Improving epilepsy diagnosis across the lifespan: approaches and innovations

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Epilepsy diagnosis is often delayed or inaccurate, exposing people to ongoing seizures and their substantial consequences until effective treatment is initiated. Important factors contributing to this problem include delayed recognition of seizure symptoms by patients and eyewitnesses; cultural, geographical, and financial barriers to seeking health care; and missed or delayed diagnosis by health-care providers. Epilepsy diagnosis involves several steps. The first step is recognition of epileptic seizures; next is classification of epilepsy type and whether an epilepsy syndrome is present; finally, the underlying epilepsy-associated comorbidities and potential causes must be identified, which differ across the lifespan. Clinical history, elicited from patients and eyewitnesses, is a fundamental component of the diagnostic pathway. Recent technological advances, including smartphone videography and genetic testing, are increasingly used in routine practice. Innovations in technology, such as artificial intelligence, could provide new possibilities for directly and indirectly detecting epilepsy and might make valuable contributions to diagnostic algorithms in the future.

Introduction

Epilepsy encompasses a range of diseases with an enduring predisposition to generate unprovoked seizures.[1] More than 50 million people live with epilepsy worldwide, and the disorder exerts a substantial global burden on disability-adjusted life years and mortality.[2] The scope of clinical presentations, causes, and comorbidities can make the diagnosis of epilepsy challenging; yet, prompt diagnosis is crucial for guiding treatment.

Antiseizure medications can control seizures in up to 80% of people with epilepsy,[3] reducing seizure-related morbidity and mortality. Unfortunately, delays in treatment initiation are frequent and can lead to reduced quality of life and increased risk of injury, admission to hospital, and death.[4–6] Many factors contribute to treatment delays. For example, subtle or nuanced seizure signs and symptoms can go unrecognised by people living with epilepsy and eye-witnesses or be misdiagnosed by health-care providers. This diagnostic gap is crucial to identify and resolve, particularly in older adults for whom the majority of new-onset seizures have non-convulsive symptoms.[7]

Once seizures are recognised, diagnosis of the epilepsy type and, if applicable, the epilepsy syndrome is key to inform appropriate treatment decisions. In 2022, the International League Against Epilepsy (ILAE) published a formal classification of epilepsy syndromes across the lifespan to assist with syndrome identification.[8–13] The importance of rapid and accurate epilepsy diagnosis is now a widely recognised issue, as reflected by WHO's *Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031* (IGAP), which was approved by the World Health Assembly in 2022.[14] The IGAP represents a culmination of substantial work by WHO, the International Bureau for Epilepsy, and the ILAE in their Global Campaign Against Epilepsy to raise epilepsy awareness, increase epilepsy education, and help close diagnostic and treatment gaps for people with epilepsy.[15]

In this Review, we discuss the causes and consequences of diagnostic delay in people with epilepsy, describe common comorbidities and unique diagnostic considerations across the lifespan, highlight the importance of epilepsy classification and syndrome identification, and describe emerging investigative tools for diagnosis.

The importance of early and accurate epilepsy diagnosis

Initial diagnostic hurdles

Epilepsy can be over-diagnosed and under-diagnosed. An estimated 20% of cases are erroneously diagnosed, with non-epileptic seizure-like events caused most commonly by syncope, functional seizures, or cardiovascular conditions.[16,17] Over-diagnosis of epilepsy has immense implications, including unnecessary exposure to antiseizure medications and their adverse events, social ramifications including driving and work restrictions, and delay in initiation of appropriate investigations and interventions. Previous work has addressed differential diagnosis of seizure-like events in detail.[3]

Under-diagnosis of epilepsy is also important. Diagnostic delay occurs in up to 77% of people with epilepsy.[18] Many factors can contribute to diagnostic delay, including missed or misdiagnosed signs or symptoms and barriers to accessing health care.[18] Unrecognised seizures are the primary cause of delayed diagnosis;[7,19] seizure signs and symptoms unrecognised by individuals or eye-witnesses can lead to diagnostic delay spanning months and sometimes years.
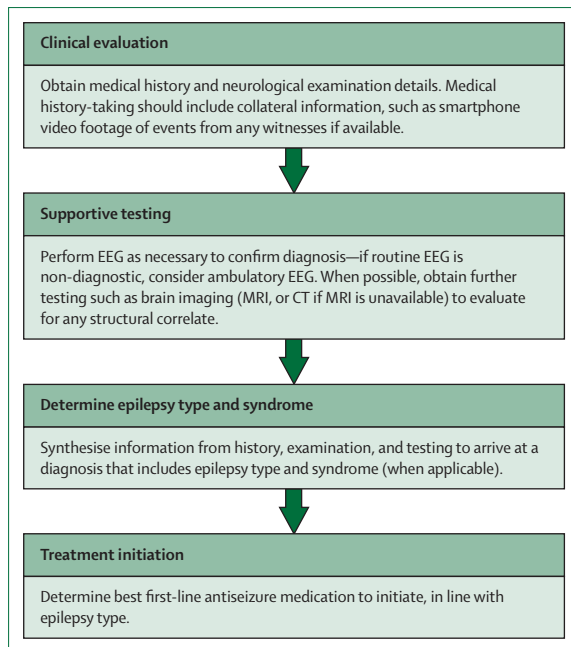
After diagnosis, further delays are common on the path to treatment optimisation and, where indicated, epilepsy surgery.[20] Barriers to treatment include perceived stigma, health literacy, language, geography, cultural factors, and financial problems.[18] Perceived stigma is the subjective awareness of social stigma or expected reaction from others that people with new-onset seizures might feel. It is associated with lower quality of life, social isolation, and psychiatric comorbidities, whereas higher

Clinical evaluation

Obtain medical history and neurological examination details. Medical history-taking should include collateral information, such as smartphone video footage of events from any witnesses if available.

Supportive testing

Perform EEG as necessary to confirm diagnosis—if routine EEG is non-diagnostic, consider ambulatory EEG. When possible, obtain further testing such as brain imaging (MRI, or CT if MRI is unavailable) to evaluate for any structural correlate.

Determine epilepsy type and syndrome

Synthesise information from history, examination, and testing to arrive at a diagnosis that includes epilepsy type and syndrome (when applicable).

Treatment initiation

Determine best first-line antiseizure medication to initiate, in line with epilepsy type.

Figure 1: **Overview of epilepsy diagnosis**
The primary steps in making an epilepsy diagnosis involve first obtaining a thorough medical history and examination, ordering testing to help support diagnosis and evaluation of underlying causes, and then initiating treatment when appropriate.

self-efficacy (an individual's belief in their own capabilities) as well as greater health literacy and good social support are associated with less perceived stigma.[21–23] Public education can mitigate the effect of stigma on time to diagnosis.[24] Improving public awareness and knowledge of epilepsy might reduce diagnostic barriers, in parallel with ongoing medical education that raises the profile of epilepsy and its various manifestations among clinicians, particularly those working in primary care and emergency settings.

Arriving at a diagnosis

Once people with suspected epilepsy access medical services, early diagnosis and initiation of appropriate medication are crucial for delivering optimal care because antiseizure medications reduce the odds of seizure recurrence and epilepsy-related morbidity and mortality.[20] Health-care providers should follow several steps to make an accurate epilepsy diagnosis and ensure that appropriate treatment is initiated.[25] In line with ILAE guidelines,[1] the crucial first step in diagnosis is determining whether the seizure event is epilepsy, which is achieved through obtaining a thorough medical history; clinical examination, smartphone video footage, and investigations such as EEG and neuroimaging can support the diagnosis. When epileptic seizures are confirmed, the next step is to ascertain whether ILAE diagnostic criteria are fulfilled.[1] Epilepsy type and syndrome, and conditions with causative or bidirectional

relationships with epilepsy, should be identified as per the ILAE diagnostic schema. In addition to history-taking and clinical examination, targeted investigations (eg, genetic testing for specific phenotypes or neurocognitive testing for cases of suspected neurodegenerative conditions) might be helpful in identifying the epilepsy type, epilepsy syndrome, and other conditions with causative or bidirectional relationships with epilepsy. Underlying conditions causing seizures that require urgent medical attention—eg, tumour, infection, or haemorrhage—should be identified at the time of initial medical evaluation.

The diagnostic investigation comprises a detailed clinical history, which alone might secure the diagnosis, and corroborating evidence such as video footage of the seizure event, an EEG that captures interictal epileptiform discharges or electrographic seizure activity, and neuroimaging such as MRI or CT (if MRI is unavailable) that shows a potential epileptogenic brain lesion (figure 1). Notably, apart from formal characterisation on video EEG, no single event or testing modality in isolation can be used to make an epilepsy diagnosis; as per ILAE guidelines, epilepsy is a clinical diagnosis.[1] For example, an epileptiform discharge on EEG in the absence of a supportive clinical history does not meet epilepsy diagnostic criteria. The diagnosis can be made on the basis of clinical history alone because investigations such as EEG and MRI are often either non-contributory or not available.

Many people who experience a first convulsive seizure present to emergency departments (panel 1). Half have experienced preceding non-motor seizures,[5,26,27] with more subtle clinical manifestations,[28] underscoring the importance of detailed history-taking as part of epilepsy diagnostic evaluations. As signs and symptoms of focal seizures are manifold, health-care providers should find value in asking for both specific features (eg, presence of intense intrusive déjà vu) and more common characteristics, such as the presence of unprovoked, short-duration (typically ≤2 min), stereotyped (always the same for an individual), or strange or unusual symptoms from affected individuals, or signs noticed by eye-witnesses.[29]

Consequences of delayed diagnosis

Consequences of diagnostic delay affect individuals, communities, and health-care systems. People with untreated epilepsy are at increased risk of injuries, motor vehicle collisions, and mortality, including sudden unexpected death in epilepsy (SUDEP).[4,7,30] SUDEP has an incidence of 0·09–2·4 deaths per 1000 person-years, and young age, a structural cause for the epileptic seizures, and drug resistance are independent predictors of this outcome, and it is possible that delayed diagnosis and treatment might also contribute to SUDEP.[30] An analysis of baby monitoring system videos suggested that unexplained death in toddlers could often be associated

with seizures.[31] Young adults are also disproportionately affected, leading to an augmented health-economic burden through increased disability-adjusted life years.[32] People with undiagnosed and untreated epilepsy also experience increased health-care utilisation, because unrecognised seizures lead to recurrent emergency department visits, hospital admissions, and redundant medical testing.[33,34] Additional indirect consequences resulting from undiagnosed epilepsy include negative effects on cognition, emotional well-being, and social functioning; reduced productivity while at school or work; and a higher burden of informal care needs such as unpaid care provided by friends and family.[35] Epilepsy comorbidities, such as depression and anxiety, might be exacerbated by diagnostic delay, potentially further contributing to barriers in help-seeking.[36,37]

Diagnosing epilepsy across the lifespan
History and examination
The first step in the diagnosis of epilepsy is correctly identifying whether events are epileptic seizures.[1] Most children and adolescents attending emergency departments or medical clinics with paroxysmal events do not have epilepsy; therefore, clinicians must be skilful in recognising the myriad of epilepsy mimics.[38] A detailed medical history—including all circumstances before the event, the nature of the event, course, timing, and post event signs and symptoms—should be elicited (panel 2). Paediatric specialists often have the benefit of a parent or carer as witness to the event; however, the child must also be encouraged to describe their experiences in their own language. Descriptions from a 9-year-old such as a "fuzzy feeling in my mouth and not being able to talk" might indicate a focal seizure typical of self-limited epilepsy with centrotemporal spikes.[10] A younger child might not be able to articulate their symptoms but, with colouring pencils, might draw the brightly coloured circles and other shapes characteristic of the onset of focal seizures in childhood occipital visual epilepsy.[10] These are practical methods that health-care providers can implement in practice.

Observation of a child's behaviour in the clinic and other aspects of clinical examination are important at the time of epilepsy diagnosis and might aid in diagnosing the epilepsy syndrome. Cognitive, behavioural, and motor comorbidities are most common in early, childhood-onset, developmental and epileptic encephalopathies, with particular patterns giving clues to underlying causes, guiding investigations and future management.[39–41] When developmental regression or stagnation is associated with clusters of spasm-like movements in an infant, a diagnosis of infantile epileptic spasms syndrome is likely and can be confirmed by capturing a video of an event, which can then be supported by an EEG.[9] In an older child with infrequent focal to bilateral tonic-clonic seizures in sleep but regression in behaviour, cognition, or speech and language, the diagnosis could be epileptic

encephalopathy with spike-wave activation in sleep, which can only be confirmed by a sleep EEG recording.[10] A history of progressive visual loss in the years following a diagnosis of epileptic seizures in a pre-school child should raise suspicion for ceroid lipofuscinosis type 2. This previously fatal disease can now be treated with intrathecal enzyme replacement therapy.[42]

Panel 1: Consequences of delayed diagnosis

A 35-year-old right-handed woman with no past medical history began experiencing recurrent events characterised by altered sensation and behaviour.

Seizure 1
She experienced what she described as a "loss of time" while driving. She received an email from her insurance company telling her she was involved in a hit and run—she thought this was a mistake until she went to look at her car and noticed it was dented and leaking fluid.

Seizure 2
1 week after the first seizure, she had another seizure while driving; she collided with another vehicle, there were no injuries, and she had no recollection of what happened. Following this seizure, she went to an emergency department for assessment of her symptoms, which she described as a memory lapse. In the emergency department, she underwent CT of the head, blood work, and had an electrocardiogram, with no abnormalities, and she was discharged without a diagnosis.

Seizure 3
1 week after the second seizure, she was driving to work when she experienced loss of awareness, resulting in a more severe vehicle collision during which she fractured her sternum. She was taken to an emergency department for care and evaluation, and underwent MRI of the brain, which showed no abnormalities. After this seizure, she stopped driving, but continued having events of altered awareness, and was not diagnosed with epilepsy for another 2 months.

This case report is of a participant in the Human Epilepsy Project, a study that enrolled people with newly diagnosed and treated focal epilepsy between 2012 and 2017.

Panel 2: Identifying a history of non-motor seizures

Eliciting a history of unrecognised focal non-motor seizures might be facilitated by asking questions about events with these characteristics:

Unprovoked
Events start without clear explanation or obvious triggers

Short-lasting
Less than a few minutes in duration

Stereotyped
An individual will experience exactly the same symptoms during each event

Strange or unusual symptoms
Intense, disruptive symptoms, including psychic phenomena (eg, deju vu, jamais vu, depersonalisation), olfactory or gustatory aura, and epigastric rising. These symptoms are especially important to enquire about during history-taking, because patients might not volunteer these symptoms and might not realise their importance.

For more on the **Human Epilepsy Project** see https://www.humanepilepsyproject.org/

Similarly, for adults presenting with possible seizures, clinicians should try to obtain a medical history from affected individuals and eye-witnesses, as this substantially improves diagnostic accuracy.[43,44] Medical history-taking might be facilitated by using structured interview questionnaires, such as the Diagnostic Interview for Seizure Classification Outside of Video-EEG Recording (for both affected individuals and observers), the Paroxysmal Event Profile (for affected individuals), and Paroxysmal Event Observer (for observers).[43–45] A UK multicentre study of patients aged 16 years and older provides class III evidence that a tool based on patient and witness reports helps discriminate between syncope, epilepsy, and functional seizures, which together account for more than 90% of cases of transient loss of consciousness.[46] Having access to these questionnaires might improve the ability of health-care providers to diagnose seizures. In future clinical practice, machine learning might exploit non-linear interactions between structured questionnaire items to further improve diagnostic accuracy.[46]

Smartphone videograph

Smartphone video footage of events can be a useful adjunct to medical history-taking, especially if the history is limited in detail or ambiguous. Smartphones are practicable, portable, and ubiquitous, with an estimated 6·9 billion smartphones in use worldwide in 2023, and with a smartphone present in more than 80% of households in high-income countries and in about 30% of households in low-income countries.[47] Smartphone videography has an increasingly important role in epilepsy diagnosis in children and adolescents. For example, a US multicentre retrospective study of 80 consecutive cases of confirmed infantile spasms demonstrated that smartphone video recordings enabled earlier diagnosis and treatment by an average of 17 days.[48] In this study, parents filmed events, compared them to events on public video streaming sites, and then presented their child and videorecording to health-care services. The benefits of using smartphone video to aid in diagnosis in paediatric populations are perhaps best exemplified by a secure, cloud-based, web application called vCreate Neuro, which supports the diagnosis and management of epilepsy and other neurological disorders. It is used in more than 100 centres in the UK, with more than 40 000 video clips uploaded by more than 20 000 affected individuals and their families or caregivers to date. Videos are peer-reviewed by clinicians who then communicate diagnosis and management plans with families. A 2022 Scottish Health Technology Group assessment found this platform—developed with the support of National Health Service Scotland—reduced time to diagnosis by an average of 2 weeks, facilitated rapid decision making, and prioritised specific tests or prevented unnecessary investigations. These findings lend support to the establishment of similar programmes elsewhere.[49]

In adults, a comparison of a smartphone video with subsequent video-EEG monitoring in a prospective masked diagnostic accuracy study revealed that the odds of receiving a correct diagnosis was 5·45 times higher (95% CI 1·01–54·3; p=0·02) with smartphone video plus history and physical examination than with history and physical examination alone.[50] Smartphone videography discriminates between epileptic seizures and non-epileptic seizures with high accuracy. A prospective study comparing epileptologist diagnosis based on smartphone video with video-EEG review demonstrated 94% diagnostic concordance between expert-reviewed smartphone and video-EEG footage of events for the same affected individuals.[51,52] A prospective multicentre study exploring outpatient smartphone video quality recommended that smartphone video recordings should include interactivity with affected individuals to determine their awareness and ability to respond, and capture early and late ictal and post-ictal features, because these clinical features can help distinguish between epileptic seizures and other events.[52,53] Health-care providers might instruct people with frequent patient contact to record events on smartphones, which can be shared during follow-up visits, or uploaded securely through online patient portals.

EEG

Once an event is deemed a probable or definite epileptic seizure, EEG can help to confirm the diagnosis and determine the epilepsy type. Epileptic seizures have a high incidence in neonates; however, the only seizure types that can be diagnosed with certainty on purely clinical grounds are focal clonic and focal tonic seizures.[54] The ILAE Neonatal Seizure Task Force has recommended that paroxysmal events in the neonate require EEG or amplitude-integrated EEG to confirm their epileptic nature.[55] Acknowledging that EEG technology is not readily available in most neonatal centres, ILAE guidelines provide a degree of diagnostic certainty for different seizure types in such circumstances and provide leverage for centres with limited resources to advocate for improved facilities.

Extending the duration of the EEG increases the yield of information,[56] but prolonged in-hospital monitoring is resource intensive and not readily available. An emerging alternative is ambulatory video-EEG monitoring, which requires a similar duration to inpatient video EEG to achieve comparable diagnostic and classification results.[57] A retrospective analysis of a home video-EEG monitoring system, utilising a shoulder-worn EEG and a telescopic pole-mounted camera, demonstrated an event capture rate of EEG for more than 99·8% of events, and video footage for 95% of events.[58] A prospective study in 100 patients at a single centre who experience a first unprovoked seizure found that a 24-h ambulatory EEG captured epileptiform discharges and seizures with a sensitivity of 72%, compared with 11% for a single 30-min

EEG and 22% if the 30 min study was repeated.[59] The development of comfortable polymer-based water-soluble EEG adhesive, providing high-integrity EEG recordings that can be maintained by individuals in their homes,[60] as well as minimally invasive sub-scalp devices[61] promise robust seizure detection and forecasting opportunities. Artificial intelligence might further increase the utility of EEG. A single centre study analysed interictal EEGs of 70 adults with first unprovoked seizures and demonstrated that quantification of paroxysmal slow wave events predicted the development of epilepsy.[62] The ILAE has published minimum recording standards for routine and sleep EEG to help guide the conduct and interpretation of this testing.[63]

Neuroimaging
Neuroimaging can identify underlying structural causes of epilepsy, thereby assisting with the identification of the epilepsy type (ie, focal epilepsy) and prognosis. A prospective study reported that epileptogenic lesions were identified on neuroimaging for 29% of people with first-ever seizures, supporting the diagnosis of focal epilepsy in the appropriate clinical context.[64] Compared with CT, MRI significantly increases diagnostic yield of epileptogenic lesions.[56,64] The ILAE has published the Harmonised Neuroimaging of Epilepsy Structural Sequences-MRI protocol for new onset focal epilepsy to optimise use of MRI in epilepsy diagnostic investigations.[65] In a 10-year prospective observational study from Australia of more than 1000 adults with first seizures, a focal abnormality on EEG was the strongest predictor of an MRI epileptogenic lesion,[64] and the presence of epileptogenic lesions was associated with higher seizure recurrence risk.[64] Seizure recurrence risk might exceed 60% in the case of remote brain insults from stroke, trauma, or CNS infections, meeting epilepsy diagnostic criteria after a single seizure. Other brain lesions (eg, tumours) have wide-ranging seizure recurrence risks and need to be interpreted within their specific contexts.[1,66] There are increasing applications for artificial intelligence in neuroimaging, such as in aiding discrimination between subtle radiological features of temporal lobe epilepsy and Alzheimer's disease.[67]

Genetic testing
Some epilepsy syndromes are defined by a genetic variant or a metabolic or structural cause and cannot be diagnosed without a relevant test.[13] Certain epilepsy syndromes take months or years to evolve; however, if they are strongly associated with a particular gene, finding a pathogenic variant in that gene will increase the clinician's confidence of a syndrome diagnosis at an earlier stage, which can be beneficial into adulthood as knowing a syndrome earlier can help with prognosis and anticipating associated comorbidities.[68] Notably, a single gene mutation can be linked to several dissimilar syndromes. For example, variants in the neuronal sodium channel *SCN1A* gene can be associated with severe infantile onset developmental and epileptic encephalopathy, Dravet syndrome, or the self-limited epilepsy called genetic epilepsy with febrile seizures plus.[69] With use of machine learning on large datasets, a phenotype prediction model has been developed that utilises age of first seizure and gene variant characteristics.[70] This model has the potential to provide earlier access to potentially disease-modifying gene-related therapies that are being trialled in children with Dravet syndrome (NCT06112275).

Community-based monitoring
Emerging low-cost and long-term home video-only monitoring systems with accompanying artificial intelligence can discriminate between epileptic and non-epileptic seizures with a high degree of accuracy. This possibility has been shown in prospective studies comparing video footage alone with video-EEG characterisation of events, as well as machine learning algorithms for distinguishing between epilepsy and non-epilepsy diagnoses based on patient-reported symptoms.[46,51] An example of a low-cost solution is a seizure detection system developed with a specialised high-definition camera and microphone that can be placed in the affected individual's bedroom, which streams data to a central computer using a secure internet connection.[71] Machine learning processes these data and detects clinical events in real time, and these videos are then sent to human experts for their review. A systematic review describing home video in epilepsy diagnosis confirmed its utility but commented on the need to address cultural factors, privacy, and ethical issues as telemedicine applications are developed.[47]

Advanced testing
Advanced testing—such as magnetoencephalography and transcranial magnetic stimulation (TMS)—are commonly used in high-resource settings when assessing suitability for epilepsy surgery, which is a common treatment pathway for individuals who continue to have seizures despite optimisation of antiseizure medications. Pilot studies suggest a possible role for TMS-EEG in idiopathic generalised epilepsy diagnosis and for cases in which repeated EEGs, including sleep-deprived EEGs, have been non-diagnostic in people with suspected epilepsy.[72,73] However, future studies are needed to clarify the role that these modalities have in routine epilepsy diagnostic investigations.[74]

Epilepsy comorbidities across the lifespan
Following the diagnosis of epilepsy, efforts should turn to identifying relevant comorbidities. This process is emphasised in the 2017 ILAE Classification of the Epilepsies position paper, in which the important and often bidirectional interaction of comorbidities with epilepsy is recognised.[25]
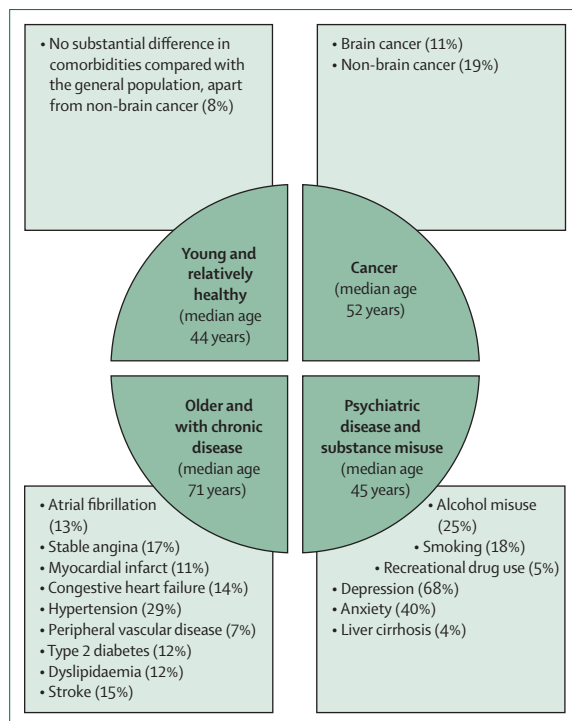
Figure 2: **Clinical presentations at epilepsy onset**
Findings of a retrospective cohort study of 10 499 adults with new-onset epilepsy drawn from the Health Improvement Network database (UK)[75] suggested that individuals fit into four distinct clinical presentation groups, with little overlap between the groups.

Although associations between clinical diagnoses of childhood diseases and seizure risk can be estimated on the basis of epidemiological data, genetic diagnoses can make risk assessment more certain. For example, in children, a definitive diagnosis of tuberous sclerosis complex before the onset of seizures allows clinicians and carers to be vigilant for seizure onset and to monitor cardiac, skin, renal, and other systems that might be affected by this disorder.[73,74]

Four distinct groups of clinical presentations that apply to adults with new-onset epilepsy are illustrated in figure 2.[76] Clinicians might consider targeting investigations for clusters of comorbidities based on these findings.

In adults, epilepsy shares common risk factors with stroke and dementia and is associated with an increased risk of cardiovascular disorders, including coronary heart disease, myocardial infarction, and hypertension.[77] In an analysis of a longitudinal community-based cohort from the Framingham Heart Study, including 2986 people aged 45 years and older with information on cardiac risk factors and mean follow-up of 19 years, hypertension was associated with a nearly twofold increased risk of developing epilepsy (HR 1·93 [95% CI 1·36–4·35; p=0·0030).[78] Stroke is the most common cause of new-onset epilepsy in people aged 60 years and older, according to a prospective multicentre European study

that included 4229 adults with confirmed stroke.[79] A retrospective observational study from Argentina of 691 adults with ischaemic stroke and at least 1 year of follow-up reported that 6·2% had developed post-stroke epilepsy.[80] The development of post-stroke epilepsy was associated with several factors including previous ischaemic stroke, higher score on the National Institutes of Health Stroke Scale on admission (a quantitative 15-item assessment tool for measuring stroke-related neurological deficit), cortical involvement, and acute symptomatic seizures.[80] Dementia, particularly Alzheimer's disease and vascular dementia, commonly cause seizures in older people, which are also increasingly considered to contribute to the pathogenesis of dementia in a bidirectional relationship. A 2020 review provides an informative in-depth discussion regarding the association between dementia and epilepsy.[81]

Almost 40% of adults with new-onset epilepsy have mood and anxiety disorders, similar to people with established epilepsy, and have a greater than twofold risk of developing mood and anxiety disorders during their lifetime than does the general population.[37] A nationwide register-based matched cohort study from Denmark evaluated the diagnosis of epilepsy and depression over 36 years, revealing a strong bidirectionality between epilepsy and depression, for which the peak incidence of one diagnosis was shortly followed by the diagnosis of the other, with the peak extending several years before and after the index diagnosis.[82] Several screening instruments have been validated for diagnosing mood disorders and anxiety in people with epilepsy, including the Neurological Disorders Depression Inventory–Epilepsy and the Epilepsy Anxiety Screening Instrument (EASI), along with its brief version known as brEASI.[83] The ILAE has published guidelines on treatment of depression in people with epilepsy to improve recognition and management of this condition.[84]

Seizure classification and epilepsy syndromes
It is important to recognise that the diagnostic procedure is not complete after only distinguishing epileptic seizures from non-epileptic events, or after confirming the presence or absence of epilepsy. Ideally, all patients, carers, and physicians should understand the type of seizures and the epilepsy syndrome, if possible. Otherwise, a referral to an epilepsy centre for classification is recommended. Classification is important for prognosis and selection of appropriate treatment as part of personalised care, taking individual factors such as genetic information into consideration.

The ILAE updated the classification of seizures and epilepsy in 2017.[25,53] This initiative focused on creation of a clinically useful classification system with treatment implications.[76,85] Thus, clinicians can use it as a so-called roadmap for approaching classification in people with newly diagnosed epilepsy. Briefly, seizures are classified as focal, generalised, or unknown onset. The epilepsies
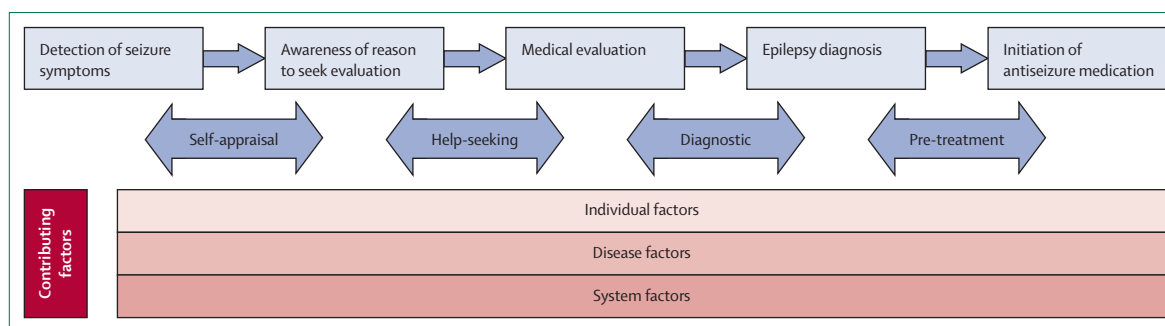
Figure 3: **Modified Andersen Model of total delay in epilepsy**
Based on the most widely cited theoretical framework for delay in cancer diagnoses, the Andersen Model[89] can be similarly applied as a conceptual framework for understanding diagnostic delay in people with epilepsy to help identify pathways for potential interventions designed to improve time to diagnosis and treatment. Individual factors are those that can vary from person to person, such as life circumstance, education, experiences, and perceived stigma. Disease factors are those related to the underlying cause that can influence disease severity at onset, progression, and comorbidities. System factors include access to care and health-care resources. Top rows (blue) indicate the overall process for an individual from initial symptoms to treatment initiation, with arrows indicating parts of the pathway that can be bidirectional. Bottom rows (red) indicate overlying factors that influence the duration of this process.

can be divided into those with seizures arising exclusively from an epileptic focus (focal epilepsy), seizures that are exclusively generalised in onset (generalised epilepsy), or both (epilepsy with combined focal and generalised seizures).

Focal epilepsy is common, occurring in about two-thirds of cases and at any age, and comprising 99% of cases with onset after age 25 years, according to a worldwide meta-analysis estimating the burden of active and lifetime epilepsy.[86] Because most people with both focal and generalised seizures have substantially disrupted brain networks, most will have a developmental and epileptic encephalopathy with seizure onset before age 5 years, although rarely seizure onset can occur later in childhood.[41,87] If seizures cannot be classified, the individual is believed to have epilepsy of unknown onset.

Classification is guided by the component of the clinical history or test results that are most clear. For example, if a person is already known to have a seizure focus based on EEG, aetiology, or imaging, they are likely to have focal epilepsy. In this case, seizure types will be focal (focal aware, focal with impaired awareness, or focal to bilateral tonic-clonic). In this example, a staring spell should be classified as a focal seizure with impaired awareness, rather than an absence seizure, which is a generalised seizure type. For this case, the type of epilepsy provides the diagnosis for the seizure type. On the other hand, in a newly diagnosed individual with a normal routine EEG and MRI, a clinical history of seizures that begin focally (eg, with a Jacksonian march) suggests focal epilepsy. Therefore, a seizure type provides the diagnosis for the epilepsy type.

Once a patient has been identified to have one of the three epilepsy types, they might have an epilepsy syndrome. An epilepsy syndrome is defined as a constellation of distinctive clinical and EEG features with imaging, aetiological, prognostic, and treatment implications. Examples of epilepsy syndromes include temporal lobe epilepsy (focal), juvenile myoclonic epilepsy (generalised), and Lennox-Gastaut syndrome (combined focal and generalised). Syndromes are relatively common; for example, according to a cohort study of children who experienced their first seizure before age 2 years, a syndrome was identified in more than half of cases.[88] In 2022, the ILAE published definitions for the epilepsy syndromes across different ages, from the neonatal period to adulthood, as well as syndromes that can occur at variable ages.[9–11,13] The ILAE also redefined the four syndromes that comprise idiopathic generalised epilepsy, namely childhood absence epilepsy, juvenile absence epilepsy, juvenile myoclonic epilepsy, and idiopathic generalised epilepsy with generalised tonic-clonic seizures.[12] People with idiopathic generalised epilepsy comprise about 20% of all those with epilepsy and comprise the largest generalised epilepsy subset. It is important to recognise this subset of patients because their seizures do not necessarily respond to antiseizure medications approved for focal epilepsy.

Clinicians should also try to identify the cause of epilepsy because identification can have treatment implications. For this reason, ILAE classification has subdivided causes into structural, genetic, infectious (referring to the sequelae of infective processes), metabolic, immune, and unknown and an individual might have more than one underlying cause for their seizures.[25]

Conclusions and future directions

The importance of early and accurate epilepsy diagnosis cannot be overstated. Worldwide, epilepsy is under-recognised and under-diagnosed, resulting in treatment delays associated with otherwise avoidable seizure-related morbidity and mortality. Diagnosis is a multistep process, affected by factors related to the individual, the disease, and the environment. For example, the severity of seizure symptoms at epilepsy onset can influence self-recognition and motivation to seek evaluation, and

algorithms in the future. New applications for existing technologies, such as using smartphones to record events, are likely to become an increasingly important diagnostic adjunct, particularly in resource-limited settings where standard EEG and neuroimaging might not be readily available. These advances support rapid identification and diagnosis of epilepsy, which remains the foundational step in treatment optimisation.

This Review covers the gold standard epilepsy diagnostic investigations and innovations typically available in high-income countries, but it is essential for global efforts to focus on the 80% of people with epilepsy who live in low-income and middle-income countries (panel 3).

external factors such as stigma and systemic barriers to health care can affect the time to medical evaluation (figure 3).

Medical education should reinforce the importance of history-taking for identification of subtle non-motor seizures before clinical assessment. In many cases, history-taking might allow an epilepsy diagnosis to be made and treatment to be initiated early, avoiding recurrent seizures and related accidents, injuries, and hospital admissions.

Health-care providers should be encouraged to refer to the relevant ILAE position papers to accurately determine epilepsy type and, if applicable, syndrome, and tailor their treatment plans accordingly. Identifying and managing comorbidities sharing bidirectional relationships with epilepsy through a holistic approach is needed to optimally treat these interconnected conditions. The advent of artificial intelligence affords new possibilities for directly and indirectly detecting epilepsy and will probably make valuable contributions to diagnostic

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