatment between non-responders at baseline and subjects enrolled into the study. The response rate, at follow-up, differed significantly between the groups, being lowest in the Chalfont group (P <0.001). Considering those who responded at baseline, there was no difference in seizure frequency, at baseline, by final responder status (Table 5.3). There were also no differences by responder status for years of education, employment status, source of income or marital status (Table 5.4). A comparison of baseline SHE scores of responders with non-responders at follow-up revealed that non responders scored marginally lower on the Social scale and the Change scale (Table 5.5, P<0.05).

A similar comparison for the ESI-55 revealed that non-responders at follow-up scored significantly lower on all the "role" scales (Table 5.5; role-physical ($P < 0.01$), role-emotional, role-memory, and summary role ($P < 0.05$)). Thus, the impact of epilepsy on daily activity at baseline, as measured by the SHE and ESI-55, was marginally greater on those who failed to respond at follow-up. The subjects who failed to respond at follow-up were also more likely than responders to have had psychiatric symptoms recorded in the hospital case record (Table 5.6; χ^2 13.1, P=0.0014). However, non-responders at follow-up did not have a higher prevalence of psychiatric "caseness" on either the HAD or GHQ scales. The baseline characteristics of the non-responders at follow-up in the Chalfont group were specifically explored because in this group they represented a significant fraction of the original sample. No differences with respect to sex, age, seizure frequency, SHE scale score, ESI-55 scale score, HAD score, or GHQ score were observed according to responder status. However, Chalfont non-responders were more likely to have had a diagnosis of purely non-epileptic attacks made. Over half of these did not complete follow-up assessments. Psychiatric symptoms were also more common (77% of non-responders versus 43% of responders; $P< 0.001$).

Table 5.3 Clinical characteristics of responders and non-responders

Characteristic	Baseline and follow-up	Baseline only	Never
Number of subjects	288	104	90
Male	137	48	50
Female	151	56	40
Median age (years)	34	31	31
Duration of epilepsy (years)	21	18	21
Epilepsy syndrome classification (%)			
Focal epilepsy	79	72	75
Idiopathic generalized epilepsy	15	12	11
Symptomatic generalized epilepsy	2	1	4
Non-epileptic seizures*	3	11	2
Unclassified	1	4	8
Overall seizure frequency (%)			
In 2 Year remission	7	5	21*
In 1-2 Year remission	5	5	19
Simple partial seizures only	1	3	2
Less than 1 seizure per month	11	12	12
1-4 seizures per month	20	20	29
More than 4 seizures per month	56	55	17
Frequency of tonic-clonic seizures			
None	51	44	n/a
1 per Year	10	9	n/a
2-11 per year	13	13	n/a
1-4 per month	17	18	n/a
More than 4 per month	9	16	n/a
Number of anti-epileptic drugs at baseline			
None	3	5	2
One	24	22	22
Two	42	43	54
Three	25	27	21
Four	6	3	1

* Diagnosis of non-epileptic seizures at follow-up; n/a = not available.

* Responder status (ever v never) by seizure frequency ; χ^2=43.1 P=0.00001

Table 5.4 Demographic details of responders and non-responders at follow-up

Characteristic	Baseline and follow-up	Baseline only
Years of education (years)	11	11
Mean Verbal IQ	93	87
Mean Performance IQ	91	87
Highest educational achievement		
Degree	10	12
A level	8	4
O / GCSE level	42	33
Vocational	8	6
Other qualifications	7	11
Nil	25	34
Employment status		
Employed	43	32
In education or training	8	9
Disabled or unemployed	38	46
Housewife	9	12
Retired	2	1
Main source of income		
Own salary	29	25
Partner	10	8
Parents	14	4
Benefits	44	62
Pension	3	1
Currently living with		
Partner and/or children	45	50
Alone	15	19
Parents	35	23
With others	5	8

"A" level = National examination taken at 18 years,

"O" / GCSE level = National examination taken at 16 Years.

Table 5.5 Mean SHE and ESI-55 score (and 95% Confidence interval) for responders at baseline only and at baseline and follow-up

Responder status	**Mean Score**						
	SHE scale						
	Work	Social	Physical	Self Perception	Life-Satisfaction	Change	
Baseline Only (102)	47 (42,52)	60* (54,65)	43 (39,47)	42 (37,46)	54 (51,58)	47* (43,50)	
Baseline + Follow-up (288)	52 (50,55)	66 (63,69)	46 (44,49)	45 (42,48)	58 (56,60)	50 (48,52)	
	ESI-55 scale						
	Physical Function	Role-Physical	Role-Emotional	Vitality	Health Perception	Social Function	Mental Health
Baseline Only (102)	81 (77,85)	50** (43,58)	56* (48,64)	47 (42,51)	58 (55,62)	64 (58,70)	59 (55,63)
Baseline + Follow-up (288)	83 (80,86)	62 (57,66)	65 (60,70)	49 (46,51)	62 (60,64)	70 (67,74)	61 (59,64)
	Cognitive	Pain	Role-Memory	Quality of Life	Total Physical	Total Mental	Total Role
Baseline Only (102)	55 (50,60)	66 (60,72)	57* (50,65)	56 (53,60)	63* (59,67)	57 (53,60)	57** (51,62)
Baseline + Follow-up (288)	61 (58,64)	72 (69,75)	67 (62,71)	58 (56,60)	68 (66,71)	60 (58,62)	65 (62,68)

Significant difference in mean score for comparison of "responded at baseline only" versus "responded at both times" ** P <0.01, * P<0.05.

Table 5.6 Psychiatric status at baseline according to responder status (%)

Responder status:	Psychiatric symptoms recorded	HAD "Case"	GHQ "Case"
	%	%	%
No baseline response	23	n/a	n/a
Baseline only	49*	37	54
Baseline and follow-up	32	35	48

* (χ^2=13.1, P=0.0014)

Table 5.7 Clinical characteristics in the four groups at baseline

Characteristic	Surgery	Non-operated	Chalfont	Clinic
Male N(%)	19 (44)	40 (49)	38 (56)	40 (42)
Median age in years (range)	33 (21-52)	34 (18-57)	30 (16-60)	34 (16-74)
Median duration of epilepsy in years	20	22	17	22
Syndrome classification (%)				
Focal epilepsy	100	100	63	63
Idiopathic generalized	0	0	19	31
Symptomatic generalized	0	0	4	3
Non-epileptic attacks*	0	0	13	0
Unclassified	0	0	0	3
Seizure frequency (%)				
In more than 2 Year remission	0	0	3	18 ¶
In 1-2 Year remission	0	0	0	15
Simple partial seizures only	0	0	0	3
Less than 1 seizure per month	4	2	3	27
1-4 seizures per month	33	27	20	9
More than 4 seizures month	63	71	74	28
Frequency of tonic-clonic seizures (%)				
None	45	50	37	64*
1 per Year	12	4	6	17
2-11 per Year	21	16	6	13
1-4 per month	17	25	26	4
More than 4 per month	5	5	25	2
Number of AEDs(%)				
None	0	1	8	3†
1	12	22	15	38
2	74	34	28	44
3	9	39	33	14
4	5	4	16	1

¶ χ^2=118.6 P = 0.00001

* χ^2= 15.4.8 P = 0.001 (No generalized seizures versus any generalized seizures)

† χ^2= 23.2 P = 0.000094 (One or less AEDs versus two or more)

Table 5.8. Baseline demographic and psychosocial characteristics in the four groups

Characteristics	Surgery	Non-operated	Chalfont	Clinic
Median years of education	11 (9-15)	11 (10-14)	11 (7-14)	11 (10-14)
Median Verbal IQ (range)	91 (66-123)	91 (70-137)	84 (66-115)	98 (72-122)
Median Performance IQ(range)	98 (68-137)	97 (69-136)	87 (65-125)	89 (64-136)
Educational achievement (%)				
Degree	7	8	4	16
A level	9	6	4	9
O level	37	45	50	36
Vocational	12	6	5	12
Other	12	9	3	6
None	23	26	34	21
Employment status (%)				
Employed	44	46	19	56
In education or training	9	9	9	7
Disabled or unemployed	33	33	68	24
Housewife	14	11	4	9
Retired	0	1	0	4
Main source of income (%)				
Own salary	37	31	13	36
Partner	14	13	4	11
Parents	19	7	17	19
Benefits	35	49	66	27
Pension	0	0	0	7
Currently living with: (%)				
Partner and/or children	40	60	28	45
Alone	9	12	15	21
Parents	44	24	50	31
With others	7	4	7	3

5.3.2 Baseline clinical characteristics

The clinical characteristics at baseline (syndrome, seizure frequency and AED usage) of the subjects in the Surgical and Non-operated groups were almost identical (Table 5.7). The Chalfont group was similar to the Surgical and Non-operated groups, except for presence of subjects with idiopathic epilepsy. The occurrence of generalized seizures was not equal amongst the groups (χ^2= 15.4.8 P = 0.001, Table 5.7), being highest in the Chalfont group. The Clinic group were more often treated with AED monotherapy (χ^2= 23.2 P = 0.00004). The Clinic cohort was the only group with a significant number of seizure free subjects. The neuropsychological and psychosocial characteristics of the Surgical, Non-operated and Clinic group were also similar (Table 5.8). The Chalfont cohort had more subjects who were either unemployed, disabled or living with parents. They also had lower IQ scores.

5.3.3 Baseline differences in the outcome measures

The Clinic group scored higher at baseline on all SHE scales implying that they had the least handicap (P<0.05; Table 5.9). The other groups were well matched in terms of subjective handicap. On the ESI-55, the groups were generally well matched at baseline (Table 5.10). However, on four subscales, and 2 summary scales (Physical function, Role-Physical, Role-Emotional, Social Function, Total Physical and Total Role), the Chalfont group had significantly inferior health status. On 2 scales (Mental health and Quality of Life) the Clinic cohort had higher scores than the other groups (Table 5.10, P<0.05). Between a third and a half of the subjects were classified as cases on the HAD and GHQ scales. The mean scores were slightly higher in the Chalfont group and lower in the Clinic group (Table 5.11). Thus, the SHE, ESI-55 and the psychiatric scores implied that, at baseline, the Chalfont group were the most affected by their epilepsy and the Clinic cohort the least.

Table 5.9 Baseline SHE scale scores

Treatment group	SHE scale score					
	Work and Activity	Social	Physical	Self-Perception	Life-Satisfaction	Change
Surgery (42)	49 (43,55)	64 (57,72)	47 (41,52)	39 (33,46)	55 (49,62)	47 (43,51)
Non-operated (81)	45 (40,49)	62 (56,68)	38 (33,42)	38 (33,44)	55 (51,60)	47 (45,50)
Chalfont (67)	43 (38,49)	58 (52,64)	40 (34,45)	41 (34,47)	55 (49,60)	45 (41,50)
Clinic (95)	67* (63,72)	75* (70,80)	58* (55,62)	57* (51,63)	64* (60,68)	58* (55,61)

* Significantly greater mean SHE scale score for "Clinic" v all other groups $P<0.05$.

Table 5.10 Mean ESI-55 scale scores (95% confidence intervals)

Treatment group	Mean ESI-55 scale score						
	Physical Function	Role-Physical	Role-Emotional	Vitality	Health Perception	Social Function	Mental Health
Surgery (42)	88 (82,95)	64 (53,76)	65 (52,78)	44 (37,52)	64 (59,70)	72 (64,79)	57 (50,64)
Non-operated (82)	85 (81,90)	60 (51,69)	71 (62,79)	47 (42,52)	61 (57,65)	70 (63,76)	61 (57,65)
Chalfont (67)	72* (65,79)	41*(32,50)	49*(38,60)	46(41,52)	55 (50,61)	58*(49,66)	56 (50,62)
Clinic (95)	86 (82,91)	75 (69,82)	71 (64,78)	54 (49,58)	65 (62,69)	79 (74,84)	67†(63,72)
	Cognition	Pain	Role-Memory	Quality of Life	Total Mental	Total Physical	Total Role
Surgery (42)	63 (55,70)	84#(76,91)	69 (58,81)	53 (50,58)	57 (52,63)	73 (68,78)	67 (58,75)
Non-operated (81)	54 (49,59)	66 (60,72)	64 (58,72)	56 (52,60)	58 (54,61)	67 (63,71)	64 (59,70)
Chalfont (67)	56 (49,63)	63 (56,71)	54 (44,65)	52 (46,57)	54 (49,59)	57* (52,63)	52*(46,60)
Clinic (95)	69 (64,73)	77#(72,82)	76(69,83)	66†(62,69)	66†(63,69)	74 (70,78)	73 (69,79)

* Mean Chalfont score lower than all other groups P<0.05,
† Mean Clinic group score higher than all other groups P<0.05
# Clinic and Surgery group higher mean score than other groups P<0.05

Table 5.11 Psychiatric status at baseline

Responder : status	Mean HAD Anxiety	Mean HAD Depression	"Case" on HAD %	Mean GHQ	"Case" on GHQ %
Surgical	9.0	4.4	37	31	45
Non-operated	9.4	5.3	37	33.5	54
Chalfont	9.1	6.3	41	38†	62
Clinic	7.5*	3.9¶	27	28	37

* Clinic patients less anxious than Non-operated group ($P < 0.05$)

¶ Clinic patients less depressed than Chalfont group ($P < 0.05$)

† Higher GHQ score in Chalfont than Surgical and Clinic patients ($P < 0.05$)

5.3.4 Interventions for the four groups

5.3.4.1 Surgery

Temporal lobe resection (23 left and 12 right lobectomies, and 1 lesionectomy) was the commonest surgical procedure. Four extra-temporal procedures and 3 callosotomies accounted for the remainder. The histology of resected specimens was available for 32 patients (hippocampal sclerosis 23, cavernous angioma 2, dysembryoplastic neuroepithelial tumour 2, dysplasia 1, glioma 1, and normal or non-diagnostic in 4). After 1 year about half the surgically treated group remained on the same medication and about a third had undergone a partial drug reduction (Table 5.12). Few of the Non-operated patients had a drug reduction.

5.3.4.2. Chalfont and clinic populations

Nearly half the Chalfont group had either reduced or stopped medication. Only 7% had an increase (Table 5.12). The majority of the Clinic group had no drug changes (Table 5.12). Eighty five percent of the referrals to the Chalfont centre came from neurologists without particular expertise in epilepsy (Table 5.13). The average length of stay at Chalfont was 6 weeks, though some patients stayed several months. Nearly all Chalfont patients were assessed with MRI, EEG, neuropsychology and by a specialist medical social worker (Table 5.13). A third were seen by a psychiatrist with expertise in epilepsy, and a third received psychotherapy. Establishing, or confirming, a diagnosis (of seizure type or epilepsy syndrome) was the major diagnostic objective for most of the Chalfont patients (Table 5.14). Seizure frequency reduction was the major treatment aim. The neurologist in charge of the assessment unit expected a seizure frequency reduction of more than 50% in only 13% of cases (Table 5.14). At the end of the assessment about half the subjects left with a new seizure or syndrome diagnosis. A quarter of the subjects were found to have non-epileptic attacks either alone or in combination with epilepsy. Thirteen percent had only non-epileptic attacks.

Table 5.12 Antiepileptic drug therapy (%)

Treatment	Group			
	Surgical	Non-operated	Chalfont	Clinic
AED therapy started	0	0	3	0
More AEDs	7	13	7	14
Fewer AEDs	31	17	40	9
AEDs stopped	0	1	8	2
Same number of AEDs				
drugs identical	50	42	21	60
drugs changed	12	27	21	15

Abbreviations: AEDs = antiepileptic drugs

Table 5.13 Process of care in the Chalfont group

Source of referral (%)	
Consultant Neurologist	65
Epileptologist	15
Primary Care Physician	20
Mean duration of stay in days (range)	43 (9-115)
Mean follow-up interval (days)	362
Investigations performed (%)	
MRI	82
EEG	100
Ambulatory EEG	63
Video-EEG telemetry	16
Neuropsychology	93
Social worker assessment	100
Neuropsychiatric assessment	39
Psychotherapy / counselling (%)	37

Table 5.14. Aims of admission and diagnostic outcome at Chalfont (%)

Diagnostic aim	
To make a diagnosis	44
To confirm/clarify a diagnosis	49
No diagnostic aim	7
Expectation for achievable reduction in seizure frequency	
More than 50% reduction expected	13
Less than 50% reduction expected	66
Seizure reduction not a major aim	21
Principal aim for antiepileptic drug treatment	
Seizure frequency reduction	70
Drug side-effect reduction	4
Institute monotherapy	3
Stop Antiepileptic drugs	3
None	20
Diagnostic Outcome	
New syndrome or seizure classification	49
New MRI findings	35
New diagnosis of Non-epileptic attack	26

5.3.5 Seizure outcome

At one year, 24% of the surgically treated cases had been completely seizure free. A further 33% had experienced only auras and 7% isolated seizures (Table 5.15). Thirty six percent were still experiencing regular seizures. The other three groups experienced little change in seizure frequency compared with baseline. According to the subjective seizure rating scale 81% of the surgery group felt their seizure control was better (or seizure free) (Table 5.16). The proportions who felt seizure frequency was improved compared with baseline in the other groups were: Chalfont 60%, Non-operated 36%, and Clinic group 28%.

Table 5.15 Seizure classification at follow-up (Number and percentage in each seizure frequency category)

Group	Seizure status											
	Seizure free < 2 years		Seizure free 1-2 Years		Auras only		<1 Seizure / Month		1-4 Seizures / Month		>4 Seizures / Month	
Surgery	0	(0)	10	(24)	14	(33)	3	(7)	6	(14)	9	(22)
Non-operated	0	(0)	1	(1)	0	(0)	11	(13)	16	(20)	54	(66)
Chalfont	1	(1)	2	(3)	2	(3)	8	(12)	13	(19)	41	(62)
Clinic	21	(22)	10	(11)	3	(3)	26	(28)	8	(9)	26	(28)

Table 5.16 Seizure classification using a subjective rating scale at follow-up (Number and percentage in each category)

Group	**Seizure status (Subjective)**							
	None*		**Better**		**Unchanged**		**Worse**	
Surgery	16	(38)	18	(43)	2	(5)	6	(14)
Non-operated	1	(1)	28	(36)	22	(28)	27	(35)
Chalfont	3	(5)	40	(60)	11	(16)	13	(19)
Clinic	31	(38)	25	(28)	16	(19)	13	(15)

* "None" category includes subjects who rated themselves as seizure free despite having simple partial seizures

5.3.6 Subjective Handicap of Epilepsy

The surgically treated group improved very significantly in terms of handicap. All scales except Life-satisfaction revealed differences for Surgery compared with the Non-operated subjects (Table 5.17; Ancova, $P<0.0001$). The size of the improvement was between 11-23 scale points, an effect size of approximately one. This is generally regarded as a large effect (Kazis *et al.*, 1989). The Chalfont group significantly improved compared with the combined Non-operated and Clinic groups on the SHE Change scale (Table 5.17, Anova, $P<0.0001$). The other SHE scales did not reveal improvement. About half of the Surgery group were classified as having experienced a major improvement in handicap post-operatively (effect size >1) on three of the scales (Physical, Self-Perception and Change; Table 5.18). Thirty eight percent had a major improvement on the "Work and activity" scale. About a quarter of the Chalfont patients experienced major improvement across the scales (Table 5.18). The proportion of patients in the control groups that experienced major improvement in handicap scores was in the range 10-20%. The Life-satisfaction scale demonstrated least change across all groups.

There were four reasons for not proceeding to surgery amongst the non-operated group; that the investigations for epilepsy surgery had not finished, that the patient was not suitable, that a decision had been deferred because seizures were better or that the patient declined (usually because the odds of success were not sufficient to warrant proceeding). The median SHE scale scores at baseline, and change scores at follow-up, for the subgroups are shown in table 5.20. Using the Kruskal-Wallis test (because of the small cell sizes), no differences between these groups emerged on SHE scores. A similar result emerged for the ESI-55 (data not shown).

5.3.7 ESI-55 scores

The outcome on the ESI-55 scale using a difference score (follow-up - baseline) is presented in Table 5.19. Positive values represented an improvement in health

status. The Surgical group had a significantly greater improvement than the Non-operated group on 5 subscales (Mental Health and Quality of life, P<0.005; Vitality, Health perceptions and Change, P<0.05; Table 5.19) and 1 summary scale (Total Mental Health; P<0.005). The Chalfont group improved significantly more than the combined Non-operated and Clinic groups on 6 scales (Cognition, Role-memory, Quality of life P<0.01; Physical Function, Mental Health, Change P<0.05, Table 5.19) and two summary scales (Total Mental Health P<0.05; and Total Role-functioning P<0.01, Table 5.19).

The analysis for the ESI-55 scales, on which it will be recalled the Chalfont group improved, was repeated but the effect of non-response due to absence of benefit was modelled by including all subjects in the analysis and setting the follow-up scores to equal the baseline scores for the non-respondents in each group (hence zero benefit). In this simulation, the Chalfont group still demonstrated a significant benefit on the Mental Health, Cognition, Role-memory, Quality of Life, Change and Total Role-functioning scales (Table 5.21). The benefit on the Physical Function and Total Mental Health scales was no longer significant. The improvement seen on the SHE Change scale also remained highly significant (data not shown). The simulation, therefore, suggested that the benefits seen in the Chalfont group were robust.

In summary, on the ESI-55, the Surgical group showed improvements in comparison to the control group in measures of mental health, vitality and overall quality of life, whereas the Chalfont group showed improvements in cognitive functioning, mental health and overall quality of life.

Table 5.17 Mean follow-up SHE scale scores (95% confidence interval) and **mean change score** (95% confidence interval)

Treatment group	SHE scale score					
	Work and Activity	Social	Physical	Self-Perception	Life-Satisfaction	Change
Surgery (42)	68 (61,75)*	76 (69,82)*	64 (57,71)*	62 (54,69)*	60 (53,67)	71 (64,77)†
	+20 (13,26)	**+11** (3,20)	**+18** (11,25)	**+23** (15,31)	**+5** (-3,12)	**+23** (15,32)
Non-operated (81)	48 (43,53)	66 (60,72)	42 (38,46)	43 (37,49)	56 (52,60)	50 (47,54)
	+3 (-1,8)	**+4** (-1,9)	**+5** (1,9)	**+5** (0,10)	**+3** (-2,5)	**+4** (0,7)
Chalfont (67)	52 (47,58)	66 (60,72)	47 (41,54)	52 (45,58)	56 (51,61)	59 (55,63)#
	+9 (2,14)	**+7** (0,13)	**+7** (1,12)	**+10** (4,16)	**+1** (-5,7)	**+13** (8,19)
Clinic (95)	72 (68,77)	81 (76.85)	60 (56,64)	64 (59,69)	68 (64,72)	58 (55,61)
	+5 (2,8)	**+6** (2,9)	**+1** (-2,4)	**+7** (4,11)	**+4** (2,7)	**0** (-3,3)

* Significant difference "Surgical" v "Non-operated" group (Ancova P<0.0001)

Significant difference "Chalfont" versus "Non-operated" and "Clinic" (Ancova P<0.001)

† Significant difference Surgery versus Non-operated group (Anova P<0.0001)

Table 5.18 Percentage of subjects who improved by more than one effect size at follow-up on the SHE and ESI-55 subscales.

Group	SHE scale					
	Work	Social	Physical	Self-Perception	Satisfaction	Change
Surgery	38	24	45	45	17	55
Non-operated	14	21	16	17	5	13
Chalfont	23	23	15	28	15	36
Clinic	11	9	10	17	13	7

	ESI-55 scale						
	Physical	Role-Physical	Role-Emotional	Vitality	Health Perception	Social	Mental Health
Surgery	10	33	26	37	30	20	22
Non-operated	7	25	16	15	13	16	9
Chalfont	21	24	30	16	21	21	23
Clinic	5	11	22	12	21	11	7

	Cognition	Pain	Role-Memeory	Quality of Life	Change	Total Physical	Total Mental	Total Role
Surgery	26	7	18	37	66	21	35	21
Non-operated	12	13	10	11	33	12	7	13
Chalfont	29	20	35	25	55	20	24	25
Clinic	7	14	16	9	17	8	10	14

Table 5.19 Mean follow-up **ESI-55 change score** *(and 95% confidence interval)*

Group	Mean Change in ESI-55 scale score							
	Physical Function	Role-Physical	Role-Emotional	Vitality	Health Perception	Social	Mental	
Surgery	**1.3** *(-6.3, 8.9)*	**14.9** *(1,29)*	**7.7** *(-4.2,19.5)*	**10.6*** *(2.7,18.5)*	**9.4*** *(3.2,15.5)*	**4.5** *(-4.8,13.7)*	**11.4**** [1] *(3.9,18.9)*	
Non-operated	**0** *(-3.6,3.7)*	**9.5** *(0,19)*	**-2.0** *(-11.3,7.2)*	**1.5** *(-2.8,5.7)*	**1.7** *(-1.5,5.1)*	**2.3** *(-4.2,8.9)*	**1.5** *(-2.5,5.4)*	
Chalfont	**5.2†** *(-1.1,11.5)*	**12.1** *(2.5,21.6)*	**13.7** *(-0.3,27.6)*	**4.5** *(-2,11.1)*	**2.8** *(-2.3,7.9)*	**8.1** *(-0.9,17.1)*	**6.6†** *(1.2,11.9)*	
Clinic	**-1.7** *(-5.8,2.4)*	**-0.7** *(-6.5,5.1)*	**7.7** *(0.1,15.3)*	**-1.4** *(-5.5,2.7)*	**4.0** *(0.8,7.3)*	**1.2** *(-3.7,6.0)*	**-0.9** *(-4.1,2.2)*	
	Cognition	Pain	Role-Memory	Quality of Life	Change	Total Physical	Total Mental	Total Role
Surgery	**7.5** *(-1.4,16.2)*	**2.0** *(-6.9,10.9)*	**1.0** *(-10.6,12.6)*	**14.3**** *(7.0,21.6)*	**25.6*** *(15.4,35.8)*	**6.7** *(0,13.4)*	**10.7**** [1] *(4.6,16.5)*	**8.0** *(0,15.9)*
Non-operated	**3.0** *(-1.4,7.4)*	**2.6** *(-3.4,8.6)*	**-2.3** *(-9.1,4.4)*	**3.6** *(0.2,7.1)*	**8.5** *(3.0,14.0)*	**3.3** *(-0.2,6.8)*	**2.3** *(-0.6,5.2)*	**1.4** *(-3.7,6.6)*
Chalfont	**10.1††** *(3.3,16.9)*	**2.5** *(-6.3,11.3)*	**15.7†† [1]** *(3.4,28.0)*	**8.5†† [1]** *(2.6,14.5)*	**19.9††† [1]** *(11.1,28.7)*	**5.4** *(0,10.9)*	**6.4†** *(1.3,11.6)*	**12.5†† [1]** *(4.7,20.4)*
Clinic	**1.6** *(-1.9,4.9)*	**2.3** *(-2.9,7.6)*	**3.5** *(-3.1,10.0)*	**0.2** *(-3.1,3.6)*	**-5.9** *(-10.6,-1.2)*	**0.3** *(-2.9,3.4)*	**0.6** *(-1.8,3.0)*	**3.5** *(-0.6,7.5)*

Significant difference in mean ESI-55 score; Surgery greater than Non-operated: ** P< 0.005, * P < 0.05
Significant difference in mean ESI-55 score; Chalfont greater than Non-operated and Clinic: †† P < 0.01, † P < 0.05 ;
[1] remains significant after Scheffe procedure.

Table 5.20

Median SHE scale score at baseline and median change in SHE score at follow-up for the subgroups of the non-operated group according to the reason for not proceeding to surgery

Scale	Investigations continue (N=21)	Not Suitable (N=50)	Deferred (N=5)	Declined (N=6)
Median baseline score Median Change score (25,75%ile)				
Work	47 -6(-12,3)	44 6(-7,13)	41 9(-5,39)	57 -10(-13,0)
Social	62 6(-12,12)	62 6(-12,25)	75 10(-13,19)	78 6(0,6)
Physical	38 0(-7,12)	38 3(-12,13)	31 22(13,41)	35 -6(-6,31)
Self-Perception	35 0(-10,5)	35 5(-5,20)	55 12(-5,42)	45 0(0,15)
Life-Satisfaction	56 0(-6,6)	59 0(-7,13)	50 3(0,6)	72 -6(-19,0)
Change	50 0(-10,11)	50 0(-7,18)	43 7(7,7)	52 -2(-11,0)

Table 5.21 Mean ESI-55 scale change scores for follow-up responders and modeling the effect of subjects droping out at follow-up (change score set to zero for non-responders)

Group	Mean Change in ESI-55 scale score -- responders only -- *all baseline subjects assuming zero change in non-responders*							
	Physical Function	Role-Physical	Role-Emotional	Vitality	Health Perception	Social	Mental	
Surgery	1.3 *1.2*	14.9 *14.2*	7.7 *7.3*	10.6* *10.2**	9.4* *8.9**	4.5 *4.3*	11.4** *10.8 ***	
Non-operated	0 *0*	9.5 *7.9*	-2.0 *-1.7*	1.5 *1.2*	1.7 *1.5*	2.3 *2.0*	1.5 *1.3*	
Chalfont	5.2† *2.0*	12.1 *7.7*	13.7 *8.7*	4.5 *3.0*	2.8 *1.9*	8.1 *5.2*	6.6 † *4.3 †*	
Clinic	-1.7 *-1.2*	-0.7 *-0.5*	7.7 *5.5*	-1.4 *-1.0*	4.0 *2.9*	1.2 *0.9*	-0.9 *-0.7*	
	Cognition	Pain	Role-Memory	Quality of Life	Change	Total Physical	Total Mental	Total Role
Surgery	7.5 *7.1*	2.0 *1.9*	1.0 *1.0*	14.3** *13.6 ***	25.6* *24.4 **	6.7 *6.3*	10.7** *10.1 ***	8.0 *7.6*
Non-operated	3.0 *2.5*	2.6 *2.2*	-2.3 *-1.9*	3.6 *3.1*	8.5 *7.2*	3.3 *2.8*	2.3 *1.9*	1.4 *1.2*
Chalfont	10.1†† *6.5 †*	2.5 *1.6*	15.7 †† *10.1 ††*	8.5 †† *5.6 †*	19.9††† *13.1 †††*	5.4 *3.5*	6.4† *4.2*	12.5†† *7.9 †*
Clinic	1.6 *1.1*	2.3 *1.7*	3.5 *2.6*	0.2 *0.2*	-5.9 *-4.3*	0.3 *0.2*	0.6 *0.5*	3.5 *2.5*

Significant difference in mean ESI-55 score; Surgery greater than Non-operated: ** P< 0.005, * P < 0.05
Significant difference in mean ESI-55 score; Chalfont greater than Non-operated and Clinic: †† P < 0.01, † P < 0.05 ;

5.3.8 Psychiatric outcome

The mean change in HAD anxiety score declined significantly more in the Surgical group than the Non-operated group (P <0.05, Table 5.22). The mean depression score declined more in the Chalfont group than the Clinic group (P< 0.05, Table 5.22). The percentage of subjects classified as "cases" by the HAD scale dropped from 37% to 17% in the Surgical group, and from 41% to 30% at follow-up in the Chalfont group. It remained unchanged in the other groups. The ESI-55 Total Mental Health scale also showed a significant improvement in the Surgical group at follow-up compared with the Non-operated group (Table 5.19; P< 0.005). The Chalfont group showed a similar, though smaller, improvement on the ESI-55 Mental Health scale compared to the Non-operated and Clinic groups (Table 5.19; P<0.05).

Table 5.22 Psychiatric scale scores at follow-up

	Mean HAD Anxiety Change (95% C.I.)	Mean HAD Depression Change (95% C.I.)	HAD "Case" (%)
Surgical	-3.4 (-4.7,-2)*	-1.1 (-2.5,+0.2)	17
Non-operated	-0.7 (-1.6,+0.1)	-0.3 (-0.9,+0.2)	37
Chalfont	-1.5 (-2.7,-0.3)	-1.7 (-2.9,-0.5)†	30
Clinic	-0.7 (-1.3,-0.1)	0 (-0.5,+0.5)	27

* Surgical versus Non-operated P < 0.05.

† Chalfont versus Clinic P < 0.05.

5.3.9 Objective handicap

For all groups about 10% of persons gained or lost a position in employment, education or training over the course of the study (Table 5.23). The majority of subjects remained either employed or "disabled". Only 1 subject in the Surgical group, and 2 in the Chalfont group, obtained paid employment at follow-up, if social security benefits were the main source of income at baseline.

Table 5.23 Occupational outcome in terms of a position gained, maintained or lost (number and percentage of entire treatment group).

Treatment group	Position in employment / training *		
	Gained	Maintained	Lost
Surgery (42)	6 (14)	14 (33)	5 (12)
Non-operated (82)	4 (5)	36 (44)	4 (5)
Chalfont (68)	7 (10)	14 (21)	4 (6)
Clinic (90)	6 (7)	50 (53)	4 (4)

* Table does not include persons remaining on disability benefits or as homemakers

5.3.10 Qualitative observations

Of the 42 subjects in the longitudinal study of epilepsy surgery, 39 provided extra comments, 21 of which were more than 1 or 2 sentences. Twelve comments are reproduced in the appendix to this chapter. In the retrospective study (Section 3.2.7.2), 67 of 105 produced comments, a representative 17 of which are reproduced in the appendix. Forty seven of 67 Chalfont subjects replied to the supplementary questions, 21 providing more than very brief responses, and 15 are reproduced in the appendix.

The surgical subjects reported major changes in their life. Subjects typically spoke in terms of "life changing completely" and of "life having just begun". It was striking how many felt they were a "new person" or that they "were normal" again. Subjects in the retrospective group, who had longer duration of follow-up, were particularly likely to report that their life had changed "completely". Relief at being able to abandon a stigmatized *persona* was common. Many noted an increase in confidence and sense of independence. Many reported that they had stopped worrying about seizures. Some subjects commented that they were unaware just how much epilepsy affected them until they were relieved of the seizures. A few subjects remarked on the difficulties relatives had in coming to terms with the change in their health and a reduced need for help. Some relationships broke down in the context of seizure relief. Several patients commented on a phase of a depression or increased emotionality after the operation, but only two reported very severe symptoms beyond one year. Memory problems were the typical adverse effect of the surgery. The comments of subjects who were not relieved of the seizures (excluding auras) were fewer and qualitatively very different. Subjects rarely noted dramatic benefits, few describing it in terms of "becoming normal". Some spoke of their disappointment. From the qualitative evidence of the longitudinally studied subjects there appeared to be little difference between those with and without auras, though the numbers are too small for a confident conclusion.

The Chalfont subjects never spoke of dramatic improvements in their life. Sixty of the 67 respondents said they were glad they had been at the centre. Of the 47 comments most were brief comments about seizures or treatment. Ten remarked that no improvements had occurred and 18 that seizure control was better. Ten mentioned improvements in drug treatment, but 6 commented that the drug changes had not helped. Of the more extended comments, one theme predominated; the benefit of meeting others with severe epilepsy or non-epileptic seizures. Typically

subjects spoke of realizing that they were "not alone" and welcomed the opportunity of finding out how others coped with epilepsy. Others said that learning more about their condition helped them. A few mentioned that their diagnosis had been clarified or that psychotherapy had helped. The common criticisms of the process of care at the centre were boredom during the long assessment and the inadequacies of the residential facilities.

5.4 **Discussion**

The main findings of the study were that patients after epilepsy surgery were significantly improved on measures of handicap, quality of life, psychiatric symptoms and seizure frequency. The comprehensive assessment group also experienced quality of life gains, particularly in terms of self-assessed cognition, overall quality of life and mental health. Handicap improved in the comprehensive assessment group to a lesser extent, only one SHE scale (Change) detecting significant improvement. When expressed as the proportion of subjects experiencing a major improvement in handicap over the course of the study, approximately one half improved after surgery, a quarter after comprehensive assessment, and 10-15% in the control groups.

There are several important caveats regarding the interpretation of the study. First, and most important, is that the absence of randomization, weakens the confidence with which one can attribute the differences in outcome to the interventions used. However, for the reasons discussed, randomization was considered impracticable and unethical. An assessment of the bias introduced by lack of randomization was obtained by detailing the differences at baseline in clinical and social characteristics between the groups. Three of the groups (Surgery, Non-operated and Chalfont) differed little at baseline in terms of seizure frequency, though the Clinic group clearly had the mildest epilepsy. The psychosocial characteristics were also broadly similar at baseline, though the Chalfont group again had the greatest level of

objective handicap (e.g. lack of paid employment). The ANCOVA procedure was used to reduce the effect of differences in baseline subjective handicap on the outcome scores. It showed that, allowing for the baseline differences, handicap improved considerably in the Surgery group, a little in the Chalfont group, and negligibly in the two control groups. The non-operated group probably did differ aetiologically from the operated group, but it is unlikely that this accounted for the major difference in psychosocial outcome. At baseline, both on objective characteristics, and on scale scores, the groups were well matched. In addition, in the analysis of scores at follow-up of non-operated subjects, subdivided by reason for not having surgery, there was no difference between those rejected as unsuitable and those in whom investigations were continuing. This suggested that the rejected group were not especially disadvantaged.

The second reservation related to how representative of the general population of epilepsy the original and the follow-up samples were. The original sampling frame was highly selected because all patients came from a specialist centre. However, the degree of handicap in the treatment study was very similar to that noted in patients with frequent seizures from the unselected population in section 4 (see comparison of SHE scores for patients with frequent seizures on Table 4.5 and 5.9). This suggested that with respect to the social impact of the epilepsy, the patients in the hospital sample were representative of the general population of severe epilepsy. However, the Chalfont sample may have been especially disadvantaged (see low SHE scores on Table 5.9 and demographic characteristics on Table 5.8). The only exclusion criterion in the study was learning difficulties sufficient to preclude completion of the questionnaires. Different methods will be required to assess the impact of treatment on people with learning difficulties, because of the methodological problems involved and the particular difficulties faced by such persons.

The response rates at baseline and at follow-up were high. At follow-up, the only group with a low response rate was the Chalfont group. At least three factors may have been involved. First, more than one half of the Chalfont cohort had returned to follow-up by their referring physicians, which made compliance with follow-up assessments more difficult. Second, patients with non-epileptic attacks had a higher than expected non-response rate; and third, the non-responders had an unusually high rate of psychiatric symptoms recorded at baseline. It is uncertain whether the Chalfont non-responders had a particularly unfavourable outcome. If this were the case, then the overall benefits of the comprehensive assessment group may have been over estimated. An attempt was made to adjust for this by performing a simulation exercise, assuming that all non-respondents in the study obtained no benefit. The improvement, as a group, seen in the Chalfont group remained. However, if the non-respondents in the Chalfont had a differentially poorer outcome compared with the non-respondents in the other groups (i.e. actually worsened as a result of their assessment), the possibility remains that the estimate of benefit is biased.

A third consideration is the heterogeneity of the clinical problems referred to the Chalfont program and the variety of treatment approaches used. The patients presented with a combination of diagnostic, therapeutic and social difficulties. In some, clarifying the seizure syndrome led to AED treatment changes, and in others a reduction in drug treatment. In those with non-epileptic attacks, drugs were generally completely withdrawn and psychological therapies initiated. Identifying which aspects of assessment and treatment were responsible for the outcome was not possible. The current study is an overall assessment of outcome.

Patients who had extratemporal resections and callosotomies were included together with operations known to be associated with a good outcome (temporal lobectomy) because it was considered illogical to exclude cases felt to have a reduced chance of

a "good" outcome in the surgery group, in the same way as no-one was excluded from the Chalfont group on the basis of a predicted poor outcome. Heterogeneity of "input" is typical of referrals to an epilepsy centre. The present study was carried out to assess what can be done "overall" in either a surgery or a comprehensive assessment program.

Another limitation of the study is that one year of follow-up was a relatively short. It is conceivable that further benefits could have accrued with longer observation. However, as duration of follow-up increases in observational studies of this type so does the difficulty, and cost, of achieving high rates of follow-up. Differential follow-up rates could clearly have confounded the interpretation of the study. Logistical constraints apart, one year was chosen as a compromise.

What can be concluded about the outcomes in the study ? The seizure outcome in the Surgical group, is somewhat lower than that reported in other surgical case series (Engel *et al.*, 1993). This was because patients reporting any auras, or seizures in the first post-operative year, were classed as not being seizure free. No allowances were made for "post-operative" seizures. In addition, this case series included procedures which rarely result in seizure freedom. The percentage of patients with hippocampal sclerosis in the resected specimen who were seizure free (or with auras) was 74%, which is keeping with the results from other centres.

The reduction in subjective handicap was greatest in the Surgical group, reflecting the major impact of seizure frequency on handicap. The benefits of surgery as assessed by the ESI-55 in this study closely match the previous prospective study (McLachlan *et al.*, 1997). He found that at 12 months after surgery two ESI-55 scales detected a benefit (Health perception and quality of life), and at 24 months five did. The current study found benefits at 12 months on four main scales (Health perception, Quality of life, Mental Health and Vitality) and one summary scale (the

Change scale was not reported by McLachlan). He argued that it may take at least 24 months for the main benefits to occur. The differences between the studies may be due to sample size (the control group in the current study was four times the size of McLachlan's study).

The Chalfont group improved significantly only on the SHE Change scale. On the ESI-55, however, the Chalfont group changed significantly on several measures, in some cases more so than the Surgical group. Particular improvements were noted on the Cognition, Role-memory scales and Quality of Life scale. This may have related to changes in anti-epileptic medication that were made in this group. No simple relation existed between change in number of drugs and ESI-55 scores (data not shown). It should be noted that the confidence intervals around the change in the 3 ESI-55 role scales (Role-physical, Role-emotional, and Role-memory) were very wide indicating either heterogeneity in outcome or measurement error. The benefits that were detected on the ESI-55 Mental Health, Role-emotional scales and Quality of Life visual analogue scale were mirrored by a drop in the HAD scores for the group, suggesting improvement in emotional health in the Chalfont group.

It was noteworthy that the Chalfont subjects improved more on the ESI-55 scale than on the SHE scale. One interpretation is that the SHE scale measured the more enduring impact of epilepsy whereas the ESI-55 was more symptom oriented. The period of comprehensive assessment was able to alleviate some of the cognitive and psychological effects of epilepsy and AED treatment, but the social and vocational consequences were much more difficult to change. There is clearly further scope to develop innovative rehabilitation programs to try and address these issues.

It was interesting that the Clinic sample experienced no change in seizure frequency. Scores on the SHE, ESI-55 or HAD scales also did not change over the course of the study. Only 10% of the clinic patients were classified as having a major

improvement in handicap, quality of life or general health status (Table 5.19). This suggests that patients undergoing routine follow-up in an epilepsy clinic have a rather fixed health status. Further research into the value of prolonged specialist follow-up is called for.

The qualitative observations served to underscore the major benefits of successful epilepsy surgery. The manner in which patients spoke of the effect of the intervention suggests it can be considered "a cure", though the benefits may take some time to accrue and some adjustment on the part of the subject and his/her family is often needed. Surgery which does not result in complete seizure relief appeared to have much less benefit. Comprehensive assessment did not result in dramatic changes, but it was of considerable interest that patients reported that meeting others with severe epilepsy (often for the first time) was a help in coming to terms with their condition. This may be similar to the support patients obtain from attending self-help groups.

The SHE work, physical, and self-perception scales were the most sensitive to differences between the groups, followed by the ESI-55 vitality, health perception and mental health scales. This replicated the findings in the validation study (section 3.2.7.2b). Both Change scales were also highly sensitive to improvement, though less informative about *what* had improved.

In conclusion, this is the first study to prospectively measure the impact, over one year, of epilepsy surgery and comprehensive assessment on the handicap and quality of life of people with severe epilepsy. Epilepsy surgery had considerable impact on subjective handicap and quality of life. Patients, who were not suitable for surgery, derived benefit, from intensive multi-disciplinary medical and psychosocial assessment at an epilepsy centre. The principal gains related to the cognition and mental health rather than subjective handicap. There were no changes in objective

indices of handicap. The study emphasizes the difficulties encountered when trying to improve the quality of life of people with severe epilepsy if it is not possible to render them seizure free.

5.5 Summary and Conclusions

(1) In the study, two treatment groups were recruited: 45 patients undergoing epilepsy surgery and 104 comprehensive assessment at an epilepsy centre. Two control groups were enrolled: 113 patients assessed for surgery but not operated upon, and 130 patients in an epilepsy follow-up clinic. The subjects were assessed at baseline and after one year on measures of subjective handicap, quality of life, mental health and seizure frequency.

(2) Significant improvements in seizure control, subjective handicap, quality of life and psychiatric status were seen in the surgically treated patients compared with the non-operated group. About half of the surgery group experienced a major reduction in subjective handicap one year after treatment.

(3) Improvement on some measures of quality of life and handicap occurred in the comprehensive assessment patients compared with the two control groups, despite no change in overall seizure frequency. About 25% of the Chalfont group reported a significant reduction in subjective handicap on follow-up.

(4) Complete remission of seizures appears to have a primary role in achieving major quality of life gains for patients with severe epilepsy , though smaller but significant gains can be obtained by skilled multi-disciplinary assessment.

Appendix to section 5

Comments by subjects at follow-up.

Longitudinal Surgery patients : Seizure free patients (with or without auras)

Key: N000 = Subject Number

1.

N212. Female, 30. Epilepsy onset age 11. 1 year after temporal lobectomy. Seizure free except some auras. Unemployed.

[The benefits are...] My life has changed completely. I had to rely on people, I could not live on my own, I could not go out on my own. Whereas now I don't need to rely on anybody, and I now know that everybody likes me, whereas before the surgery I thought everybody hated me because I had epilepsy. I found it very hard to make friends but I have got so many now. Thanks to the surgery everyone says I am a different person for the better. Because I thought I never had a life, now my life has just begun and I am enjoying my life so much.

[On the negative side...] The only people it has been difficult for is my mum and dad, they cannot handle the thought of me not needing them so much. It has caused so many arguments. They still haven't come to terms with it in over a year. I don't think they ever will.

2.

N214. Female, 30. Epilepsy onset age 11. 1 year after L. temporal lobectomy for HS. Seizure free except auras. Teacher.

[The benefits are...] Psychologically I am more able to make realistic judgements on how I feel. My job is far easier as I am able to be 100% concentrating and not worrying about fits. I am much happier, more stable, more relaxed more interested in life, more positive and am starting to enjoy life again after 17 years of intermittent hell.

[On the negative side] ...I suffer from tinnitus-which changes frequency and timing and ear from day to day. I still have auras which prevent the driving. I suffered severe clinical depression not long after the operation and am still on antidepressants.

[I would have liked...] help from a support group set up by people who have already undergone the operation.

3.

N242. Female, 28. Epilepsy onset 11. 1 year after L. temporal lobectomy for HS. Seizure free. Secretary.

[The benefits are...] My life has improved brilliantly. I no longer have epileptic fits and therefore feel 100% (almost all of the time). The stigma of being an epileptic has been taken away. I am able to drive and this has changed my life, and also my family's and friends lives. I feel as though I have independence and I am a normal person.

[On the negative side...] There has been a slight change to my memory. I don't remember names of people very easily or lists of things.

4.

N229. Female, 29. Epilepsy onset age 6. 1 year after L. temporal lobectomy for HS Seizures free now except auras. Works in marketing.

[The benefits are...] My memory has shown signs of improvement. [There is a ..] a sense of relief for both myself and my family. I now have a full night's sleep rather than a disturbed one. [I had a ...] short period of post operative depression. [I am...] accepting that I may not be 100% seizure free.

Talking to a counsellor prior to surgery may have been useful, to help in getting myself prepared for how I might feel afterwards. I also feel that a counsellor during my stage of depression , as those around me could not really help-being too close to me. They were also unable to relate to what I was going through having had no similar experience.

5.

N244. Male, 28. Epilepsy onset 2. 1 year after L. temporal lobectomy for HS. Seizure free except auras. Unemployed.

[The benefits are...] Doing things what I hadn't done before. I seem to be more out-going, a bit more of sense of humour at times, and more confident in my self. Being able to go out without thoughts of having a seizure.

[On the negative side..] My parents seem to be still on edge, as though they think I am still going to have a seizure at any time.

6.

N235. Female, 35. Epilepsy onset age 21. 1 Year after R. temporal lobectomy for HS.
Seizure free except auras. Housewife.

[The benefits are...] Having no seizures since surgery has given me a lot more confidence in my ability to do more activities with my children, without the worry that if I had a seizure, who would look over them until I recovered. (e.g.. we have been swimming, to the park, shopping, to the pictures, out walking the dog etc.) without needing another adult with us. So I have great deal more freedom without the family worrying.

I am not so tired as I was before and do not need so much sleep. The greatest problem has been loss of memory, especially for words. I have tried hard to explain many simple things to the children and found this hard as the as the words do not come although I know what I am trying to tell them. My husband and I found it hard to adjust to the fact that I am not so tired and want more out of my life.

[On the negative side...] I have found that I have less patience with other people and have found it hard to adjust to the fact that my family no longer feel I need someone with me and spend a great deal of time on my own and a lot of activities that I would have company (e.g. shopping) - I now find I'm alone.

7.

N246. Female, 24. Epilepsy onset age 1. 1 year after L. temporal lobectomy for HS. Seizure free except auras. Dental assistant.

The benefits are that you don't have to tell people that you are on medication for epilepsy when you meet them. Also you don't have to worry about having a epileptic fit. Also my mother does not worry like she used to.

[On the negative side...] My moods are worse than they were before, I am more impatient.

8.

N216. Male, 34 . Epilepsy onset age 14. 1 year after L. temporal lobectomy for HS. Seizure free. Silversmith, lives alone.

[Benefits are...] No attacks so far. I am able to work part-time without the threat of attacks or auras (only occasional) sick feeling or fear which is nothing compared to an attack or previous aura. More confidence. Patience and determination. Happier on the outside, but fed up inside. Once at work full-time I shall be a lot happier all over.

[On the negative side...] It is taking a long time to get over the feeling of tiredness and exhaustion. This has prevented me from having a social life. Also not being able to carry out a full working day makes the situation worse. I am sure that once I am back at work full-time this will change and life will be much better. In fact with the tiredness, exhaustion, sometimes depression and anxiety, I forgot that hopefully I got rid of the worst thing -epilepsy! When I realise this I feel much better.

9.

N280. Female, 32. Epilepsy onset age 7. 1 year after R. temporal lobectomy Seizure free except auras. Housewife.

[The benefits are...] Since my operation my sexual relationship with my husband has improved. I feel more confident and others can see this in me too. I have more energy than I used to which is probably why I don't sit [around] so much anymore. I have also started to take driving lessons.

[One the negative side...] My family says I have become more quick tempered. This may be due to feeling less inhibited. I had a big panic attack soon after coming home which was worrying. And pains in the head which later could only be described as muscles contracting. Depression started soon after I came home this has not helped by family matters although it is now getting better. I think it is now down to family and not post-operative.

10.

N209. Male, 25. Epilepsy onset age 9. 1 year after R. temporal lobectomy for HS. Seizure free. Spot welder.

[The benefits are...] I am seizure free since the op. Memory [has] improved, confidence has improved. I find my sense has improved as in sick sense of humour.

Retrospective study of epilepsy surgery: Seizure free patients.

11.

N002. Female, 36. Epilepsy onset age 21. 2 years after L. temporal lobectomy for HS. Seizure free. Unemployed pre-operatively, now care assistant with disabled children. Married.

[The benefits are...] I didn't realise how much I was missing out on until now... Life is GREAT.

12.

N008. Male, 20. Epilepsy onset age 1. 2.5 Years after R temporal lobectomy for a DNT. Seizure free. Lives with parents, working in a residential home hoping to be a nurse.

[The benefits are...] Overall, since my operation life is cool. BUT it does annoy me somewhat that people can't forget my history, I CAN. I like to live life to the max. I love danger and I love being involved with dangerous sports. But, yet again, my history goes against me- but it shouldn't it is history....As far as I am concerned. I am just the same as anyone else; prospective employers have always seemed keen, until I mention epilepsy. On many occasions I have been referred to medical advisors etc. etc.. to see if I am suitable for employment - I take great offence by this 'procedure' which I have been through many times.

13.

N077. Female, 39. Epilepsy onset age 21. 5 years after amygdalo-hippocampectomy for HS. Seizure free.

[The benefits are...] I had my operation in 1988 and since that time I haven't had any problems. I have now got my licence back and have clocked up over 60,000 [miles] since getting my licence back. My husband left me because of my epilepsy but myself joining a social club has made life a lot better. It is just so lovely to be independent again as I was off the road for 9 years.

14.

N078. Female, 36. Epilepsy onset age 21. 2 years after L. temporal lobectomy for HS. Seizure free.

[The benefits are...] Epilepsy no longer affects my life as I no longer have epilepsy. It did affect my life in every way, before my operation I was always tired and afraid of every thing and everyone, with no confidence. ... The only problem I have is still taking medication which makes me feel like I am still holding on to the past. I believe that I no longer need the medication as I no longer have the illness.

15.

N093. Female, 28. Epilepsy onset age 2. 2.5 years after temporal lobectomy for HS. Seizure free. Unemployed before surgery, now care assistant. Lives with parents.

[The benefits are...] Until two years ago I still carried my epileptic label which stopped me from doing the work I wanted to. I felt very guilty when I applied for a new job - after two years fit free and I could honestly write "good health" in the medical section. Now being able to drive has allowed my independence to increase although after such a long time away from some social groups it is taking time to get invited and involved. It has certainly been easier making new friends than connecting up with some who were scared by my fits. Emotions are still a problem. Now I look and act normal, people expect me to act my age emotionally. I missed my teens and mid-twenties due to "drug numbness". I am still learning about my self - making teenage mistakes. Sexually I still hold back and I am scared in case I am still not 100%.

16.

N092. Female, 31. Epilepsy onset age 3. 4 years after amygdalo-hippocampectomy. Seizure free.

[The benefits are...] I had epilepsy all my life and realised it affected my life style, but did not realise to what extent until after my surgery, since which I have had no seizures. My schooling was greatly affected both due to my lack of concentration and also by the way I was treated by other pupils. The teachers were also very ignorant about epilepsy and didn't make things easier. I enrolled in a typing course with [a newspaper], then I was asked to leave following a seizure. The principal said the course was not suitable for people with epilepsy. ...[after the surgery...] I have had the opportunity to work for myself.

17.

N068 Male, 24. Epilepsy since age 1. 2.5 years after temporal lobectomy for HS. Seizure free. Since surgery has started at horticultural college.

[The benefits are...] Straight after the operation my awareness was heightened tremendously. This had pros and cons, for good things seemed 10 times as good, bad things ten times as bad. Despite my operation, I still have epilepsy stamped on my forehead when it comes to job applications. The operation was a great success in halting my seizures. My memory still remains a problem in my life generally. However, I wish to keep my chin up. For the more I achieve the better my chance of proving that epilepsy is a thing of the past. My specialists have toyed with the idea of reducing my medication. However, I wish to leave things as they are, because although the question remains -'would he have a seizure if medication was reduced?' I do not want to be a role model for experiments. My driving licence is due to be a big step forward when I pass my test. Being at a residential college means I have my own life to lead and I am not under the pressure of my fathers roof.

18.

N113. Female, 32. Epilepsy onset age 1. 7 years after temporal lobectomy. Seizure free. Housewife with children.

[The benefits are...] Since my operation I have not had any fits and the quality of my life is excellent compared to before the operation. Because I had suffered from epilepsy most of my life, I didn't realise until after the operation how it had affected me so much e.g. feeling tired all the time, nervous about going out, depressed etc. I feel the first 24 years of my life are a blur because epilepsy affected my memory do much. I also feel quite bitter that I could not pursue the career of my choice. It affected so many aspects of my life, even my sex life. Often intercourse would be interrupted by a fit or an aura.

19.

N126. female, 20. 3 years after lesionectomy for extratemporal low grade glioma. Seizure free. College student, living with parents

[The benefits are...] My lifestyle has improved immensely. I am now taking a B.Tec. in travel and tourism. It is easy for me to forget about my history because I want to forget it, but other people don't find it so easy. I have travelled around Europe without my family last year. Personally I feel as normal as anyone else....It is not that the epilepsy sometimes makes it difficult to make friends but the mental scars of always having to be on the defence at school when I did have the seizures.

20.

N009. Female. Epilepsy onset age 11. 19 months after R. temporal lobectomy for HS.

Seizure free. Pre-operatively, Florist and married.

[The benefits are...] Since the operation my health and happiness had improved 100% until my husband unexpectedly left me....If this had happened before the operation I know my health would have suffered greatly as stress and emotional upset would always trigger the seizures. I think, therefore, that being healthy has helped me cope with the shock and recover much faster than I would have before. The only difficulty since the operation, my memory for faces and names and events has seemed to worsen slightly and it was quite bad before, causing quite a few rather embarrassing situations with friends and family. I don't recognise them after not seeing them for maybe six to eight weeks! But I find this minor compared to the problems I had before the operation caused by epilepsy i.e. being frightened to go out on my own, constantly worrying about when the next fit would come, totally unhappy with my quality of life in general and very often depressed. Life is really worth living now and all other problems I now have to face really are minor now I have my health back.

21.

N051. Female, 31. Epilepsy onset 4. 1.5 years after Temporal lobectomy. for HS Auras post-op. Living with parents, working as a secretary.

With regard to my personal life, I am disappointed that it has not developed more quickly. I had hoped that my operation would automatically open a whole new life for me, but knowing that I am not going to have a fit has not been enough to give me the confidence to go ahead and do all the things I thought I would be doing now. I still feel restricted in making relationships, but I have just started counselling, which I really hope will help me. Family relationships have, on occasions, been strained but I believe this has partly due to the fact that my work situation has made it difficult for me to snap out of the depression I suffered after the operation.

22.

N102. Female, 29. Epilepsy onset age 9. 1.5 years after temporal lobectomy for HS. Seizure free. Unemployed preoperatively. Now doing voluntary work in Oxfam shops .

[The benefits are...] Since the operation my life has changed totally. I now live alone as I wanted to be totally independent, so I moved out and left my boyfriend. We are still the best of friends, but it was not until after the operation when I regained good health, free of seizures that I realised I didn't love him, and it was my epilepsy that kept us together. I'm glad we never married. In many ways I regret about having the operation as I've lost my home, partner and don't talk to my parents anymore. In other ways I'm doing things in my life now I could never achieve if I'd been ill, so my feelings are mixed. The past year has not been easy, but I have to admire myself for going through with it, not many people would have taken it on.

Surgery : Not completely seizure free (Both studies)

23.

N023. Female. Epilepsy onset age 11. 1 year after temporal lobectomy for a low grade glioma at age 20. Occasional seizures after surgery. Lives with parents, works as a clerical assistant.

Previous to my operation I felt that fits were part of every day. Now I am in fear of them because it is like a defeat when I have a fit.

I hope to better myself, but I am in a type of fear of rejection or changing and then quality of life going down or fits recurring".

24.

N066. Female, 35. Epilepsy onset 15. 1 year after Temporal lobectomy. Rare seizures post-op. Not in work.

[The benefits are...] My whole life has changed. All my friends and family notice it. I'm more full of life, I'm much more happier. I haven't got that blank look anymore. My hormones are back to normal. I've have a regular period. I'm more cheeky and I've put on weight.

25.

N108. Male, 32.. Epilepsy onset 12. 1.5 years after lesionectomy of DNT. Recurring seizures, but fewer severe ones. Lives with parents, doing college course.

The major bonus after my operation is that I don't have to keep going to hospital to have stitches put in my head and especially my face. Also I do not have to keep worrying about spilling things over myself. This isn't much but I never did let my epilepsy bother me before the operation.

26.

N304. Male, 40. Epilepsy onset age 24. 1 year after R. temporal lobectomy for HS. Recurrent seizures. Car dealer.

[The benefits are...] Mainly fewer fits. I don't really consider myself as a person that has a problem with quality of life, although the lack of driving licence really does upset me (having worked for a car company for over 20 years not having a licence is a bitter pill to swallow). Apart from the fits I have always been 100% healthy.

[On the negative side...] Sometimes I just cannot think of the words I would like to say in a split second. It has been more of a disappointment to have a fit now, because I really wanted to go into hospital, have the operation and be cured 100% the next day! I believe I am rational enough to know this will not happen and so try not to be too disheartened. The drugs have caused me to lose libido completely.

27.

N332. Female, 36. Epilepsy onset 28. R. Frontal lesionectomy for cavernous angioma. Recurrent seizures. Housewife.

[The benefits are..] Fits not so severe although more frequent. I feel more settled knowing I have tried another method to control even if this meant radical surgery.

[On the negative side...] Disappointment, that has been very difficult to deal with. Depression with a loss of ambition and energy. I actually feel less well physically. I have experienced lots of tiredness. I take more anti-convulsants. I am sensitive emotionally.

Surgery : Depression

28.

N072. Female, 32 . Epilepsy onset age 18. 3 years after temporal lobectomy. Occasional seizures. Severe depression post-operatively.

[On the negative side...] Since the surgery I have spent my life in and out of psychiatric hospitals, suffering with bouts of recurring depression. Although the majority of my seizures were removed through the surgery, it seems to have taken the lid off many emotional problems stored in my brain. Thus it is harder to keep negative thoughts under control. Due to the depression and suicide attempts my husband and I separated. Having coped with my severe epilepsy until the surgery, only to be replaced by a wife who was not mentally safe, he and I both realized we could not continue living together.

29.

N052. Female, 37 years. Epilepsy onset age 1. 8 months after temporal lobectomy for dysplasia. About 15 post-operative seizures. Occasional auras still. Father died suddenly recently , mother and husband unwell recently. Patient depressed.

[On the negative side...] I started to suffer from post-operative depression after 5.5 months and this is affecting me quite badly at times. I sometimes feel resentful that I had the operation - I feel that, although I couldn't control it when I had fits, I knew most times when I would have them, but now I feel I have no control over my feelings at times and it is because of what others have done to my brain. I want to know more about the actual operation, what was done and why some things are taking a long time to heal. In a lot of ways, I wish I had been told more about how I would feel post-operatively before the operation.

Chalfont assessment unit patients

30.

N903. Female, 18. Several simple partial seizures per week. Some reduction in frequency after Chalfont. Mild hemiplegia. Student.

[Benefits ...] Meeting people with problems like mine. Being able to do things without people trying to stop me (mum and dad). Showing the family that I can cope with everyday things.

31.

N920. Female, 26. Monthly complex partial seizures. Went to live with new partner after meeting him at Chalfont.

[Benefits ...] Previously my parents had done their best to raise me as a normal child and not to treat me differently in any way....Living away from them and learning to look after myself seemed a rather awe inspiring prospect. Chalfont was supposed to provide a useful stepping stone in order to help me learn to adapt to ordinary society. This was the idealistic view of my family. In actual fact I met -----, my partner, there who was about to have a brain operation [and left to look after him]. I sometimes regret that I did not complete the training I would have got in LINKS. ....My stay definitely boosted my self-confidence and helped me to make the decision to move away from home. It helped me not to feel so isolated and cut off by my epilepsy by introducing me to people from my own peer group who were living with it.

32.

N931. Male, 31. Frequent seizures, unchanged after Chalfont. On Disability benefits.

[Benefits ...] I found it helpful to get information on my condition also to be able to discuss my problems with fellow suffers. I hoped that by going to Chalfont my epilepsy would be controlled. To a certain extent the fits are less frequent but the side-effects of drugs prevent me from leading a normal life.

33.

N951. Female, 29. Juvenile myoclonic epilepsy and non-epileptic seizures. Fewer seizures after Chalfont (both types). Social worker.

[Benefits ...] The diagnosis is now absolutely clear. I have non-epileptic seizures and epilepsy. The current treatment for epilepsy is working well. I take epilim chrono and my most recent jerk was Sept. 95.. As for NES, the psychologist's client centred, task centred approach to therapy provided a very useful springboard to therapy beyond Chalfont. Her technique of relaxation and tuning in to my fears have proved invaluable. These coupled with a desensitization program late in 1995 have helped me to reduce the incidence of NES in my life. Most recent episode was Feb 1996. Prior to that was Oct. 1995. This much improved situation has found me with increased confidence, a more positive self-image and overall a much better life.

34.

N963. Female, 16. Frequent attacks on admission. All non-epileptic. Now very few.

[Benefits ...] It made me realise that I was not the only person who had non-epileptic seizures, which was very supporting. I also made a lot of friends and it gave me time to grow up, being with all those adults. I am trying to get on with my life and I am not sure why but it is embarrassing to receive letters with NSE written on it because I haven't got epilepsy.

35.

N966. Male, 17. Weekly Complex partial seizures, unchanged on follow-up. At college

[Benefits ...] I feel that the 3 months I spent at Chalfont were not a lot of good as the pills I was put on did not help. They made me put on a lot of weight and I am still having a lot of fits. The only benefit I received was a bit more confidence by being with other epilepsy suffers.

36.

N967. Female, 31. Frequent absences and generalized seizures. No sign. change.

[Benefits ...] Coming to Chalfont has helped with my epilepsy by putting me on the new drug Topiramate. It also made me realise there were people with epilepsy who were worse than myself; it gave me more confidence.

37.

N972. Female, 51. Weekly non-epileptic attacks. Some improvement with psychotherapy.

[Benefits ...] By coming to Chalfont and talking to doctors I have come to thinking I have got to do and that is I am trying to do. I am finding it hard, but with coming to Chalfont I have got positively to keep giving me and my husband a little push. [transcribed verbatim: perhaps means motivated to get better ?]

38.

N973. Female, 20. Non-epileptic attacks. Much improved.

[Benefits ...] I found out what was wrong with me which has helped. The follow-up after my stay at Chalfont started well, with me coming each week to see the psychologist. Then she got another job. It took 7 months before seeing another psychologist in London-in which time the situation got worse.

39.

N979. Male, 25. Complex partial seizures and non-epileptic attacks. No sign. change.

[Benefits ...] I found out a lot of information about my illness which has helped me to understand epilepsy a lot better. I found it good myself being at Chalfont centre. I met new people how have the same thing as me. As well staff and finding out a lot more to do with epilepsy and keeping in touch with people I met up with in there. Also found it done me the world good going into it. To find the right answer to my epilepsy which I did not know about before hand.

40.

N984. Male. 20. Frequent generalized seizures reduced to 1 in one year.

[Benefits ...] Since going to the CCE [Chalfont] my epilepsy has been a lot more controlled and my health is much better. When I went to Chalfont I met people who also had epilepsy and I didn't feel alone. I have read about people with epilepsy, but at Chalfont it actually made a difference because I now feel relieved.

41.

N994. Female, 31. Temporal lobe epilepsy. Still has frequent complex partial seizures, but some reduction after Chalfont. On disability benefits.

[Benefits ...] Before coming to Chalfont I'd never seen anyone have an epileptic fit, but being among people who all have the same complaint, and see how it affects different people in different ways made me more confident of myself.

42.

N998. Female, 27. Temporal lobe epilepsy. Weekly complex partial seizures, unchanged. On disability benefits.

[Benefits ...] The stay at the centre made me realise that I was not alone and helped me understand more about the epilepsy. The staff were very friendly and helpful and they did not wrap you in cotton wool.

43.

N1003. Male, 48. Frequent complex partial seizures, unchanged. Kitchen porter.

[Benefits ...] Being able to share experiences, living ideas, ways to cope etc. I now know what caused me to have epilepsy. I have met people with epilepsy which is far worse than mine. The small groups explaining how the brain works, how we can improve memory, was relevant and important.

44.

N925. Female, 30. Several seizures per week. On Disability benefits.

[Benefits ...] By being with others it made me realise that I was not alone with my illness and that there were many forms of epilepsy. I made new friends.

Section 6

Concluding remarks

6.0 Concluding remarks

These final remarks concern the conclusions that can be drawn from the studies presented in this thesis and possible directions for further research. The discussion will focus on four themes;

(1) What methods should be adopted in the assessment of the outcome of the treatment of epilepsy ?

(2) What has been learnt about the outcome of epilepsy surgery and what should be the direction of future studies ?

(3) What has been discovered about the effectiveness of programs of comprehensive assessment and how could these be improved ?

(5) What are the lessons for the management of epilepsy in general practice ?

6.1 What methods should be adopted to assess the outcome of epilepsy treatment ?

In the literature review it was discussed how seizure frequency had until recently been the key outcome variable in the treatment of epilepsy. It was noted that this approach had its limitations. Seizure frequency, however, has been found to be the major factor determining the impact of epilepsy on psychosocial functioning and quality of life. Are measures apart from seizure frequency, in fact, redundant ? The answer is no, for several reasons.

Firstly, the precise relationship between seizure frequency and the consequences of epilepsy remains uncertain. The major difference in the broader impact of epilepsy is the dichotomy between active and inactive epilepsy (Jacoby, 1996). In Jacoby's study, however, there was a difference in the "impact of epilepsy" between subjects experiencing more than, compared with less than, one seizure per month. In the current validation study of the SHE scale (sections 3.2) a linear trend was discovered across seizure frequencies. However, when the problem is considered longitudinally for an individual, or a group, it remains uncertain what change in seizure frequency is required to effect a clinically relevant reduction in the psychosocial consequences of epilepsy. Thus, it is unknown how often, if ever, a 50% reduction in seizure frequency is associated with broader health gains for the patient. Ideally, the current study would have collected actual seizure counts, as this would have allowed one to explore this problem. Two main considerations precluded collecting precise seizure frequency data. Firstly, baseline seizure frequency (in the form of seizure diaries) was not reliably available for all subjects. Secondly, the longitudinal studies involved approximately 500 patients, and overseeing and maintaining seizure data collection for 2 years was beyond the resources of the study. Nevertheless, further studies could usefully explore a number of issues: (1) can one generalize about the benefit (in terms of quality of life) of given levels of seizure reduction. Alternatively, is the relationship

particular to an individual ? (2) Is there a threshold of seizure frequency reduction below which no benefit accrues ? (3) Over what time course do the advantages of a decline of seizure frequency occur ? (4) Is a change in seizure frequency more usefully expressed as a percentage reduction or as a transition form one absolute state to another (i.e more than 10 seizures per year to less than 10 per year). These two methods are not necessarily equivalent. Answers to these questions would help in the design of antiepileptic drug trials. Outcomes, expressed in terms of changes in seizure frequency, would have more validity if it were known what benefits arise from a given change in seizure frequency.

The second reason for not relying on seizure frequency as the only outcome measure, is that other variables are important in determining psychosocial outcome. Seizure status, explained only 18% of the variance in "impact of epilepsy" in Jacoby's study. Other studies have documented that predictors of psychopathology (used here as a surrogate for impact of epilepsy) include social as well as seizure related variables (Hermann *et al.*, 1990; Baker *et al.*, 1996). Thus, if one wishes to understand more about the impact of epilepsy, it is advisable to measure psychosocial variables directly, rather than rely on seizure frequency.

Seizure severity has emerged an important additional measure of impairment in epilepsy. Baker has shown that seizure frequency and seizure severity are independent predictors of psychological health (Hermann *et al.*, 1990; Baker *et al.*, 1996). In addition, there is some evidence that reducing seizure severity may be an important additional outcome in AED trials (Smith *et al.*, 1995). The relationship between reductions in seizure severity and improved quality of life also needs further analysis. At present, it is conjecture that a 2-3 points change on the National Hospital Seizure Severity Scale is a clinically relevant change. The scale is now in use in three antiepileptic drug trials. It is hoped that the results will establish the responsiveness of

the scale. Another study is in progress investigating the relationship between subjective and objective seizure severity scales.

Thirdly, interventions which have long-term goals (e.g epilepsy surgery and rehabilitation) clearly require measures of the broader impact of epilepsy. A number of instruments are available and, though related, they are not equivalent. The ESI-55 and SF-36 scales are multi-dimensional scales tapping physical and mental health. They do not however deal with the typically disabling social consequences of epilepsy. The QOLIE 89 scale and the Impact of Epilepsy scale share many of the measurement aims of the SHE scale. The Impact scale is rather short, and factor analysis has suggested it contains a single dimension (Jacoby *et al.*, 1993). It may not be able to distinguish between different outcomes (i.e. work / social). The QOLIE scale is comprehensive, and deals with physical, emotional, cognitive functioning and social life. It is heavily weighted towards neuropsychological functioning (20 of the 89 items) and does not include items exploring stigma and how people feel about themselves. The thrust of the QOLIE scale is towards performance, rather than how patients see themselves. The SHE scale is conceived within the frame work of "handicap" and is weighted towards the long-term impact of epilepsy on work, daily activities, social functioning and how people perceive themselves. The scale deliberately does not set out to measure mobility or psychological symptoms. It is thus ideally placed to become a major new outcome measure for long-term interventions for epilepsy. The scale has not been designed for use in children, but this would be a useful development.

Assessment of the psychological and social effects of epilepsy is not necessary for every therapeutic trial. Interventions that are very short term, such as studies in the early phase of development of new AEDs, in which it is of interest whether the new compound has antiepileptic potential, clearly require primarily assessment of seizure

frequency. Scores on instruments such as the SHE, ESI-55 and QOLIE are unlikely to change over a matter of weeks.

Further areas of research include investigating what "value" patients attach to certain outcomes, both in terms of changes in seizure frequency, handicap and quality of life measures. These studies would be a prelude to an in-depth investigation of the cost-utility of epilepsy treatment.

An area of outcome research that has only been briefly mentioned in this thesis is the qualitative analysis of the impact of epilepsy treatment: the so-called "narrative approach" (Kleinman, 1988). This perspective is complementary to studies using standardized numerical measures. It can provide a deeper understanding of the benefits of treatment or adjusting to the failure of therapy. In section 5 the written comments of subjects were briefly analysed. The remarks tended to support the conclusions of the quantitative approach. The studies could be taken further with a systematic analysis of in depth interviews of patients during and after epilepsy interventions. It would have potential in designing rehabilitative interventions for people adjusting to becoming seizure free after surgery and for those who have no prospect of being rendered free of seizures.

Fundamentally, future investigators of the outcome of epilepsy treatment need to think carefully about which outcomes are of greatest interest to them. Thought also needs to be given to the resources available (particularly duration of follow-up) to measure these outcomes in a reliable and valid fashion. The "off-the-shelf" approach to selecting outcome measures should be avoided.

6.2 What has been learnt about the outcome of epilepsy surgery and what should be the directions of future studies ?

The study presented in section 5 has confirmed that epilepsy surgery has a significant positive impact on well-being. All but one of the previous studies have been limited by being either uncontrolled or retrospective or both. The present investigation, though non-randomized, has provided new information on the benefits of epilepsy surgery. At one year follow-up it was possible to demonstrate improvements in patients across a spectrum of measures of psychological health, quality of life and handicap. The study sample size was too small to reveal whether there is a difference in outcome (in terms of quality of life) in patients with remaining auras compared with those without. Retrospective studies have suggested that this is so (Vickrey *et al.*, 1992). A number of investigators have reported that during the first year following surgery a significant proportion of patients have mood disturbance (Blumer *et al.*, 1998; Ring *et al.*, 1998). This was not evident in the current study, probably because the these symptoms had resolved at the time of follow-up. Indeed, the psychological health of this group of surgery patients was better at follow-up then at baseline. The lack of change in employment status was notable, but this may well have been due to the relatively short period of follow-up. Other studies have documented adjustment difficulties to the state of being seizure free (Bladin, 1993). This was not explored in detail, though a few patients did report this in supplementary comments, some patients adding that they would have appreciated more counselling in the post-operative period. This an area that deserves further study. The study was too small to make comments on the relative benefits of temporal lobe surgery compared with extra-temporal and palliative procedures. This an important area for further investigation, as both these latter types of surgery have lower rates of complete seizure freedom. If complete remission is necessary for major quality of life gains, then patients need to be aware that these procedures may not radically change their lives.

Another area of potential investigation is the development of more accurate predictors, for individual patients, for seizure outcome, neuropsychological consequences and quality of life changes after surgery. This would involve detailed ratings before and longitudinally after surgery, to derive regressions equations predicting a good quality of life outcome. The numbers of subjects required is likely to be 200-300 (at least ten times the number predictor variables). This would involve multicentre collaboration.

There is great scope for work on epilepsy surgery in children. Circumstantial evidence suggests that the best social outcomes after epilepsy surgery occur if performed very early in adolescence. A randomized trial (necessarily multicentre) of early surgery, perhaps before the age of 16, versus delayed temporal lobe surgery is called for.

6.3 What has been discovered about the effectiveness of programs of comprehensive assessment and how could these be improved ?

The current study documented the overall outcome of a comprehensive assessment program. The results suggested that at one year of follow-up the long-term social and vocational handicaps were not appreciably altered, but that aspects of mood and self-rated cognition were. In addition, some patients reported feeling better able to cope with epilepsy. Overall, 90% of respondents were glad that they had been through the program of assessment. If one assumes that non-respondents did not benefit this proportion drops to two thirds.

That handicap was not ameliorated more may reflect the fact that these consequences are very difficult to change in the absence of a major reduction in seizure frequency. It also implied that the social interventions (the use of a medical social worker, a program of education about epilepsy, and the experience of being with other people with severe epilepsy) did not affect the attributes measured by the scales. Evidence

from free text comments made by some of the subjects however did suggest that the period at Chalfont had helped them "learn to live with epilepsy". Clearly further thought needs to be given to developing new social interventions.

From patients' comments it also appeared that after discharge from the centre further "therapy" came to a halt. Consideration needs to be given as to how, within available resources, liaison with the referring medical practitioners could be improved.

The conclusions of the Chalfont study are limited in a number of ways. The assessments and interventions at Chalfont were necessarily highly specialized. Some of these (diagnostic clarification and drug changes) could easily take place at another specialized centre, but the psychotherapeutic and social interventions are harder to standardize, and may be particular to the centre. It was not possible to identify specific aspects of care that proved helpful, as the number of permutations of problems at baseline, and interventions used, was too numerous. Further studies should select particular activities of the centre (e.g. drug reduction or psychotherapy) for greater attention. Patients with non-epileptic attacks posed particular problems with follow-up. Because of non-response it is not clear how successful the centre was for these patients. Another prospective study focusing on these patients is warranted.

6.4 What are the lessons for the management of epilepsy in general practice ?

The studies in section 4 illustrated that the burden of epilepsy in patients found in general practice is not negligible. The study provided evidence that active epilepsy is associated with a higher incidence of psychological symptoms than healthy persons (patients in remission who have ceased treatment). Further studies should confirm these findings by validating the diagnosis of psychiatric caseness with standardized

interviews. Circumstantial evidence also suggested that the general practitioners were often not aware of their patients' psychiatric morbidity. The questionnaire used was short and easy to complete, and the potential exists for general practitioners, or practice nurses, to use this as an aid to psychiatric case finding. More generally, the SHE scale could be used as a method for identifying persons in the practice in particular need of help. The scale also has potential for assisting in the audit of general practice care. The benefit of employing epilepsy nurse specialists in a general practice could easily be evaluated using the SHE. A more radical study would entail a randomized investigation of referral of cases of "difficult" epilepsy for specialist outpatient management at a tertiary centre.

Appendices

The National Hospital Seizure Severity Scale

The Subjective Handicap of Epilepsy Scale - Published version

The ESI-55 Scale

The Hospital Anxiety and Depression Scale

The General Health Questionnaire 30

Core demographic and clinical questionnaire

tient's me:

e:

tructions

mpletion:

ne how many erent types of ure occur (e.g a, complex ial, generalized vulsion...). these type 1-3 trarily.

ly questions 2-8 ach seizure type **arately**. As the S3 indicates rent seizure erity, **define the e frame**: e.g. 1-3 nths or time e the last clinic . Use clinical gement whether h factor occurs ne seizure type the physician des if there is a vulsion after stioning the ent). Allow the ent to judge the uency of each nt. Then tick the opposite the onse options. number in the is the score for question.

e:
. Only actual s are recorded if the seizures ld cause falls have not ause they all ured while in , then the score

refers to the e until the patient s fully functional.

e the specific ring instructions Q4. and 6.

column totals e the seizure erity score.

	Type 1	Type 2	Type 3
1. Record the name of the seizure types that occur under headings "type1,2,3...."			

since the last visit:

2. Does the patient have a generalized convulsion during this type of seizure ?			
Yes	4	4	4
No	0	0	0
3. How often has the patient fallen to the ground in this type of seizure ?			
Nearly always or always	4	4	4
Often	3	3	3
Occasionally	2	2	2
Never	0	0	0
4. Has this type of seizure caused any of the following ? (score only the worst)			
Burns,scalds, deep cuts, fractures	4	4	4
Bitten tongue or severe headaches	3	3	3
Milder injuries or mild headaches	2	2	2
No injuries	0	0	0
5. How often has the patient been incontinent of urine in this type of seizure ?			
Nearly always or always	4	4	4
Often	3	3	3
Occasionally	2	2	2
Never	0	0	0
6. If the seizure causes loss of consciousness, is there a warning long enough for the patient to protect him/herself ? (no loss of consciousness or seizures only while asleep scores 0)			
Never	2	2	2
Sometimes	1	1	1
Nearly always or always	0	0	0
7. How long is it until the patient is really back to normal after the seizure?			
Less than 1 minute	0	0	0
Between 1 and 10 minutes	1	1	1
Between 10 minutes and 1 hour	2	2	2
Between 1 and 3 hours	3	3	3
More than 3 hours	4	4	4
8. Do the following events occur in this type of seizure ?			
Seriously disruptive automatisms (e.g. shouting, wandering, undressing)	4	4	4
Mild automatisms or focal jerking	2	2	2
None	0	0	0
Add 1 point to each column	1	1	1
TOTAL SCORE FOR EACH SEIZURE TYPE			

The Subjective Handicap of Epilepsy Scale

Final version as published :

O'Donoghue MF, Duncan JS, Sander JWAS. The Subjective Handicap of Epilepsy: a new approach to measuring treatment outcome. Brain 1998; 121: 317-343.

Please read this first:

In this booklet most of the questions use the word "**epilepsy**".

* **If you are still having seizures** ("fits" or "turns"), the questions are about the effect of epilepsy on your life **now.**

* **If you have stopped having seizures** ("fits" or "turns") the questions are about whether the seizures you had in the past still have any effect on your life **now** (e.g. work, social life ...).

* To answer the questions simply place a tick in the box underneath the answer that comes closest to how you feel.

If you have any difficulties filling in the questionnaire, get someone to help you, **but the answers should be all your own.**

Now, the questions...

About your work

Here are some questions about your main day time activity. This could be either paid work, studying, a training course, looking after the home, or perhaps something else.

There are separate questions depending on your main activity:

If you are in full-time or part-time paid employment : start the questionnaire on **page 2**

If you are in full-time education or training : start the questionnaire on **page 3**

Everyone else : start the questionnaire on **page 4**

IF YOU DO PAID WORK...
Please answer the questions on this page

otherwise go on to the next page fi

1a. **In the last 6 months has epilepsy caused you problems doing your job ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
2a. **In the last 6 months have you had time off work because of epilepsy ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
3a. **In the last 6 months have you worried about losing your job because of epilepsy ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
4a. **How often do you feel tired and drowsy during the day ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
5a. **How often do you have problems with your memory ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
6a. **Does epilepsy prevent you doing the *type* of job you would really like to do ?**	Totally [ ]	A lot [ ]	Partly [ ]	A little [ ]	Not at all [ ]
7a. **How happy are you overall in your job ?**	Very Happy  [ ]	Happy [ ]	It is OK [ ]	Unhappy [ ]	Very Unhappy  [ ]

please go to question 8 on page 5

IF YOU ARE STUDYING OR ARE ON A COURSE...
Please answer the questions on this page

otherwise go on to the next page fi

1b. **In the last 6 months has epilepsy caused you problems doing your work ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
2b. **In the last 6 months have you had time off because of epilepsy ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
3b. **In the last 6 months have you been worried that you might have to stop your course because of epilepsy ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
4b. **How often do you feel tired and drowsy during the day ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
5b. **How often do you have problems with your memory ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
6b. **Does epilepsy prevent you doing the *type* of course or training you would really like to do ?**	Totally [ ]	A lot [ ]	Partly [ ]	A little [ ]	Not at all [ ]
7b. **How happy are you overall doing your course ?**	Very Happy  [ ]	Happy [ ]	It is OK [ ]	Unhappy [ ]	Very Unhappy  [ ]

please go to question 8 on page 5

EVERYONE ELSE...
Please answer the questions on this page

do not answer these questions if you filled in page 2 or 3

1c. **In the last 6 months has epilepsy caused you problems doing your usual "day-to-day" activities ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
2c. **In the last 6 months have you had to take some time off from your usual "day-to-day" activities because of epilepsy ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
3c. **Do you need help looking after your home because of your epilepsy ?**	I need help with everything [ ]	I need a lot of help [ ]	I need some help [ ]	I need a little help [ ]	I need no help [ ]
4c. **How often do you feel tired and drowsy during the day ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
5c. **How often do you have problems with your memory ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
6c. **Does epilepsy prevent you doing the *type* of job you would really like to do ?**	Totally [ ]	A lot [ ]	Partly [ ]	A little [ ]	Not at all [ ]
7c. **How happy are you overall with the way you spend your average day ?**	Very Happy  [ ]	Happy [ ]	It is OK [ ]	Unhappy [ ]	Very Unhappy  [ ]

please go to question 8 on the next page

Your personal life

Here are some questions about your relationships with other people. Some questions are quite personal, but we would find it helpful to know how epilepsy is affecting you in these matters.

8. **Does your epilepsy create problems in getting on with close relations (e.g. children, parents...) ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]	Does not apply to me [ ]
9. **Does your epilepsy cause problems in your relationship with friends ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]	
10. **Does your epilepsy cause problems making new friends ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]	
11. **Does your epilepsy make you feel lonely ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]	
12. **How happy are you overall with your social life outside the family ?**	Very Happy  [ ]	Happy [ ]	It is OK [ ]	Unhappy [ ]	Very Unhappy  [ ]	

place ticks with care !

13.	Very Happy	Happy	It is OK	Unhappy	Very Unhappy
How happy are you overall with your home life ?					
	[ ]	[ ]	[ ]	[ ]	[ ]

Here are some questions about how epilepsy affects what you do for leisure and fun.

14.	Very often	Often	Sometimes	Rarely	Never
In the last 6 months has epilepsy prevented you from doing leisure activities ?	[ ]	[ ]	[ ]	[ ]	[ ]

15.	Totally	A lot	Partly	A little	Not at all
How much does epilepsy prevent you from doing the *type* of leisure activity you would like to do ?	[ ]	[ ]	[ ]	[ ]	[ ]

16.	Very Happy	Happy	It is OK	Unhappy	Very Unhappy
How happy are you overall with the way you can spend your leisure time ?					
	[ ]	[ ]	[ ]	[ ]	[ ]

please carry on with question 17 on the next page

Thinking about the last 6 months...

17. **Has epilepsy made you feel physically unwell ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
18. **Has epilepsy caused you injury or pain ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
19. **Does epilepsy cause you annoying problems in "day-to-day" life ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
20. **Does epilepsy cause you problems travelling and getting about ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
21. **Does your epilepsy make you feel that you are not in full control of your life ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
22. **Does your epilepsy make you feel you cannot do things as well as most people ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
23. **Do you worry about having another seizure ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
24. **Do you worry about being in public because of your epilepsy ?**	Very often [ ]	Often [ ]	Sometimes [ ]	Rarely [ ]	Never [ ]
25. **Overall how much does epilepsy affect your life ?**	Totally [ ]	A lot [ ]	Quite a bit [ ]	A little [ ]	Not at all [ ]

Your life compared to 1 year ago

We would like to know if there has been any change overall in your life compared to 1 year ago.

	 Much better	Better	The same	Worse	 Much worse
26. **Overall how has your life been compared to 1 year ago ?**	[ ]	[ ]	[ ]	[ ]	[ ]
27. **Compared to 1 year ago how have your close relationships been ?**	[ ]	[ ]	[ ]	[ ]	[ ]
28. **Compared to 1 year ago how has work been for you ?**	[ ]	[ ]	[ ]	[ ]	[ ]
29. **Compared to 1 year ago how has the control of your epilepsy been?**	 [ ]	[ ]	[ ]	[ ]	 [ ]
30. **Compared to 1 year ago how has your social life been ?**	[ ]	[ ]	[ ]	[ ]	[ ]
31. **Compared to 1 year ago how has your leisure time been ?**	[ ]	[ ]	[ ]	[ ]	[ ]

and ...

	Much more	A bit more	The same	A bit less	Much less
32. **Compared to 1 year ago how much do you enjoy life ?**	[ ]	[ ]	[ ]	[ ]	[ ]

The ESI-55 Questionnaire

THE FOLLOWING QUESTIONS ASK FOR YOUR VIEWS ABOUT YOUR HEALTH, HOW YOU FEEL AND HOW WELL YOU ARE ABLE TO DO YOUR USUAL ACTIVITIES. IF YOU ARE UNSURE ABOUT HOW TO ANSWER ANY QUESTION, PLEASE GIVE THE BEST ANSWER YOU CAN AND MAKE ANY COMMENTS IN THE SPACE AVAILABLE AFTER QUESTION 16

please tick one

1. **In general would you say your health is:**

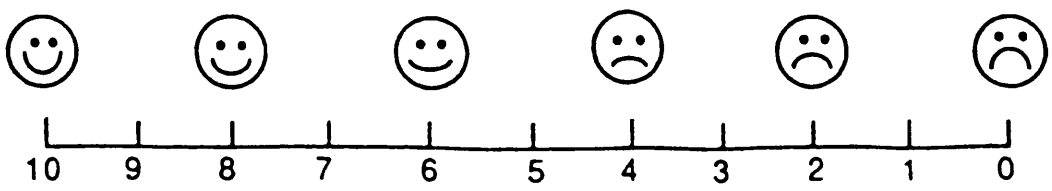
- Excellent ○
- Very Good ○
- Good ○
- Fair ○
- Poor ○

2. **Compared to <u>one year ago</u>, how would you rate your health in general <u>now</u> ?**

- Much better now than one year ago ○
- Somewhat better now than one year ago ○
- About the same ○
- Somewhat worse now than one year ago ○
- Much worse now than one year ago ○

3. **Overall how would you rate your quality-of-life ?**

Circle one number on the scale below:



Best Possible Quality-of-Life

Worst Possible Quality-of-Life

HEALTH AND DAILY ACTIVITIES

4. The following questions are about activities you might do during a typical day. Does your health limit you in these activities? If so, how much?

Please tick one circle on each line

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a. Vigorous activities, such as running, lifting heavy objects participating in strenuous sports	○	○	○
b. Moderate activities such as moving a table, pushing a vacuum cleaner, bowling or playing golf	○	○	○
c. Lifting or carrying groceries	○	○	○
d. Climbing several flights of stairs	○	○	○
e. Climbing one flight of stairs	○	○	○
f. Bending, kneeling or stooping	○	○	○
g. Walking a mile	○	○	○
h. Walking half a mile	○	○	○
i. Walking 100 yards	○	○	○
j. Bathing and dressing yourself	○	○	○

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your <u>physical health</u> ?

Answer Yes or No to each question

	Yes	No
a. Cut down on the amount of time you spent on work or other activities	○	○
b. Accomplished less than you would like	○	○
c. Were limited in the kind of work or other activities	○	○
d. Had difficulty performing the work or other activities (e.g. it took extra effort)	○	○
e. Did work or other activities less carefully than usual	○	○

6. **During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)**

Answer Yes or No to each question

	Yes	No
a. Cut down on the amount of time you spent on work or other activities	◯	◯
b. Accomplished less than you would like	◯	◯
c. Were limited in the kind of work or other activities	◯	◯
d. Had difficulty performing the work or other activities	◯	◯
e. Didn't do work or other activities as carefully as usual	◯	◯

7. **During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups ?**

please tick one

- Not at all ◯
- Slightly ◯
- Moderately ◯
- Quite a bit ◯
- Extremely ◯

8. **How much bodily pain have you had during the past 4 weeks ?**

- None ◯
- Very mild ◯
- Mild ◯
- Moderate ◯
- Severe ◯
- Very severe ◯

9. **During the past 4 weeks, how much did pain interfere with your normal work (including work both outside the home and housework)?**

Not at all	○
A little bit	○
Moderately	○
Quite a bit	○
Extremely	○

Your Feelings

10. **These questions are about how you have been feeling and how things have been with you during the past month.** *(please indicate the one answer that comes closest to the way you have been feeling)*

How much time during the past month:	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of life?	○	○	○	○	○	○
b. Have you been a very nervous person ?	○	○	○	○	○	○
c. Have you felt so down in the dumps that nothing could cheer you up ?	○	○	○	○	○	○
d. Have you felt calm and peaceful ?	○	○	○	○	○	○
e. Did you have a lot of energy?	○	○	○	○	○	○
f. Have you felt downhearted and low ?	○	○	○	○	○	○
g. Did you feel worn out ?	○	○	○	○	○	○
h. Have you been a happy person ?	○	○	○	○	○	○
i. Did you feel tired ?	○	○	○	○	○	○
j. Has health limited your social activities (like visiting friends or close relatives) ?	○	○	○	○	○	○

11. How much of the time during the past 4 weeks...

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
a. have you had difficulty concentrating and thinking ?	○	○	○	○	○	○
b. did you have trouble keeping your attention on an activity for long ?	○	○	○	○	○	○
c. have you worried about having another seizure ?	○	○	○	○	○	○
d. did you have difficulty reasoning and solving problems (for example making plans, making decisions, learning new things ?	○	○	○	○	○	○
e. were you discouraged by your health problems ?	○	○	○	○	○	○

HEALTH IN GENERAL

12. Please choose the answer that best describes how true or false each of the following statements is for you.

please tick one circle on each line

	Definitely true	Mostly true	Not sure	Mostly false	Definitely false
a. I seem to get ill more easily than other people	○	○	○	○	○
b. I am as healthy as anyone I know	○	○	○	○	○
c. I expect my health to get worse	○	○	○	○	○
d. My health is excellent	○	○	○	○	○
e. When there is an illness going around, I usually catch it	○	○	○	○	○
f. I seem to get seizures a little easier than other people with epilepsy	○	○	○	○	○

13. In the past 4 weeks, have you had any trouble with your memory ?

please tick one :

Yes, a great deal ○

Yes, somewhat ○

Yes, a little ○

No, not at all ○

14. In the past 4 weeks, have you had any trouble with your speech or language ?

Yes, a great deal ○

Yes, somewhat ○

Yes, a little ○

No, not at all ○

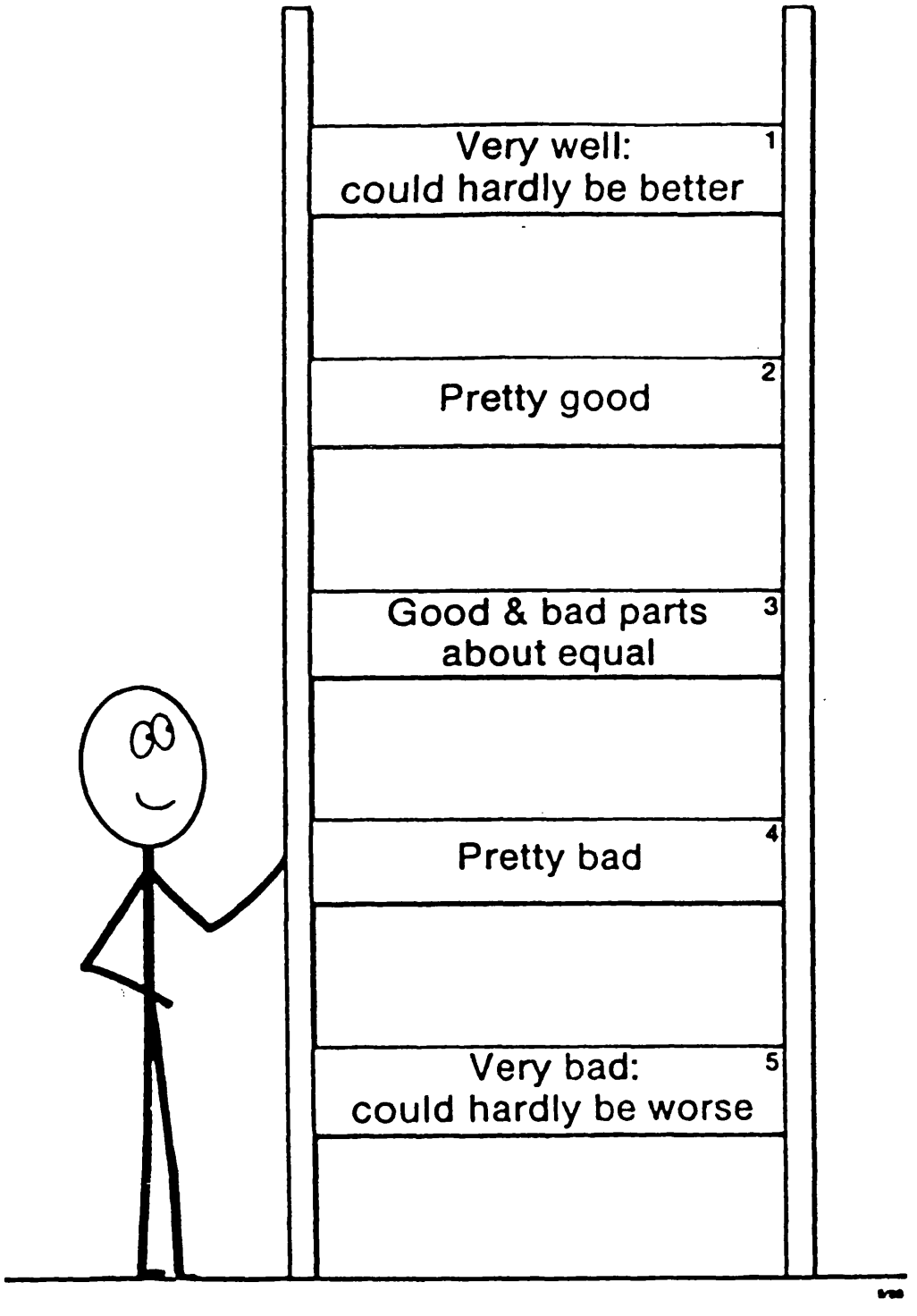
15. During the past 4 weeks have you had any of the following problems with your regular daily activities or work as a result of any memory, speech or language problems ?

Please tick either *Yes* or *No*

	Yes	**No**
Cut down on the amount of time you could spend on work or other activities	○	○
Accomplished less than you would like	○	○
Were limited in the kind of work or activities	○	○
Had difficulty performing the work or other activities	○	○
Did work or other activities less carefully than usual	○	○

16. How has the quality of your life been during the past 4 weeks
That is, how have things been going for you ?

(circle one number)



The Hospital Anxiety and Depression Scale

Please read this:
Doctors are aware that emotions play an important part in most illnesses. We would like to know more about these feelings. This questionnaire is designed to help us know how you feel. Read each question and place a firm tick in the box opposite the reply which comes closest to how you have been feeling **in the past week.** Don't take too long over your replies: your immediate reactions to each question will probably be more accurate than a long thought-out response. Please answer each question. Thank you very much.

I feel tense or 'wound-up':

- Most of the time
- A lot of the time
- Time to time, occasionally
- Not at all

I still enjoy the things I used to enjoy:

- Definitely as much
- Not quite so much
- Only a little
- Hardly at all

I get a sort of frightened feeling as if something awful is about to happen:

- Very definitely and quite badly
- Yes, but not too badly
- A little, but it doesn't worry me
- Not at all

I can laugh and see the funny side of things:

- As much as I always could
- Not quite so much now
- Definitely not so much now
- Not at all

Worrying thoughts go through my mind:

- A great deal of the time
- A lot of the time
- From time to time but not too often
- Only occasionally

I feel cheerful:

- Not at all
- Not often
- Sometimes
- Most of the time

I can sit at ease and feel relaxed:

- Definitely
- Usually
- Not often
- Not at all

I feel as if I am slowed down:

- Nearly all the time
- Very often
- Sometimes
- Not at all

I have lost interest in my appearance:

- Definitely
- I don't take as much care as I should
- I may not take quite as much care
- I take just as much care as ever

I get a sort of frightened feeling like butterflies in the stomach:

- Not at all
- Occasionally
- Quite often
- Very often

I feel restless as if I have to be on the move:

- Very much indeed
- Quite a lot
- Not very much
- Not at all

I look forward with enjoyment to things:

- As much as ever I did
- Rather less than I used to
- Definitely less than I used to
- Hardly at all

I get sudden feelings of panic:

- Very often indeed
- Quite often
- Not very often
- Not at all

I can enjoy a good book or radio or TV programme:

- Often
- Sometimes
- Not often
- Very seldom

The General Health Questionnaire 30

Please read this instruction :

We should like to know if you have had any medical complaints, and how your health has been in general **over the past few weeks.** By health we mean both epilepsy and any other medical complaints you may have. Please answer all the questions on the following pages simply by putting a **circle** around the answer which you think most nearly applies to you. Remember that we want to know about **present complaints,** not those you had in the past. Thank you.

HAVE YOU RECENTLY...

1.	**been able to concentrate on whatever you're doing ?**	Better than usual	Same as usual	Less than usual	Much less than usual
2.	**lost much sleep over worry ?**	Not at all	No more than usual	Rather more than usual	Much more than usual
3.	**been having restless, disturbed nights ?**	Not at all	No more than usual	Rather more than usual	Much more than usual
4.	**been managing to keep yourself busy and occupied ?**	More so than usual	Same as usual	Rather less than usual	Much less than usual
5.	**been getting out of the house as much as usual ?**	More so than usual	Same as usual	Less than usual	Much less than usual
6.	**been managing as well as most people would in your shoes ?**	Better than most	About the same	Rather less well	Much less well
7.	**been feeling on the whole you were doing things well ?**	Better than usual	About the same	Less well than usual	Much less well
8.	**been satisfied with the way you've carried out your task ?**	Better than usual	About the same	Less well than usual	Much less well
9.	**been able to feel warmth and affection for those near to you?**	Better than usual	About same as usual	Less well than usual	Much less well
10.	**been finding it easy to get on with other people ?**	Better than usual	About same as usual	Less well than usual	Much less well
11.	**spent much time chatting to people ?**	Not at all	No more than usual	Rather more than usual	Much more than usual
12.	**felt that you are playing a useful part in things ?**	More so than usual	Same as usual	Rather less than usual	Much less than usual
13.	**felt capable of making decisions about things ?**	More so than usual	Same as usual	Less so than usual	Much less than usual
14.	**felt constantly under strain ?**	Not at all	No more than usual	Rather more than usual	Much more than usual
15.	**felt that you couldn't overcome your difficulties ?**	Not at all	No more than usual	Rather more than usual	Much more than usual

HAVE YOU RECENTLY...

16.	**been finding life a struggle all the time ?**	Not at all	No more than usual	Rather more than usual	Much more than usual
17.	**been able to enjoy your normal day-to-day activities ?**	More so than usual	Same as usual	Less so than usual	Much less than usual
18.	**been taking things hard ?**	Not at all	No more than usual	Rather more than usual	Much more than usual
19.	**been getting scared or panicky for no good reason ?**	Not at all	No more than usual	Rather more than usual	Much more than usual
20.	**been able to face up to your problems ?**	More so than usual	Same as usual	Less able than usual	Much less able
21.	**found everything getting on top of you ?**	Not at all	No more than usual	Rather more than usual	Much more than usual
22.	**been feeling unhappy and depressed ?**	Not at all	No more than usual	Rather more than usual	Much more than usual
23.	**been losing confidence in yourself ?**	Not at all	No more than usual	Rather more than usual	Much more than usual
24.	**been thinking of yourself as a worthless person ?**	Not at all	No more than usual	Rather more than usual	Much more than usual
25.	**felt that life is entirely hopeless ?**	Not at all	No more than usual	Rather more than usual	Much more than usual
26.	**been hopeful about your own future ?**	More so than usual	About same as usual	Less so than usual	Much less than usual
27.	**been feeling reasonably happy, all things considered ?**	More so than usual	About same as usual	Less so than usual	Much less than usual
28.	**been feeling nervous and strung-up all the time ?**	Not at all	No more than usual	Rather more than usual	Much more than usual
29.	**felt that life isn't worth living ?**	Not at all	No more than usual	Rather more than usual	Much more than usual
30.	**found at times you couldn't do anything because your nerves were too bad ?**	Not at all	No more than usual	Rather more than usual	Much more than usual

Core demographic and clinical questionnaire

(minor variations in wording depending on sample)

OTHER INFORMATION

We would like some details about yourself : Please place a tick in the box next to the answer that applies to you.

1. Are you male [ ]
   female [ ]

2. What is your date of birth ?.....

3. At what age did you leave school ?.....

4. What qualifications have you obtained ?

(tick all that apply)	How many?
No official qualifications. . . . . [ ]	
CSE/ "O" Levels / GCSEs . . . . . [ ]	
"A" Levels. . . . . [ ]	
City & Guilds. . . . . [ ]	
HNC / HND. . . . . [ ]	
University / College degree . . . . . [ ]	
Other qualifications (please specify) . . . . . [ ]	

5. Has epilepsy affected your choice of education, training, job, or career ?

Yes	[ ]
No	[ ]
Not applicable to me	[ ]

6. If the answer is YES, please explain :

The following questions are about employment **now....**

7. Which of the following best describes your <u>current</u> position (in the last month) concerning employment ?

	tick one
Full time (more than 25 hours per week) paid employment	[ ]
Part time (less than 25 hours per week) paid employment.	[ ]
Housewife	[ ]
School student	[ ]
College or further education student	[ ]
Training course.	[ ]
Unemployed (but fit for work)	[ ]
Voluntary work	[ ]
Day centre.	[ ]
Permanently off work due to sickness.	[ ]
Other (please write this down)	

8. Please give the name of the job or course or activity that you do **now**:

9. Please give a short explanation of what your job or course or main activity involves:

10. Have you ever lost your job **because of epilepsy** ?

Yes [ ]
No [ ]

If yes, how many times ?

11. Have you ever been turned down for a job **because of epilepsy** ?

Yes [ ]
No [ ]

If yes, how many times ?

12. Were you ever unemployed ?

Yes [ ]
No [ ]

If Yes, for what length of time ?

13. Were you ever declared by your doctor as unfit for work (because of epilepsy or other disability) ?

Yes [ ]
No [ ]

If Yes, for what length of time ?

The following questions are about where you live **now...**

14. Do you live in:

A flat. . . . . [ ]

A house. . . . . [ ]

A hostel . . . . . [ ]

A bedsitter. . . . . [ ]

Other (please write this down)

15. How is this paid for ?

You own it. . . . . [ ]

You rent it. . . . . [ ]

It is your parents' place. . . . . [ ]

Other (please write this down)

16. Who lives with you **now** ?

A husband, wife or partner. . . . . [ ]

Your parents. . . . . [ ]

Other relatives . . . . . [ ]

Your children . . . . . [ ]

By yourself . . . . . [ ]

Other (please write this down)

17. What is the **main** source of income for paying all your bills (rent, food etc.) ?

Your wage package . . . . . [ ]

Your parents . . . . . [ ]

Your partner's wage package. . . . . [ ]

Unemployment benefits . . . . . [ ]

Disability benefits. . . . . [ ]

Other (please write this down)

18. Have you **at any stage** received any of these state benefits ?
(please tick)

Unemployment Benefit.	[ ]	Disability Living Allowance. . . .	[ ]
Income Support	[ ]	Disability Working Allowance. .	[ ]
Family Credit	[ ]		
		Other Benefits or Allowances	
Statutory Sick Pay or Sickness Benefit. .	[ ]	(please write this down)	
Invalidity Benefit	[ ]		
Severe Disablement Allowance	[ ]		

19. For how long (approximately) have you received this ?

.....months.....years

20. Are you **now** (this month) still receiving any state benefits ?
(this information will not be passed on to anyone)

Yes	[ ]
No	[ ]

21. If **yes**, please tick which ones :

Unemployment Benefit.	[ ]	Disability Living Allowance. . . .	[ ]
Income Support	[ ]	Disability Working Allowance. .	[ ]
Family Credit	[ ]		
		Other Benefits or Allowances	
Statutory Sick Pay or Sickness Benefit. .	[ ]	(please write this down)	
Invalidity Benefit	[ ]		
Severe Disablement Allowance	[ ]		

22. Do you <u>currently</u> hold a driving licence ?

Yes	[ ]
No	[ ]
Not applicable (too young)	[ ]

23. Do you travel **by yourself** on public transport?

Yes	[ ]
No	[ ]

Now some questions about your epileptic seizures (fits or attacks)

24. How old were you when you had your first epileptic seizure ?.....

25. Here are descriptions of 4 common types of epileptic seizure. Please tick the box (yes or no) if you have **ever** had one of these types of epileptic seizure.

	tick one **Yes**	**No**
A grand mal seizure (also called generalized tonic clonic convulsion) In this you are completely unconscious, and there is stiffness of the body and shaking of the arms and legs. It is often followed by sleepiness or confusion for at least several minutes.	[ ]	[ ]
Simple partial seizure (also called aura, warning or minor by some people) In this there is either jerking of an arm or leg, or odd sensations in the body (head, stomach, arms or legs, or a smell or a taste etc.). There is **no** confused behaviour and you remain **fully aware** throughout the attack and nothing else happens.	[ ]	[ ]
Complex partial seizure (also called petit mal or minor by some people) In this there is sometimes a "warning" (e.g. stomach sensations) followed by **loss of awareness**, confusion, with odd body movements like smacking of the lips, fidgeting, or wandering. Recovery takes at least 1-2 minutes usually.	[ ]	[ ]
Absence seizure (also called petit mal by some people) In this there is a sudden blank look and loss of awareness. The attack lasts only a few seconds and you recover very quickly. There is very little movement of the body, and you do not fall to the floor.	[ ]	[ ]

26. Have you had ***any*** epileptic seizure in the last 12 months ? Yes [ ]

No [ ]

27. **If Yes...**

Think about the last 12 months....

How often has each type of seizure occurred ? (on average)

(if not sure you can guess)

A grand mal seizure (also called generalized tonic clonic convulsion) In this you are completely unconscious, and there is stiffness of the body and shaking of the arms and legs. It is often followed by sleepiness or confusion for at least several minutes.	**never**..... [ ] **1 in the last year**..... [ ] **2 to 11 per year** ..... [ ] **1 to 4 per month**..... [ ] **more than 1 per week** . [ ] **several per day**..... [ ]
Simple partial seizure (also called aura, warning or minor by some people) In this there is either jerking of an arm or leg, or odd sensations in the body (head, stomach, arms or legs, or a smell or a taste etc.). There is **no** confused behaviour and you remain **fully aware** throughout the attack and nothing else happens.	**never**..... [ ] **1 in the last year**..... [ ] **2 to 11 per year** ..... [ ] **1 to 4 per month**..... [ ] **more than 1 per week** . [ ] **several per day**..... [ ]
Complex partial seizure (also called petit mal or minor by some people) In this there is sometimes a "warning" (e.g. stomach sensations) followed by **loss of awareness**, confusion, with odd body movements like smacking of the lips, fidgeting, or wandering. Recovery takes at least 1-2 minutes usually.	**never**..... [ ] **1 in the last year**..... [ ] **2 to 11 per year** ..... [ ] **1 to 4 per month**..... [ ] **more than 1 per week** . [ ] **several per day**..... [ ]
Absence seizure (also called petit mal by some people) In this there is a sudden blank look and loss of awareness. The attack lasts only a few seconds and you recover very quickly. There is very little movement of the body, and you do not fall to the floor.	**never**..... [ ] **1 in the last year**..... [ ] **2 to 11 per year** ..... [ ] **1 to 4 per month**..... [ ] **more than 1 per week** . [ ] **several per day**..... [ ]

28. **If** your last attack was **more than 12 months ago**, can you tell us roughly when it was:

Between 1 and 2 years ago.	[ ]
Between 2 and 5 years ago.	[ ]
Between 5 and 10 years ago.	[ ]
Between 10 and 20 years ago.	[ ]
More than 20 years ago.	[ ]

29. Do you know the date ?.....

30. Is there any other type of attack not mentioned in the box on the previous page that you have at the moment ?

If **yes,** please describe this below:

1.	**none. . . . . .**	[ ]
	1 in the last year.	[ ]
	2 to 11 per year.	[ ]
	1 to 4 per month.	[ ]
	more than 1 per week. . .	[ ]
	several per day.	[ ]
2.	**none. . . . . .**	[ ]
	1 in the last year.	[ ]
	2 to 11 per year.	[ ]
	1 to 4 per month.	[ ]
	more than 1 per week. . .	[ ]
	several per day.	[ ]

31. How <u>often</u> are you having seizures **now** compared to **12 months ago** ?
(including all types of attack)

(tick one only)

Much more often **now** than 12 months ago	↑↑↑	[ ]
Quite a bit more often **now** than 12 months ago	↑↑	[ ]
A little more often **now** than 12 months ago	↑	[ ]
The same as 12 months ago	–	[ ]
A little less often **now** than 12 months ago	↓	[ ]
Quite a bit less often **now** than 12 months ago	↓↓	[ ]
Much less often **now** than 12 months ago	↓↓↓	[ ]

32. Do you have any medical condition or disability apart from epilepsy ?

Yes	[ ]
No	[ ]

If the answer is YES, please write this down :

33. Has any event or change in your life, **not directly connected with your epilepsy**, affected your "quality of life" in an important way in the last year ?

Yes	[ ]
No	[ ]

If the answer is YES, please explain :

And in the last year what has affected your "quality of life" more overall; epilepsy or other changes in your life ?

	tick only one
Epilepsy has affected my "quality of life" more overall	[ ]
Other changes in my life have affected my "quality of life" more overall	[ ]

Do you think of yourself as still having epilepsy ?	YES [ ]	NO [ ]
Did anyone help you fill in this questionnaire ?	YES [ ]	NO [ ]

If YES, who ?

- Is there anything more you would like to tell us about how epilepsy has affected your quality of life in general ? (work, personal life, how you feel about yourself... or anything you think is important).

Please feel free to write this below and on the next page:

⇒ **please check that you have answered all the questions that apply to you**

THANK YOU VERY MUCH FOR FILLING IN THIS LONG QUESTIONNAIRE !!

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