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Abstract

Objective

To determine the clinical characteristics, management and outcomes of patients taken to hospital by emergency ambulance after a suspected seizure.

Design

Quantitative cross-sectional study of a consecutive series of patients.

Setting

An acute hospital trust in a large city in England.

Participants

Patients were initially identified from the records of the regions ambulance service. In 2012/13 there were 605,481 emergency incidents, 74,141 originated from Sheffield (a large city in the region). Of these 2,121/74,141 (2.9%) were suspected seizures and 178 occurred in May 2012. We undertook detailed analysis of the medical records of those patients who were transported by ambulance to the city's acute hospital.

Results

2.4% of patients were seizing on arrival in the Emergency Department (ED), 19.5% were post-ictal and 69.5% were alert. 74.7% of suspected seizures were diagnosed as epileptic but only 30.8% already had a diagnosis of epilepsy. 11.0% were psychogenic non-epileptic seizures (PNES) and 9.9% were cardiogenic. Non-compliance with AEDs was documented in 18.8%. 63.4% were discharged at the end of their ED attendance and 31.7% were admitted to an in-patient ward. 36.5% of those discharged from ED and 33.3% of those discharged from in-patient wards had no documented referral or follow-up in specialised epilepsy services.

Conclusions

This paper has provided detailed data on the aetiology of suspected seizures in this population. Most suspected seizures are actually epileptic seizures but this is a diagnostically heterogeneous group. Only a small minority of patients require emergency medical care but most are transported to hospital and many are admitted generating significant costs. Despite incurring these costs few patients receive expert review and many are discharged home without referral to specialised epilepsy services leaving them at risk of further seizures and the associated morbidity, mortality and health services costs of poorly controlled epilepsy.

Strengths and Limitations of this Study

This is the first study to describe the clinical characteristics, management and outcomes of patients taken to hospital by emergency ambulance after a suspected seizure.

Our sample was relatively small but a larger sample would not have been feasible because of the time consuming nature of extracting data from clinical records.

The triangulation of data drawn from pre-hospital records and hospital medical records (ED, in-patient and epilepsy clinic) resulted in richer and more robust data than data drawn from a single source.

Although this study was conducted in a single hospital trust it is one of the largest acute care providers in the United Kingdom and its Emergency Department provides emergency services for a large socioeconomically mixed population.

The themes identified in this paper resonate with previous studies reflecting practice across the UK and across the world and are therefore of international significance.

INTRODUCTION

Background

Epilepsy is an ambulatory care sensitive condition (ACSC) (1) and sub-optimal ambulatory care (also known as routine or scheduled care) leads to unnecessary demand for emergency care. The majority of epileptic seizures do not require emergency treatment but ambulance services are often called. By the time the ambulance arrives most seizures and have terminated spontaneously, nevertheless the majority of patients are transported to hospital (2) (3). Precise estimates vary, but in England (population 52.96 million, 42.96 million adults) seizures give rise to approximately 211,000 calls to ambulance services per year (3.3% of all emergency calls) (4). It is estimated that there are 60,000 seizure-related Emergency Department (ED) attendances per year (2-3% of all attendances) (5), and 40,000 hospital admissions which represent 9.5% of all admissions for ACSCs (5) (6). There are currently no published studies of care pathways for people who have presented as an emergency with a suspected seizure which aim to facilitate urgent specialist review (7, 8) and avoid unnecessary transport to hospital. Clinical guidelines for paramedics provide little guidance on the community management and/or referral of patients after a seizure and focus almost exclusively on medical emergencies which are rare (9).

Active epilepsy should trigger urgent specialist review to prevent further seizures and/or to refine the patients emergency care plan but this opportunity is often missed (5) (10) (11) (12). Patients therefore remain at risk of further seizures and the associated morbidity (13), mortality (14) and health services costs (15) (16) of poorly controlled epilepsy. Approximately 70% of people with epilepsy (PWE) could become seizure-free with optimal treatment (17) (18) (19) but internationally actual seizure freedom rates are significantly lower than this. There is little published data on seizure-freedom rates in individual countries (17) (20) (21) and there are no published international comparisons of seizure-freedom rates. The overall seizure freedom rate in the UK is thought to be 50% (22) (23) (24, 25). Some epilepsy services in the United Kingdom (UK) are world-leading but the quality of care is highly geographically variable, and patients in many areas do not have access to optimal monitoring and treatment. This means that approximately one-in-five patients with epilepsy are unnecessarily having seizures (17).

EPIC (Epilepsy Pre-Hospital Interventions and Care)

The EPIC study was designed to generate data to support improvements in emergency care after a seizure. Despite its importance, this aspect of epilepsy care has received relatively scant academic attention to date. In EPIC1 (26) we described the pre-hospital management of a series of consecutive incidents with suspected seizures. The present study, EPIC2, focusses on the group of patients that was transported to hospital after a suspected seizure with the aim of determining the clinical characteristics of these patients, their management and their outcomes based on data collected from ED, in-patient wards and the epilepsy clinic. The emergency care structure in the UK, with its universal access to healthcare, unitary emergency call handling service and non-overlapping ambulance service and emergency department provisions offers opportunities to researchers to study emergency presentations with seizures which do not exist in many other countries.

METHODS

Local Context and Patient Selection

Patients were initially identified from the records of the Yorkshire Ambulance Service (YAS) (4). Emergency incidents which were categorised as suspected seizures by call handlers during the period 1st April 2012 and 31st March 2013 were included. YAS is a regional ambulance service in England (one of the four devolved nations of the UK) covering 9,656 square kilometres and is the sole provider of ambulance and paramedic services for its population of 4,019,610 adults (4,954,876

adults and children) (27). Sheffield is one of the major urban centres within the area served by YAS and has a population of 451,100 adults (551,756 adults and children) which is served by a single hospital-based Emergency Department (ED) for adults at the Northern General Hospital (NGH) site of the Sheffield Teaching Hospitals NHS Foundation Trust (STH) (28).

Data Collection and Analysis

Our analysis is based on YAS and STH medical records of all patients initially categorised as having "suspected seizures" who were transported to hospital during the study period. Data were extracted by one of the authors (HD) using a data extraction tool (available as additional online content) developed by all the authors which was revised after an initial pilot. Some variables such as the working diagnosis changed throughout the care pathway and so we report the results separately at each stage in the pathway: 1) ED, 2) in-patient wards, 3) out-patient epilepsy clinic and 4) combined data from all three sources. The data presented in section (4) was drawn together by HD from all available sources (ED notes, in-patient notes, epilepsy clinic notes) to document an overview of the hospital management of each incident taking into account the opinion of all the clinicians involved throughout the care pathway. This data allowed us to determine the best available aetiological explanation for the index event. The care pathway from emergency call to discharge from hospital is complex. Figure 1 illustrates the care pathway and how the denominator changes at different stages.

In this paper we report the data as it was recorded in the notes by the clinicians involved in the incidents with as little interpretation from the authors as possible. Where interpretation was required we included definitions within the data collection tool to inform these judgements; these are described below. We analysed each incident separately (some patients attended more than once during the study period and therefore generated multiple incidents). To calculate the number of incidents in which all physiological parameters were normal we used the following parameters: heart rate (60-100bpm), respiratory rate (14-18 breaths per minute), systolic BP (100-140mmHg), blood glucose (3.5-11.1 mmol/l), temperature (36.5-37.5°C), O2 saturations (<94%) and GCS (15/15). We excluded low temperature (<36.5°C) from this calculation because it is very unlikely that any patients truly had hypothermia in May in England (a low temperature measurement is likely to reflect inaccuracy of peripheral temperature recording). We recorded the Sheffield Early Warning Score (SHEWS) which is based on the National Early Warning Score (29). It is a composite score based on heart rate, respiratory rate, oxygen saturation, systolic blood pressure, urine output and consciousness level, which is intended to identify patients who may be acutely ill so that their care can be stepped-up if necessary. Numerical data was entered into SPSS which was used for calculating summary statistics. Chi-Square tests were used to assess relationships between categorical variables.

Definitions

The latest ILAE definitions of epilepsy and seizures (30) (31) were applied during data collection. We categorised the indication for admission: medical (seizure-related), medical (not seizure-related) and social. Medical (seizure-related) admissions were those where the principal reason for admission was seizure(s), for example, patients who were still post-ictal at the end of their ED attendance. Medical (not seizure-related) admissions were those where the principal reason for admission was not a seizure, for example, lower respiratory tract infection or unexplained pyrexia. Social admissions were those where there was no medical reason for admission but it was not possible to discharge the patient directly from the ED e.g. because a home care package had to be put in place. We categorised those with and without a self-reported diagnosis of epilepsy prior to the index event. Historical diagnoses of epilepsy were determined from the records of the ED doctors and often only brief information was available. In addition to the seizure we determined if the patient had any other acute clinical problems. Alcohol was deemed to be a clinical problem if there was

documentation of excessive alcohol ingestion which occurred around the time of the index event or if there was a history of alcohol abuse (such as alcohol dependency or withdrawal seizures). Patients were deemed to have recovered fully if they were recorded as having returned to their normal level of functioning with no acute medical problems that required hospital assessment and/or treatment, and were not thought to be post-ictal (notwithstanding tiredness, headache and myalgia).

RESULTS

Case Ascertainment, Exclusions and Missing Data

Between 1 April 2012 and 31 March 2013 the Yorkshire Ambulance Service dealt with 605,481 emergency incidents in adults (≥16 years old). 19,799 (3.3%) of these incidents were suspected seizures, 2,121 originated from Sheffield (a large city in the region) and 178 occurred in May 2012 (this month was chosen after preliminary analysis of the summary statistics showed it to be a typical month (4)). After non-seizure diagnoses and other exclusions were removed 132 incidents were analysed in detail and 98 were transported to hospital. The initial call-handling and out-of-hospital management of these patient was the focus of EPIC1 (4).

Of the 98 incidents from EPIC1 that were transported to hospital, 4/98 incidents were transported to an ED outside Sheffield and 3/98 patients were not identifiable on the STH's computer system so medical records were available for 91/98 incidents. 8/91 (8.8%) incidents were given non-seizure diagnoses in ED so no further data was collected for these incidents. All available hospital records relating to the remaining 83 incidents were obtained. Exclusions and missing data from the EPIC study (EPIC1 and EPIC2) are summarised in Figure 1.

Demographics and Repeat Attendances

The patients' median age was 40 (IQR 30, range 16-97). Males accounted for 54.2% and females 45.8% of incidents. The 83 incidents relate to 79 patients. 4/79 (5.1%) patients generated two incidents during the one-month study period. The time intervals between the repeat attendances were: 1 day, 3 days, 13 days and 15 days.

Management in the Emergency Department

Past Medical History

82/83 incidents were seen in ED, one incident was admitted directly to a neurology ward (without being seen in ED). The ED records documented a history of a seizure disorder in 43.9% (36/82) of all incidents: epilepsy 36.6% (30/82), psychogenic non-epileptic seizures (PNES) 6.1% (5/82), epilepsy plus PNES 1.2% (1/82).

Clinical details

In 2.4% (2/82) of incidents the patient was seizing on arrival at the ED. 69.5% (57/82) were alert on arrival and 19.5% (16/82) were post-ictal. All physiological parameters were normal (or not recorded) in 28/82 (34.1%) of incidents (see Figure 2) but often only one parameter was abnormal and often this was mild tachycardia or mild hypertension. In the incidents in which the seizure had terminated prior to arrival in the ED, 76.25% (61/80) had no subsequent seizures during their hospital stay. 17.5% (14/80) had recurrent seizures either in the ED or after transfer to a hospital ward. In 7.3% (6/82) of incidents emergency medication for the termination of seizures was administered in the ED. 70.7% (58/82) of cases had recovered fully by the end of the ED attendance.

Final Diagnosis at the End of the ED Attendance

In the opinion of the ED clinicians, 63/82 incidents were likely to have been epileptic seizures: 13.4% (11/82) had experienced a first fit, 35.4% (29/82) had experienced an epileptic seizure in the context of an established diagnosis of epilepsy (diagnosis reported by the patient as having been made by an appropriately qualified doctor), 28.0% (23/82) had experienced an epileptic seizure with a history of recurrent seizures but without an established diagnosis of epilepsy. 7.3% (6/82) were diagnosed with an acute symptomatic seizure. 9.8% (8/82) were diagnosed with a PNES. The diagnosis was unknown in 2.4% (2/82), and in 3.7% (3/82) no diagnosis was recorded.

Other Clinical Problems

47.6% (39/82) of cases had another clinical problem(s) in addition to the suspected seizure. This was sometimes secondary to the suspected seizure but was often unrelated or only tangentially related to it. 35.4% (29/82) had one additional clinical problem, 8.5% (7/82) had two, 2.4% (2/82) had three and 1.2% (1/82) had four. In total there were 53 additional clinical problems amongst the 82 incidents. 41.5% (22/53) of these were alcohol, 15.0% (8/53) were injuries, 9.4% (5/53) were illicit drug use and 34.0% (18/53) were 'other' (for example, brain tumour, pyrexia, acidosis, psychiatric problems and abdominal pain).

Discharge and Referral from ED

63.4% (52/82) of patients were discharged home at the end of their ED attendance, 31.7% (26/82) were admitted to an in-patient ward from ED (another patient who was taken directly to a ward by ambulance without attending ED), and 4.9% (4/82) self-discharged. The indication for admission was related to the seizure in 61.5% (16/26) of cases. In 26.9% (7/26) of cases it was due to a medical problem which was not obviously related to the seizure (e.g. chest infection, GI problems, infective rash) and in 11.5% (3/26) of cases the reason for admission was social. Of the patients who were discharged home from the ED, only 61.5% (32/52) had documented referral or follow-up advice. 34.6% (18/52) were referred to an epilepsy clinic, 25.0% (13/52) were referred to their GP, and 1.9% (1/52) were referred to an epilepsy specialist nurse. 36.5% (19/52) had no documented referral, and 52.6% (10/19) of these had not been seen in the epilepsy clinic before the event. There was a relationship between SHEWS and GCS on arrival in ED with disposal (admission or discharge). Patients with an abnormal SHEWS on arrival were more likely to be admitted to hospital and less likely to be discharged ($\chi 2$ (1, N=45) = 10.385, p=0.001), likewise for patients with a reduced GCS on arrival ($\chi 2$ (1, N=68) = 15.451, p=0.000085).

2) Inpatient Management

Length of stay and speciality

27 patients were admitted to an in-patient medical ward. The median duration of admission was 2.0 days (IQR 5.0, range 0-17). 66.7% (18/27) were admitted to a general medical ward, 18.5% (5/27) were admitted under neurology, 7.4% (2/27) were admitted to ICU, and the remaining 7.4% (2/27) were admitted under other specialities (infectious diseases and the surgical admissions centre). 29.6% (8/27) were transferred to another speciality during their admission (four to gastroenterology, two to neurology and two to general medicine).

Final diagnosis at the end of the In-Patient Admission

Of those that were diagnosed with an epileptic seizure: 44.4% (12/27) had an established diagnosis of epilepsy (diagnosis documented in the medical records or reported by the patient as being made by an appropriately qualified doctor), 22.2% (6/27) had a history of recurrent seizures without an established diagnosis of epilepsy, and none) had experienced a first fit. 14.8% (4/27) were diagnosed with an acute symptomatic seizure and 7.4% (2/27) with a non-epileptic attack.

Discharge and referral

66.7% (18/27) were eventually discharged home from the hospital ward. All 18 were fully recovered at discharge. 11.1% (3/27) self-discharged without waiting for medical assessment. Of the patients who were discharged, 33.3% (6/18) had no documented referral or follow-up. 44.4% (8/18) were referred to an epilepsy clinic and 11.1% (2/18) were referred to an epilepsy specialist nurse. 2/6 (33.3%) patients with no referral were already under the care of the epilepsy clinic and may have had direct access to their services making formal referral unnecessary and one patient (1/18, 5.6%) already had an epilepsy clinic appointment scheduled for the next day.

3) Epilepsy clinic data

63.4% (52/82) of all patients transported to the ED during the study period had been seen in the only specialist epilepsy clinic in the city. 51.9% (27/52) of these had been seen before the index event and 25/52 (48.1%) had been seen after the index event. In 75.0% (39/52) of these patients a diagnosis of epilepsy was made in the clinic (either before or after the index event). In 66.7% (26/39), the diagnosis was localisation-related epilepsy, in 17.9% (7/39) it was generalised epilepsy, in 15.4% (6/39) the epilepsy type was undetermined. In 15.4% (8/52) a diagnosis of (PNES) was made in the epilepsy clinic.

4) Data from all sources

Epilepsy medication

38.6% (32/83) had a documented history of AED use at the time of the index event: 56.3% (18/32) were receiving mono-therapy and 43.8% (14/32) poly-therapy. A suspicion of non-compliance with medication was documented in 18.8% (6/32).

General management and seizure-related injuries

AED regimes were changed or AEDs started during the hospital attendance/admission in 16.9% (14/83) of cases (in the ED or on the wards). Excluding the treatment of injuries, 36.1% (30/83) received some form of acute medical treatment (including complex treatments, such as for alcohol withdrawal, as well as relatively minor treatments such as pain relief with paracetamol or codeine). 7.2% (6/83) of incidents sustained an injury but only 1.2% (1/83) received major treatment (defined as that which probably required an acute hospital) for their injury (shoulder dislocation) and 2.4% (2/83) received minor treatment (defined as that which probably could have been delivered elsewhere) (wound care and treatment for an avulsed toenail). Although there was no tangible intervention in many incidents, all the patients received monitoring, assessment and diagnosis from a doctor and/or other clinicians.

Investigations

22.9% (19/83) had neuroimaging at some point during their attendance or admission. No patients had an EEG performed in the ED or as an in-patient. EEG tests, if considered necessary, were carried out as routine outpatient tests after the patient's discharge from their emergency care episode.

Seizure recurrence

In 73.5% (61/83) of incidents, the index event was the only seizure the patient had experienced in the 24 hours prior to their arrival in the ED. 21.7% (18/83) had experienced at least one other seizure in the previous 24 hours ('recurrent seizures'). Of those admitted after a single seizure, 14.8% (9/61) went on to have a subsequent seizure(s) in hospital. Of those with recurrent seizures, 27.8% (5/18) went on to have subsequent seizures in hospital. A Chi-Square test of independence was performed to examine the relationship between seizure presentation on arrival (single or recurrent) and seizure recurrence during the hospital stay. The relationship was not significant, χ^2 (1, *N*=83) = 1.38, p = 0.24. 10.8% (9/83) of patients had emergency medication administered by either a carer or ambulance

crew before arrival in the ED. Of these, 77.8% (7/9) were either still seizing on arrival in the ED or went on to have recurrent seizures during their hospital attendance.

Best Available Aetiological Explanation for the Index Event

The majority of suspected seizures in EPIC2 were epileptic 68/91 (74.7%) (including acute symptomatic seizures) but only 28/91 (30.8%) had a diagnosis of epilepsy. The epileptic seizures fall into the following four categories: a first epileptic seizure (13.2%, 12/91), an epileptic seizure in a patient with a formal diagnosis of epilepsy (30.8%, 28/91) an epileptic seizure in a patient known to have recurrent seizures but without a formal diagnosis of epilepsy (20.9%, 19/91) and acute symptomatic seizures in 9.9% (9/91). The other two important diagnostic categories were PNES 11.0% (10/91) and cardiogenic events 9.9% (9/91). The best available aetiological explanation for the index event is summarised in Figure 3 and Figure 4 shows diagnoses at each stage in the care pathway.

Diagnostic accuracy in the ED

87.8% (72/82) of diagnoses recorded at time of initial ED admission concurred with diagnoses made after more specialist or prolonged assessment during an inpatient stay or in a specialist in clinic. In those with an ED diagnosis of epileptic seizure, 98.3% (58/59) had a concordant diagnosis after inpatient admission or more specialist review.

DISCUSSION

Aetiology and Significance of Emergency Calls for Suspected Seizures

This is the first study to accurately quantify diagnoses amongst pre-hospital patients after a suspected seizure. Our data show that 74.7% of our patients had suffered an epileptic seizure, 11.0% a PNES and 9.9% a cardiogenic event (see Figure 3). The patients with epilepsy fall into three sub-groups all of whom could benefit from urgent review by an epilepsy specialist after a seizure. This also applies to the patients with PNES. Despite clear clinical need for specialist review our data is consistent with other large studies (5) which show that most patients are discharged without the input of an epilepsy specialist or follow-up. This leaves all these patients (not just those with epilepsy and PNES) at risk of recurrence and the associated morbidity, mortality and health services costs of these events.

Medical Emergencies and Clinical Risk Management

A large majority of the patients in our study were not acutely unwell on arrival at hospital. These results are consistent with qualitative data suggesting that a major factor in deciding to transport patients to hospital after a suspected seizure is lack of confidence amongst paramedics rather than true clinical need (2) (3). We were unable to define the exact proportion of patients that were potentially suitable for community management without transport to hospital or discharge from ED. This would require a criterion-based approach and further research would be required to define criteria which can be used to identify patients suitable for non-transport and how to overcome barriers to community management such as the presence of other clinical problems, risk stratification for recurrence of seizures, appropriate levels of supervision and safe management of the post-ictal phase.

The risk of seizure recurrence and the phenomenon of seizure clusters are a major factor in management decisions by clinicians but they are poorly understood (32). We are not aware of any prospective studies specifically looking at the short-term risk of seizure recurrence in the community. The published evidence in this area focusses on long-term recurrence risk after a seizure (33) (34) and the treatment of status epilepticus (35) (defined as ongoing seizure activity or recurrent seizures). Our data showed that, further recurrence is not more likely in patients who

have presented with more than one seizure, compared with those who present with a single seizure, but the numbers in each group were small and further research is required.

Non-Compliance, Alcohol and Difficult to Reach Groups

20.9% (19/91) of patients in our study with recurrent seizures did not have a formal epilepsy diagnosis. This result is consistent with the NASH audit (5), a large national audit conducted in the NHS, and it is not clear why this might be the case. We did not collect data to analyse this phenomenon further but we did find that alcohol use and illicit drugs were common clinical problems as was non-adherence with AED treatment. Non-adherence is associated with increased seizure frequency, adverse outcomes and increased hospital attendance/admission and higher health care costs (36) (37) (38). These data suggest that these patients may not understand the importance and benefits of medical advice, may be socially isolated and are perhaps living chaotic lifestyles. Simply improving access to medical services may not be an effective solution and more active outreach programmes may be required to reach this group (39).

Demographics, Re-Attendance and Specialist Review

5.1% (4/79) of our patients re-attended within the one-month study period. This probably under-estimates the true repeat attendance rate because of the short time window. Other studies have estimated this figure as to be as high as 60% within one year (40). The age-histogram of our cohort was uni-modal with a cut-off at age 16 (children were excluded) and a peak incidence at age 40. However, the age-related incidence curve of epilepsy has two peaks, one in childhood and the other in old age (41). This inconsistency which has been reported elsewhere (42) may be explained by underlying seizure frequency in this group but other factors are likely to be more important such as alcohol use and thresholds for accessing care (43) (44). Consistent with the NASH audit, our data has shown sub-optimal rates of referral to specialised epilepsy services and low rates of intervention such as in-patient specialist review, epilepsy-specific investigations or modification of AEDs.

Conclusions

Suspected seizures generate significant demand for emergency care (pre-hospital and hospital). Most suspected seizures are epileptic and often reflect failed ambulatory care for epilepsy. Emergency calls to ambulance services are an opportunity to improve seizure freedom rates by facilitating urgent review by a specialised epilepsy service. Many patients do not require emergency hospital treatment and there is the potential to develop pathways which both avoid unnecessary hospital attendance/admission and facilitate specialised review. The EPIC study (EPIC1 and EPIC2) provides good quality data to stimulate further research and to conceptualise the reconfiguration of services which aim to maximise seizure freedom rates in people with epilepsy and to prevent avoidable attendances at hospital.

Ethics approval: This study was categorised as a service evaluation and received approval from the Clinical Governance Group at YAS, from the Clinical Effectiveness Unit at STH and from the University of Sheffield Research Ethics Committee (Ref 002558). We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Data Sharing Statement: No data sharing agreements are in place but the authors welcome queries from people interested in viewing the original data.

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Contributorship Statement

The research was suggested by MR and RAG. They provided important advice and comments on the protocol and manuscript throughout. JMD took the lead with the study design, contacting collaborators, submitting ethics applications and other permissions, supervision of HD and writing the manuscript. HD took the lead for data collection, data analysis, presentation and interpretation of the results. She wrote some parts of the manuscript and reviewed the manuscript throughout its preparation by JMD. SM and JS were involved in study design, data collection and provided advice and comments on the protocol and manuscript throughout. JMD and HD and joint first authors and RAG and MR are joint senior authors.

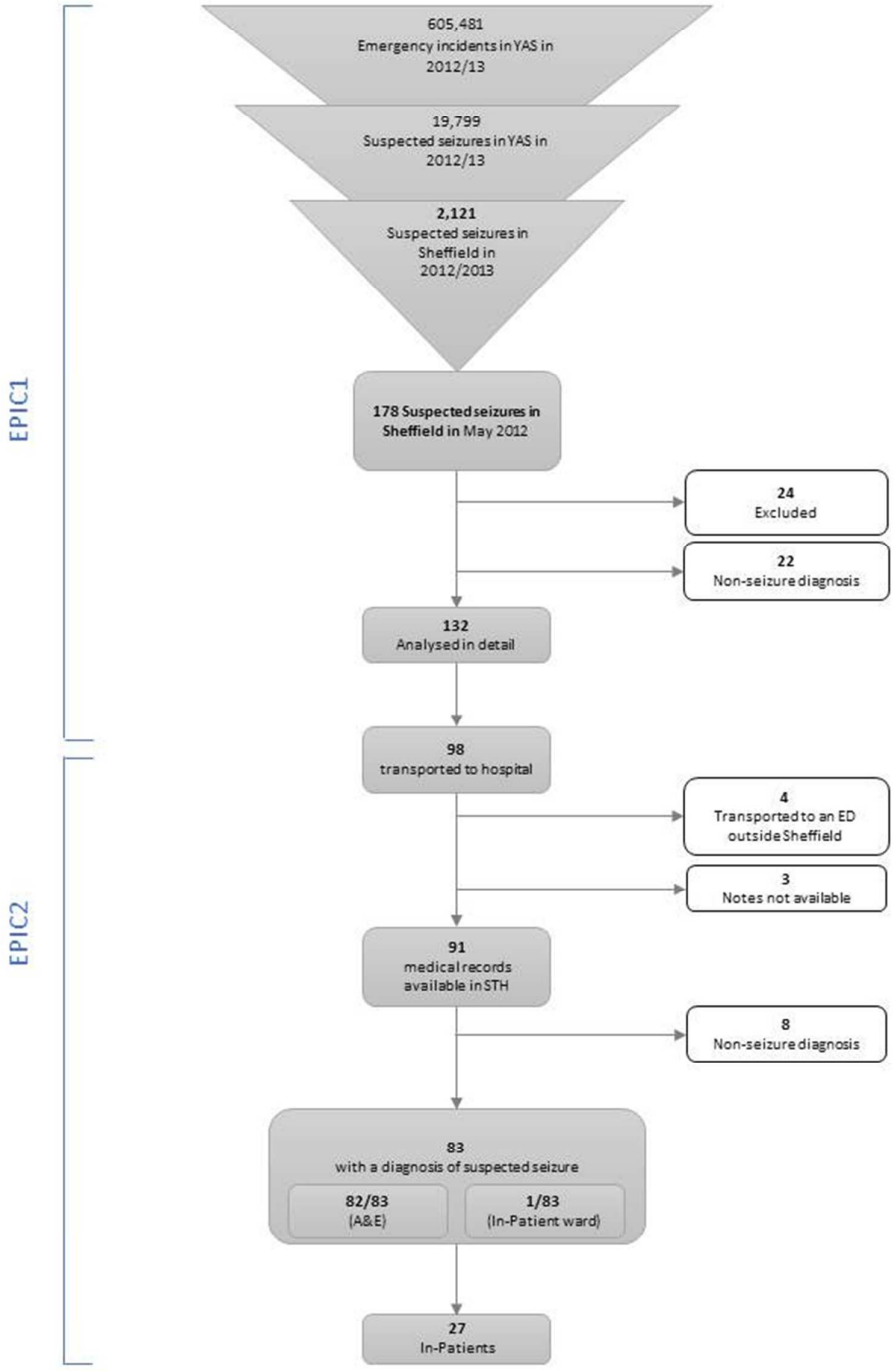


Figure 1. Flow chart to illustrate the care pathway and exclusions throughout the EPIC study (EPIC1 and EPIC2). The EPIC1 exclusions were: missing/inadequate data (18/178) and miscellaneous, for example, hoax call (6/178). The non-seizure diagnoses in EPIC1 were: syncope (3), intoxicated/passed out (2), tremor/spasm (2), fall (2), rigours (2), twitching (1), panic attack (1), anxiety/hyperventilation (2), abnormal behaviour (1), social/miscellaneous/inappropriate (6). The non-seizure diagnoses in EPIC2 were (5/8 vasovagal, 1/8 syncope, 1/8 complete heart block, 1/8 'collapse').

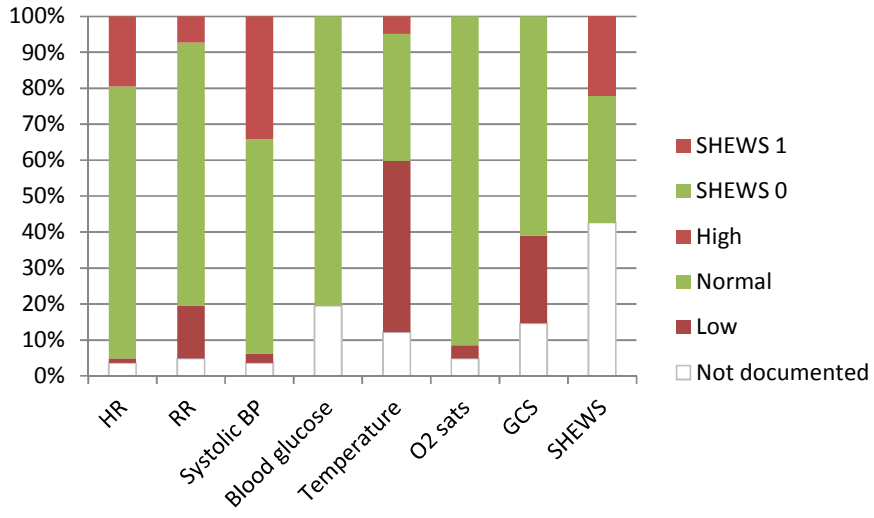


Figure 2 Physiological parameters and the Sheffield Early Warning Score (SHEWS) for each of the patients on arrival in ED. No patients had a SHEWS score recorded that was higher than 1. HR = heart rate, RR = respiratory rate, BP = blood pressure. O_2 sats. = oxygen saturations, GCS = Glasgow coma score.

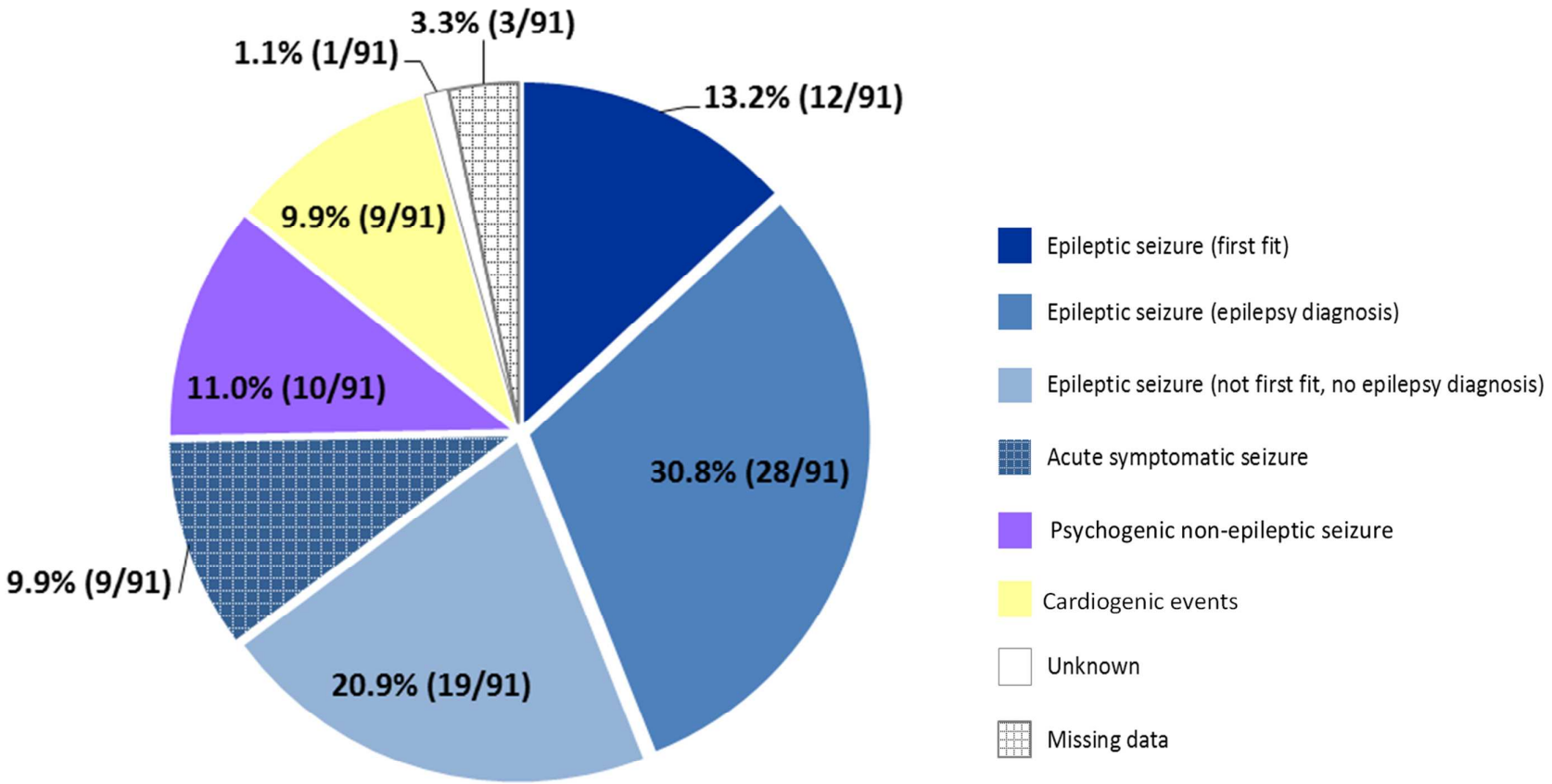
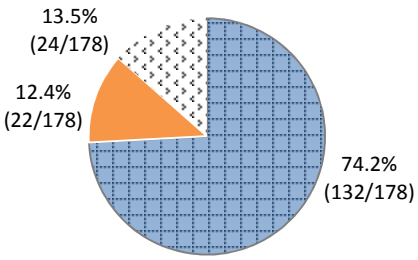


Figure 3: Best available aetiological explanation for the index event. Acute symptomatic causes were: alcohol withdrawal (6), head injury (1), hypoglycaemia (1), and transient ischaemic attack (1). The cardiogenic events: vasovagal episode (6), syncope (1), complete heart block (1), and collapse (1).

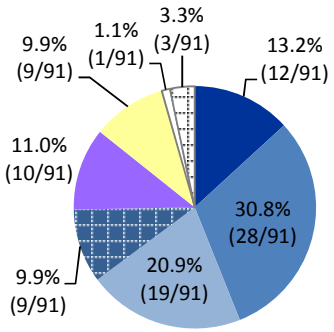
Pre-hospital Diagnosis (EPIC1)

a)

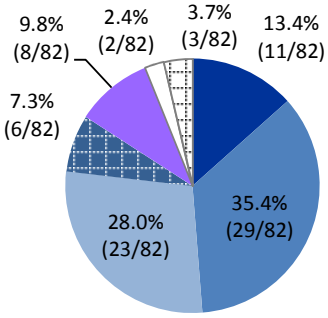


Hospital Diagnoses (EPIC2)

b) Best Available Diagnosis (EPIC2)



c) Emergency Department Diagnosis (EPIC2)



d) In-patient Diagnosis (EPIC2)

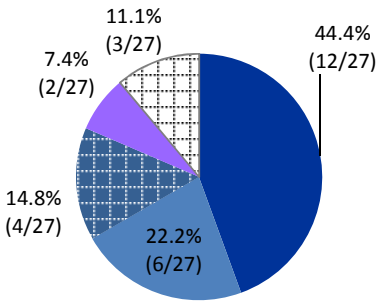


Figure 4. Data from EPIC1 and EPIC2 to illustrate diagnoses, exclusions and missing data at each stage in the care pathway.

Pre-Hospital Diagnoses (Fig a)

In Sheffield May 2012 there were 178 suspected seizures for which 999 was called. 24/178 were excluded and 22/178 were not seizures leaving 132/178 suspected seizure incidents that were studied in detail in EPIC1. Exclusions: missing/inadequate data (18/178, 10.1%), miscellaneous e.g. hoax call (6/178, 3.4%). The clinical impression of the ambulance clinicians was that there was no evidence of seizure activity in 22/178 (12.4%). Not seizure diagnoses: syncope (3), intoxicated/passed out (2), tremor/spasm (2), fall (2), rigours (2), twitching (1), panic attack (1), anxiety/hyperventilation (2), abnormal behaviour (1), social/miscellaneous/inappropriate (6).

Hospital Diagnoses (Figs b-d)

Best Available Diagnoses

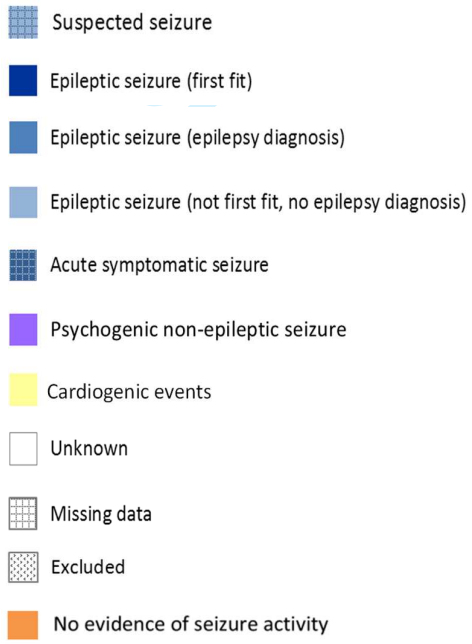
The hospital notes of 91/132 were analysed in detail (98/132 were transported to hospital but 4/98 transported to an hospital outside Sheffield and 3/98 sets of notes were not available). The best available data for the aetiology of the 91 events is shown in Figure 4b (this is based on data from all sources: ED notes, in-patient notes and epilepsy clinic notes). Aetiology of acute symptomatic seizures: alcohol withdrawal (6), head injury (1), hypoglycaemia (1) and transient ischaemic attack (1).

Emergency Department Diagnoses

82/91 that were transported to ED at STH were suspected seizures (Fig 4c). 9/91 were given non-seizure diagnoses: vasovagal episode (6), syncope (1), complete heart block (1), and collapse (1). NB/ An addition 1/91 suspected seizure was transported direct to an in-patient ward so 82/91 were diagnosed with suspected seizures.

In-Patient Diagnoses

27/132 were admitted to an in-patient ward (Fig 3d).



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Location	Variable	Categories	Notes
ED	ED area	1 Minors 2 Majors 3 Resus 4 Not documented	The highest dependency area that the patient went to during the ED attendance.
	HR on arrival	1 Normal 2 Low 3 High 4 Not documented	Normal heart rate (HR) = 60-100 beats per minute
	RR on arrival	1 Normal 2 Low 3 High 4 Not documented	Normal respiratory rate (RR) = 14-18 breaths per minute (male) and 16-20 breaths per minute (female)
	Systolic BP on arrival	1 Normal 2 Low 3 High 4 Not documented	Normal systolic blood pressure (BP) = 100-140 mmHg
	BM on arrival	1 Normal 2 Low 3 High 4 Not documented	Normal blood glucose (BM) = 3.5-11.1 mmol/l
	GCS on arrival	3 4 5 etc. 15 16 Not documented	GCS (Glasgow coma scale) is used to assess the state of consciousness of the patient. 3/15 (lowest score) = completely unresponsive 15/15 (highest score) = conscious, orientated, and responding well to questions

	Temperature on arrival	1 Normal 2 Low 3 High 4 Not documented	Normal temperature = 36.5-37.5°C
	O_2 sats	1 Normal 2 Low 3 Not documented	Low O_2 sats = < 94%
	SHEWS score on arrival	0 1 2 3 4 Not recorded	Sheffield hospitals early warning score (SHEWS) is an early warning system used to determine the degree of illness of a patient based on their HR, systolic BP, RR, temperature and level of alertness. Based on a scale from 0 to 3, where 0 is normal and 1-3 are outside the normal range, and 3 represents the greatest deviation from normal.
	Formal diagnosis of epilepsy?	1 Yes 2 No	A 'formal diagnosis of epilepsy' was as documented by the ED doctor on the ED card - as part of the medical history or documentation that the patient was known epileptic. Formal diagnosis means a diagnosis made by an appropriately qualified clinician - in most cases this would be a neurologist by could also include general physicians. Includes both idiopathic and symptomatic epilepsies. Non-epileptic attacks and alcohol-related seizures were not included unless a clear diagnosis of epilepsy was recorded as well.
	Documented history of PNES	1 Yes 2 No	

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	Suspicion of non-epileptic seizure documented	1 Yes 2 No	If clinician had a suspicion that the event was a non-epileptic attack.
	Seizure presentation on arrival (1)	1 Single seizure 2 Recurrent seizures	This variable was copied directly from the pre-hospital (EPIC1) data, as it is difficult to determine recurrence from the ED card. Seizures were divided into patients for which this was their first seizure in the previous 24 hours (single) and patients who had experienced more than one seizure in the previous 24 hours (recurrent).
	Seizure presentation on arrival (2)	1 Complete 2 Ongoing	
	Seizures during ED attendance	1 Yes 2 No	This includes unwitnessed seizures where the patient was found to be post-ictal.

	Other clinical problem (1)	1 None 2 Syncope 3 Stroke/TIA/CVA 4 Hypoglycaemia 5 Arrhythmias 6 Alcohol 7 Injury 8 Drugs 9 Other (specify)	This encompasses other clinical problems which may be acutely present in addition to the seizure, which requires hospital treatment and/or assessment. This would include, for example, a head injury requiring CT but no treatment, but would exclude bruising/grazes to the limbs. They may be the cause of the seizure, a complication of the seizure, or unrelated to the seizure. Arrhythmias: Does not include sinus tachycardia or sinus bradycardia. Alcohol: refers to any recent alcohol use and past alcohol abuse suggested by the past medical or drug history and of the patients such as a history of withdrawal seizures or alcohol dependent. The only exception is where alcohol consumption was indicated but was specifically noted to be below the recommended daily allowance (2-3 units for women, 3-4 units for men) with no reference to previous alcohol abuse. Drugs: includes illicit drug use as well as overdose on prescribed medication.
	Other clinical problem (1) (other)		

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	Other clinical problem (2)	1 None 2 Syncope 3 Stroke/TIA/CVA 4 Hypoglycaemia 5 Arrhythmias 6 Alcohol 7 Injury 8 Drugs 9 Other (specify)	
	Other clinical problem (2) (other)		
	Other clinical problem (3)	1 None 2 Syncope 3 Stroke/TIA/CVA 4 Hypoglycaemia 5 Arrhythmias 6 Alcohol 7 Injury 8 Drugs 9 Other (specify)	
	Other clinical problem (3) (other)		

	Documented alcohol dependency	1 Yes 2 No	Where there is a clear statement that the patient has documented current alcohol dependency. Alcohol dependency is defined by the DSM-IV criteria as: “A maladaptive pattern of alcohol use leading to clinically significant impairment or distress, as manifested by three or more of the following seven criteria, occurring at any time in the same 12-month period: Tolerance; withdrawal; alcohol is often taken in larger amounts or over a longer period than was intended; there is a persistent desire or there are unsuccessful efforts to cut down or control alcohol use; a great deal of time is spent in activities necessary to obtain alcohol, use alcohol or recover from its effects; important social, occupational, or recreational activities are given up or reduced because of alcohol use; alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the alcohol”.[180]

	Clinical condition on arrival	1 Alert 2 Post-ictal 3 Ictal 4 Other (specify)	Taken from the nurses notes on arrival or ED notes if the clinical condition on arrival is clearly stated. The postictal state is the abnormal condition occurring between the end of an epileptic seizure and return to baseline condition. We operationalised our definition of post-ictal to only include symptoms that were a barrier to the patient being safely discharge home. It specifically did not include tiredness, headache or myalgia. The main feature which would mean safe discharge was not possible are reduced consciousness, significant drowsiness, neurological deficits etc.
	Clinical condition on arrival (other)		
	Seizure-related Injuries	1 Yes (specify) 2 No	Here injuries are only included if they required hospital assessment or treatment (in ED or as in-patient).
	Injuries (specify)		

	Fully recovered at the end of attendance	1 Yes 2 No	The patient was fully recovered if they had returned to their normal level of functioning with no acute medical problems that required hospital assessment and/or treatment, and were not post-ictal. We operationalised our definition of post-ictal to only include symptoms that were a barrier to the patient being safely discharge home. It specifically did not include tiredness, headache or myalgia. The main feature which would mean safe discharge was not possible are reduced consciousness, significant drowsiness, neurological deficits etc.
	Pregnancy	1 Yes 2 No	
	Illicit drug abuse documented/suspected	1 Yes 2 No	
	Medication in ED (1)	1 Yes 2 No	Anticonvulsant medication used for the termination of seizures.
	Medication in ED (2)	1 Lorazepam 2 Phenytoin 3 Diazepam 4 Midazolam 5 Other (specify)	
	Medication in ED (2) (Other)		
	HES code (local)		
	HES code (national)		

	ED disposal	1 Discharged home 2 Discharged elsewhere 3 Admitted (specify where) 4 Death 5 Self-discharge	
	Admitted to	1 General medicine 2 ICU 3 Neurology 4 Other (specify where)	
	Admitted to (other)		
	Referral / Post-seizure follow up advice	1 Epilepsy clinic/first fit clinic 2 Epilepsy specialist nurse (referral or verbal advice) 3 GP 4 Other	The patient was said to have been referred to their GP if the patient was advised to see their GP for reasons relating to the care of their epilepsy. The ED physician may have written a letter to the GP.
	Referral (other)		
	Final diagnosis/impression of ED clinician (1)	1 Epileptic seizure (first fit) 2 Epileptic seizure (not first fit, no formal diagnosis of epilepsy) 3 Epileptic seizure (formal epilepsy diagnosis) 4 Non-epileptic attack	This is the diagnosis of the suspected seizure event. "not seizure" cases were included in this variable. Here, a 'formal epilepsy diagnosis' is one documented by the ED clinician.

		5 Acute symptomatic seizure (specify) 6 Not seizure (specify)	
	Final diagnosis/impression of ED clinician (1) (acute symptomatic - specify)		
	Final diagnosis/impression of ED clinician (1) (not seizure - specify)		
	Final diagnosis/impression of ED clinician (2)		
	Indication for admission	1 Social 2 Medical (seizure-related) (specify) 3 Medical (not seizure-related) (specify)	Social admissions are those where there is no medical reason for admission e.g. unable to put care package in place for discharge.
	Indication for admission (seizure-related - specify)		
	Indication for admission (not seizure-related - specify)		
In-patient	Date of admission		
	Date of discharge		
	Duration of admission		

	Seizures during admission	1 Yes 2 No	This includes unwitnessed seizures where the patient was found to be post-ictal.
	Final discharge destination	1 Home 2 Death 3 Self-discharge 4 Other (specify)	Home' was defined as the current or usual residence of the patient. This included rented or owned properties as well as institutions such as nursing or care homes. If the patient was discharged somewhere new, for example a patient previously living at home being discharged to a care home, this was documented as 'other'.
	Final discharge destination (other)		
	Transferred to another speciality during inpatient admission	1 Yes (specify) 2 No	
	Transferred to another speciality during inpatient admission (specify)		
	Fully recovered at the end of attendance	1 Yes 2 No	The patient was fully recovered if they had returned to their normal level of functioning with no acute medical problems that required hospital assessment and/or treatment, and were not-post ictal. We operationalised our definition of post-ictal to only include symptoms that were a barrier to the patient being safely discharge home. It specifically did not include tiredness, headache or myalgia. The main feature which would mean safe discharge was not possible are reduced consciousness, significant drowsiness, neurological deficits etc.

	Referral / Post-seizure follow up advice	1 Epilepsy clinic/first fit clinic 2 Epilepsy specialist nurse (referral or verbal advice) 3 GP 4 Other	The patient was said to have been referred to their GP if the patient was advised to see their GP for reasons relating to the care of their epilepsy. The physician may have written a letter to the GP.
	Referral (other)		
	Diagnosis at discharge	1 Epileptic seizure (first fit) 2 Epileptic seizure (not first fit, no formal diagnosis of epilepsy) 3 Epileptic seizure (formal epilepsy diagnosis) 4 Non-epileptic attack 5 Acute symptomatic seizure (specify) 6 Not seizure (specify)	Taken from discharge sheet, if no discharge sheet then final diagnosis documented in progress record or clerking sheet.
	Diagnosis at discharge (acute symptomatic - specify)		
	Diagnosis at discharge (not seizure - specify)		
Epilepsy clinic	Ever seen in epilepsy clinic?	1 Yes 2 No	

	Seen in epilepsy clinic before the index event?	1 Yes 2 No	
	Seen in epilepsy clinic (or specialised epilepsy services) as a result of the index event?	1 Yes 2 No	
	Does the patient have a diagnosis of epilepsy that was made in the epilepsy clinic? If yes, specify.	1 Yes 2 No	Regardless of when this diagnosis was made.
	Epilepsy clinic epilepsy diagnosis	1 Localisation-related epilepsy (focal, local, partial) 2 Generalised epilepsy 3 Undetermined whether focal or general 4 Special syndromes	These categories are based on the ILAE Proposal for Revised Classification of Epilepsies and Epileptic Syndromes - Epilepsia (1989) 30(4): 389-399.
	Does the patient have a diagnosis of PNES that was made in the epilepsy clinic? If yes, specify.	1 Yes 2 No	
From all sources	AEDs	1 Yes (state which) 2 No	AEDs at the time of the ED attendance in May 2012.

	Which AED (1)	1 Sodium valproate 2 Carbamazepine 3 Levetiracetam 4 Phenytoin 5 Phenobarbital 6 Not documented 7 Other (state which)	
	Which AED (1) (Other)		
	Which AED (2)	1 Sodium valproate 2 Carbamazepine 3 Levetiracetam 4 Phenytoin 5 Phenobarbital 6 Not documented 7 Other (state which)	
	Which AED (2) (Other)		
	Non-concordance with AEDs	1 Yes 2 No	At the time of the event in May 2012. This refers to patients who have not taken their AED medication as prescribed including cases where patients have run out of AEDs or forgotten to take their medication, as well as patients who have overdosed. Includes suspected non-adherence.

	"Best available" aetiological explanation for the index event .	1 Epileptic seizure (first fit) 2 Epileptic seizure (not first fit, no diagnosis of epilepsy) 3 Epileptic seizure (epilepsy diagnosis) 4 Non-epileptic attack 5 Acute symptomatic seizure (specify) 6 Not seizure (specify)	"Not seizure" cases included in this variable.
	"Best available" aetiological explanation for the index event (acute symptomatic - specify)	1 Yes 2 No	
	"Best available" aetiological explanation for the index event (not seizure - specify)	1 Yes 2 No	
	Hospital management		These variables pertain to key features of hospital management received by the patient. The list is not exhaustive. This includes treatments that were not specifically to treat the seizure in the case of complex patients with more than one clinical problem.
	Expert opinion	1 Yes 2 No	Expert opinion from any hospital specialist on diagnosis, investigations or management.
	Was an AED regime started or modified during the admission?	1 Yes 2 No	Either in ED or in-patient.
	Neuroimaging	1 Yes 2 No	Acute neuroimaging especially CT head scan.

	Acute medical treatment (specify)	1 Yes 2 No	Excluding injuries. Including: parenteral drugs to terminate seizures, IV fluids, etc.
	Acute treatment of injuries (major)	1 Yes 2 No	Dressings, sutures, shoulder relocation etc. which probably required hospital treatment.
	Acute treatment of injuries (minor)	1 Yes 2 No	Dressings, sutures, shoulder relocation etc. which probably did not require hospital treatment.
	Other (specify)	1 Yes 2 No	
	Other (specify)		Narrative account of hospital treatment

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	3-5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	3-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3-5
Bias	9	Describe any efforts to address potential sources of bias	3-5
Study size	10	Explain how the study size was arrived at	3-5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	3-5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	3-5
		(*b*) Describe any methods used to examine subgroups and interactions	3-5
		(*c*) Explain how missing data were addressed	3-5
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	3-5
		(*e*) Describe any sensitivity analyses	N/A

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5-8
		(b) Give reasons for non-participation at each stage	5-8
		(c) Consider use of a flow diagram	Fig 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5-8
		(b) Indicate number of participants with missing data for each variable of interest	5-8
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	5-8
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	5-8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5-8
		(*b*) Report category boundaries when continuous variables were categorized	5-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5-8
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5-8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8-9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8-9, 1
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-9
Generalisability	21	Discuss the generalisability (external validity) of the study results	8-9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Cross-sectional study of the hospital management of adult patients with a suspected seizure (EPIC2)

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Cross-sectional study of the hospital management of adult patients with a suspected seizure (EPIC2)

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Abstract

Objective

To determine the clinical characteristics, management and outcomes of patients taken to hospital by emergency ambulance after a suspected seizure.

Design

Quantitative cross-sectional retrospective study of a consecutive series of patients.

Setting

An acute hospital trust in a large city in England.

Participants

In 2012/13 the regions ambulance service managed 605,481 emergency incidents, 74,141/605,481 originated from Sheffield (a large city in the region), 2,121/74,141 (2.9%) were suspected seizures and 178/2,121 occurred in May 2012. We undertook detailed analysis of the medical records of the 91/178 patients who were transported to the city's acute hospital. After undertaking a retrospective review of the medical records the best available aetiological explanation for the seizures was determined.

Results

The best available aetiological explanation for 74.7% (68/91) of the incidents was an epileptic seizure, 11.0% (10/91) were psychogenic non-epileptic seizures (PNES) and 9.9% (9/91) were cardiogenic events. The epileptic seizures fall into the following four categories: first epileptic seizure (13.2%, 12/91), epileptic seizure with a historical diagnosis of epilepsy (30.8%, 28/91), recurrent epileptic seizures without a historical diagnosis of epilepsy (20.9%, 19/91), and acute symptomatic seizures (9.9%, 9/91). Of those with seizures (excluding cardiogenic events), 2.4% (2/82) of patients were seizing on arrival in the Emergency Department (ED), 19.5% (16/82) were post-ictal and 69.5% (57/82) were alert. 63.4% (52/82) were discharged at the end of their ED attendance and 36.5% (19/52) of these had no referral or follow-up.

Conclusions

Most suspected seizures are epileptic seizures but this is a diagnostically heterogeneous group. Only a small minority of patients require emergency medical care but most are transported to hospital. Few patients receive expert review and many are discharged home without referral to an epilepsy specialist leaving them at risk of further seizures and the associated morbidity, mortality and health services costs of poorly controlled epilepsy.

Strengths and Limitations of this Study

This is the first study to describe the clinical characteristics, management and outcomes of patients taken to hospital by emergency ambulance after a suspected seizure. The themes identified in this paper resonate with previous studies reflecting practice across the world.

The triangulation of data drawn from pre-hospital records and hospital medical records (ED, in-patient and epilepsy clinic) resulted in richer and more robust data than data drawn from a single source.

Our sample was small and data extraction could have been given added rigour by involving a second rater. Manual data extraction from clinical notes is time consuming which constrained our study methods and is the major limitation to the study.

Although this study was conducted in a single hospital trust it is one of the largest acute care providers in the United Kingdom and its Emergency Department provides emergency services for a large socioeconomically mixed population.

INTRODUCTION

Background

Epilepsy is an ambulatory care sensitive condition (ACSC) (1) and sub-optimal ambulatory care (also known as routine or scheduled care) leads to unnecessary demand for emergency care (2). The majority of epileptic seizures do not require emergency treatment but ambulance services are often called. Calls are rapidly triaged by specialised call handlers, an emergency response vehicle is usually dispatched, but by the time the ambulance arrives most seizures and have terminated spontaneously, nevertheless the majority of patients are transported to hospital (3) (4). Precise estimates vary, but in England (population 52.96 million, 42.96 million adults) seizures give rise to approximately 211,000 calls to ambulance services per year (3.3% of all emergency calls) (5). It is estimated that there are 60,000 seizure-related Emergency Department (ED) attendances per year (2-3% of all attendances) (6), and 40,000 hospital admissions which represent 9.5% of all admissions for ACSCs (6) (7). There are currently no published studies of care pathways for people who have presented as an emergency with a suspected seizure which aim to facilitate urgent medical review (8) and avoid unnecessary transport to hospital (9, 10). Clinical guidelines for paramedics provide little guidance on the community management and/or referral of patients after a seizure and focus almost exclusively on medical emergencies which are rare (11).

An epileptic seizure may be the result of sub-optimal treatment and should lead to consideration of whether specialist review is required. But this opportunity to prevent further seizures and/or to refine the patients emergency care plan is often missed (6) (8) (12) (13). Many patients therefore unnecessarily remain at risk of further seizures and the associated morbidity (14), mortality (15) and health services costs (2) (16) of poorly controlled epilepsy. Approximately 70% of people with epilepsy (PWE) could become seizure-free (≥12 months) with optimal treatment (17) (18) (19) but internationally actual seizure freedom rates are significantly lower than this. There is little published data on seizure-freedom rates in individual countries (17) (20) (21) and there are no published international comparisons of seizure-freedom rates. The overall seizure freedom rate in the UK is thought to be 50% (22) (23) (24, 25). Some epilepsy services in the United Kingdom (UK) are world-leading but the quality of care is highly geographically variable, and patients in many areas do not have access to optimal monitoring and treatment. This means that as many as one-in-five patients with epilepsy may be unnecessarily having seizures (17).

EPIC (Epilepsy Pre-Hospital Interventions and Care) Study

The EPIC study was designed to generate data to support improvements in emergency care after a suspected seizure. Despite its importance, this aspect of epilepsy care has received relatively scant academic attention to date. In EPIC1 (5) we described the pre-hospital management of a series of consecutive incidents with suspected seizures. The present study, EPIC2, focusses on the sub-group of these patients that was transported to hospital after a suspected seizure with the aim of determining their clinical characteristics, their management and their outcomes based on data collected from ED, in-patient wards and the epilepsy clinic. The emergency care structure in the UK, with its universal access to healthcare, unitary emergency call handling service and non-overlapping ambulance service and emergency department provisions offers opportunities to researchers to study emergency presentations with seizures which do not exist in many other countries.

METHODS

Local Context and Patient Selection

YAS is a regional ambulance service in England (one of the four devolved nations of the UK) covering 9,656 square kilometres and it is the sole provider of ambulance and paramedic services for its population of 4,019,610 adults (4,954,876 adults and children) (26). Sheffield is one of the major

urban centres within the area served by YAS and has a population of 451,100 adults (551,756 adults and children) which is served by a single hospital-based Emergency Department (ED) for adults at the Northern General Hospital (NGH) site of the Sheffield Teaching Hospitals NHS Foundation Trust (STH) (27).

Case Ascertainment, Exclusions and Missing Data

Patients were retrospectively identified from the records of the Yorkshire Ambulance Service (YAS). Between 1 April 2012 and 31 March 2013 the Yorkshire Ambulance Service dealt with 605,481 emergency incidents in adults (≥16 years old). 19,799 (3.3%) of these incidents were suspected seizures, 2,121 originated from Sheffield (a large city in the region) and 178 occurred in May 2012. We analysed data from a sample month, May 2012, which was chosen after preliminary analysis of the summary statistics showed it to be a typical month (5). After non-seizure diagnoses and other exclusions were removed 132 incidents were analysed in detail and 98 were transported to hospital. The initial call-handling and out-of-hospital management of these patient was the focus of EPIC1 (5).

Of the 98 incidents from EPIC1 that were transported to hospital, 4/98 incidents were transported to an ED outside Sheffield and 3/98 patients were not identifiable on the STH's computer system so medical records were available for 91/98 incidents. The focus of this paper is the analysis of these 91 incidents although 8/91 (8.8%) incidents were given non-seizure diagnoses in ED so no further data was collected for these. Detailed data extraction was undertaken for the remaining 83 incidents. The care pathway from emergency call to discharge from hospital including exclusions is complex. It is summarised in Figure 1.

Data Collection and Analysis

Data were extracted by one of the authors (HD) using a data extraction tool (see Supplementary File) which was developed by all the authors and was revised after an initial pilot. Some variables such as the working diagnosis changed throughout the care pathway and so we report the results separately at each stage in the pathway: 1) ED, 2) in-patient wards, 3) out-patient epilepsy clinic and 4) combined data from all three sources. The data presented in section (4) was drawn together by HD from all available sources (ED notes, in-patient notes, epilepsy clinic notes) to document an overview of the hospital management of each incident taking into account the opinion of all the clinicians involved throughout the care pathway. This allowed triangulation of the data, which allowed resolution of inconsistencies between, for example, accounts in the ED notes and in the epilepsy clinic notes, and it allowed us to draw robust conclusions about the best available aetiological explanation for the index event. If the best available aetiological explanation for the suspected seizure was an epileptic seizure it allowed us to determine if the patient had a historical diagnosis of epilepsy.

In this paper we report the data as it was recorded in the notes by the clinicians involved in the incidents with as little interpretation from the authors as possible. Where interpretation was required we included definitions within the data collection tool to inform these judgements; these are described below. We analysed each incident separately (some patients attended more than once during the study period and therefore generated multiple incidents). To calculate the number of incidents in which all physiological parameters were normal we used the following parameters: heart rate (60-100bpm), respiratory rate (14-18 breaths per minute), systolic BP (100-140mmHg), blood glucose (3.5-11.1 mmol/l), temperature (36.5-37.5°C), O2 saturations (<94%) and GCS (15/15). We excluded low temperature (<36.5°C) from this calculation because it is very unlikely that any patients truly had hypothermia in May in England (a low temperature measurement is likely to reflect inaccuracy of peripheral temperature recording). We recorded the Sheffield Early Warning Score (SHEWS) which is based on the National Early Warning Score. SHEWS is a composite score based on heart rate, respiratory rate, oxygen saturation, systolic blood pressure, urine output and

consciousness level. A score above 0 identifies patients who may be acutely ill so that their care can be stepped-up: 1 = increase frequency of observations and inform nurse, 2 = hourly observations and consider medical review, 3 = immediate medical review. Numerical data was entered into SPSS which was used for calculating summary statistics. Chi-Square tests were used to assess relationships between categorical variables. Where there was missing data it was coded as such in SPSS. Variables with large numbers of missing data points were excluded from the analysis and are not reported in the Results. Small numbers of missing data points in specific variables are not reported in the Results.

Definitions

The latest International League Against Epilepsy (ILAE) definitions of epilepsy and seizures (28) (29) were applied during data collection. We categorised the indication for admission: medical (seizure-related), medical (not seizure-related) and social. Medical (seizure-related) admissions were those where the principal reason for admission was seizure(s), for example, patients who were still post-ictal at the end of their ED attendance. Medical (not seizure-related) admissions were those where the principal reason for admission was not a seizure, for example, lower respiratory tract infection or unexplained pyrexia. Social admissions were those where there was no medical reason for admission but it was not possible to discharge the patient directly from the ED e.g. because a home care package had to be put in place. We categorised those with and without a self-reported diagnosis of epilepsy prior to the index event. Historical diagnoses of epilepsy were determined from the records of the ED doctors and often only brief information was available. In addition to the seizure we determined if the patient had any other acute clinical problems. Alcohol was deemed to be a clinical problem if there was documentation of excessive alcohol ingestion which occurred around the time of the index event or if there was a history of alcohol abuse (such as alcohol dependency or withdrawal seizures). Patients were deemed to have recovered fully if they were recorded as having returned to their normal level of functioning with no acute medical problems that required hospital assessment and/or treatment, and were not thought to be post-ictal (notwithstanding tiredness, headache and myalgia).

RESULTS

Demographics and Repeat Attendances

The patients' median age was 40 (IQR 30, range 16-97). Males accounted for 54.2% of incidents. The 83 incidents relate to 79 patients. 4/79 (5.1%) patients generated two incidents during the one-month study period. The time intervals between the repeat attendances were: 1 day, 3 days, 13 days and 15 days.

Management in the Emergency Department

Past Medical History

82/83 incidents were seen in ED, one incident was admitted directly to a neurology ward (without being seen in ED). The ED records documented a history of a seizure disorder in 43.9% (36/82) of all incidents: epilepsy 36.6% (30/82), psychogenic non-epileptic seizures (PNES) 6.1% (5/82), epilepsy plus PNES 1.2% (1/82).

Clinical details

In 2.4% (2/82) of incidents the patient was seizing on arrival at the ED, 69.5% (57/82) were alert on arrival, 19.5% (16/82) were post-ictal and in 6/82 (7.3%) their status was not clear from the notes. All physiological parameters were normal (or not recorded) in 28/82 (34.1%) of incidents but often only one parameter was abnormal and often this was mild tachycardia or mild hypertension (see Figure 2). In the incidents in which the seizure had terminated prior to arrival in the ED, 76.25%

(61/80) had no subsequent seizures during their hospital stay. 17.5% (14/80) had recurrent seizures either in the ED or after transfer to a hospital ward. In 7.3% (6/82) of incidents emergency medication for the termination of seizures was administered in the ED. 70.7% (58/82) of cases had recovered fully by the end of the ED attendance.

Final Diagnosis at the End of the ED Attendance

In the opinion of the ED clinicians, 63/82 incidents were likely to have been epileptic seizures: 13.4% (11/82) had experienced a first fit, 35.4% (29/82) had experienced an epileptic seizure in the context of an historical diagnosis of epilepsy, 28.0% (23/82) had experienced an epileptic seizure with a history of recurrent seizures but without an historical diagnosis of epilepsy. 7.3% (6/82) were diagnosed with an acute symptomatic seizure. 9.8% (8/82) were diagnosed with a PNES. The diagnosis was unknown in 2.4% (2/82), and in 3.7% (3/82) no diagnosis was recorded.

Other Clinical Problems

47.6% (39/82) of cases had another clinical problem(s) in addition to the suspected seizure. This was sometimes secondary to the suspected seizure but was often unrelated or only tangentially related to it. 35.4% (29/82) had one additional clinical problem, 8.5% (7/82) had two, 2.4% (2/82) had three and 1.2% (1/82) had four. In total there were 53 additional clinical problems amongst the 82 incidents. 41.5% (22/53) of these were alcohol, 15.0% (8/53) were injuries, 9.4% (5/53) were illicit drug use and 34.0% (18/53) were 'other' (for example, brain tumour, pyrexia, acidosis, psychiatric problems and abdominal pain).

Discharge and Referral from ED

63.4% (52/82) of patients were discharged home at the end of their ED attendance, 31.7% (26/82) were admitted to an in-patient ward from ED (another patient who was taken directly to a ward by ambulance without attending ED), and 4.9% (4/82) self-discharged. The indication for admission was related to the seizure in 61.5% (16/26) of cases. In 26.9% (7/26) of cases it was due to a medical problem which was not obviously related to the seizure (e.g. chest infection, GI problems, infective rash) and in 11.5% (3/26) of cases the reason for admission was social. Of the patients who were discharged home from the ED, only 61.5% (32/52) had documented referral or follow-up advice. 34.6% (18/52) were referred to an epilepsy clinic, 25.0% (13/52) were referred to their GP, and 1.9% (1/52) were referred to an epilepsy specialist nurse. 36.5% (19/52) had no documented referral, and 52.6% (10/19) of these had not been seen in the epilepsy clinic before the event. There was a relationship between SHEWS and GCS on arrival in ED with disposal (admission or discharge). Patients with an abnormal SHEWS on arrival were more likely to be admitted to hospital and less likely to be discharged ($\chi 2$ (1, N=45) = 10.385, p=0.001), likewise for patients with a reduced GCS on arrival ($\chi 2$ (1, N=68) = 15.451, p=0.000085).

2) Inpatient Management

Length of stay and speciality

27 patients were admitted to an in-patient medical ward. The median duration of admission was 2.0 days (IQR 5.0, range 0-17). 66.7% (18/27) were admitted to a general medical ward, 18.5% (5/27) were admitted under neurology, 7.4% (2/27) were admitted to ICU, and the remaining 7.4% (2/27) were admitted under other specialities (infectious diseases and the surgical admissions centre). 29.6% (8/27) were transferred to another speciality during their admission (4 to gastroenterology, 2 to neurology and 2 to general medicine).

Final diagnosis at the end of the In-Patient Admission

Of those that were diagnosed with an epileptic seizure: 44.4% (12/27) had an historical diagnosis of epilepsy, 22.2% (6/27) had a history of recurrent seizures without an historical diagnosis of epilepsy,

and none) had experienced a first fit. 14.8% (4/27) were diagnosed with an acute symptomatic seizure and 7.4% (2/27) with a non-epileptic attack.

Discharge and referral

66.7% (18/27) were eventually discharged home from the hospital ward. All 18 were fully recovered at discharge. 11.1% (3/27) self-discharged without waiting for medical assessment. Of the patients who were discharged, 33.3% (6/18) had no documented referral or follow-up. 44.4% (8/18) were referred to an epilepsy clinic and 11.1% (2/18) were referred to an epilepsy specialist nurse. 2/6 (33.3%) patients with no referral were already under the care of the epilepsy clinic and may have had direct access to their services making formal referral unnecessary and one patient (1/18, 5.6%) already had an epilepsy clinic appointment scheduled for the next day.

3) Epilepsy clinic data

63.4% (52/82) of all patients with a suspected seizure who were transported to the ED during the study period had been seen in the only specialist epilepsy clinic in the city. 51.9% (27/52) of these had been seen before the index event and 25/52 (48.1%) had been seen after the index event. In 75.0% (39/52) of these patients a diagnosis of epilepsy was made in the clinic (either before or after the index event). In 66.7% (26/39), the diagnosis was localisation-related epilepsy, in 17.9% (7/39) it was generalised epilepsy, in 15.4% (6/39) the epilepsy type was undetermined. In 15.4% (8/52) a diagnosis of (PNES) was made in the epilepsy clinic.

4) Data from all sources

Epilepsy medication

38.6% (32/83) had a documented history of anti-epileptic drug (AED) use at the time of the index event: 56.3% (18/32) were receiving mono-therapy and 43.8% (14/32) poly-therapy. A suspicion of non-compliance with medication was documented in 18.8% (6/32).

General management and seizure-related injuries

AED regimes were changed or AEDs started during the hospital attendance/admission in 16.9% (14/83) of cases (in the ED or on the wards). Excluding the treatment of injuries, 36.1% (30/83) received some form of acute medical treatment (including complex treatments, such as for alcohol withdrawal, as well as relatively minor treatments such as pain relief with paracetamol or codeine). 7.2% (6/83) of incidents sustained an injury but only 1.2% (1/83) received major treatment (defined as that which probably required an acute hospital) for their injury (shoulder dislocation) and 2.4% (2/83) received minor treatment (defined as that which probably could have been delivered elsewhere) (wound care and treatment for an avulsed toenail). Although there was no tangible intervention in many incidents, all the patients received monitoring, assessment and diagnosis from a doctor and/or other clinicians.

Investigations

22.9% (19/83) had neuroimaging at some point during their attendance or admission. No patients had an EEG performed in the ED or as an in-patient. EEG tests, if considered necessary, were carried out as routine outpatient tests after the patient's discharge from their emergency care episode.

Seizure recurrence

In 73.5% (61/83) of incidents, the index event was the only seizure the patient had experienced in the 24 hours prior to their arrival in the ED. 21.7% (18/83) had experienced at least one other seizure in the previous 24 hours ('recurrent seizures'). Of those admitted after a single seizure, 14.8% (9/61) went on to have a subsequent seizure(s) in hospital. Of those with recurrent seizures, 27.8% (5/18) went on to have subsequent seizures in hospital. A Chi-Square test of independence was performed

to examine the relationship between seizure presentation on arrival (single or recurrent) and seizure recurrence during the hospital stay. The relationship was not significant, χ^2 (1, *N*=83) = 1.38, p = 0.24. 10.8% (9/83) of patients had emergency medication administered by either a carer or ambulance crew before arrival in the ED. Of these, 77.8% (7/9) were either still seizing on arrival in the ED or went on to have recurrent seizures during their hospital attendance.

Best Available Aetiological Explanation for the Index Event

The majority of suspected seizures in EPIC2 were epileptic 68/91 (74.7%) (including acute symptomatic seizures) but only 28/91 (30.8%) had a diagnosis of epilepsy. The epileptic seizures fall into the following four categories: a first epileptic seizure (13.2%, 12/91), an epileptic seizure in a patient with a formal diagnosis of epilepsy (30.8%, 28/91) an epileptic seizure in a patient known to have recurrent seizures but without a formal diagnosis of epilepsy (20.9%, 19/91) and acute symptomatic seizures in 9.9% (9/91). The other two important diagnostic categories were PNES 11.0% (10/91) and cardiogenic events 9.9% (9/91). The best available aetiological explanation for the index event is summarised in Figure 3 and Figure 4 shows diagnoses at each stage in the care pathway.

Diagnostic accuracy in the ED

87.8% (72/82) of diagnoses recorded at time of initial ED admission concurred with diagnoses made after more specialist or prolonged assessment during an inpatient stay or in a specialist in clinic. In those with an ED diagnosis of epileptic seizure, 98.3% (58/59) had a concordant diagnosis after inpatient admission or more specialist review.

DISCUSSION

Aetiology and Significance of Emergency Calls for Suspected Seizures

This is the first study to quantify diagnoses amongst pre-hospital patients after a suspected seizure. Our data show that 74.7% of our patients had suffered an epileptic seizure, 11.0% a PNES and 9.9% a cardiogenic event (see Figure 3). The patients with epilepsy fall into three sub-groups: epileptic seizure (first fit), epileptic seizure (epilepsy diagnosis) and epileptic seizure (not first fit, no epilepsy diagnosis). Although many of these patients did not require emergency treatment, patients in all three groups could benefit from urgent review by an epilepsy specialist after a seizure (8) (this also applies to the patients with PNES). Despite this, our data is consistent with other large studies (6) which show that most patients are discharged without the input of an epilepsy specialist or follow-up. This leaves all these patients (not just those with epilepsy and PNES) at risk of recurrence and the associated morbidity, mortality and health services costs of these events (2).

Medical Emergencies and Clinical Risk Management

A large majority of the patients in our study were not acutely unwell on arrival at hospital. These results are consistent with qualitative data suggesting that major factors in deciding to call for an emergency ambulance and transporting patients to hospital after a suspected seizure are lack of confidence, and medico-legal concerns, amongst patients, carers, the public and paramedics rather than true clinical need (3) (4) (30). We were unable to define the exact proportion of patients that were potentially suitable for community management without transport to hospital or discharge from ED. This would require a criterion-based approach and further research would be required to define criteria which can be used to identify patients suitable for non-transport and how to overcome barriers to community management such as the presence of other clinical problems, risk stratification for recurrence of seizures, appropriate levels of supervision and safe management of the post-ictal phase.

The risk of seizure recurrence and the phenomenon of seizure clusters are a major factor in management decisions by clinicians but they are poorly understood (31). We are not aware of any

prospective studies specifically looking at the short-term risk of seizure recurrence in the community. The published evidence in this area focusses on long-term recurrence risk after a seizure (32) (33) and the treatment of status epilepticus (34) (defined as ongoing seizure activity or recurrent seizures). Our data showed that, short-term recurrence is not more likely in patients who have presented with more than one seizure, compared with those who present with a single seizure, but the numbers in each group were small and further research is required.

Non-Compliance, Alcohol and Difficult to Reach Groups

20.9% (19/91) of patients in our study with recurrent seizures did not have an historical epilepsy diagnosis. This might partly be a reflection of inadequate medical records, but this result may reflect a more substantial problem of unmet need and is consistent with the national audit of seizure management in hospitals (NASH) (6), a large national audit conducted in the National Health Service (NHS) in the UK. We did not collect data to analyse this phenomenon further but we did find that alcohol use and illicit drugs were common clinical problems as was non-adherence with AED treatment. Non-adherence is associated with increased seizure frequency, adverse outcomes and increased hospital attendance/admission and higher health care costs (35) (36) (37). These data suggest that these patients may not understand the importance and benefits of medical advice, may be socially isolated and are perhaps living chaotic lifestyles. Simply improving access to medical services may not be an effective solution and more active outreach programmes may be required to reach this group (38). Hospital-based alcohol nurses and ambulance-service alcohol referral pathways may be able to intervene in these cases and facilitate joint working between epilepsy services and alcohol services.

Demographics, Re-Attendance and Specialist Review

5.1% (4/79) of our patients re-attended within the one-month study period. This probably under-estimates the true repeat attendance rate because of the short time window. Other studies have estimated this figure as to be as high as 60% within one year (39). The age-histogram of our cohort was uni-modal with a cut-off at age 16 (children were excluded) and a peak incidence at age 40. However, the age-related incidence curve of epilepsy has two peaks, one in childhood and the other in old age (40). This inconsistency which has been reported elsewhere (41) may be explained by underlying seizure frequency in this group but other factors are likely to be more important such as alcohol use and thresholds for accessing care (42) (43). Consistent with the NASH audit, our data has shown sub-optimal rates of referral to epilepsy specialists and low rates of intervention such as in-patient specialist review, epilepsy-specific investigations or modification of AEDs (8). Follow-up by specialist epilepsy nurses has been shown to be associated with earlier discharge from hospital (39). Expansion of the specialist nurse role may be a solution to problems with lack of capacity in some consultant-led services (44).

Conclusions

Suspected seizures generate significant demand for emergency care (pre-hospital and hospital). Most suspected seizures are epileptic and often reflect failed ambulatory care for epilepsy. Emergency calls to ambulance services are an opportunity to improve seizure freedom rates by facilitating urgent review by an epilepsy specialist. Many patients do not require emergency hospital treatment and there is the potential to develop pathways which both avoid unnecessary hospital attendance/admission and facilitate specialist review. The EPIC study (EPIC1 and EPIC2) provides good quality data to stimulate further research and to conceptualise the reconfiguration of services which aim to maximise seizure freedom rates in people with epilepsy and to prevent avoidable attendances at hospital.

Ethics approval: This study was categorised as a service evaluation and received approval from the Clinical Governance Group at YAS, from the Clinical Effectiveness Unit at STH and from the University

of Sheffield Research Ethics Committee (Ref 002558). We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Data Sharing Statement: No data sharing agreements are in place but the authors welcome queries from people interested in viewing the original data.

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Contributorship Statement

The research was suggested by MR and RAG. They provided important advice and comments on the protocol and manuscript throughout. JMD took the lead with the study design, contacting collaborators, submitting ethics applications and other permissions, supervision of HD and writing the manuscript. HD took the lead for data collection, data analysis, presentation and interpretation of the results. She wrote some parts of the manuscript and reviewed the manuscript throughout its preparation by JMD. SM and JS were involved in study design, data collection and provided advice and comments on the protocol and manuscript throughout. JMD and HD and joint first authors and RAG and MR are joint senior authors.

Figure 1. Flow chart to illustrate the care pathway and exclusions throughout the EPIC study (EPIC1 and EPIC2). The EPIC1 exclusions were: missing/inadequate data (18/178) and miscellaneous, for example, hoax call (6/178). The non-seizure diagnoses in EPIC1 were: syncope (3), intoxicated/passed out (2), tremor/spasm (2), fall (2), rigours (2), twitching (1), panic attack (1), anxiety/hyperventilation (2), abnormal behaviour (1), social/miscellaneous/inappropriate (6). The non-seizure diagnoses in EPIC2 were (5/8 vasovagal, 1/8 syncope, 1/8 complete heart block, 1/8 'collapse').

Figure 2 Physiological parameters and the Sheffield Early Warning Score (SHEWS) for each of the patients on arrival in ED. SHEWS score: 1 = increase frequency of observations and inform nurse, 2 = hourly observations and consider medical review, 3 = immediate medical review. No patients had a SHEWS score recorded that was higher than 1. HR = heart rate, RR = respiratory rate, BP = blood pressure. O_2 sats. = oxygen saturations, GCS = Glasgow coma score. Normal ranges: heart rate (60-100bpm), respiratory rate (14-18 breaths per minute), systolic BP (100-140mmHg), blood glucose (3.5-11.1 mmol/l), temperature (36.5-37.5°C), O2 saturations (<94%) and GCS (15/15).

Figure 3: Best available aetiological explanation for the index event. Acute symptomatic causes were: alcohol withdrawal (6), head injury (1), hypoglycaemia (1), and transient ischaemic attack (1). The cardiogenic events: vasovagal episode (6), syncope (1), complete heart block (1), and collapse (1).

Figure 4a-d. Data from EPIC1 and EPIC2 to illustrate diagnoses, exclusions and missing data at each stage in the care pathway. Pre-Hospital Diagnoses (Fig 4a). In Sheffield May 2012 there were 178 suspected seizures for which 999 was called. 24/178 were excluded and 22/178 were not seizures leaving 132/178 suspected seizure incidents that were studied in detail in EPIC1. Exclusions: missing/inadequate data (18/178, 10.1%), miscellaneous e.g. hoax call (6/178, 3.4%). The clinical impression of the ambulance clinicians was that there was no evidence of seizure activity in 22/178 (12.4%). Not seizure diagnoses: syncope (3), intoxicated/passed out (2), tremor/spasm (2), fall (2), rigours (2), twitching (1), panic attack (1), anxiety/hyperventilation (2), abnormal behaviour (1), social/miscellaneous/inappropriate (6). **Hospital Diagnoses (Figs 4b-d).** Best Available Diagnoses (Fig 4b). The hospital notes of 91/132 were analysed in detail (98/132 were transported to hospital but 4/98 transported to an hospital outside Sheffield and 3/98 sets of notes were not available). The best available data for the aetiology of the 91 events is shown in Figure 4b (this is based on data from all sources: ED notes, in-patient notes and epilepsy clinic notes). Aetiology of acute symptomatic seizures: alcohol withdrawal (6), head injury (1), hypoglycaemia (1) and transient ischaemic attack (1). Emergency Department Diagnoses (Fig 4c). 82/91 that were transported to ED at STH were suspected seizures (Fig 4c). 9/91 were given non-seizure diagnoses: vasovagal episode (6), syncope (1), complete heart block (1), and collapse (1). NB/ An addition 1/91 suspected seizure was transported direct to an in-patient ward so 82/91 were diagnosed with suspected seizures. In-Patient Diagnoses (Fig 4d) 27/83 were admitted to an in-patient ward.

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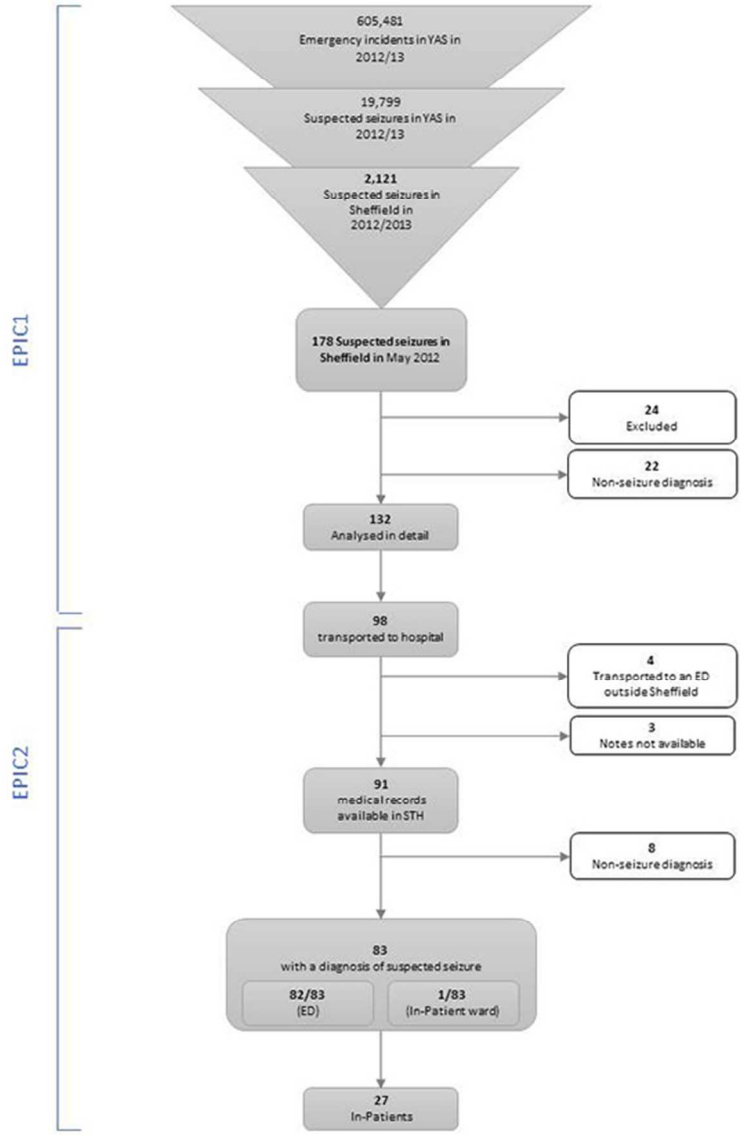

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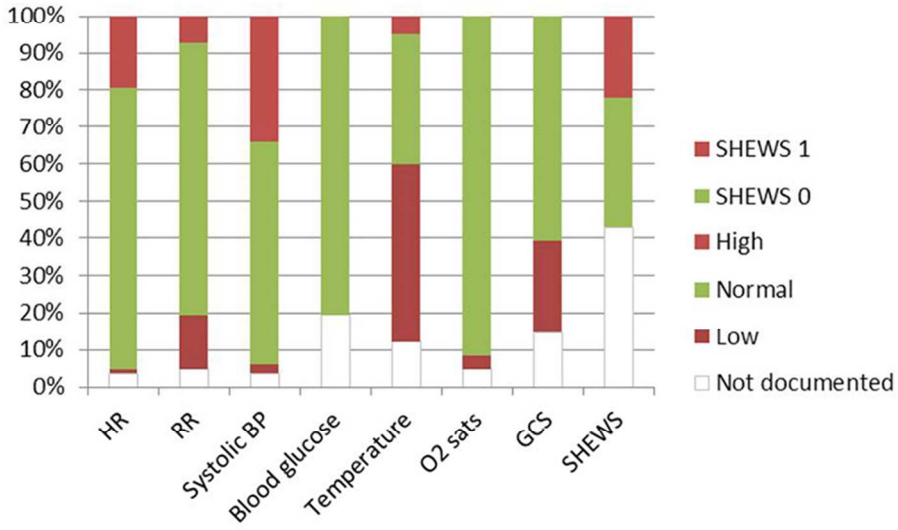

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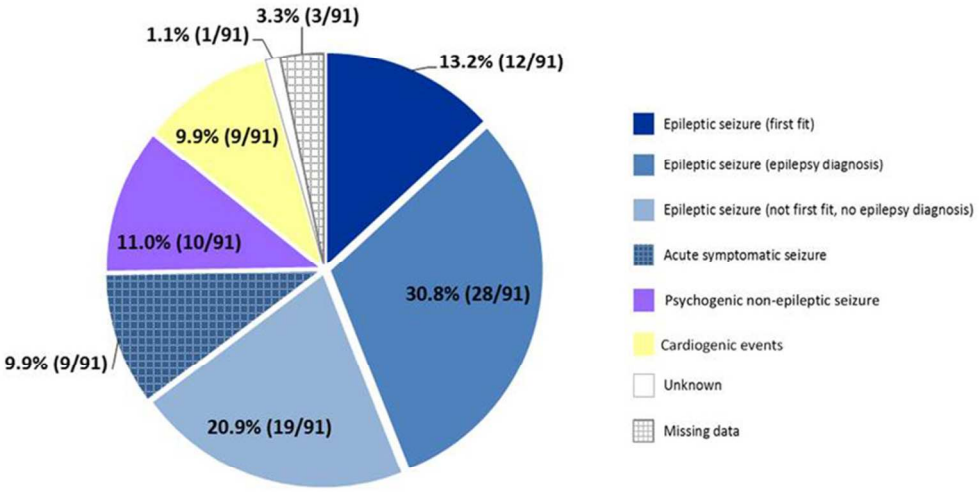

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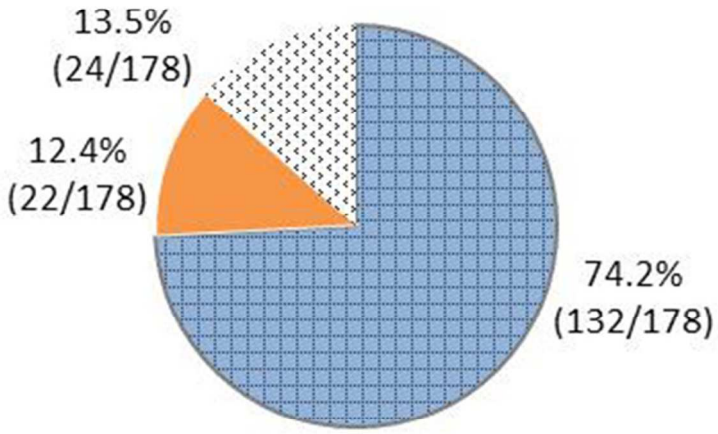

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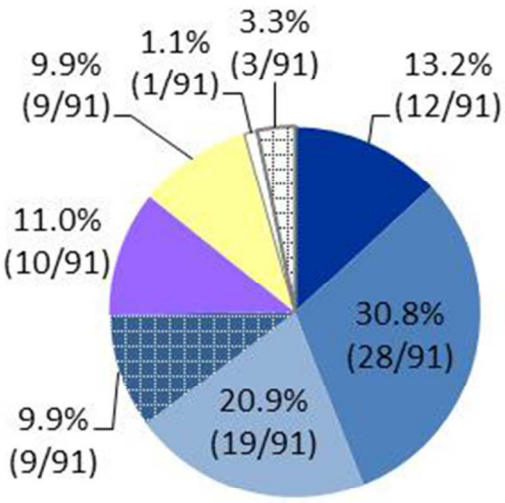

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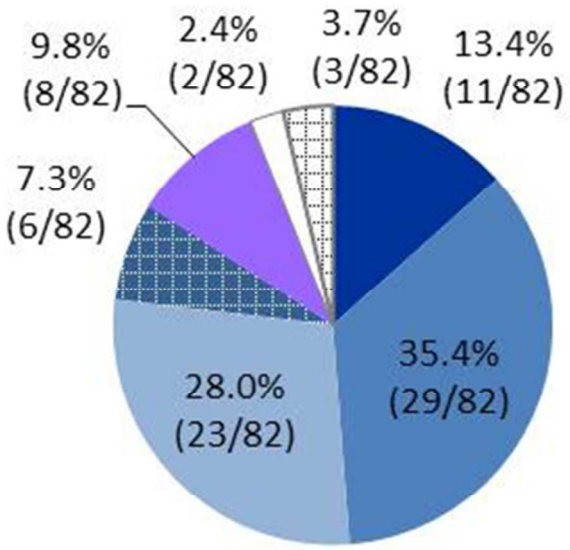

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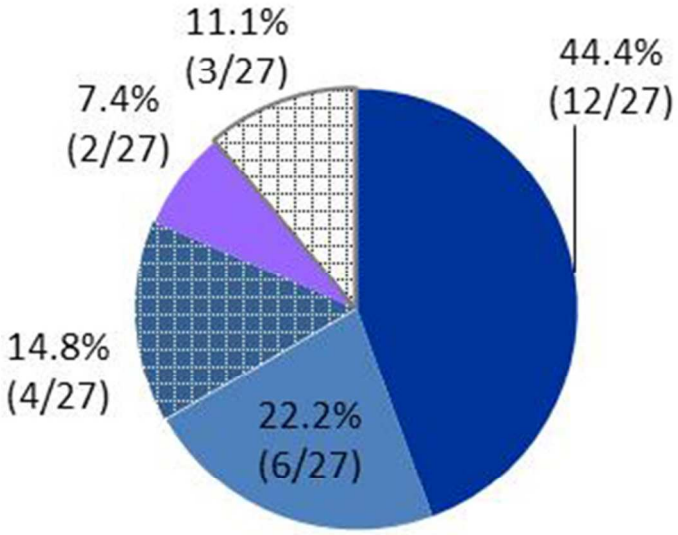

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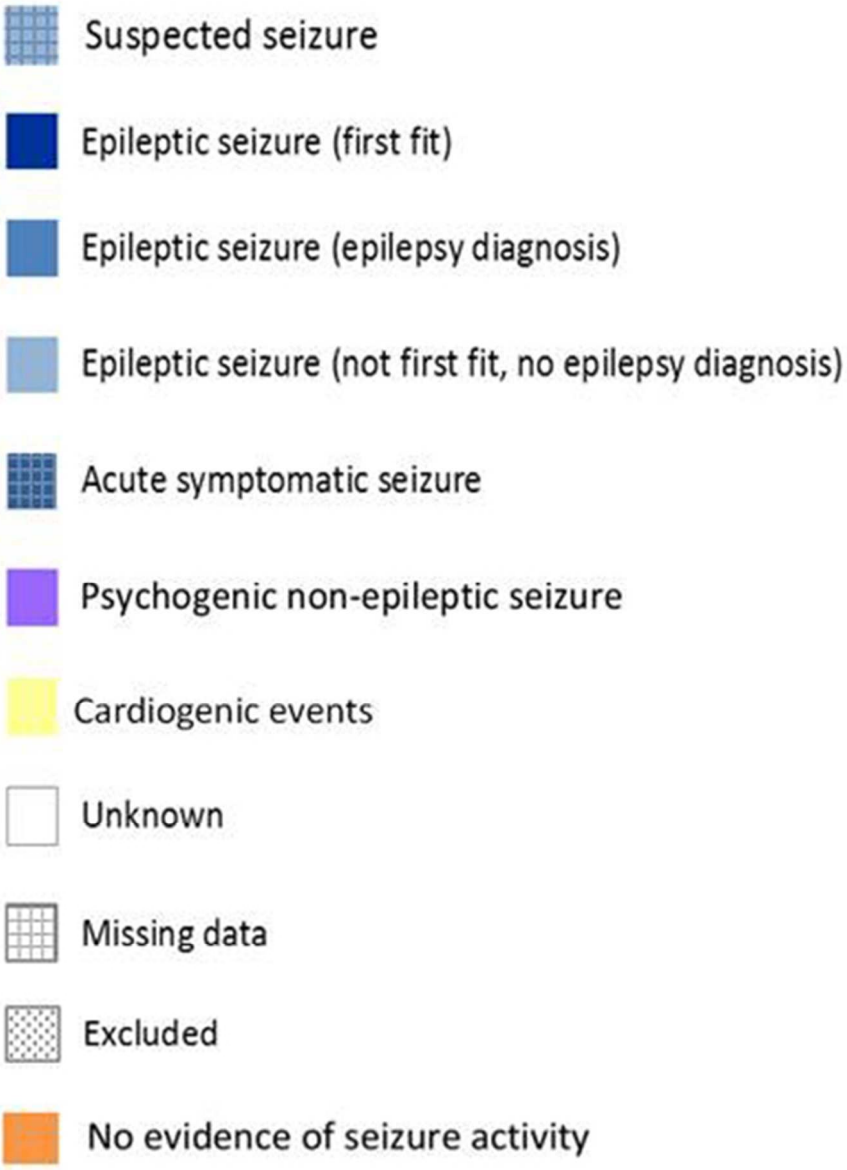

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Location	Variable	Categories	Notes
ED	ED area	1 Minors 2 Majors 3 Resus 4 Not documented	The highest dependency area that the patient went to during the ED attendance.
	HR on arrival	1 Normal 2 Low 3 High 4 Not documented	Normal heart rate (HR) = 60-100 beats per minute
	RR on arrival	1 Normal 2 Low 3 High 4 Not documented	Normal respiratory rate (RR) = 14-18 breaths per minute (male) and 16-20 breaths per minute (female)
	Systolic BP on arrival	1 Normal 2 Low 3 High 4 Not documented	Normal systolic blood pressure (BP) = 100-140 mmHg
	BM on arrival	1 Normal 2 Low 3 High 4 Not documented	Normal blood glucose (BM) = 3.5-11.1 mmol/l
	GCS on arrival	3 4 5 etc. 15 16 Not documented	GCS (Glasgow coma scale) is used to assess the state of consciousness of the patient. 3/15 (lowest score) = completely unresponsive 15/15 (highest score) = conscious, orientated, and responding well to questions

	Temperature on arrival	1 Normal 2 Low 3 High 4 Not documented	Normal temperature = 36.5-37.5°C
	O_2 sats	1 Normal 2 Low 3 Not documented	Low O_2 sats = < 94%
	SHEWS score on arrival	0 1 2 3 4 Not recorded	Sheffield hospitals early warning score (SHEWS) is an early warning system used to determine the degree of illness of a patient based on their HR, systolic BP, RR, temperature and level of alertness. Based on a scale from 0 to 3, where 0 is normal and 1-3 are outside the normal range, and 3 represents the greatest deviation from normal.
	Formal diagnosis of epilepsy?	1 Yes 2 No	A 'formal diagnosis of epilepsy' was as documented by the ED doctor on the ED card - as part of the medical history or documentation that the patient was known epileptic. Formal diagnosis means a diagnosis made by an appropriately qualified clinician - in most cases this would be a neurologist by could also include general physicians. Includes both idiopathic and symptomatic epilepsies. Non-epileptic attacks and alcohol-related seizures were not included unless a clear diagnosis of epilepsy was recorded as well.
	Documented history of PNES	1 Yes 2 No	

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	Suspicion of non-epileptic seizure documented	1 Yes 2 No	If clinician had a suspicion that the event was a non-epileptic attack.
	Seizure presentation on arrival (1)	1 Single seizure 2 Recurrent seizures	This variable was copied directly from the pre-hospital (EPIC1) data, as it is difficult to determine recurrence from the ED card. Seizures were divided into patients for which this was their first seizure in the previous 24 hours (single) and patients who had experienced more than one seizure in the previous 24 hours (recurrent).
	Seizure presentation on arrival (2)	1 Complete 2 Ongoing	
	Seizures during ED attendance	1 Yes 2 No	This includes unwitnessed seizures where the patient was found to be post-ictal.

	Other clinical problem (1)	1 None 2 Syncope 3 Stroke/TIA/CVA 4 Hypoglycaemia 5 Arrhythmias 6 Alcohol 7 Injury 8 Drugs 9 Other (specify)	This encompasses other clinical problems which may be acutely present in addition to the seizure, which requires hospital treatment and/or assessment. This would include, for example, a head injury requiring CT but no treatment, but would exclude bruising/grazes to the limbs. They may be the cause of the seizure, a complication of the seizure, or unrelated to the seizure. Arrhythmias: Does not include sinus tachycardia or sinus bradycardia. Alcohol: refers to any recent alcohol use and past alcohol abuse suggested by the past medical or drug history and of the patients such as a history of withdrawal seizures or alcohol dependent. The only exception is where alcohol consumption was indicated but was specifically noted to be below the recommended daily allowance (2-3 units for women, 3-4 units for men) with no reference to previous alcohol abuse. Drugs: includes illicit drug use as well as overdose on prescribed medication.
	Other clinical problem (1) (other)		

	Other clinical problem (2)	1 None 2 Syncope 3 Stroke/TIA/CVA 4 Hypoglycaemia 5 Arrhythmias 6 Alcohol 7 Injury 8 Drugs 9 Other (specify)	
	Other clinical problem (2) (other)		
	Other clinical problem (3)	1 None 2 Syncope 3 Stroke/TIA/CVA 4 Hypoglycaemia 5 Arrhythmias 6 Alcohol 7 Injury 8 Drugs 9 Other (specify)	
	Other clinical problem (3) (other)		

	Documented alcohol dependency	1 Yes 2 No	Where there is a clear statement that the patient has documented current alcohol dependency. Alcohol dependency is defined by the DSM-IV criteria as: “A maladaptive pattern of alcohol use leading to clinically significant impairment or distress, as manifested by three or more of the following seven criteria, occurring at any time in the same 12-month period: Tolerance; withdrawal; alcohol is often taken in larger amounts or over a longer period than was intended; there is a persistent desire or there are unsuccessful efforts to cut down or control alcohol use; a great deal of time is spent in activities necessary to obtain alcohol, use alcohol or recover from its effects; important social, occupational, or recreational activities are given up or reduced because of alcohol use; alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the alcohol”.[180]

	Clinical condition on arrival	1 Alert 2 Post-ictal 3 Ictal 4 Other (specify)	Taken from the nurses notes on arrival or ED notes if the clinical condition on arrival is clearly stated. The postictal state is the abnormal condition occurring between the end of an epileptic seizure and return to baseline condition. We operationalised our definition of post-ictal to only include symptoms that were a barrier to the patient being safely discharge home. It specifically did not include tiredness, headache or myalgia. The main feature which would mean safe discharge was not possible are reduced consciousness, significant drowsiness, neurological deficits etc.
	Clinical condition on arrival (other)		
	Seizure-related Injuries	1 Yes (specify) 2 No	Here injuries are only included if they required hospital assessment or treatment (in ED or as in-patient).
	Injuries (specify)		

	Fully recovered at the end of attendance	1 Yes 2 No	The patient was fully recovered if they had returned to their normal level of functioning with no acute medical problems that required hospital assessment and/or treatment, and were not post-ictal. We operationalised our definition of post-ictal to only include symptoms that were a barrier to the patient being safely discharge home. It specifically did not include tiredness, headache or myalgia. The main feature which would mean safe discharge was not possible are reduced consciousness, significant drowsiness, neurological deficits etc.
	Pregnancy	1 Yes 2 No	
	Illicit drug abuse documented/suspected	1 Yes 2 No	
	Medication in ED (1)	1 Yes 2 No	Anticonvulsant medication used for the termination of seizures.
	Medication in ED (2)	1 Lorazepam 2 Phenytoin 3 Diazepam 4 Midazolam 5 Other (specify)	
	Medication in ED (2) (Other)		
	HES code (local)		
	HES code (national)		

	ED disposal	1 Discharged home 2 Discharged elsewhere 3 Admitted (specify where) 4 Death 5 Self-discharge	
	Admitted to	1 General medicine 2 ICU 3 Neurology 4 Other (specify where)	
	Admitted to (other)		
	Referral / Post-seizure follow up advice	1 Epilepsy clinic/first fit clinic 2 Epilepsy specialist nurse (referral or verbal advice) 3 GP 4 Other	The patient was said to have been referred to their GP if the patient was advised to see their GP for reasons relating to the care of their epilepsy. The ED physician may have written a letter to the GP.
	Referral (other)		
	Final diagnosis/impression of ED clinician (1)	1 Epileptic seizure (first fit) 2 Epileptic seizure (not first fit, no formal diagnosis of epilepsy) 3 Epileptic seizure (formal epilepsy diagnosis) 4 Non-epileptic attack	This is the diagnosis of the suspected seizure event. "not seizure" cases were included in this variable. Here, a 'formal epilepsy diagnosis' is one documented by the ED clinician.

		5 Acute symptomatic seizure (specify) 6 Not seizure (specify)	
	Final diagnosis/impression of ED clinician (1) (acute symptomatic - specify)		
	Final diagnosis/impression of ED clinician (1) (not seizure - specify)		
	Final diagnosis/impression of ED clinician (2)		
	Indication for admission	1 Social 2 Medical (seizure-related) (specify) 3 Medical (not seizure-related) (specify)	Social admissions are those where there is no medical reason for admission e.g. unable to put care package in place for discharge.
	Indication for admission (seizure-related - specify)		
	Indication for admission (not seizure-related - specify)		
In-patient	Date of admission		
	Date of discharge		
	Duration of admission		

	Seizures during admission	1 Yes 2 No	This includes unwitnessed seizures where the patient was found to be post-ictal.
	Final discharge destination	1 Home 2 Death 3 Self-discharge 4 Other (specify)	Home' was defined as the current or usual residence of the patient. This included rented or owned properties as well as institutions such as nursing or care homes. If the patient was discharged somewhere new, for example a patient previously living at home being discharged to a care home, this was documented as 'other'.
	Final discharge destination (other)		
	Transferred to another speciality during inpatient admission	1 Yes (specify) 2 No	
	Transferred to another speciality during inpatient admission (specify)		
	Fully recovered at the end of attendance	1 Yes 2 No	The patient was fully recovered if they had returned to their normal level of functioning with no acute medical problems that required hospital assessment and/or treatment, and were not-post ictal. We operationalised our definition of post-ictal to only include symptoms that were a barrier to the patient being safely discharge home. It specifically did not include tiredness, headache or myalgia. The main feature which would mean safe discharge was not possible are reduced consciousness, significant drowsiness, neurological deficits etc.

	Referral / Post-seizure follow up advice	1 Epilepsy clinic/first fit clinic 2 Epilepsy specialist nurse (referral or verbal advice) 3 GP 4 Other	The patient was said to have been referred to their GP if the patient was advised to see their GP for reasons relating to the care of their epilepsy. The physician may have written a letter to the GP.
	Referral (other)		
	Diagnosis at discharge	1 Epileptic seizure (first fit) 2 Epileptic seizure (not first fit, no formal diagnosis of epilepsy) 3 Epileptic seizure (formal epilepsy diagnosis) 4 Non-epileptic attack 5 Acute symptomatic seizure (specify) 6 Not seizure (specify)	Taken from discharge sheet, if no discharge sheet then final diagnosis documented in progress record or clerking sheet.
	Diagnosis at discharge (acute symptomatic - specify)		
	Diagnosis at discharge (not seizure - specify)		
Epilepsy clinic	Ever seen in epilepsy clinic?	1 Yes 2 No	

	Seen in epilepsy clinic before the index event?	1 Yes 2 No	
	Seen in epilepsy clinic (or specialised epilepsy services) as a result of the index event?	1 Yes 2 No	
	Does the patient have a diagnosis of epilepsy that was made in the epilepsy clinic? If yes, specify.	1 Yes 2 No	Regardless of when this diagnosis was made.
	Epilepsy clinic epilepsy diagnosis	1 Localisation-related epilepsy (focal, local, partial) 2 Generalised epilepsy 3 Undetermined whether focal or general 4 Special syndromes	These categories are based on the ILAE Proposal for Revised Classification of Epilepsies and Epileptic Syndromes - Epilepsia (1989) 30(4): 389-399.
	Does the patient have a diagnosis of PNES that was made in the epilepsy clinic? If yes, specify.	1 Yes 2 No	
From all sources	AEDs	1 Yes (state which) 2 No	AEDs at the time of the ED attendance in May 2012.

	Which AED (1)	1 Sodium valproate 2 Carbamazepine 3 Levetiracetam 4 Phenytoin 5 Phenobarbital 6 Not documented 7 Other (state which)	
	Which AED (1) (Other)		
	Which AED (2)	1 Sodium valproate 2 Carbamazepine 3 Levetiracetam 4 Phenytoin 5 Phenobarbital 6 Not documented 7 Other (state which)	
	Which AED (2) (Other)		
	Non-concordance with AEDs	1 Yes 2 No	At the time of the event in May 2012. This refers to patients who have not taken their AED medication as prescribed including cases where patients have run out of AEDs or forgotten to take their medication, as well as patients who have overdosed. Includes suspected non-adherence.

	"Best available" aetiological explanation for the index event .	1 Epileptic seizure (first fit) 2 Epileptic seizure (not first fit, no diagnosis of epilepsy) 3 Epileptic seizure (epilepsy diagnosis) 4 Non-epileptic attack 5 Acute symptomatic seizure (specify) 6 Not seizure (specify)	"Not seizure" cases included in this variable.
	"Best available" aetiological explanation for the index event (acute symptomatic - specify)	1 Yes 2 No	
	"Best available" aetiological explanation for the index event (not seizure - specify)	1 Yes 2 No	
	Hospital management		These variables pertain to key features of hospital management received by the patient. The list is not exhaustive. This includes treatments that were not specifically to treat the seizure in the case of complex patients with more than one clinical problem.
	Expert opinion	1 Yes 2 No	Expert opinion from any hospital specialist on diagnosis, investigations or management.
	Was an AED regime started or modified during the admission?	1 Yes 2 No	Either in ED or in-patient.
	Neuroimaging	1 Yes 2 No	Acute neuroimaging especially CT head scan.

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	Acute medical treatment (specify)	1 Yes 2 No	Excluding injuries. Including: parenteral drugs to terminate seizures, IV fluids, etc.
	Acute treatment of injuries (major)	1 Yes 2 No	Dressings, sutures, shoulder relocation etc. which probably required hospital treatment.
	Acute treatment of injuries (minor)	1 Yes 2 No	Dressings, sutures, shoulder relocation etc. which probably did not require hospital treatment.
	Other (specify)	1 Yes 2 No	
	Other (specify)		Narrative account of hospital treatment

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STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	3-5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	3-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3-5
Bias	9	Describe any efforts to address potential sources of bias	3-5
Study size	10	Explain how the study size was arrived at	3-5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	3-5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	3-5
		(*b*) Describe any methods used to examine subgroups and interactions	3-5
		(*c*) Explain how missing data were addressed	3-5
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	3-5
		(*e*) Describe any sensitivity analyses	N/A

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5-8
		(b) Give reasons for non-participation at each stage	5-8
		(c) Consider use of a flow diagram	Fig 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5-8
		(b) Indicate number of participants with missing data for each variable of interest	5-8
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	5-8
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	5-8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5-8
		(*b*) Report category boundaries when continuous variables were categorized	5-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5-8
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5-8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8-9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8-9, 1
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-9
Generalisability	21	Discuss the generalisability (external validity) of the study results	8-9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Cross-sectional study of the hospital management of adult patients with a suspected seizure (EPIC2)

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Cross-sectional study of the hospital management of adult patients with a suspected seizure (EPIC2)

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Abstract

Objective
To determine the clinical characteristics, management and outcomes of patients taken to hospital by emergency ambulance after a suspected seizure.

Design
Quantitative cross-sectional retrospective study of a consecutive series of patients.

Setting
An acute hospital trust in a large city in England.

Participants
In 2012/13 the regions ambulance service managed 605,481 emergency incidents, 74,141/605,481 originated from Sheffield (a large city in the region), 2,121/74,141 (2.9%) were suspected seizures and 178/2,121 occurred in May 2012. We undertook detailed analysis of the medical records of the 91/178 patients who were transported to the city's acute hospital. After undertaking a retrospective review of the medical records the best available aetiological explanation for the seizures was determined.

Results
The best available aetiological explanation for 74.7% (68/91) of the incidents was an epileptic seizure, 11.0% (10/91) were psychogenic non-epileptic seizures (PNES) and 9.9% (9/91) were cardiogenic events. The epileptic seizures fall into the following four categories: first epileptic seizure (13.2%, 12/91), epileptic seizure with a historical diagnosis of epilepsy (30.8%, 28/91), recurrent epileptic seizures without a historical diagnosis of epilepsy (20.9%, 19/91), and acute symptomatic seizures (9.9%, 9/91). Of those with seizures (excluding cardiogenic events), 2.4% (2/82) of patients were seizing on arrival in the Emergency Department (ED), 19.5% (16/82) were post-ictal and 69.5% (57/82) were alert. 63.4% (52/82) were discharged at the end of their ED attendance and 36.5% (19/52) of these had no referral or follow-up.

Conclusions
Most suspected seizures are epileptic seizures but this is a diagnostically heterogeneous group. Only a small minority of patients require emergency medical care but most are transported to hospital. Few patients receive expert review and many are discharged home without referral to a specialist leaving them at risk of further seizures and the associated morbidity, mortality and health services costs of poorly controlled epilepsy.

Strengths and Limitations of this Study

This is the first study to describe the clinical characteristics, management and outcomes of patients taken to hospital by emergency ambulance after a suspected seizure. The themes identified in this paper resonate with previous studies reflecting practice across the world.

The triangulation of data drawn from pre-hospital records and hospital medical records (ED, in-patient and epilepsy clinic) resulted in richer and more robust data than data drawn from a single source.

Our sample was small and data extraction could have been given added rigour by involving a second rater. Manual data extraction from clinical notes is time consuming which constrained our study methods and is the major limitation to the study.

Although this study was conducted in a single hospital trust it is one of the largest acute care providers in the United Kingdom and its Emergency Department provides emergency services for a large socioeconomically mixed population.

INTRODUCTION

Background

Epilepsy is an ambulatory care sensitive condition (ACSC) (1) and sub-optimal ambulatory care (also known as routine or scheduled care) leads to unnecessary demand for emergency care (2). The majority of epileptic seizures do not require emergency treatment but ambulance services are often called. Calls are rapidly triaged by specialised call handlers, an emergency response vehicle is usually dispatched, but by the time the ambulance arrives most seizures and have terminated spontaneously, nevertheless the majority of patients are transported to hospital (3) (4). Precise estimates vary, but in England (population 52.96 million, 42.96 million adults) seizures give rise to approximately 211,000 calls to ambulance services per year (3.3% of all emergency calls) (5). It is estimated that there are 60,000 seizure-related Emergency Department (ED) attendances per year (2-3% of all attendances) (6), and 40,000 hospital admissions which represent 9.5% of all admissions for ACSCs (6) (7). There are currently no published studies of care pathways for people who have presented as an emergency with a suspected seizure which aim to facilitate urgent medical review (8) and avoid unnecessary transport to hospital (9, 10). Clinical guidelines for paramedics provide little guidance on the community management and/or referral of patients after a seizure and focus almost exclusively on medical emergencies which are rare (11).

An epileptic seizure may be the result of sub-optimal treatment and should lead to consideration of whether specialist review is required. But this opportunity to prevent further seizures and/or to refine the patients emergency care plan is often missed (6) (8) (12) (13). Many patients therefore unnecessarily remain at risk of further seizures and the associated morbidity (14), mortality (15) and health services costs (2) (16) of poorly controlled epilepsy. Approximately 70% of people with epilepsy (PWE) could become seizure-free (≥12 months) with optimal treatment (17) (18) (19) but internationally actual seizure freedom rates are significantly lower than this. There is little published data on seizure-freedom rates in individual countries (17) (20) (21) and there are no published international comparisons of seizure-freedom rates. The overall seizure freedom rate in the UK is thought to be 50% (22) (23) (24, 25). Some epilepsy services in the United Kingdom (UK) are world-leading but the quality of care is highly geographically variable, and patients in many areas do not have access to optimal monitoring and treatment. This means that as many as one-in-five patients with epilepsy may be unnecessarily having seizures (17).

EPIC (Epilepsy Pre-Hospital Interventions and Care) Study

The EPIC study was designed to generate data to support improvements in emergency care after a suspected seizure. Despite its importance, this aspect of epilepsy care has received relatively scant academic attention to date. In EPIC1 (5) we described the pre-hospital management of a series of consecutive incidents with suspected seizures. The present study, EPIC2, focusses on the sub-group of these patients that was transported to hospital after a suspected seizure with the aim of determining their clinical characteristics, their management and their outcomes based on data collected from ED, in-patient wards and the epilepsy clinic. The emergency care structure in the UK, with its universal access to healthcare, unitary emergency call handling service and non-overlapping ambulance service and emergency department provisions offers opportunities to researchers to study emergency presentations with seizures which do not exist in many other countries.

METHODS

Local Context and Patient Selection

YAS is a regional ambulance service in England (one of the four devolved nations of the UK) covering 9,656 square kilometres and it is the sole provider of ambulance and paramedic services for its population of 4,019,610 adults (4,954,876 adults and children) (26). Sheffield is one of the major

urban centres within the area served by YAS and has a population of 451,100 adults (551,756 adults and children) which is served by a single hospital-based Emergency Department (ED) for adults at the Northern General Hospital (NGH) site of the Sheffield Teaching Hospitals NHS Foundation Trust (STH) (27).

Case Ascertainment, Exclusions and Missing Data

Patients were retrospectively identified from the records of the Yorkshire Ambulance Service (YAS). Between 1 April 2012 and 31 March 2013 the Yorkshire Ambulance Service dealt with 605,481 emergency incidents in adults (≥16 years old). 19,799 (3.3%) of these incidents were suspected seizures, 2,121 originated from Sheffield (a large city in the region) and 178 occurred in May 2012. We analysed data from a sample month, May 2012, which was chosen after preliminary analysis of the summary statistics showed it to be a typical month (5). After non-seizure diagnoses and other exclusions were removed 132 incidents were analysed in detail and 98 were transported to hospital. The initial call-handling and out-of-hospital management of these patient was the focus of EPIC1 (5).

Of the 98 incidents from EPIC1 that were transported to hospital, 4/98 incidents were transported to an ED outside Sheffield and 3/98 patients were not identifiable on the STH's computer system so medical records were available for 91/98 incidents. The focus of this paper is the analysis of these 91 incidents although 8/91 (8.8%) incidents were given non-seizure diagnoses in ED so no further data was collected for these. Detailed data extraction was undertaken for the remaining 83 incidents. The care pathway from emergency call to discharge from hospital including exclusions is complex. It is summarised in Figure 1.

Data Collection and Analysis

Data were extracted by one of the authors (HD) using a data extraction tool (see Supplementary File) which was developed by all the authors and was revised after an initial pilot. Some variables such as the working diagnosis changed throughout the care pathway and so we report the results separately at each stage in the pathway: 1) ED, 2) in-patient wards, 3) out-patient epilepsy clinic and 4) combined data from all three sources. The data presented in section (4) was drawn together by HD from all available sources (ED notes, in-patient notes, epilepsy clinic notes) to document an overview of the hospital management of each incident taking into account the opinion of all the clinicians involved throughout the care pathway. This allowed triangulation of the data, which allowed resolution of inconsistencies between, for example, accounts in the ED notes and in the epilepsy clinic notes, and it allowed us to draw robust conclusions about the best available aetiological explanation for the index event. If the best available aetiological explanation for the suspected seizure was an epileptic seizure it allowed us to determine if the patient had a historical diagnosis of epilepsy.

In this paper we report the data as it was recorded in the notes by the clinicians involved in the incidents with as little interpretation from the authors as possible. Where interpretation was required we included definitions within the data collection tool to inform these judgements; these are described below. We analysed each incident separately (some patients attended more than once during the study period and therefore generated multiple incidents). To calculate the number of incidents in which all physiological parameters were normal we used the following parameters: heart rate (60-100bpm), respiratory rate (14-18 breaths per minute), systolic BP (100-140mmHg), blood glucose (3.5-11.1 mmol/l), temperature (36.5-37.5°C), O2 saturations (<94%) and GCS (15/15). We excluded low temperature (<36.5°C) from this calculation because it is very unlikely that any patients truly had hypothermia in May in England (a low temperature measurement is likely to reflect inaccuracy of peripheral temperature recording). We recorded the Sheffield Early Warning Score (SHEWS) which is based on the National Early Warning Score. SHEWS is a composite score based on heart rate, respiratory rate, oxygen saturation, systolic blood pressure, urine output and

consciousness level. A score above 0 identifies patients who may be acutely ill so that their care can be stepped-up: 1 = increase frequency of observations and inform nurse, 2 = hourly observations and consider medical review, 3 = immediate medical review. Numerical data was entered into SPSS which was used for calculating summary statistics. Chi-Square tests were used to assess relationships between categorical variables. Where there was missing data it was coded as such in SPSS. Variables with large numbers of missing data points were excluded from the analysis and are not reported in the Results. Small numbers of missing data points in specific variables are not reported in the Results.

Definitions

The latest International League Against Epilepsy (ILAE) definitions of epilepsy and seizures (28) (29) were applied during data collection. We categorised the indication for admission: medical (seizure-related), medical (not seizure-related) and social. Medical (seizure-related) admissions were those where the principal reason for admission was seizure(s), for example, patients who were still post-ictal at the end of their ED attendance. Medical (not seizure-related) admissions were those where the principal reason for admission was not a seizure, for example, lower respiratory tract infection or unexplained pyrexia. Social admissions were those where there was no medical reason for admission but it was not possible to discharge the patient directly from the ED e.g. because a home care package had to be put in place. We categorised those with and without a self-reported diagnosis of epilepsy prior to the index event. Historical diagnoses of epilepsy were determined from the records of the ED doctors and often only brief information was available. In addition to the seizure we determined if the patient had any other acute clinical problems. Alcohol was deemed to be a clinical problem if there was documentation of excessive alcohol ingestion which occurred around the time of the index event or if there was a history of alcohol abuse (such as alcohol dependency or withdrawal seizures). Patients were deemed to have recovered fully if they were recorded as having returned to their normal level of functioning with no acute medical problems that required hospital assessment and/or treatment, and were not thought to be post-ictal (notwithstanding tiredness, headache and myalgia).

RESULTS

Demographics and Repeat Attendances

The patients' median age was 40 (IQR 30, range 16-97). Males accounted for 54.2% of incidents. The 83 incidents relate to 79 patients. 4/79 (5.1%) patients generated two incidents during the one-month study period. The time intervals between the repeat attendances were: 1 day, 3 days, 13 days and 15 days.

Management in the Emergency Department

Past Medical History

82/83 incidents were seen in ED, one incident was admitted directly to a neurology ward (without being seen in ED). The ED records documented a history of a seizure disorder in 43.9% (36/82) of all incidents: epilepsy 36.6% (30/82), psychogenic non-epileptic seizures (PNES) 6.1% (5/82), epilepsy plus PNES 1.2% (1/82).

Clinical details

In 2.4% (2/82) of incidents the patient was seizing on arrival at the ED, 69.5% (57/82) were alert on arrival, 19.5% (16/82) were post-ictal and in 6/82 (7.3%) their status was not clear from the notes. All physiological parameters were normal (or not recorded) in 28/82 (34.1%) of incidents but often only one parameter was abnormal and often this was mild tachycardia or mild hypertension (see Figure 2). In the incidents in which the seizure had terminated prior to arrival in the ED, 76.25%

(61/80) had no subsequent seizures during their hospital stay. 17.5% (14/80) had recurrent seizures either in the ED or after transfer to a hospital ward. In 7.3% (6/82) of incidents emergency medication for the termination of seizures was administered in the ED. 70.7% (58/82) of cases had recovered fully by the end of the ED attendance.

Final Diagnosis at the End of the ED Attendance

In the opinion of the ED clinicians, 63/82 incidents were likely to have been epileptic seizures: 13.4% (11/82) had experienced a first fit, 35.4% (29/82) had experienced an epileptic seizure in the context of an historical diagnosis of epilepsy, 28.0% (23/82) had experienced an epileptic seizure with a history of recurrent seizures but without an historical diagnosis of epilepsy. 7.3% (6/82) were diagnosed with an acute symptomatic seizure. 9.8% (8/82) were diagnosed with a PNES. The diagnosis was unknown in 2.4% (2/82), and in 3.7% (3/82) no diagnosis was recorded.

Other Clinical Problems

47.6% (39/82) of cases had another clinical problem(s) in addition to the suspected seizure. This was sometimes secondary to the suspected seizure but was often unrelated or only tangentially related to it. 35.4% (29/82) had one additional clinical problem, 8.5% (7/82) had two, 2.4% (2/82) had three and 1.2% (1/82) had four. In total there were 53 additional clinical problems amongst the 82 incidents. 41.5% (22/53) of these were alcohol, 15.0% (8/53) were injuries, 9.4% (5/53) were illicit drug use and 34.0% (18/53) were 'other' (for example, brain tumour, pyrexia, acidosis, psychiatric problems and abdominal pain).

Discharge and Referral from ED

63.4% (52/82) of patients were discharged home at the end of their ED attendance, 31.7% (26/82) were admitted to an in-patient ward from ED (another patient who was taken directly to a ward by ambulance without attending ED), and 4.9% (4/82) self-discharged. The indication for admission was related to the seizure in 61.5% (16/26) of cases. In 26.9% (7/26) of cases it was due to a medical problem which was not obviously related to the seizure (e.g. chest infection, GI problems, infective rash) and in 11.5% (3/26) of cases the reason for admission was social. Of the patients who were discharged home from the ED, only 61.5% (32/52) had documented referral or follow-up advice. 34.6% (18/52) were referred to an epilepsy clinic, 25.0% (13/52) were referred to their GP, and 1.9% (1/52) were referred to an epilepsy specialist nurse. 36.5% (19/52) had no documented referral, and 52.6% (10/19) of these had not been seen in the epilepsy clinic before the event. There was a relationship between SHEWS and GCS on arrival in ED with disposal (admission or discharge). Patients with an abnormal SHEWS on arrival were more likely to be admitted to hospital and less likely to be discharged ($\chi 2$ (1, N=45) = 10.385, p=0.001), likewise for patients with a reduced GCS on arrival ($\chi 2$ (1, N=68) = 15.451, p=0.000085).

2) Inpatient Management

Length of stay and speciality

27 patients were admitted to an in-patient medical ward. The median duration of admission was 2.0 days (IQR 5.0, range 0-17). 66.7% (18/27) were admitted to a general medical ward, 18.5% (5/27) were admitted under neurology, 7.4% (2/27) were admitted to ICU, and the remaining 7.4% (2/27) were admitted under other specialities (infectious diseases and the surgical admissions centre). 29.6% (8/27) were transferred to another speciality during their admission (4 to gastroenterology, 2 to neurology and 2 to general medicine).

Final diagnosis at the end of the In-Patient Admission

Of those that were diagnosed with an epileptic seizure: 44.4% (12/27) had an historical diagnosis of epilepsy, 22.2% (6/27) had a history of recurrent seizures without an historical diagnosis of epilepsy,

and none) had experienced a first fit. 14.8% (4/27) were diagnosed with an acute symptomatic seizure and 7.4% (2/27) with a non-epileptic attack.

Discharge and referral

66.7% (18/27) were eventually discharged home from the hospital ward. All 18 were fully recovered at discharge. 11.1% (3/27) self-discharged without waiting for medical assessment. Of the patients who were discharged, 33.3% (6/18) had no documented referral or follow-up. 44.4% (8/18) were referred to an epilepsy clinic and 11.1% (2/18) were referred to an epilepsy specialist nurse. 2/6 (33.3%) patients with no referral were already under the care of the epilepsy clinic and may have had direct access to their services making formal referral unnecessary and one patient (1/18, 5.6%) already had an epilepsy clinic appointment scheduled for the next day.

3) Epilepsy clinic data

63.4% (52/82) of all patients with a suspected seizure who were transported to the ED during the study period had been seen in the only specialist epilepsy clinic in the city. 51.9% (27/52) of these had been seen before the index event and 25/52 (48.1%) had been seen after the index event. In 75.0% (39/52) of these patients a diagnosis of epilepsy was made in the clinic (either before or after the index event). In 66.7% (26/39), the diagnosis was localisation-related epilepsy, in 17.9% (7/39) it was generalised epilepsy, in 15.4% (6/39) the epilepsy type was undetermined. In 15.4% (8/52) a diagnosis of (PNES) was made in the epilepsy clinic.

4) Data from all sources

Epilepsy medication

38.6% (32/83) had a documented history of anti-epileptic drug (AED) use at the time of the index event: 56.3% (18/32) were receiving mono-therapy and 43.8% (14/32) poly-therapy. A suspicion of non-compliance with medication was documented in 18.8% (6/32).

General management and seizure-related injuries

AED regimes were changed or AEDs started during the hospital attendance/admission in 16.9% (14/83) of cases (in the ED or on the wards). Excluding the treatment of injuries, 36.1% (30/83) received some form of acute medical treatment (including complex treatments, such as for alcohol withdrawal, as well as relatively minor treatments such as pain relief with paracetamol or codeine). 7.2% (6/83) of incidents sustained an injury but only 1.2% (1/83) received major treatment (defined as that which probably required an acute hospital) for their injury (shoulder dislocation) and 2.4% (2/83) received minor treatment (defined as that which probably could have been delivered elsewhere) (wound care and treatment for an avulsed toenail). Although there was no tangible intervention in many incidents, all the patients received monitoring, assessment and diagnosis from a doctor and/or other clinicians.

Investigations

22.9% (19/83) had neuroimaging at some point during their attendance or admission. No patients had an EEG performed in the ED or as an in-patient. EEG tests, if considered necessary, were carried out as routine outpatient tests after the patient's discharge from their emergency care episode.

Seizure recurrence

In 73.5% (61/83) of incidents, the index event was the only seizure the patient had experienced in the 24 hours prior to their arrival in the ED. 21.7% (18/83) had experienced at least one other seizure in the previous 24 hours ('recurrent seizures'). Of those admitted after a single seizure, 14.8% (9/61) went on to have a subsequent seizure(s) in hospital. Of those with recurrent seizures, 27.8% (5/18) went on to have subsequent seizures in hospital. A Chi-Square test of independence was performed

to examine the relationship between seizure presentation on arrival (single or recurrent) and seizure recurrence during the hospital stay. The relationship was not significant, χ^2 (1, *N*=83) = 1.38, p = 0.24. 10.8% (9/83) of patients had emergency medication administered by either a carer or ambulance crew before arrival in the ED. Of these, 77.8% (7/9) were either still seizing on arrival in the ED or went on to have recurrent seizures during their hospital attendance.

Best Available Aetiological Explanation for the Index Event

The majority of suspected seizures in EPIC2 were epileptic 68/91 (74.7%) (including acute symptomatic seizures) but only 28/91 (30.8%) had a diagnosis of epilepsy. The epileptic seizures fall into the following four categories: a first epileptic seizure (13.2%, 12/91), an epileptic seizure in a patient with a historical diagnosis of epilepsy (30.8%, 28/91) an epileptic seizure in a patient known to have recurrent seizures but without a historical diagnosis of epilepsy (20.9%, 19/91) and acute symptomatic seizures in 9.9% (9/91). The other two important diagnostic categories were PNES 11.0% (10/91) and cardiogenic events 9.9% (9/91). The best available aetiological explanation for the index event is summarised in Figure 3 and Figure 4 shows diagnoses at each stage in the care pathway.

Diagnostic accuracy in the ED

87.8% (72/82) of diagnoses recorded at time of initial ED admission concurred with diagnoses made after more specialist or prolonged assessment during an inpatient stay or in a specialist in clinic. In those with an ED diagnosis of epileptic seizure, 98.3% (58/59) had a concordant diagnosis after inpatient admission or more specialist review.

DISCUSSION

Aetiology and Significance of Emergency Calls for Suspected Seizures

This is the first study to quantify diagnoses amongst pre-hospital patients after a suspected seizure. Our data show that 74.7% of our patients had suffered an epileptic seizure, 11.0% a PNES and 9.9% a cardiogenic event (see Figure 3). The patients with epilepsy fall into three sub-groups: epileptic seizure (first fit), epileptic seizure (epilepsy diagnosis) and epileptic seizure (not first fit, no epilepsy diagnosis). Although many of these patients did not require emergency treatment, patients in all three groups could benefit from a review in the next few days by an epilepsy specialist after a seizure (8) (this also applies to the patients with PNES). Despite this, our data is consistent with other large studies (6) which show that most patients are discharged without the input of an epilepsy specialist or follow-up. This leaves all these patients (not just those with epilepsy and PNES) at risk of recurrence and the associated morbidity, mortality and health services costs of these events (2).

Medical Emergencies and Clinical Risk Management

A large majority of the patients in our study were not acutely unwell on arrival at hospital. These results are consistent with qualitative data suggesting that major factors in deciding to call for an emergency ambulance and transporting patients to hospital after a suspected seizure are lack of confidence, and medico-legal concerns, amongst patients, carers, the public and paramedics rather than true clinical need (3) (4) (30). We were unable to define the exact proportion of patients that were potentially suitable for community management without transport to hospital or discharge from ED. This would require a criterion-based approach and further research would be required to define criteria which can be used to identify patients suitable for non-transport and how to overcome barriers to community management such as the presence of other clinical problems, risk stratification for recurrence of seizures, appropriate levels of supervision and safe management of the post-ictal phase.

The risk of seizure recurrence and the phenomenon of seizure clusters are a major factor in management decisions by clinicians but they are poorly understood (31). We are not aware of any prospective studies specifically looking at the short-term risk of seizure recurrence in the community. The published evidence in this area focusses on long-term recurrence risk after a seizure (32) (33) and the treatment of status epilepticus (34) (defined as ongoing seizure activity or recurrent seizures). Our data showed that, short-term recurrence is not more likely in patients who have presented with more than one seizure, compared with those who present with a single seizure, but the numbers in each group were small and further research is required.

Non-Compliance, Alcohol and Difficult to Reach Groups

20.9% (19/91) of patients in our study with recurrent seizures did not have an historical epilepsy diagnosis. This might partly be a reflection of inadequate medical records, using additional data sources such as GP records may have reduced the number in this category. But this result may reflect a more substantial problem of unmet need and is consistent with the national audit of seizure management in hospitals (NASH) (6), a large national audit conducted in the National Health Service (NHS) in the UK. We did not collect data to analyse this phenomenon further but we did find that alcohol use and illicit drugs were common clinical problems as was non-adherence with AED treatment. Non-adherence is associated with increased seizure frequency, adverse outcomes and increased hospital attendance/admission and higher health care costs (35) (36) (37). These data suggest that these patients may not understand the importance and benefits of medical advice, may be socially isolated and are perhaps living chaotic lifestyles. Simply improving access to medical services may not be an effective solution and more active outreach programmes may be required to reach this group (38). Hospital-based alcohol nurses and ambulance-service alcohol referral pathways may be able to intervene in these cases and facilitate joint working between alcohol services and services for people with epilepsy.

Demographics, Re-Attendance and Specialist Review

5.1% (4/79) of our patients re-attended within the one-month study period. This probably under-estimates the true repeat attendance rate because of the short time window. Other studies have estimated this figure as to be as high as 60% within one year (39). The age-histogram of our cohort was uni-modal with a cut-off at age 16 (children were excluded) and a peak incidence at age 40. However, the age-related incidence curve of epilepsy has two peaks, one in childhood and the other in old age (40). This inconsistency which has been reported elsewhere (41) may be explained by underlying seizure frequency in this group but other factors are likely to be more important such as alcohol use and thresholds for accessing care (42) (43). Consistent with the NASH audit, our data has shown sub-optimal rates of referral to epilepsy specialists and low rates of intervention such as in-patient specialist review, epilepsy-specific investigations or modification of AEDs (8). Follow-up by specialist epilepsy nurses has been shown to be associated with earlier discharge from hospital (39). Expansion of the specialist nurse role may be a solution to problems with lack of capacity in some consultant-led services (44).

Conclusions

Suspected seizures generate significant demand for emergency care (pre-hospital and hospital). Most suspected seizures are epileptic and often reflect failed ambulatory care for epilepsy. Emergency calls to ambulance services are an opportunity to improve seizure freedom rates by facilitating urgent review by an epilepsy specialist. Many patients do not require emergency hospital treatment and there is the potential to develop pathways which both avoid unnecessary hospital attendance/admission and facilitate specialist review. The EPIC study (EPIC1 and EPIC2) provides good quality data to stimulate further research and to conceptualise the reconfiguration of services which aim to maximise seizure freedom rates in people with epilepsy and to prevent avoidable attendances at hospital.

Ethics approval: This study was categorised as a service evaluation and received approval from the Clinical Governance Group at YAS, from the Clinical Effectiveness Unit at STH and from the University of Sheffield Research Ethics Committee (Ref 002558). We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Competing interests: JMD received a grant of £3,500 in 2014 from UCB Pharma Limited (paid to The University of Sheffield) to study unscheduled admissions for seizures using Hospital Episode Statistics. UCB had no direct input into the project. The other authors have no competing interests.

Data Sharing Statement: No data sharing agreements are in place but the authors welcome queries from people interested in viewing the original data.

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Contributorship Statement

The research was suggested by MR and RAG. They provided important advice and comments on the protocol and manuscript throughout. JMD took the lead with the study design, contacting collaborators, submitting ethics applications and other permissions, supervision of HD and writing the manuscript. HD took the lead for data collection, data analysis, presentation and interpretation of the results. She wrote some parts of the manuscript and reviewed the manuscript throughout its preparation by JMD. SM and JS were involved in study design, data collection and provided advice and comments on the protocol and manuscript throughout. JMD and HD and joint first authors and RAG and MR are joint senior authors.

Figure 1. Flow chart to illustrate the care pathway and exclusions throughout the EPIC study (EPIC1 and EPIC2). The EPIC1 exclusions were: missing/inadequate data (18/178) and miscellaneous, for example, hoax call (6/178). The non-seizure diagnoses in EPIC1 were: syncope (3), intoxicated/passed out (2), tremor/spasm (2), fall (2), rigours (2), twitching (1), panic attack (1), anxiety/hyperventilation (2), abnormal behaviour (1), social/miscellaneous/inappropriate (6). The non-seizure diagnoses in EPIC2 were (5/8 vasovagal, 1/8 syncope, 1/8 complete heart block, 1/8 'collapse').

Figure 2 Physiological parameters and the Sheffield Early Warning Score (SHEWS) for each of the patients on arrival in ED. SHEWS score: 1 = increase frequency of observations and inform nurse, 2 = hourly observations and consider medical review, 3 = immediate medical review. No patients had a SHEWS score recorded that was higher than 1. HR = heart rate, RR = respiratory rate, BP = blood pressure. O_2 sats. = oxygen saturations, GCS = Glasgow coma score. Normal ranges: heart rate (60-100bpm), respiratory rate (14-18 breaths per minute), systolic BP (100-140mmHg), blood glucose (3.5-11.1 mmol/l), temperature (36.5-37.5°C), O2 saturations (<94%) and GCS (15/15).

Figure 3: Best available aetiological explanation for the index event. Acute symptomatic causes were: alcohol withdrawal (6), head injury (1), hypoglycaemia (1), and transient ischaemic attack (1). The cardiogenic events: vasovagal episode (6), syncope (1), complete heart block (1), and collapse (1).

Figure 4a-d. Data from EPIC1 and EPIC2 to illustrate diagnoses, exclusions and missing data at each stage in the care pathway. Pre-Hospital Diagnoses (Fig 4a). In Sheffield May 2012 there were 178 suspected seizures for which 999 was called. 24/178 were excluded and 22/178 were not seizures leaving 132/178 suspected seizure incidents that were studied in detail in EPIC1. Exclusions: missing/inadequate data (18/178, 10.1%), miscellaneous e.g. hoax call (6/178, 3.4%). The clinical impression of the ambulance clinicians was that there was no evidence of seizure activity in 22/178 (12.4%). Not seizure diagnoses: syncope (3), intoxicated/passed out (2), tremor/spasm (2), fall (2), rigours (2), twitching (1), panic attack (1), anxiety/hyperventilation (2), abnormal behaviour (1), social/miscellaneous/inappropriate (6). **Hospital Diagnoses (Figs 4b-d).** Best Available Diagnoses (Fig 4b). The hospital notes of 91/132 were analysed in detail (98/132 were transported to hospital but 4/98 transported to an hospital outside Sheffield and 3/98 sets of notes were not available). The best available data for the aetiology of the 91 events is shown in Figure 4b (this is based on data from all sources: ED notes, in-patient notes and epilepsy clinic notes). Aetiology of acute symptomatic seizures: alcohol withdrawal (6), head injury (1), hypoglycaemia (1) and transient ischaemic attack (1). Emergency Department Diagnoses (Fig 4c). 82/91 that were transported to ED at STH were suspected seizures (Fig 4c). 9/91 were given non-seizure diagnoses: vasovagal episode (6), syncope (1), complete heart block (1), and collapse (1). NB/ An addition 1/91 suspected seizure was transported direct to an in-patient ward so 82/91 were diagnosed with suspected seizures. In-Patient Diagnoses (Fig 4d) 27/83 were admitted to an in-patient ward.

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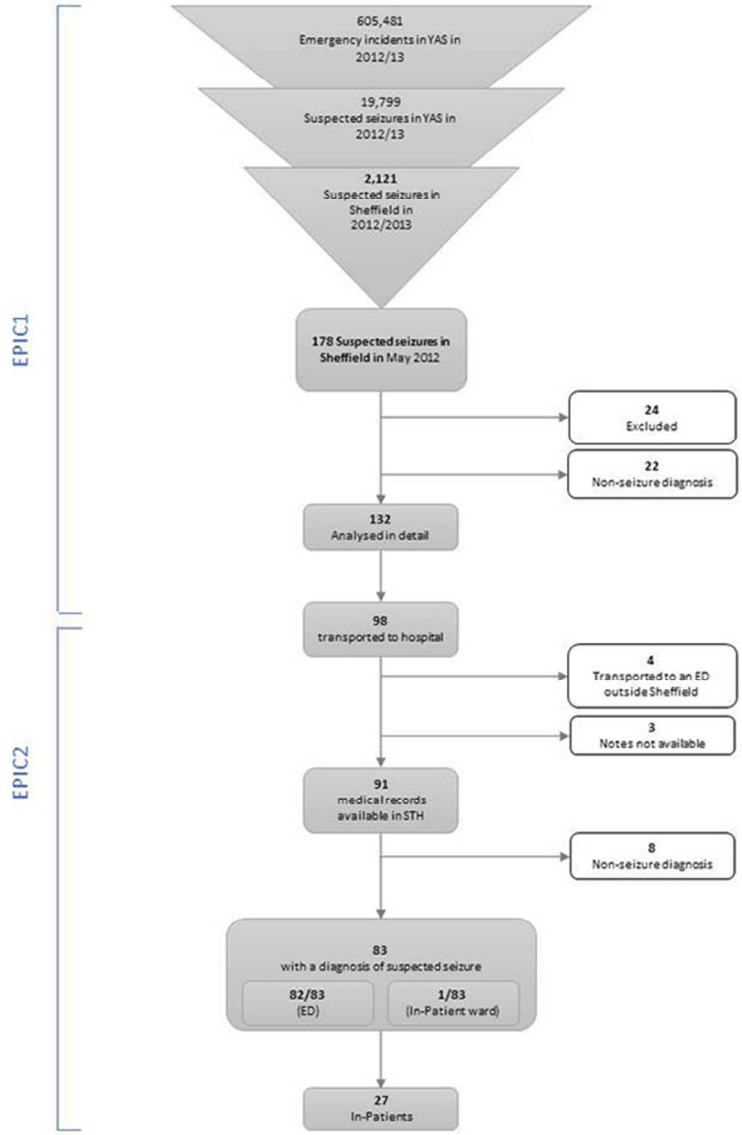

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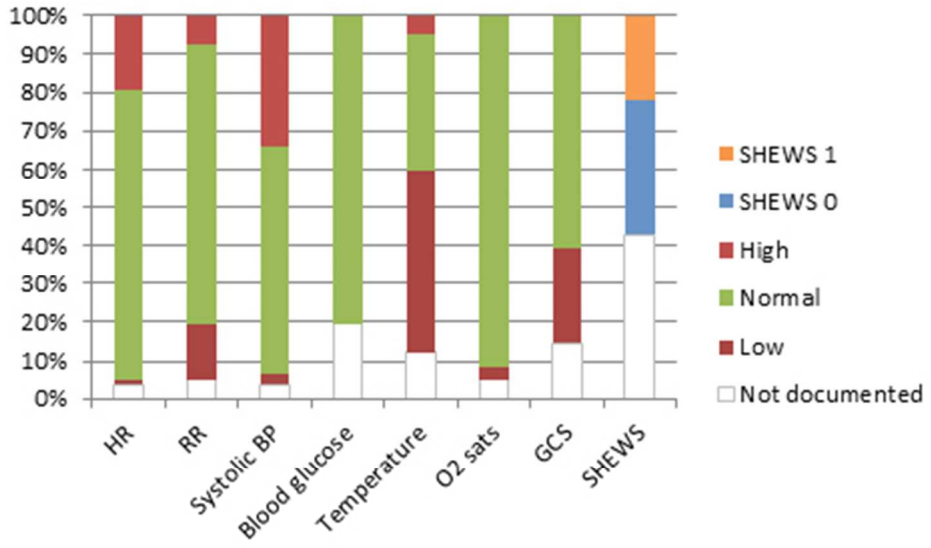

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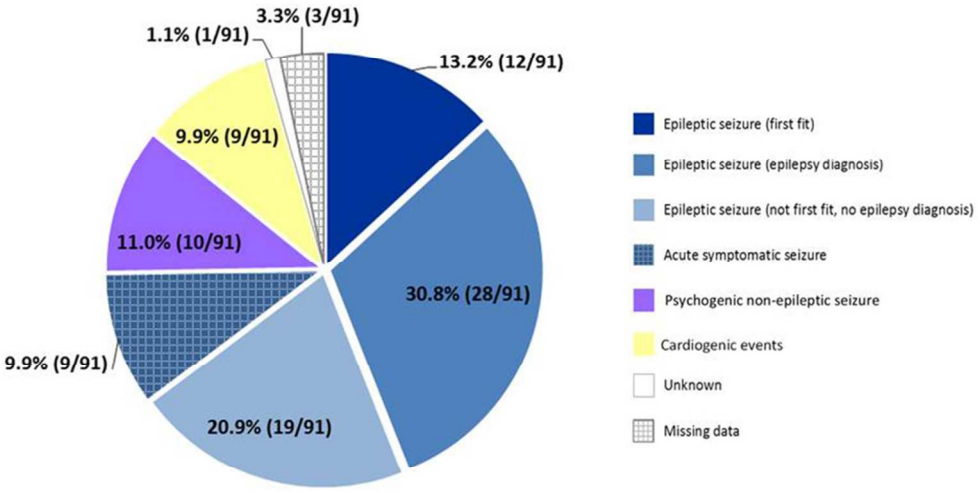

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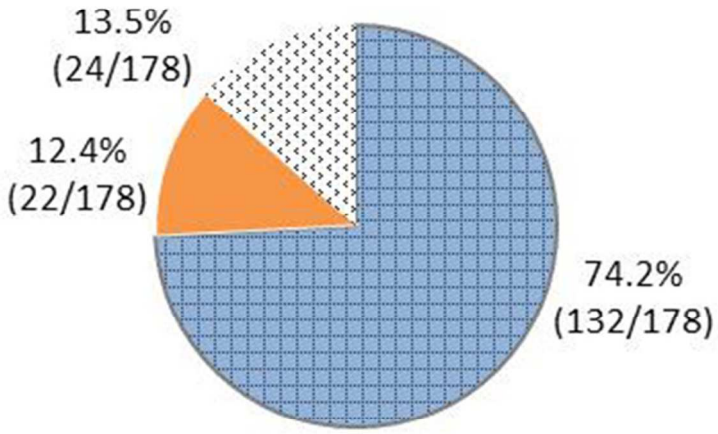

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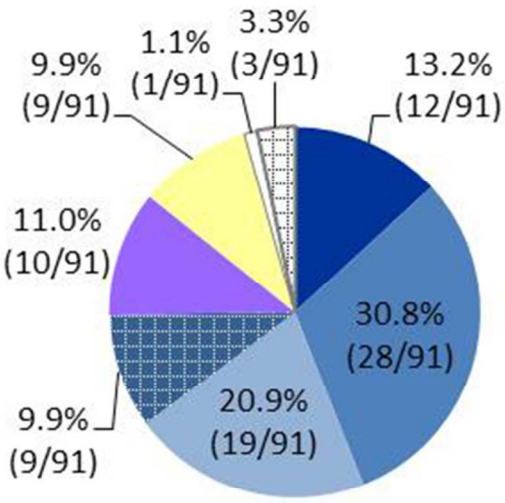

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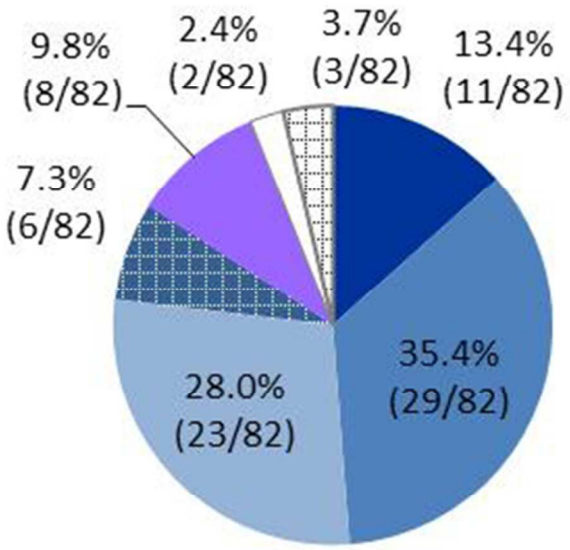

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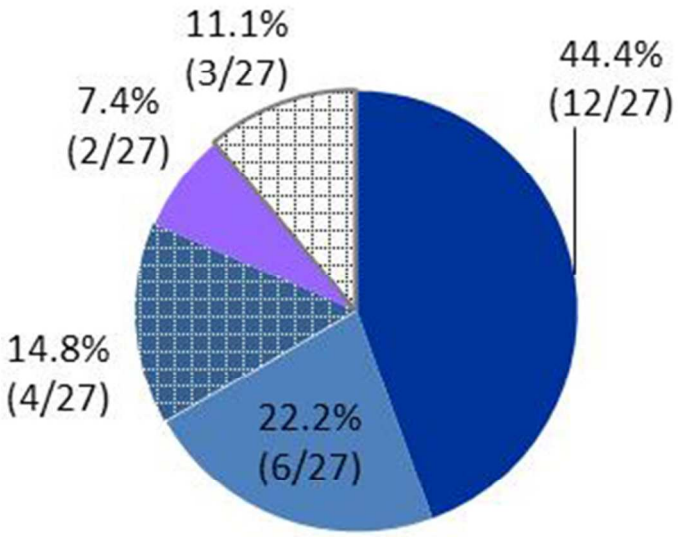

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Location	Variable	Categories	Notes
ED	ED area	1 Minors 2 Majors 3 Resus 4 Not documented	The highest dependency area that the patient went to during the ED attendance.
	HR on arrival	1 Normal 2 Low 3 High 4 Not documented	Normal heart rate (HR) = 60-100 beats per minute
	RR on arrival	1 Normal 2 Low 3 High 4 Not documented	Normal respiratory rate (RR) = 14-18 breaths per minute (male) and 16-20 breaths per minute (female)
	Systolic BP on arrival	1 Normal 2 Low 3 High 4 Not documented	Normal systolic blood pressure (BP) = 100-140 mmHg
	BM on arrival	1 Normal 2 Low 3 High 4 Not documented	Normal blood glucose (BM) = 3.5-11.1 mmol/l
	GCS on arrival	3 4 5 etc. 15 16 Not documented	GCS (Glasgow coma scale) is used to assess the state of consciousness of the patient. 3/15 (lowest score) = completely unresponsive 15/15 (highest score) = conscious, orientated, and responding well to questions

	Temperature on arrival	1 Normal 2 Low 3 High 4 Not documented	Normal temperature = 36.5-37.5°C
	O_2 sats	1 Normal 2 Low 3 Not documented	Low O_2 sats = < 94%
	SHEWS score on arrival	0 1 2 3 4 Not recorded	Sheffield hospitals early warning score (SHEWS) is an early warning system used to determine the degree of illness of a patient based on their HR, systolic BP, RR, temperature and level of alertness. Based on a scale from 0 to 3, where 0 is normal and 1-3 are outside the normal range, and 3 represents the greatest deviation from normal.
	Formal diagnosis of epilepsy?	1 Yes 2 No	A 'formal diagnosis of epilepsy' was as documented by the ED doctor on the ED card - as part of the medical history or documentation that the patient was known epileptic. Formal diagnosis means a diagnosis made by an appropriately qualified clinician - in most cases this would be a neurologist by could also include general physicians. Includes both idiopathic and symptomatic epilepsies. Non-epileptic attacks and alcohol-related seizures were not included unless a clear diagnosis of epilepsy was recorded as well.
	Documented history of PNES	1 Yes 2 No	

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	Suspicion of non-epileptic seizure documented	1 Yes 2 No	If clinician had a suspicion that the event was a non-epileptic attack.
	Seizure presentation on arrival (1)	1 Single seizure 2 Recurrent seizures	This variable was copied directly from the pre-hospital (EPIC1) data, as it is difficult to determine recurrence from the ED card. Seizures were divided into patients for which this was their first seizure in the previous 24 hours (single) and patients who had experienced more than one seizure in the previous 24 hours (recurrent).
	Seizure presentation on arrival (2)	1 Complete 2 Ongoing	
	Seizures during ED attendance	1 Yes 2 No	This includes unwitnessed seizures where the patient was found to be post-ictal.

	Other clinical problem (1)	1 None 2 Syncope 3 Stroke/TIA/CVA 4 Hypoglycaemia 5 Arrhythmias 6 Alcohol 7 Injury 8 Drugs 9 Other (specify)	This encompasses other clinical problems which may be acutely present in addition to the seizure, which requires hospital treatment and/or assessment. This would include, for example, a head injury requiring CT but no treatment, but would exclude bruising/grazes to the limbs. They may be the cause of the seizure, a complication of the seizure, or unrelated to the seizure. Arrhythmias: Does not include sinus tachycardia or sinus bradycardia. Alcohol: refers to any recent alcohol use and past alcohol abuse suggested by the past medical or drug history and of the patients such as a history of withdrawal seizures or alcohol dependent. The only exception is where alcohol consumption was indicated but was specifically noted to be below the recommended daily allowance (2-3 units for women, 3-4 units for men) with no reference to previous alcohol abuse. Drugs: includes illicit drug use as well as overdose on prescribed medication.
	Other clinical problem (1) (other)		

	Other clinical problem (2)	1 None 2 Syncope 3 Stroke/TIA/CVA 4 Hypoglycaemia 5 Arrhythmias 6 Alcohol 7 Injury 8 Drugs 9 Other (specify)	
	Other clinical problem (2) (other)		
	Other clinical problem (3)	1 None 2 Syncope 3 Stroke/TIA/CVA 4 Hypoglycaemia 5 Arrhythmias 6 Alcohol 7 Injury 8 Drugs 9 Other (specify)	
	Other clinical problem (3) (other)		

	Documented alcohol dependency	1 Yes 2 No	Where there is a clear statement that the patient has documented current alcohol dependency. Alcohol dependency is defined by the DSM-IV criteria as: “A maladaptive pattern of alcohol use leading to clinically significant impairment or distress, as manifested by three or more of the following seven criteria, occurring at any time in the same 12-month period: Tolerance; withdrawal; alcohol is often taken in larger amounts or over a longer period than was intended; there is a persistent desire or there are unsuccessful efforts to cut down or control alcohol use; a great deal of time is spent in activities necessary to obtain alcohol, use alcohol or recover from its effects; important social, occupational, or recreational activities are given up or reduced because of alcohol use; alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the alcohol”.[180]

	Clinical condition on arrival	1 Alert 2 Post-ictal 3 Ictal 4 Other (specify)	Taken from the nurses notes on arrival or ED notes if the clinical condition on arrival is clearly stated. The postictal state is the abnormal condition occurring between the end of an epileptic seizure and return to baseline condition. We operationalised our definition of post-ictal to only include symptoms that were a barrier to the patient being safely discharge home. It specifically did not include tiredness, headache or myalgia. The main feature which would mean safe discharge was not possible are reduced consciousness, significant drowsiness, neurological deficits etc.
	Clinical condition on arrival (other)		
	Seizure-related Injuries	1 Yes (specify) 2 No	Here injuries are only included if they required hospital assessment or treatment (in ED or as in-patient).
	Injuries (specify)		

	Fully recovered at the end of attendance	1 Yes 2 No	The patient was fully recovered if they had returned to their normal level of functioning with no acute medical problems that required hospital assessment and/or treatment, and were not post-ictal. We operationalised our definition of post-ictal to only include symptoms that were a barrier to the patient being safely discharge home. It specifically did not include tiredness, headache or myalgia. The main feature which would mean safe discharge was not possible are reduced consciousness, significant drowsiness, neurological deficits etc.
	Pregnancy	1 Yes 2 No	
	Illicit drug abuse documented/suspected	1 Yes 2 No	
	Medication in ED (1)	1 Yes 2 No	Anticonvulsant medication used for the termination of seizures.
	Medication in ED (2)	1 Lorazepam 2 Phenytoin 3 Diazepam 4 Midazolam 5 Other (specify)	
	Medication in ED (2) (Other)		
	HES code (local)		
	HES code (national)		

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	ED disposal	1 Discharged home 2 Discharged elsewhere 3 Admitted (specify where) 4 Death 5 Self-discharge	
	Admitted to	1 General medicine 2 ICU 3 Neurology 4 Other (specify where)	
	Admitted to (other)		
	Referral / Post-seizure follow up advice	1 Epilepsy clinic/first fit clinic 2 Epilepsy specialist nurse (referral or verbal advice) 3 GP 4 Other	The patient was said to have been referred to their GP if the patient was advised to see their GP for reasons relating to the care of their epilepsy. The ED physician may have written a letter to the GP.
	Referral (other)		
	Final diagnosis/impression of ED clinician (1)	1 Epileptic seizure (first fit) 2 Epileptic seizure (not first fit, no formal diagnosis of epilepsy) 3 Epileptic seizure (formal epilepsy diagnosis) 4 Non-epileptic attack	This is the diagnosis of the suspected seizure event. "not seizure" cases were included in this variable. Here, a 'formal epilepsy diagnosis' is one documented by the ED clinician.

		5 Acute symptomatic seizure (specify) 6 Not seizure (specify)	
	Final diagnosis/impression of ED clinician (1) (acute symptomatic - specify)		
	Final diagnosis/impression of ED clinician (1) (not seizure - specify)		
	Final diagnosis/impression of ED clinician (2)		
	Indication for admission	1 Social 2 Medical (seizure-related) (specify) 3 Medical (not seizure-related) (specify)	Social admissions are those where there is no medical reason for admission e.g. unable to put care package in place for discharge.
	Indication for admission (seizure-related - specify)		
	Indication for admission (not seizure-related - specify)		
In-patient	Date of admission		
	Date of discharge		
	Duration of admission		

	Seizures during admission	1 Yes 2 No	This includes unwitnessed seizures where the patient was found to be post-ictal.
	Final discharge destination	1 Home 2 Death 3 Self-discharge 4 Other (specify)	Home' was defined as the current or usual residence of the patient. This included rented or owned properties as well as institutions such as nursing or care homes. If the patient was discharged somewhere new, for example a patient previously living at home being discharged to a care home, this was documented as 'other'.
	Final discharge destination (other)		
	Transferred to another speciality during inpatient admission	1 Yes (specify) 2 No	
	Transferred to another speciality during inpatient admission (specify)		
	Fully recovered at the end of attendance	1 Yes 2 No	The patient was fully recovered if they had returned to their normal level of functioning with no acute medical problems that required hospital assessment and/or treatment, and were not-post ictal. We operationalised our definition of post-ictal to only include symptoms that were a barrier to the patient being safely discharge home. It specifically did not include tiredness, headache or myalgia. The main feature which would mean safe discharge was not possible are reduced consciousness, significant drowsiness, neurological deficits etc.

	Referral / Post-seizure follow up advice	1 Epilepsy clinic/first fit clinic 2 Epilepsy specialist nurse (referral or verbal advice) 3 GP 4 Other	The patient was said to have been referred to their GP if the patient was advised to see their GP for reasons relating to the care of their epilepsy. The physician may have written a letter to the GP.
	Referral (other)		
	Diagnosis at discharge	1 Epileptic seizure (first fit) 2 Epileptic seizure (not first fit, no formal diagnosis of epilepsy) 3 Epileptic seizure (formal epilepsy diagnosis) 4 Non-epileptic attack 5 Acute symptomatic seizure (specify) 6 Not seizure (specify)	Taken from discharge sheet, if no discharge sheet then final diagnosis documented in progress record or clerking sheet.
	Diagnosis at discharge (acute symptomatic - specify)		
	Diagnosis at discharge (not seizure - specify)		
Epilepsy clinic	Ever seen in epilepsy clinic?	1 Yes 2 No	

	Seen in epilepsy clinic before the index event?	1 Yes 2 No	
	Seen in epilepsy clinic (or specialised epilepsy services) as a result of the index event?	1 Yes 2 No	
	Does the patient have a diagnosis of epilepsy that was made in the epilepsy clinic? If yes, specify.	1 Yes 2 No	Regardless of when this diagnosis was made.
	Epilepsy clinic epilepsy diagnosis	1 Localisation-related epilepsy (focal, local, partial) 2 Generalised epilepsy 3 Undetermined whether focal or general 4 Special syndromes	These categories are based on the ILAE Proposal for Revised Classification of Epilepsies and Epileptic Syndromes - Epilepsia (1989) 30(4): 389-399.
	Does the patient have a diagnosis of PNES that was made in the epilepsy clinic? If yes, specify.	1 Yes 2 No	
From all sources	AEDs	1 Yes (state which) 2 No	AEDs at the time of the ED attendance in May 2012.

	Which AED (1)	1 Sodium valproate 2 Carbamazepine 3 Levetiracetam 4 Phenytoin 5 Phenobarbital 6 Not documented 7 Other (state which)	
	Which AED (1) (Other)		
	Which AED (2)	1 Sodium valproate 2 Carbamazepine 3 Levetiracetam 4 Phenytoin 5 Phenobarbital 6 Not documented 7 Other (state which)	
	Which AED (2) (Other)		
	Non-concordance with AEDs	1 Yes 2 No	At the time of the event in May 2012. This refers to patients who have not taken their AED medication as prescribed including cases where patients have run out of AEDs or forgotten to take their medication, as well as patients who have overdosed. Includes suspected non-adherence.

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	"Best available" aetiological explanation for the index event .	1 Epileptic seizure (first fit) 2 Epileptic seizure (not first fit, no diagnosis of epilepsy) 3 Epileptic seizure (epilepsy diagnosis) 4 Non-epileptic attack 5 Acute symptomatic seizure (specify) 6 Not seizure (specify)	"Not seizure" cases included in this variable.
	"Best available" aetiological explanation for the index event (acute symptomatic - specify)	1 Yes 2 No	
	"Best available" aetiological explanation for the index event (not seizure - specify)	1 Yes 2 No	
	Hospital management		These variables pertain to key features of hospital management received by the patient. The list is not exhaustive. This includes treatments that were not specifically to treat the seizure in the case of complex patients with more than one clinical problem.
	Expert opinion	1 Yes 2 No	Expert opinion from any hospital specialist on diagnosis, investigations or management.
	Was an AED regime started or modified during the admission?	1 Yes 2 No	Either in ED or in-patient.
	Neuroimaging	1 Yes 2 No	Acute neuroimaging especially CT head scan.

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	Acute medical treatment (specify)	1 Yes 2 No	Excluding injuries. Including: parenteral drugs to terminate seizures, IV fluids, etc.
	Acute treatment of injuries (major)	1 Yes 2 No	Dressings, sutures, shoulder relocation etc. which probably required hospital treatment.
	Acute treatment of injuries (minor)	1 Yes 2 No	Dressings, sutures, shoulder relocation etc. which probably did not require hospital treatment.
	Other (specify)	1 Yes 2 No	
	Other (specify)		Narrative account of hospital treatment