

## Appendix G

### The costs of epilepsy misdiagnosis

*Also, see the section on Diagnosis in the full guideline*

#### 1.1 Introduction.

Epilepsy is a common chronic neurological condition. The available data indicate an annual incidence of 40-70 per 100,000 in developed countries, and a lifetime prevalence of 5-10/1000.<sup>1-3</sup> Epilepsy is not a diagnosis *per se* but a symptom of an underlying central nervous system (CNS) disorder. It can have a wide range of aetiologies. Though the diagnosis of epilepsy can be straightforward, it can also be a difficult clinical challenge. The problem of misdiagnosis is not small and according to the literature the rate of misdiagnosis in the UK falls between 20-31%.<sup>4-6</sup> The human and financial costs of failing to achieve the correct diagnosis are considerable.

This paper provides some information on the financial costs of epilepsy misdiagnosis with the specific purpose of highlighting the magnitude of the problem and the need for practitioners to follow clinical guidelines in order to reduce the occurrence of this problem.

The total number of misdiagnosed cases in epilepsy should include the number of *true epilepsy cases diagnosed as other non-epileptic condition + the number of non-epileptic conditions diagnosed as epilepsy*. This analysis will focus only on estimating the costs of wrongly diagnosed other conditions as epilepsy for two main reasons: a) the evidence found focused on this particular problem and b) according to the literature this is the most common mistake done.

Calculating the cost of misdiagnosis in epilepsy involves the estimation of the economic value of resources consumed or not produced because of the misdiagnosed illness. In this paper we apply standard costing methods to estimate the costs attributable to epilepsy misdiagnosis. In this study, for congruency with papers<sup>7:8</sup> that are used in the analysis we use the following

cost definitions and terms<sup>a</sup>. A direct cost is defined as the economic burden of resource utilisation required in the care of the misdiagnosed epilepsy, and it includes the medical costs such as primary care, hospital care, drugs, investigations, and the non-medical costs such as residential care and community care.<sup>7</sup> An indirect cost is defined as the lost productivity due to morbidity and mortality and includes unemployment, under-employment and decreased household work. In this study the indirect costs would need to refer to the lost productivity due to morbidity or mortality for not treating the underlying condition and/or for being stigmatized as an individual with epilepsy (such as problems with employment or mobility problems due to driving restrictions).

We focus specifically on the estimation of direct epilepsy misdiagnosis costs for two main reasons: first there is lack of published data on the consequences of lost productivity due to misdiagnosis and second, there exists a current controversy in the health economics literature on the best method to estimate indirect costs (lost productivity)<sup>b</sup>.

A series of assumptions were made in this study based mainly on published literature and on expert opinion. The derived figures can therefore be considered only approximations; nevertheless they are, we believe, close figures to the real values and one of the few attempts in the literature to measure the burden of epilepsy misdiagnosis from an economic point of view. Most of all we hope that this study highlights the magnitude of the problem of

---

<sup>a</sup> These terms are becoming less used in the literature due to inconsistencies across studies. Drummond et al explained direct costs across studies could refer to resources in the health care sector but sometimes would include patient's out of pocket expenses or resources from other statutory agencies.<sup>9</sup> To avoid confusion, present studies do not use the direct and indirect cost definitions but refer specifically to health care sector costs, patient costs and costs in other sectors. For indirect costs it is now more common to use the term productivity loss to avoid confusion with the definition of indirect costs used by the accountancy profession to denote overhead costs.

<sup>b</sup> One methodology supported by economists is the human capital approach and consists of estimating the unemployment productivity loss due to illness by calculating gross earnings of those who are employed. However it is frequently argued that these valuations overstate the true costs to society. Consequently other methodologies have emerged as the friction cost method.<sup>10</sup> This methodology considers that, from a societal perspective, if an individual becomes unemployed and remains unemployed because of illness, only a limited period of his or her unemployment or absence from work should be counted as costs. After this period, called the friction period, he or she is replaced. Thus, the real costs to a society are only the short-term production losses and the cost of replacement.<sup>11</sup>

Deleted: statutory

misdiagnosis in epilepsy not only in terms of human suffering but also in terms of the unnecessary economic burden that it represents to society and to the National Health System in terms of waste of resources.

## **1.2 Methodology**

This is a prevalence-based study and the main methodological steps are:

- to estimate the number of misdiagnosed patients in England and Wales assuming prevalence and misdiagnosis rates figures based on published literature and applying these to the 2002 population of England and Wales.
- to estimate the annual average uses of resources and costs incurred by a misdiagnosed individual based on assumptions derived from published literature.
- to estimate national figures of the cost consequences of epilepsy misdiagnosis by extrapolating the average estimated annual cost per individual to the estimated national number of misdiagnosed cases.

### **Step 1.**

#### **Estimate the number of misdiagnosed patients in England and Wales**

We first estimated the possible number of persons with epilepsy. For these estimations we used a population of 52,041,916 in England and Wales (according to the 2002 census) and a range of prevalence between 5-8/1000 according to the recent literature.<sup>3</sup> The results in table 1 show that the possible number of epilepsy cases falls within the range of 260,209 to 416,335.

England & Wales population (Census 2002)	Prevalence 5-10/1000  (according to different studies)	Calculated number of persons with epilepsy	Calculated number of misdiagnosed	Calculated number of misdiagnose	Calculated number of misdiagnosed
			<u>lower band</u> (assuming 20%)	<u>middle band</u> (assuming 23%)	<u>upper band</u> (assuming 30%)
52,041,916	5/1000	260,209	52,041	59,848	78,062
	7/1000	364,293	72,858	83,787	109,288
	7.7/1000	400,722	80,144	92,166	120,216
	8/1000	416,335	83,267	95,757	124,900

**Table 1 Estimation of number of misdiagnosed (England and Wales) assuming different estimates of prevalence and misdiagnosis (according to different evidence in the literature)**

In table 1 we estimated the possible number of misdiagnosed patients in England and Wales. In this estimation we assumed different rates of misdiagnosis derived from the literature (see table 2). These numbers depend also on the prevalence chosen, giving a broad range estimation of 52,041 (with prevalence of 5/1000 and misdiagnosis rate of 20%) to 124,900 (with prevalence of 8/1000 and misdiagnosis rate of 30%) misdiagnosed cases. Although for the rest of the analysis we will use a prevalence of 7.7/1000 and misdiagnosis rate of 23% given an estimated total 92,166 persons misdiagnosed per year (see table 1), we thought it was important to highlight that there can be variations to our estimations if different figures are assumed. The 7.7 /1000 prevalence was chosen because it is very close to one of the latest studies in the UK:<sup>3</sup> 7.7 per 1000 males [95%CI 7.5, 7.9] and 7.6 per 1000 females [95%CI 7.4-7.8]. The 23% misdiagnosis rate was derived from Scheepers' paper<sup>5</sup> that was used as the baseline for this study (see table 1).

It is important to highlight that misdiagnosis rates are based on studies focused on adult misdiagnosis. However, the problem could be worse in children given that the range of paroxysmal disorder occurring in children,

which are often misdiagnosed as epileptic seizures is far greater than that encountered in adults.<sup>12-14</sup>

Evidence/Author-Studies	Smith <i>et al</i> (1999) <sup>8</sup>	Scheepers <i>et al</i> (1998) <sup>5,4</sup>	Zaidi <i>et al</i> (2000) <sup>5,4</sup>	Taoufik <i>et al</i> (2004) <sup>16,7</sup>
Overall misdiagnosis rate	26.1% (46/184)	23.2% (49/212) min (35%)max	41.9% (31/74)	24% (29/121)
Rate of misdiagnosis according to underlying condition:				
Syncope and cerebrovascular	13/184 (7.06%)	20/214 (7.07% and 2.35% respectively, total 9.3%)	19/74 (25.7%)	31% (cardiovascular)
Psychogenic/NEA	19/184 (10.32%)	10/214, 4.6% (psychopathology)	2/74 (2.7%)	
Mixed diagnosis	6/ 184 (3.26%)			
One seizure		7/214 (3.3%)		
Alcohol related		6/214 (2.83%)		
Migraine		3/214(1.41%)		
Other	8/46 (4.34%)	3/214 (1.41%)		
Method of detecting misdiagnose	-Specialist (clinical) where required: -IEEG -AEEG -Imaging	-Specialist (clinical) where required:  -EEG -MRI - head up tilting	-Head up tilt test and carotid sinus massage during continuous electrocardiography  - Electroencephalography  -Blood pressure monitoring  -ECG (on 10 patients)	-Specialist -VET
Notes	Group of patients referred to epileptic clinic and taking epileptic medication	Community based study	Refractory epilepsy	-Only referred by neurologists -Refractory epilepsy (and taking drugs)

**Table 2 Summary of evidence on misdiagnosis studies****Steps 2 and 3****Estimate the average uses of resources and costs incurred by misdiagnosed patients and estimation of national figures**

With the purpose of providing as much information as possible we estimated misdiagnosis in epilepsy following three different approaches:

- Apply unit costs to data on resource consumption by misdiagnosed group of patients and extrapolate figures to national numbers. Wrongly diagnosed individuals with epilepsy suffering instead from other underlying condition may have a different pattern of resource use than the average and 'real' person with epilepsy so estimating the costs of misdiagnosis by imputing average costs of epilepsy per person to this group of individuals could be biased. The most direct form for estimating the costs burden by the person misdiagnosed is to use a bottom-up individual related approach where cost estimates of the number and type of health care and social services consumed by individuals are derived from observational studies, or alternatively, based on hypothetical information provided by expert panels and related literature.

This implies to first measure the use of resource quantities by those misdiagnosed and then use unit costs or market prices to cost these resources. In this section we have tried as much as possible to follow this methodology. However, when it was not possible due to lack of data we had to make assumptions about the use and costs of some resources. Lack of data also forced us to estimate only the cost of resources consumed in the health care sector that for consistency with other studies on the costs of epilepsy will be referred as direct medical costs given that no information in the use of non-medical direct resources by misdiagnosed individuals was available in the literature. Indirect costs were not estimated mainly because of lack of existing

literature.

We identified only one paper<sup>5</sup> that describes most of the yearly use of medical resources by a group of misdiagnosed individuals because of their 'epilepsy'. This study was based in a population of approximately 40,000, where 261 were identified as having a primary diagnosis of epilepsy. These 214 cases were reviewed and it was found out that 49 of these did not have epilepsy (see appendix for a more detailed description of study). We used this study as our main source to identify the resources used by individuals who are misdiagnosed. Even if, in terms of an epidemiological study, the population sampled in Scheepers' paper is relatively small, the detail of the study allows us to identify particular issues of interest.

Column 2, table 3 describes the yearly use of medical resources by the group of individuals misdiagnosed in Scheepers study. We attached a cost to the use of these resources using when possible unit cost from different sources (described in table 4). In the case of GP contacts and the cost on the use of AEDS the different problems on cost estimations and assumptions made are described as follows:

- Scheepers study<sup>5</sup> did not give the number of GP contacts by the group of those misdiagnosed so we just assumed that each misdiagnosed person contacts her//his GP as many times per year as the average person with epilepsy and so incurs the same average costs, this data was taken from Cockerell et al.<sup>7</sup>
- Scheepers study<sup>5</sup> reported data on the number of people among the misdiagnosed group that are on AEDs, but does not specify with detail drug and doses of drugs taken. For this purpose we attached the average cost on AEDs consumption per person estimated by Jacoby et al<sup>8</sup> of £161 to the proportion of misdiagnosed individuals on AED therapy. We used this study as our reference because it is one of the latest published studies

in the UK to estimate average cost of drugs use per person with epilepsy and may better reflect changes in prescribing patterns towards newer and more expensive drugs.<sup>3</sup>

In column 5 of table 3, we extrapolated our results to national figures using a 23% of misdiagnosis rate<sup>5</sup> and an assumed prevalence rate of 7.7/1000 (column 4 table 3). It is important to notice from table 4 column 4 that the average estimated medical cost per person of £263 is lower than the average estimated cost per person with epilepsy in Cockerell's study<sup>7</sup> of £488 (at 2002 prices) but similar to the average medical cost of an individual in the second year of their epilepsy estimated by Cockerell equal to £288 (at 2002 prices). Some of these differences are due to different patterns in selection of samples in the studies but others could be due to different rates of consumption between the average person with epilepsy and the misdiagnosed individual. Unfortunately with the data available, it is difficult to disentangle and specify the differences. We can notice for example that in contrast with Scheepers study, in the Cockerell study sample participants were selected only if they were taking AEDs. Instead in Scheepers study, individuals entered the sample if they were identified as having a primary diagnosis of epilepsy. In fact, only 19/49 (38.5%) of those misdiagnosed were on AEDs. Also, this group of people did not receive any test related to diagnosis (for example, CTs or EEGs) in the previous year of the study while in Cockerell some did. This could explain why our costs are more similar to the average costs estimated by Cockerell for those in the second year of their epilepsy where it is rare to have diagnostic tests. The distribution of medical costs by individuals who are misdiagnosed is presented in column 6 of table 3. We can see that hospital costs represent 49% of the economic burden followed by the use of AEDs with 23%.



1 n=49 (as in Scheepers et al.)	2 No	3 Annual Cost (£)	4 Annual Cost per patient (£)	5 Medical national direct costs* (£)	6 Distribution of medical direct costs %
hospital inpatient visits	4	6,336	129.3	11,917,658	49
AEDs	19	3,059	62.4	5,753,806	24
a&e	9	675	13.77	1,269,636	5
specialist visits	17	2,229	31.22	2,877,843	12
GPs	49	1,323	27	2,488,488	10
total		12,923	263	24,307,433	100

All prices and costs were adjusted for inflation by the hospital and community health services (HCHS) pay and price index.

**Table 3 The costs of epilepsy misdiagnosis. Prevalence rate assumed is 7.7/1000 (making a total of 36,4293 epilepsy cases) Misdiagnosis rate assumed at 23% of epilepsy cases (making a total of 83787 cases)**

	Value £	Source	Notes
Inpatient episodes	1,584		HRG label: Epilepsy <70 w/o cc. Average length of stay is 4 days.
GP contacts	27	Personal Social Services Research Unit (PSSRU), Unit costs of health and social care 2002	Assumes 12.6 minutes per clinic consultation
Specialist contact	115	Reference costs 2002	NHS Trust outpatient attendance follow up data for Neurology
A&E	75	Personal Social Services Research Unit (PSSRU), Unit costs of health and social care 2002	Cost per outpatient attendance

**Table 4 Different sources of the unit cost used to estimate the economic value of the resources consumed by misdiagnosed individuals.**

- Apply average costs of resource consumption by epilepsy patients to estimated number of misdiagnosed patients.

Some authors have estimated the costs of misdiagnosis by attaching the average cost per person from cost of illness studies to an estimated number of misdiagnosed cases.<sup>6</sup> In the next section we estimate the national costs of misdiagnosis by applying the average costs as above. The reasons for this are to allow for comparison, and to have another estimation that could allow us to generate a range where the real cost of misdiagnosis falls. This will also give an estimation of the total medical and non-medical direct costs.

In table 5 we estimated the financial cost of misdiagnosis on direct medical costs by applying the number of estimated misdiagnosed cases to the average yearly cost per person with epilepsy as estimated by Cockerell (1994) and Jacoby (1998) the only two cost of illness papers found for the UK<sup>7,8</sup>. We also add the estimated average non-medical direct cost in these studies to the medical costs estimated on the previous section. With this information we have an estimated range of the direct medical costs of epilepsy misdiagnosis of £24,307,433 to £82,941,252., and for total direct costs of £130,120,729to £188,754,549.

Source of costs		Direct medical national costs	Direct total (medical+non medical)national medical cost
Jacoby <sup>2</sup>	Upper band	82,941,252	188,754,549
Cockerell <sup>1</sup>	Middle band	47,670,153	163,715,680
Using own medical direct costs estimations (table 4) +non medical direct from the literature	Lower band	24,307,433	130,120,729 <sup>4</sup> 140,352,959 <sup>3</sup>

1. Using per person medical cost of 396 and non medical direct costs of 964 updated to 2002 prices.
2. using per person medical cost of 689 and non-medical direct costs of 879 updated to 2002 prices.
3. taking direct non-medical costs from Cockerell study<sup>7</sup>
4. taking direct non medical costs from Jacoby's study<sup>8</sup>

**Table 5 The costs of epilepsy misdiagnosis. Prevalence rate assumed is 7/1000 (making a total of 36,4293 epilepsy cases) Misdiagnosis rate assumed at 23% of epilepsy cases (making a total of 83787 cases). England and Wales**

- Estimation of costs of misdiagnosis by true underlying condition. We consider it important to highlight that there are two specific groups of conditions systematically misdiagnosed as epilepsy: cardiovascular and psychological. This section aims to give an approximation to the cost of misdiagnosis by underlying condition. Note that as mentioned before this estimation does not consider the costs incurred for not treating the real condition and as a consequence having people with a deteriorating health status. But we aim more to highlight the problem of misdiagnosis by estimating some, if not all of the significant financial

consequences.

We estimated the number of misdiagnosed persons by real underlying condition assuming misdiagnosis rates estimated mainly in two studies<sup>5,6</sup> (table 2). These rates were used to estimate national figures of misdiagnosed persons by underlying condition and then costs were assigned to these figures. The costs used are those estimated in section b (considering only the lower and middle band). This implies that the average use of resources by people misdiagnosed is the same by type of underlying condition. This assumption is difficult to justify but there is no alternative for the analysis since no study was found that specifies consumption of resources by real underlying condition. Table 6 reports the estimated number of cases of misdiagnosis according to condition most commonly mistaken as epilepsy using the rates in the studies mention above (see table 3). We can see that the number of misdiagnosed cases with cardiovascular or cerebrovascular underlying condition could have a prevalence of 26,046 to 37,618 cases per year with direct medical costs lying between £6,8969,492 and £19,457,205 and direct total costs of £39,664,966 and £66,822,726. The number of misdiagnosed cases with an underlying psychopathological condition was estimated between 18,809 and 38,068 with an estimated range of direct medical costs of £4,960,700 to £19,689,846 and direct total medical costs of £28,643,461 to £67,621,694.

Number of misdiagnosed as epilepsy by underlying condition	Number	Direct medical costs		Total direct costs		
		lower range	upper range	lower range	upper range	
Cardiovascular	lower range <sup>a</sup>	26,046	6,869,492	13,472,000	39,664,966	46,267,474
	upper range <sup>b</sup>	37,618	9,921,401	19,457,205	57,286,922	66,822,726
Psychopathology	lower range <sup>c</sup>	18,809	4,960,700	9,728,602	28,643,461	33,411,363
	upper range <sup>d</sup>	38,068	10,040,026	19,689,846	57,971,874	67,621,694

a Misdiagnosis rate of 28% of the total misdiagnosis as in Smith's paper<sup>6</sup>

b Misdiagnosis rate of 41% of total misdiagnosis as in Scheepers' paper (includes 5 % of cerebrovascular conditions)<sup>5</sup>

c Misdiagnosis rate of 20% % of total misdiagnosis as in Scheepers' paper<sup>5</sup>

d Misdiagnosis rate of 41% of total misdiagnosis as in Smith's paper<sup>6</sup>

**Table 6 Number of cases of misdiagnosis (England and Wales) according to condition most commonly mistaken as epilepsy (assuming prevalence of 7/1000 and population of 52,041,916 and considering yearly direct costs of £1360 as in the study of Cockerell)**

### 1.3 Discussion and Conclusions

In the present study we examined the economic burden of misdiagnosis in epilepsy from the Health Sector point of view. The results presented must be treated with caution since we have relied on various assumptions. Despite this, we believe the results are important and highlight the problem from an economic perspective. Even when the lower bands (and probably underestimated) of the estimations are considered the value of the resources wasted due to misdiagnosis is significant. Indirect costs (costs of lost productivity) were not estimated for reasons already mentioned. However, they may be large if we consider that Cockerell<sup>7</sup> estimated the average indirect costs per person with epilepsy to be £3,770 due to unemployment and in Smith's paper 23/46 misdiagnosed were unemployed, or under threat of job loss.<sup>6</sup>

Other important costs and consequences of misdiagnosis which are not considered in this study (mainly for lack of reliable data) are: the cost of side effects caused by incorrect treatment on misdiagnosed persons, and the forgone benefits in terms of health, quality of life and productivity for receiving the correct treatment. Also, we did not consider the direct costs for the patients and their families (for example, transport costs to the health centre hospital). And the costs of legal settlements for both misdiagnosed persons and the NHS (for example, during 2002/3 the families of children misdiagnosed in Leicester and Coroners Inquests).

To summarise, we can say that the opportunity costs of misdiagnosis are considerable high. This is especially true if we account for the fact that a large amount of lost resources could be used to give the correct treatment to misdiagnosed persons and to improve the quality of the treatment received by patients with epilepsy. We hope that with this analysis we have highlighted the magnitude of the problem and the need for practitioners to follow clinical guidelines in order to reduce the occurrence of this problem.

#### References

1. Sander JW, Shorvon SD. Epidemiology of the epilepsies. *Journal of Neurology, Neurosurgery, and Psychiatry* 1996;**61**:433-43.
2. Cockerell OC, Eckle I, Goodridge DM, Sander JW, Shorvon SD. Epilepsy in a population of 6000 re-examined: secular trends in first attendance rates, prevalence, and prognosis. *J Neurol Neurosurg Psychiatry* 1995;**58**:570-6.
3. Purcell B, Gaitatzis A, Sander JW, Majeed A. Epilepsy prevalence and prescribing patterns in England and Wales. *Health Statistics* 2002;**15**:23-31.
4. Chadwick D, Smith D. The misdiagnosis of epilepsy. *British Medical Journal* 2002;**324**:495-6.
5. Scheepers B, Clough P, Pickles C. The misdiagnosis of epilepsy: Findings of a population study. *Seizure* 1998;**7**:403-6.
6. Smith D, Defalla BA, Chadwick DW. The misdiagnosis of epilepsy and the management of refractory epilepsy in a specialist clinic. *Quarterly Journal of Medicine* 1999;**92**:15-23.
7. Cockerell OC, Hart YM, Sander JW, Shorvon SD. The cost of epilepsy in the United Kingdom: an estimation based on the results of two population-based studies. *Epilepsy Research* 1994;**18**:249-60.
8. Jacoby A, Buck D, Baker G, McNamee P, Graham-Jones S, Chadwick D. Uptake and costs of care for epilepsy: findings from a U.K. regional study. *Epilepsia* 1998;**39**:776-86.
9. Drummond, M., O'Brien, B., Stoddart, G., and Torrance, W. Methods for the economic evaluation of health care programmes. 1986. Oxford, Oxford Medical Publications.
10. Koopmanschap MA, Rutten FF, van Ineveld BM, van Roijen L. The friction cost method for measuring indirect costs of disease. *J Health Econ.* 1995;**14**:171-89.
11. van Hout B. Determining costs and cost-effectiveness of epilepsy. *Am.J Manag.Care* 1998;**4**:S501-S509.
12. Gibbs J, Appleton RE. False diagnosis of epilepsy in children. *Seizure* 1992;**1**:15-8.
13. Daley HM, Appleton RE. Fits, faints and funny turns. *Current Paediatrics* 2000;. **10**.

14. Appleton RE. Misdiagnosis of epilepsy. Misdiagnosis occurs particularly in children. *BMJ* 2002;**324**:1219.
15. Zaidi A, Clough P, Cooper P, Scheepers B, Fitzpatrick AP. Misdiagnosis of epilepsy: many seizure-like attacks have a cardiovascular cause. *J Am Coll Cardiol*. 2000;**36**:181-4.
16. Taoufik MA, Thieman C, Shatzel A, Farias S. Video-EEG telemetry can be a crucial tool for neurologists experienced in epilepsy when diagnosing seizure disorders. *Seizure* 2004;**13**:32-4.