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Epilepsy in the UK: Misdiagnosis, mistreatment, and undertreatment? The Wrexham area epilepsy project

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Summary

Objective: To assess the diagnostic and therapeutic difficulties in patients with epilepsy who had never come into contact with specialist services.
Methods: Assessment was offered to 676 patients diagnosed as having epilepsy and receiving anti-epileptic drug therapy (AED), who had no previous contact with the local epilepsy services. Two hundred and seventy-five patients gave consent and attended for reassessment. We identified the proportion of patients (a) who had previously seen a neurologist, (b) in whom the diagnosis of epilepsy was not secure, (c) in whom planned AED withdrawal could be considered (d) in whom seizure control could be improved.
Results: 53/275 (19.3%) of those attending for review had previously been seen by a neurologist. 87/275 (31.6%) patients ultimately received continued specialist care.

Diagnostic doubt was expressed in 3/53 (5.6%) and 42/222 (18.9%) of patients diagnosed by neurologist and non-specialist, respectively.

Of 133/219 (60.7%) of patients whose epilepsy was in remission, only 6 elected to withdraw or change medication. Of 18 patients with diagnostic doubt who accepted follow-up, 12 successfully stopped treatment.

17/55 (30.9%) patients with active epilepsy (10 partial, 7 generalised) achieved at least a 1 year remission consequent upon treatment in this clinic. In 15 cases this was a first ever remission.
Conclusion: Approximately 55% of the population of adults receiving treatment for epilepsy have never received specialist advice. Reassessment of these patients uncovers diagnostic uncertainty, failure to classify (leading to sub-optimal therapy) and lack of information and advice about all aspects of epilepsy care.

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The development of integrated services for people with epilepsy (PWE) must take account of this hidden need. The new General Medical Services contract for general practitioners will bring this need to our attention, and our experience will help predict the measures required to deal with the under-treatent and mistreatment of this group. The majority of PWE, not currently receiving shared care, merit reassessment and approximately one-third will require continued specialist care. Existing services do not have the capacity to process a marked increase in rate of referral. This project informs prioritisation of referrals and service reorganisation.

Introduction

Epilepsy is one of the commonest neurological conditions[1,2] with an estimated prevalence of epilepsy in the UK of 0.7%. For each of the 350,000 affected people, this diagnosis carries associated medical and social sequelae. Across three decades, government-sponsored reports from Reid[3] to Kitson[4] recommend that all patients with suspected new epilepsy should see a neurologist or other specialist for accurate diagnosis and optimal management.

Single[5] and multi-practice audits[6–8] and a large national survey[2] indicate that most patients have been seen in a hospital clinic but the proportion diagnosed and managed by specialists remains unclear. The vast majority of patients are quickly discharged to primary care where subsequent follow-up arrangements are widely reported to be inadequate.[5,7,8]

Documented consequences of this approach to the care of people with a common chronic disorder include misdiagnosis[5,9,10] inadequate classification and sub-optimal therapy[5,6,9] unnecessary poor control and toxicity[11] lack of knowledge about current seizure control[7,8] and necessity for long-term treatment,[7] widespread poor compliance, including injudicious cessation of treatment[6,12] and lack of awareness about patients anxieties about many aspects of their care.[13] Given these problems, it would appear important that all patients with the label ‘epilepsy’ require specialist assessment.

The afore-mentioned studies were incomplete: data were obtained from case-note review or personal review by GP but rarely included direct specialist support.[6,10] Additionally, the larger studies[7,8] were never designed to complete the audit cycle and the reporting of intervention and subsequent outcome is unique.[10]

Our original project involved the individual review, by a specialist registrar with interest in epilepsy (JPL or AN), of 275 patients with subsequent follow-up in a consultant-led epilepsy clinic in 87 cases. The intention was to estimate the therapeutic and diagnostic gaps in a District General Hospital catchment area with an established epilepsy clinic. The local and national implications of our findings for the future planning of services is discussed.

Methods

The partners in all 26 general practices located within the Wrexham Maelor hospital catchment area (of approximately 200,000 people) accepted the invitation to participate. All patients with a diagnosis of epilepsy, on anti-epileptic drug therapy, were identified from practice records. Letters were sent from the practice requesting permission to release details to the investigating team. Once signed consent was received, patients were invited to attend for review of their condition.

One hundred and eighty-three children under 16 years of age and 357 adults already attending the local epilepsy clinic were excluded from further review. After several frail individuals attended we excluded the remaining 123 patients aged over 80 years.

Initial assessments were undertaken by experienced specialist registrars; JPL (249) and AN (26). Data collection included history of seizure disorder, results of previous investigations and nature of all current and previous treatments. Information was obtained from patients, carers, relatives, and any existing correspondence.

Diagnosis of epilepsy was categorised as secure or doubtful. Diagnostic doubt, based on clinical grounds, was expressed if (a) there was an alternative explanation for the attacks or (b) insufficient evidence to support a confident diagnosis of epilepsy. Frequency, or remission, of events were recorded, with remission defined as at least 12 months event-free. Patients whose epilepsy was in remission received individualised estimates of risk of relapse on drug withdrawal.[14]

It emerged that many patients had attended seeking specific information and their concerns were recorded. After consultation, consultant follow-up was arranged if a treatment change was offered and accepted. Otherwise, patients were discharged.

Table 1 Estimation of proportion of prevalent population never seen by specialist.

Catchment population	194187
Patients with epilepsy (prevalence)	1339 (0.69%)
Adults (>16 years) with epilepsy	1156
Never attended local epilepsy clinic	799
Eligible for reassessment (after exclusion of 123 people aged over 80 years)	676
Attended for reassessment	275
Number (%) attending who had previously been seen by a neurologist	53 (19.3%)

The denominator is adults with epilepsy (1156). Three hundred and fifty-seven were attending local epilepsy clinic. 19.3% of those attending for review had previously seen a neurologist. 19.3% of all adults not attending the epilepsy clinic is 154. 357 + 154 = 511 patients had ever seen specialist. Therefore, assuming representative sample (see discussion), the remainder 645/1156 (55.8%) had never seen a specialist.

Results

The prevalence of epilepsy in this catchment area of 0.69% is consistent with UK estimates.[3] 275/676 (40.7%) of those eligible attended for reassessment, of whom 53/275 (19.3%) had been previously seen by a neurologist. Assuming this sample to be representative of the whole prevalent population we estimate that ~56% of adults with epilepsy had never received specialist advice (Table 1).

Initial categorisation of patients and recommended follow-up is shown in Table 2. Consultant opinion differed significantly from that of the specialist registrar in only 4/87 cases.

Table 4a Outcome: diagnostic uncertainty.

Outcome	Number
Positive: stopped AEDs, no events	9[a]
Stopped AEDs, events—not seizures	4
Neutral: stopped AEDS then DNA	2
Treatment continued	3
Negative: reduced AEDs, definite seizure	1
Total	19

[a] Includes one patient with single seizure.

Diagnostic doubt was expressed in 3/53 (5.6%) and 42/222 (18.9%) of patients diagnosed by neurologists and non-specialists respectively. Nineteen of these patients continued to experience events. Sixteen patients who were event-free and seven with ongoing attacks elected to remain on treatment and were not followed up. 9/31 women whose diagnosis was questioned had received AEDs during their child-bearing years.

The overall remission rate was 133/219 (60.7%). Remission rates in patients diagnosed by neurologists and non-specialists were broadly similar, although failure to recognise the idiopathic generalised epilepsies[15] resulted in poorer than expected[15] outcome in some individuals (Table 3).

87/275 (31.6%) patients ultimately received continued specialist care. Medium-term outcomes are displayed in Tables 4a–4c, respectively. Specific details of those achieving remission are given in Table 5.

Table 2 Follow-up according to initial assessment category.

Category	Number	Offered follow-up	Accepted follow-up	Continued follow up
Single seizure	12	10	6	1
Diagnostic doubt	45	38	22	18[a]
Epilepsy (remission)	133	59	23	13[b]
Epilepsy (active)	86	78	57	55[c]
Total	275	177 (64.3%)	108 (39.2%)	87 (31.6%)

[a] One patient with definite epilepsy who had tonic-clonic seizure on reduction of therapy.
[b] One patient initially considered to be in remission but, after review, found to have active epilepsy.
[c] Two patients initially considered to have active epilepsy but, after review, thought to be in remission.

Table 3 Remission rate according to initial classification of epilepsy.

Classification of epilepsy	Diagnosed by neurologist	Diagnosed by non-specialist	Total
Partial	23/34 (67.6%)	77/126 (61.1%)	100/160 (62.5%)
Idiopathic generalised	7/10 (70%)	11/23 (47.8%)	18/33 (54.5%)
Symptomatic generalised	0/2	2/5 (40%)	2/7 (28.6%)
Unclassified	2/4 (50%)	11/15 (73.3%)	13/19 (68.4%)
Total	32/50 (64%)	101/169 (59.8%)	133/219 (60.7%)

Table 4b Outcome: epilepsy in remission.

Outcome	Number
Positive: stopped AEDs, no relapse	2
Changed treatment, side effects resolved	4
Neutral: treatment continued	5
Not in remission	1
Negative: stopped AEDs, relapse	1
Total	13

Table 4c Outcome: active epilepsy.

Outcome	Number
Positive: new remission >1 year	17
Improved[a]	20
Neutral: unchanged	11
Uncertain—lost to follow-up	4
Epilepsy not active	2
Negative: worse[b]	1
Total	55

[a] Worthwhile reduction in seizure frequency or severity, or resolution of side effects.
[b] Transient deterioration in seizure control.

Discussion

The existing literature indicates the likelihood of significant deficiencies in the care of patients with epilepsy managed in the community. That the extent of these problems remains unknown, represents an impediment to the planning of service provision locally and nationally.[2]

Previous community-based audits have usually been GP-led, with little specialist support, but reporting benefit in small numbers of patients. The Community Awareness and Resources for Epilepsy (CARE) project[10] involved collaboration between primary and secondary care but outcome was reported only in terms of misdiagnosis. Larger projects[7,8] were not designed to influence patient outcome or inform service development.

Our study is original in several respects; patients volunteered to be reviewed, initial and subsequent assessment was conducted by trained specialists, and positive outcomes are reported in patients with active epilepsy. While all aspects of care of PWE are under scrutiny, these findings inform clinicians about the extent of unmet need and the implications for service development and re-organisation.

Table 5 Epilepsy type and treatment change leading to remission.

Epilepsy syndrome	Patient	Longest previous remission	Current seizure types	Existing treatment	Treatment change	Duration new remission
Cryptogenic partial	AB	10 months	SGTC	PHT 100 mg tds	PHT 300 mg od	15 months
	SH	3 months	CP, SGTC	PHT + PB	LTG replaced PB then PHT withdrawn	28 months
	RH	1 month	CP, SGTC	CBZ 1.2 g	TPM added	22 months
	AJ	3 months	CP	PHT	Switchover to TPM	42 months
	JJ	6 months	SP	CBZ 800 mg	Increased to 1 g	18 months
	RJ	1 month	SGTC	PHT	LTG added	25 months
	LW	1 month	CP, SGTC	CBZ 100 mg	Increased to 600 mg	14 months
Symptomatic partial	HA	3 months	CP	PHT	LTG added	24 months
	JC	6 months	SP	PHT	Switchover to LTG	27 months
	AR	6 months	CP, SGTC	VPS + PHT	TPM replaced PHT	31 months
Idiopathic generalised	GF	1 month	Myoclonus, absences, PGTC	PHT	Switchover to TPM	24 months
	LF	Days	Absences	VPS + LTG	VPS dose increased	19 months
	SG	5 months	Myoclonus	VPS 1.0 g	Increased to 1.4 g	42 months
	JL	5 Years	Myoclonus, PGTC	VPS	LTG added	41 months
	DP	1 month	Myoclonus	PHT	Switchover to TPM, then VPS, then LTG	32 months
	KP	1 year	Myoclonus, PGTC	PB + PHT	VPS replaced PHT	17 months
Symptomatic Generalised	GE	2 months	PGTC	VPS + LTG	LTG dose increased	12 months

SP: simple partial; PHT: phenytoin; CP: complex partial; PB: phenobarbitone; SGTC: secondary generalised tonic-clonic; CBZ: carbamazepine; PGTC: primary generalised tonic-clonic; VPS: sodium valproate; LTG: lamotrigine; TPM: topiramate.

Community diagnostic uncertainty

There is no gold standard for the diagnosis of epilepsy and there will often be uncertainty about diagnoses made many years ago. However, the level of agreement between specialist registrar and consultant was high and the reporting of negative outcomes is evidence that this was not contrived. Importantly, 12/18 patients with alternative diagnoses stopped treatment without problems.

The rate of misdiagnosis (16.3%) is within the range of 5 and 23% reported in community-based studies.[6,10] No-one can completely avoid mistakes but doctors with appropriate training will be less likely to misdiagnose epilepsy. The relative rates of misdiagnosis made by neurologists (5.6%) and non-specialists (19.3%) lends support to this assertion. A low rate of specialist misdiagnosis has been confirmed by the rate of misdiagnosis in cases entered into Standard And New Anti-epileptic Drug (SANAD) trial[16] between January 1999 and January 2002 by a single specialist (DS); 5/278 (1.8%) new patients have subsequently been withdrawn due to misdiagnosis.

Epilepsy in remission

The overall remission rate of 60.7% is consistent with published literature.[7,8] That there was no significant difference in outcome for patients with partial epilepsies, whether diagnosed by neurologists or not, can be explained by the facts that their prognoses are mainly dependent upon aetiology and that all conventional AEDs possess similar efficacy against these seizure types.[17] The poorer than expected outcome in patients with idiopathic generalised epilepsies (IGE) may have been predicted, since these specifically require treatment with broad spectrum AEDs.[15]

The MRC Anti-epileptic Drug Withdrawal Study[14] produced data which allows individualised counselling about the risk of relapse on drug withdrawal. These had not been previously used to inform the need to continue treatment in our patients. In keeping with previous experience[18] most patients elected to stay on medication following counselling (usually related to concerns about driving eligibility). However, four such patients chose to stop treatment with subsequent resolution of AED-related side effects.

Active (refractory) epilepsy

Smith et al.[9] assessed 94 patients referred to a specialist in 1991 for management of 'drug-resistant epilepsy'. Twelve (13%) did not have epilepsy and 16/80 (20%) who did have epilepsy were rendered seizure-free by surgery (4) or by change of medication (12). Nearly a decade later, from a sample of patients in the community in whom hospital review was not planned, we find that 17/55 (30.7%) with active epilepsy obtained at least 1 year seizure-freedom following consultation with a specialist. This was achieved by either optimising use of conventional drugs ($n = 5$) or following introduction of newer agents ($n = 12$). It is well-recognised that use of the newer agents is largely restricted to specialist practice.[17] For 15/17 this represented a first ever remission

Patients require further information

Many patients attended the clinic seeking specific information: the commonest questions concerned the possibility of drug withdrawal (58 patients), driving regulations (27 patients), reproduction or fertility (14 patients), doubts over diagnosis (3 patients), side effects and interactions of long-term AEDs (4 patients), and safety including alcohol consumption (3 patients). These findings confirm that patients will benefit if specialists (either consultants or specialist nurses) can address specific concerns about their condition[19]. Despite preferring to receive care from their GP[2] patients are very reluctant to discuss their concerns with the family doctor.[12,13] We know that better understanding of epilepsy among patients has tangible psychological benefits and delivery of this knowledge is a key role of the epilepsy specialist nurse.[20]

An estimate of unmet need in the whole prevalent population

One can only speculate about the reasons why 401/676 (59.4%) patients did not give consent for further review. We can assume that the majority[2] of these will be seizure-free, with most of these tolerating their treatment. However, a significant minority will have active epilepsy and evidence suggests that some patients with chronic epilepsy are reluctant to access services.[21] Indeed Taylor (1987)[22] reports that people who would benefit most from intervention have to be 'sought out'. We cannot be certain about the characteristics of those not attending since no consent was given for further assessment.

If we assume that our sample is representative, then review of the entire population, would produce the following findings; a period of continued care in specialist clinic (215), removal of epilepsy label and cessation of treatment (30), in remission—with subsequent withdrawal or change of therapy (15), and

Box 1. Reorganisation of care for people with label 'epilepsy'

Early review by consultant	Active epilepsy especially if (a) tonic-clonic seizures or (b) out-dated treatment regime, e.g. low doses of phenytoin and phenobarbitone Diagnosis insecure especially if still having events; may have treatable cardiovascular condition
Early review by specialist nurse	All women of child-bearing age unless (a) clear documentation that already received counselling and open access to an epilepsy/neurology service or (b) incapable of having children
Routine review by consultant or nurse	Event-free and wishing to consider drug withdrawal
All referrals	To be accompanied by (a) relevant previous correspondence and (b) an eye-witness for attacks
Discharge from secondary care	1 year (maximum 2 year) remission; should have received counselling about pros and cons of drug withdrawal Active, but stable, epilepsy where treatment options exhausted All discharged patients to be accompanied by (a) request for annual review in community and (b) explicit guidance on re-referral
Annual review in community	Event-free, tolerating medication and driving Active epilepsy refusing referral; continue to document condition and offer referral

confirmed active epilepsy achieving first ever remission (37).

The 'Best Case' scenario is that those who did not respond are completely well. In this case, there would be 401 patients in remission, free from side-effects and well-informed about their condition. In this unlikely event, the figures among those who did respond still represent significant unmet need within the District General Hospital catchment area.

We know that the Wrexham Maelor Hospital has one of only 17 District General Hospital-based epilepsy clinics in the country.[23] While our results can be extrapolated nationwide, this greater than normal service provision ensures that this will be an underestimate of the unmet need in most other areas.

Implications for service re-organisation

The care of PWE is currently under scrutiny; epilepsy is one of ten clinical indicators in the quality and outcomes framework of the new GMS contract. While this contract requires only documentation of patients' seizure control and medication, published guidelines[24] include explicit standards of care. Furthermore, the National Primary and Care Trust Development Programme explicitly defines Primary Care Trust competencies including 'working towards guidelines'.

Consequently, as practices create disease registers, primary care, as a whole, will 'discover' hundreds of thousands of patients from which tens of thousands will merit re-assessment. Prioritisation of referrals will be difficult, and existing secondary care does not have the capacity to process a marked rise in number of referrals of people with the label 'epilepsy'. Meanwhile, however, our project should help plan provision of such services and may form a basis for coherent advice on targeting and prioritisation of referrals (Box 1).

Priority should be given to patients with continuing attacks—whether to allow manipulation of AEDs or exclusion of other treatable conditions[25]. All women of child-bearing age should be counselled about fertility and teratogenesis. People who are event-free, whether the diagnosis is secure or not, can be seen less urgently. The resultant referrals may provide a negative impact on local neurology services, with a potential later offset following the discharge of recently diagnosed patients achieving remission. Nevertheless, major resource shortfalls will be identified, creating local cases for more specialist input including, ideally, GPs with specialist interest.

Conclusion

The responses gained from around 40% of patients with epilepsy in the community show that even in an area with an established epilepsy clinic there is significant unrecognised and unmet need within the prevalent population. Nationally there is a large reservoir of misdiagnosed, sub-optimally treated and ill-informed patients. Our experience shows that patients benefit positively from exposure to specialist services.

The planning of future service provision must take account of this hidden need. The identification and

assessment of those patients meriting review requires the co-ordinated efforts of primary and secondary care on behalf of purchasers (Primary Care Trusts, local health boards) and providers, respectively. It would be perfectly feasible for lead GPs in large practices[2] or Primary Care Trust-appointed GPs to create disease registers from which, with specialist guidance, patients can be identified for management in community or medical or nursing review. Inaction is not an option, but constructive action will require careful planning and resource allocation.

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