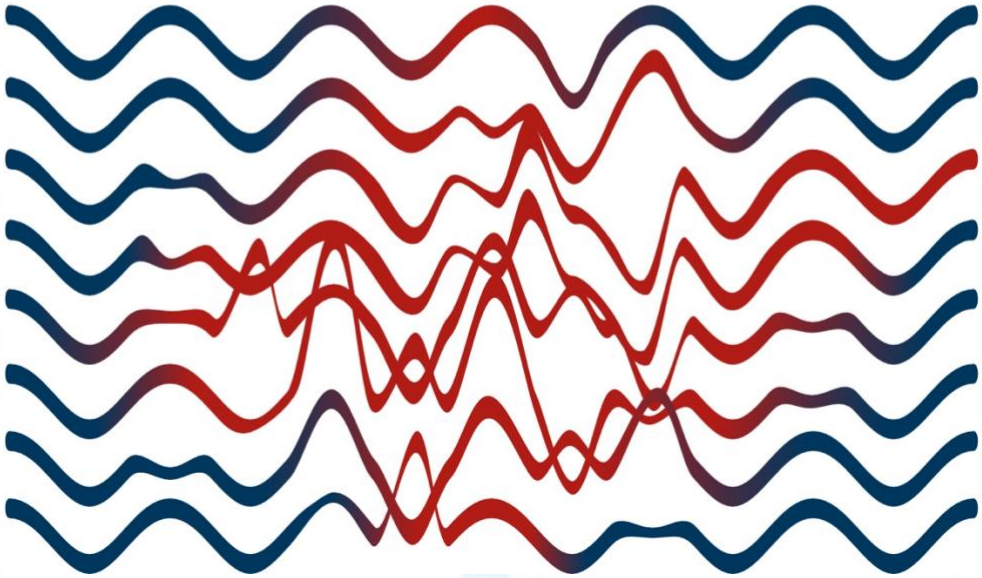
NAPIER

National Audit of Pathways in Epileptic Seizure Referrals



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CONTENTS

BACKGROUND

The diagnosis and management of suspected first seizures pose an important clinical problem. A first seizure may signal the onset of new epilepsy, previously undiagnosed epilepsy, or an underlying illness (e.g., brain tumour). Following a single unprovoked seizure, the risk of recurrence is greatest in the first 3-6 months, which has prompted the development of national guidelines setting standards of care for the management of seizures [1–3]. The National Institute of Health and Care Excellence (NICE) have set recommendations for suspected first epileptic seizures to be assessed within two weeks by a neurologist or epilepsy specialist [4]. This has led to the emergence of first seizure clinics and rapid referral pathways within secondary and tertiary centres throughout the UK and Ireland

The need for accessible and organised epilepsy care has been reinforced by the National Audit of Seizure management in Hospitals (NASH). This study demonstrated considerable variations in standards of care for seizures across the UK [5]. The rate of referral to neurology following emergency department (ED) attendance was well under 50% for almost all NHS trusts. Despite recommendations by NASH advocating separate pathways facilitating rapid referrals of suspected first seizures to specialist clinics, there exists limited organisational data at a national level regarding seizure referrals to specialists in secondary/tertiary care and their subsequent outcomes. This knowledge gap limits the development of a coherent national strategy for adult epilepsy services.

Furthermore, a considerable proportion of referrals to seizure clinics involve seizure mimics – conditions that are mistaken for true epileptic seizures (e.g. syncope, migraine, non-epileptic attacks) [6–8]. However, currently published data on the frequency of seizure mimics remain underpowered, and yet this remains an important public health concern [8–10]. Improved understanding surrounding seizure mimic referrals may provide useful data for the development of clinical biomarkers for epileptic seizures.

Established guidelines (NICE – Epilepsies: diagnosis and management) set clinical standards for the diagnosis and treatment of first seizures, and NAPIER aims to see if such standards are being met across specialist clinics throughout the UK and Ireland.

AIMS

The aims of NAPIER:

1. Audit current standards of care delivered to patients referred to first seizure clinics
    a. Management of suspected epileptic seizures and seizure mimics
    b. Onward referral to further specialist/tertiary services

OBJECTIVES

The objectives of NAPIER:

1. Identify 30 young people and adults (age ≥16) patients referred and assessed for suspected seizures at each participating specialist seizure clinic
2. Explore patient characteristics of first seizure referrals
3. Assess how standards in first seizure care vary with patient and demographical factors
4. Ascertain the annual number of patients referred to first seizure clinics from primary or secondary care
5. Identify the proportion of seizure mimics referred to first seizure clinics
6. Identify the proportion of referred patients who did not attend (DNA) their clinic appointments
7. Raise the profile of epilepsy and epilepsy research among medical students and junior doctors

AUDIT STANDARDS

The current NICE guidelines (Epilepsies: diagnosis and management) will be used as the audit standard (Appendix A)

STUDY COORDINATION

NAPIER will be coordinated by the Neurology And Neurosurgery Interest Group (NANSIG), led by Dr Seong Hoon Lee (NANSIG Vice Chair of Research, NHS Grampian Academic Foundation Doctor), under supervision from Professor Phyo Kyaw Myint (NHS Grampian Director of Clinical Academic Training & Development). NAPIER will be overseen by a national steering committee consisting of representatives from NANSIG, academic neurologists, and patient representatives.

ETHICAL APPROVAL

NAPIER is a descriptive clinical audit that will collect anonymised data to assess current standards in care for seizure management across the UK and Ireland. This will not require individual patient consent or ethical approval.

TIMELINE

The data collection period for NAPIER will run from 15th October 2021 to 31st March 2022.

	April – Sept 2021	Oct	Nov	Dec	Jan - March 2022	April	May	June	July
Protocol development and approval									
Local team recruitment									
Local project registration									
Data collection period									
Data submission deadline									
Statistical Analysis									
Preparing Manuscript(s)									
Publication and feedback to local departments									

SELECTION OF PARTICIPATING CENTRES

NAPIER is open to any hospitals in the UK or Ireland with specialist seizure clinics wishing to participate.

CASE ASCERTAINMENT

Retrospective case-note analysis: Each centre will be asked to collect anonymous data from 30 consecutive patients referred and assessed at specialist seizure clinics from 31st December 2019 going backwards (not the date of the referral request), with the duration going back as long as it needs to complete 30 consecutive cases.

Case ascertainment will vary between hospitals, most will record patient data on electronic care records and some may be paper-based.

CASE SELECTION CRITERIA

The following inclusion and exclusion criteria should be used to identify cases.

INCLUSION CRITERIA

1. They were considered an adult (age ≥16) on the day of the seizure event.
2. Referred to a specialist seizure clinic for suspected first epileptic seizure*

EXCLUSION CRITERIA

1. Patients aged <16 at time of seizure
2. Existing diagnosis of epilepsy prior to seizure clinic referral
3. Patients referred and seen outside of the study period
4. Unavailability of medical/clinic records

*Suspected first epileptic seizure: All patients suspected to have a first seizure as deemed by the referring clinician (GP/ED/secondary care clinicians)

DATA COLLECTION

Medical student and junior doctor representatives of NANSIG will be asked to identify a consultant supervisor at their respective medical school/deanery for permission and guidance to access data. This will likely be the consultant neurologist in charge of the seizure clinics in their region.

Data domains on anonymised patient demographics (age, sex) seizure characteristics, treatments and investigations requested at the seizure clinic will be collected. Patient identifiable data will not be collected. All patients will be assigned a unique study ID number to allow for traceability – these numbers will be stored securely on password-protected NHS computers and servers.

NANSIG representatives are encouraged to recruit a team of 2 or 3 medical students or junior doctors from their respective universities for the data collection process. Once the team are familiar with the data collection website, the estimated data collection time for each patient case will be 15-20 minutes.

DATA ANALYSIS

NAPIER is a clinical audit aiming to provide summary statistics and to investigate potential reasons for variability between participating centres. Descriptive data will be presented as: n (%), normally distributed continuous variables as mean (standard deviation [SD]), and skewed variables (identified statistically via skewness and kurtosis) as median (interquartile range [IQR]).

Statistical significance will be set at $\alpha < 0.05$. Differences in means and proportions will be assessed using Chi^2 and the student's T-test or the Mann-Whitney U test to investigate group differences. Statistical analyses will be performed on SPSS (Statistical Package for the Social Sciences, V.24.0, Chicago, Illinois, USA).

AUTHORSHIP ELIGIBILITY

NAPIER will use a corporate authorship model. The contribution of all local investigators will be recognised, and all work (final study results) will be submitted under a sole authorship under the name of the "NAPIER collaborative". This will encapsulate NANSIG core committee members involved with the study. If a journal does not allow a corporate authorship, named authorship will be given to contributors satisfying the following conditions defined by the International Committee of Medical Journal Editors:

i. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
ii. Drafting the work or revising it critically for important intellectual content; AND
iii. Final approval of the version to be published; AND
iv. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

STUDY STEERING COMMITTEE

NANSIG: Seong Hoon Lee, Conor Gillespie, Soham Bandyopadhyay, Suzanne Murphy, Armin Nazari, Mehdi Kahn, Setthasorn Zhi Yang Ooi, Jay Jaemin Park

Consultants/Academics: Professor Tony Marson, Professor Phyo Kyaw Myint, Dr Michael Kinney, Dr Graham Mackay, Miss Claire Taylor

Epilepsy Action: Angie Pullen, Claire Champ, Peter Burke

NATIONAL & PUBLIC ENGAGEMENT

Medical Students & Junior Doctors: NANSIG

Patient & Public Involvement: Epilepsy Action

Following data collection and analysis, a meeting will be held to interpret the findings and implications. Key areas for improvement will be identified to help guide service change. The results will be fed back to all participating centres, allowing them to compare their standards in care with the national average.

NANSIG representatives and their local team of medical students and junior doctors are encouraged to present these findings at their regional clinical neuroscience MDT meetings.

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DEFINITIONS

Electroencephalogram (EEG): An investigation that involves recording the electrical activity of the brain. Electrodes are attached to standardised points on the person's head with collodion. Recordings are usually taken across two points.

Epilepsy: A condition in which a person is prone to recurrent epileptic seizures.

Epilepsy syndrome: A distinctive disorder identifiable on the basis of a typical age of onset, seizure types, specific EEG characteristics, and often other features. Identification of epilepsy syndrome has implications for treatment, management and prognosis. (Definition from the International League Against Epilepsy [ILAE] Task Force on Classification [2001].)

Epileptic seizure: A transient occurrence of signs and/or symptoms, the result of a primary change to the electrical activity (abnormally excessive or synchronous) in the brain.

Focal seizure: A seizure that originates within networks limited to one hemisphere, discretely localised or more widely distributed. Replaces the terms partial seizure and localisation-related seizure.

Generalised seizure: A seizure that originates in, and rapidly engages, bilaterally distributed networks. Such bilateral networks can include cortical and subcortical structures but do not necessarily include the entire cortex.

Generalised tonic-clonic seizure: A seizure of sudden onset involving generalised stiffening and subsequent rhythmic jerking of the limbs, the result of rapid widespread engagement of bilateral cortical and subcortical networks in the brain.

Non-epileptic attack disorder (NEAD): A disorder characterised by episodes of change in behaviour or movement, not caused by a primary change in electrical activity of the brain. Movements are varied, and the attacks can be difficult to differentiate from epileptic seizures.

Secondary generalised seizure: Now referred to as a 'focal seizure evolving to a bilateral convulsive seizure'. (Definition from the International League Against Epilepsy [ILAE] Task Force on Classification [2001].)

Simple and complex partial epileptic seizures: These terms are no longer recommended. They have been generally replaced with the single word, 'focal'. Focal seizures should include a clear description of the impairment of consciousness. (Definition from the International League Against Epilepsy [ILAE] Task Force on Classification [2001].)

Specialist: A medical practitioner with training and expertise in epilepsy.

Syncope: A brief lapse in consciousness caused by transient reduction in blood flow to the brain. May be caused by many different factors, including emotional stress, vagal stimulation, vascular pooling in the legs, diaphoresis, or sudden change in environmental temperature or body position.

Tertiary epilepsy specialist: A tertiary epilepsy specialist is an adult or paediatric neurologist who devotes the majority of their working time to epilepsy, is working in a

multidisciplinary tertiary referral centre with appropriate diagnostic and therapeutic resources, and is subject to regular peer review.

Tertiary service: Specialist care delivery unit, to which people may be referred from secondary care.

Tonic seizure: An epileptic seizure characterised by abrupt generalised muscle stiffening possibly causing a fall. The seizure usually lasts less than a minute and recovery is rapid.

Tonic-clonic seizure: An epileptic seizure characterised by initial generalised muscle stiffening, followed by rhythmical jerking of the limbs, usually lasting a few minutes. The person may bite their tongue and may be incontinent. They may feel confused or sleepy afterwards, and take a while to recover fully.

APPENDIX A. NICE Guideline Standards (Epilepsies: diagnosis and management)

1.4.5 It is recommended that all adults having a first seizure should be seen as soon as possible by a specialist in the management of the epilepsies to ensure precise and early diagnosis and initiation of therapy as appropriate to their needs. (The Guideline Development Group considered that with a recent onset suspected seizure, referrals should be urgent, meaning that patients should be seen within 2 weeks.) **[2004]**

1.5.1 The diagnosis of epilepsy in adults should be established by a specialist medical practitioner with training and expertise in epilepsy. **[2004]**

1.5.4 A detailed history should be taken from the child, young person or adult and an eyewitness to the attack, where possible, to determine whether or not an epileptic seizure is likely to have occurred. **[2004]**

1.5.6 It may not be possible to make a definite diagnosis of epilepsy. If the diagnosis cannot be clearly established, further investigations and/or referral to a tertiary epilepsy specialist (see recommendation 1.10.2 in the section on referral for complex or refractory epilepsy) should be considered. Follow-up should always be arranged. (In this recommendation, 'centre' has been replaced with 'specialist' for consistency across recommendations.) **[2004]**

1.5.7 Where non-epileptic attack disorder is suspected, suitable referral should be made to psychological or psychiatric services for further investigation and treatment. **[2004]**

1.6.3 Children, young people and adults requiring an EEG should have the test performed soon after it has been requested. (The Guideline Development Group considered that 'soon' meant being seen within 4 weeks.) **[2004]**

1.6.4 An EEG should be performed only to support a diagnosis of epilepsy in adults in whom the clinical history suggests that the seizure is likely to be epileptic in origin. **[2004]**

1.6.6 An EEG should not be performed in the case of probable syncope because of the possibility of a false-positive result. **[2004]**

1.6.7 The EEG should not be used to exclude a diagnosis of epilepsy in a child, young person or adult in whom the clinical presentation supports a diagnosis of a non-epileptic event. **[2004]**

1.6.19 Neuroimaging should be used to identify structural abnormalities that cause certain epilepsies. **[2004]**

1.6.20 MRI should be the imaging investigation of choice in children, young people and adults with epilepsy. **[2004]**

1.6.21 MRI is particularly important in those:

- who develop epilepsy before the age of 2 years or in adulthood
- who have any suggestion of a focal onset on history, examination or EEG (unless clear evidence of benign focal epilepsy)
- in whom seizures continue in spite of first-line medication. **[2004**

1.6.22 Children, young people and adults requiring MRI should have the test performed soon. (The Guideline Development Group considered that 'soon' meant being seen within 4 weeks.) **[2004]**

1.6.23 Neuroimaging should not be routinely requested when a diagnosis of idiopathic generalised epilepsy has been made. **[2004]**

1.6.24 CT should be used to identify underlying gross pathology if MRI is not available or is contraindicated, and for children or young people in whom a general anaesthetic or sedation would be required for MRI but not CT. **[2004]**

1.6.25 In an acute situation, CT may be used to determine whether a seizure has been caused by an acute neurological lesion or illness. **[2004]**

1.6.26 Measurement of serum prolactin is not recommended for the diagnosis of epilepsy. **[2004]**

1.6.27 In adults, appropriate blood tests (for example, plasma electrolytes, glucose, calcium) to identify potential causes and/or to identify any significant comorbidity should be considered. **[2004]**

1.6.29 A 12-lead ECG should be performed in adults with suspected epilepsy. **[2004]**

1.6.31 In cases of diagnostic uncertainty, a referral to a cardiologist should be considered. **[2004]**

1.6.32 Neuropsychological assessment should be considered in children, young people and adults in whom it is important to evaluate learning disabilities and cognitive dysfunction, particularly in regard to language and memory. **[2004]**

1.7.1 Epileptic seizures and epilepsy syndromes in children, young people and adults should be classified using a multi-axial diagnostic scheme. The axes that should be considered are: description of seizure (ictal phenomenology); seizure type; syndrome and aetiology. **[2004]**

1.7.2 The seizure type(s) and epilepsy syndrome, aetiology, and comorbidity should be determined, because failure to classify the epilepsy syndrome correctly can lead to inappropriate treatment and persistence of seizures. **[2004]**

1.8.2 All children, young people and adults with epilepsy should have a comprehensive care plan that is agreed between the person, family and/or carers where appropriate, and primary care and secondary care providers. This should include lifestyle issues as well as medical issues. **[2004]**

1.8.3 Epilepsy specialist nurses (ESNs) should be an integral part of the network of care of children, young people and adults with epilepsy. The key roles of the ESNs are to support both epilepsy specialists and generalists, to ensure access to community and multi-agency services and to provide information, training and support to the child, young person or adult, families, carers and, in the case of children, others involved in the child's education, welfare and well-being. **[2004]**

1.9.2.1 AED therapy should only be started once the diagnosis of epilepsy is confirmed, except in exceptional circumstances that require discussion and agreement between the prescriber, the specialist and the child, young person or adult and their family and/or carers as appropriate. **[2004]**

1.9.2.5 Treatment with AED therapy is generally recommended after a second epileptic seizure. **[2004]**

1.9.2.6 When possible, choose which AED to offer on the basis of the presenting epilepsy syndrome. If the epilepsy syndrome is not clear at presentation, base the decision on the presenting seizure type(s). **[new 2012]**