epilepsy action

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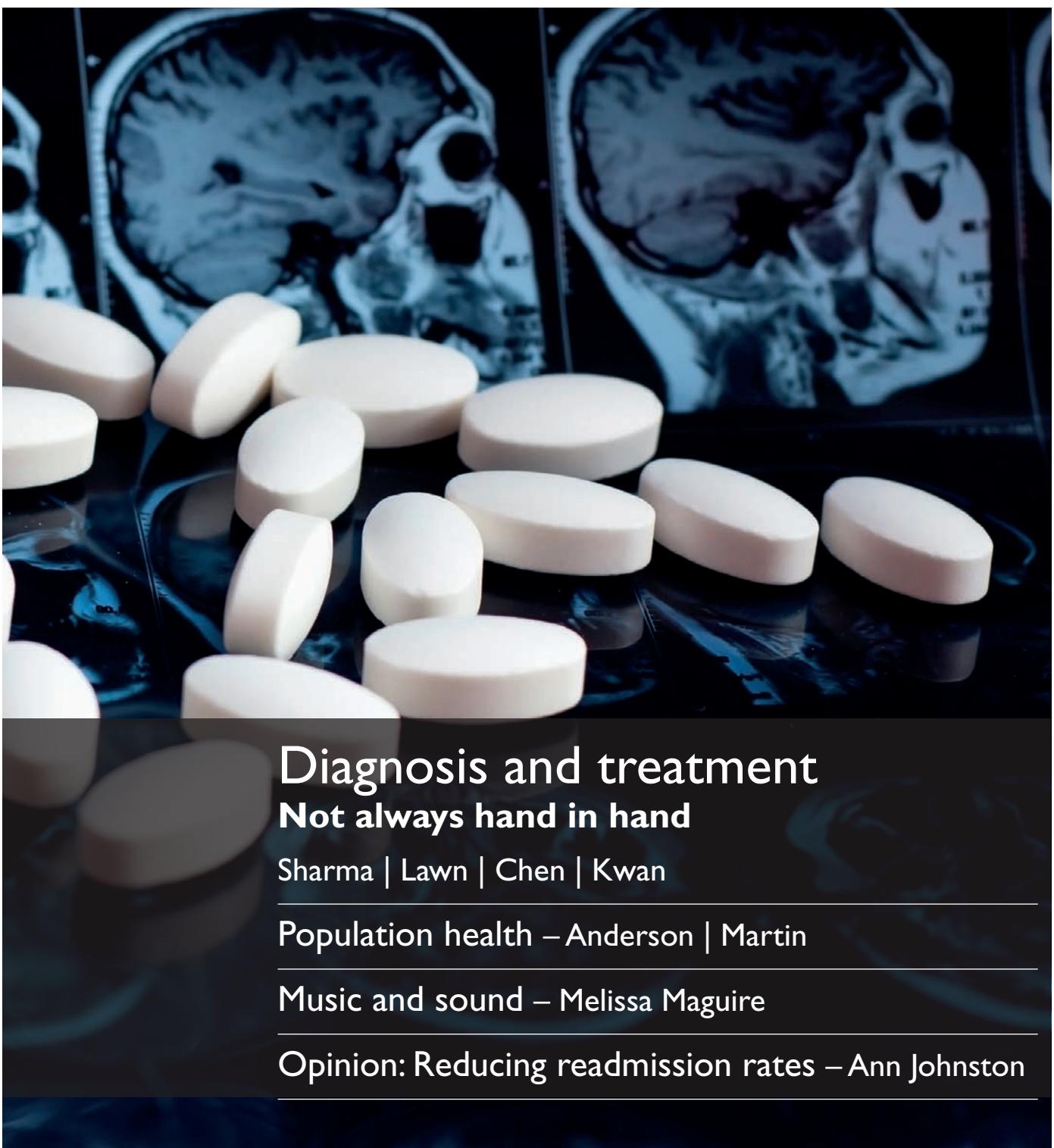

Diagnosis and treatment
Not always hand in hand

Sharma | Lawn | Chen | Kwan

Population health – Anderson | Martin

Music and sound – Melissa Maguire

Opinion: Reducing readmission rates – Ann Johnston

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1. Elliott, RE., et al., (2011) Epilepsy & Behavior. 20; 478–483.
2. Patient's Guide for Epilepsy 2021, LivaNova USA, Inc.
3. Orosz, I., et al., (2014) Epilepsia 55(10):1576-84.
4. Helmers, et al., (2011) Epilepsy Behav; 22:370-5.
5. Spindler, et al., (2019) Seizure, 69:77-79.

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LivaNova Epilepsy

The Hollywood writers are on strike, but how concerned should they be for future job security? A month ago I met up with three of my oldest friends, the best type – they are non-medical and therefore a little too impressed with their imagined idea of what I do. As a technical writer, a contract lawyer and a poet – they all (to a greater or lesser degree) depend on their use of the written word. The conversation, as it is prone to do, drifted towards artificial intelligence (AI) and tools such as ChatGPT. Is this a revolution that will help non-native speakers deliver copy in fluent English? Is this a co-pilot that can produce a first draft? Is it a threat to established careers?

One thing an AI bot struggles to do is break new ground, have truly original thought – and until that hurdle is leaped, we have bespoke high-quality writing for you in Epilepsy Professional, produced the old-fashioned way.

Joe Anderson and Elizabeth Martin from South Wales describe their clinical data dashboard (page 10). An impressive and creditable resource for individual clinicians as well as team leaders, this has a number of important uses. The ability for constant data acquisition is helpful when implementing change – or producing data about yearly trends, such as failure to attend clinics, or unscheduled care – ambulance data. Not only am I very envious of this tool, but I suspect that more is to come. This tool may be artificial (in so much that it depends on medical coding) but it certainly is intelligent.

Music and epilepsy have a rich shared heritage, including seizures triggered by certain tunes, or people trying to turn EEG in to music. Melissa Maguire is an expert in this field and logically and thoroughly builds the argument about music (or at least pulsed noise) as a potential therapeutic area that needs further exploration (page 22). It interests me that great works by European classical composers are best studied, are these effects culturally specific? More work is needed, and I would be fascinated by its answers.

Sharma, Lawn, Chen and Kwan from Monash University, Melbourne, discuss epilepsy treatment and epilepsy diagnosis by reframing the questions for an epilepsy-intelligent audience. Who with a single seizure needs medical treatment? And who with epilepsy declines or defers initial therapy? Drawing on their studies and experiences from Western Australia they unpick practice, prejudice and prescribing. Self-discontinuation of medication, meaning people who unilaterally choose to stop their anti-seizure medication, is not frequently studied and their data and outcomes deserve careful reading.

What's the future of AI writing? Will it soon be a badge of honour to be 'AI clean', the #nofilter equivalent of keeping it real? Those of you who are fans of meandering prose written to a tight deadline will note that this introduction was not doped or modified with AI. I make no promise not to flirt with the robo-co-writer in the future, and suspect that for some time the high-quality commissioned content that Epilepsy Professional provides will be delivered by the most talented of our human writers. But by 2025, just like in Blade Runner, we will need some sort of replicant test for us to know whether our epilepsy education has been provided for us by research or robot, by Prof or protocol, by scientist or cyborg.

Rhys Thomas
Consultant neurologist
Chief medical adviser
Epilepsy Professional

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music and sound

Melissa Maguire

Dr Maguire describes the evidence around infrasound, audible sound and ultrasound in affecting brain waves and the potential of sound to impact seizure activity

We often talk and think about the individual when we consider treating epilepsy. Each person is different, each situation is different, each epilepsy is different, so it stands to reason that we think about them holistically and individually.

But looking at population-level health information also has a lot of perspective to offer. Dr Anderson and Dr Martin shine a light on their data dashboard for NHS Wales, offering insights into hospital admissions, out-of-area admissions, non-epileptic attack disorder (NEAD) hospitalisations, ambulance data and more (page 10). They explain that this dashboard can also be used for patient-level data, helping epilepsy teams to stay aware of which of their patients are frequently admitted to hospital. This tool has the potential to be incredibly useful to better understand resource use, effects of the postcode lottery and where systems can be improved.

Meanwhile, on page 16, Dr Sharma, Dr Lawn, Dr Chen and Prof Kwan discuss causes for delayed treatment initiation and reasons for patients' self-discontinuation of anti-seizure medicines. This shows all the more why understanding the lives and motivations of patients is of great importance.

Finally, Dr Maguire updates us on the effects of sound and music on seizures, including audible, infra- and ultrasound and how these might impact EEG.

We hope you enjoy some time in the sun with this issue and find the articles interesting and useful.

Kami Kountcheva
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Update to sodium valproate prescription rules labelled "a risk"

Prescription rules around sodium valproate, announced in December 2022, have been called "out of proportion" by a coalition of epilepsy charities.

The organisations, including Epilepsy Action, the International League Against Epilepsy (ILAE) and SUDEP Action, are calling for the Medicines and Healthcare products Regulatory Agency (MHRA) to pause its decision.

Last year, the MHRA said no one under the age of 55 should be prescribed sodium valproate unless two epilepsy specialists independently agree it is the only suitable medicine. The new rules include boys and men for the first time.

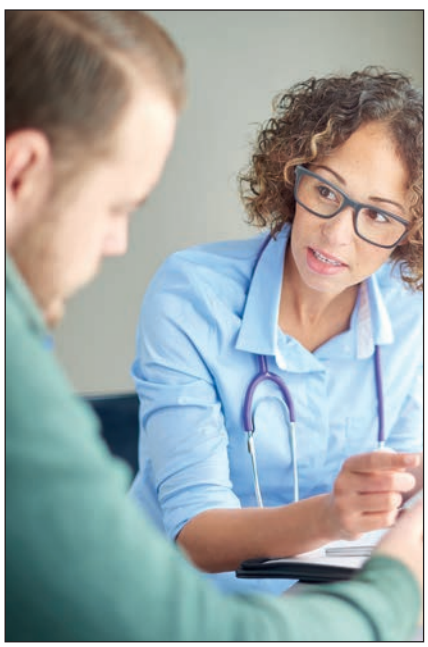
In a public statement, the coalition said: "This is a dramatic shift in practice and risk for people with epilepsy without regard to each person's situation and life choices, and totally out of proportion to the risks to patient safety."

The group has also written to the secretary of state for Health and Social Care Steve Barclay with concerns over the decision.

The MHRA previously tightened the rules around prescribing sodium valproate in 2018. These said that girls and women should not be prescribed sodium valproate unless a pregnancy prevention programme is in place.

The rules were intended to ensure women and girls were fully informed of the risks of taking sodium valproate, and the need to avoid becoming pregnant while taking the medicine.

Safety reviews have shown that the medicine can cause developmental disorders and birth defects in babies exposed to it in the womb.



With the newly announced rules from the MHRA, the coalition said there had been no consultation around this change. The organisations added they had also not been given access to the safety review results from the Commission on Human Medicines, on which the MHRA based its decision.

In their open letter, the organisations warned that for 10% of people with generalised epilepsies, sodium valproate is the "first line of defence against visits to A&E and the risk of SUDEP (sudden unexpected death in epilepsy)".

They also stressed that the new rules would increase pressure across the NHS when there are already general and epilepsy-specific workforce shortages.

For more on sodium valproate and the coalition letter visit the Epilepsy Action website: ***bit.ly/3IehrZO***.

Researchers uncover link between CBD and brain signals

A US study, published in the journal Neuron, has found that CBD affects a molecule involved in brain signalling.

In November 2018, it became legal to prescribe CBD in the UK. One CBD medicine – Epidyolex – has been legalised for use in epilepsy in the UK.

The National Institute for Health and Care Excellence (NICE) also recently approved CBD for people with tuberous sclerosis complex.

The new study, by Evan Rosenberg and colleagues, found that CBD blocks a molecule called LPI (lysophosphatidylinositol).

LPI has been found to strengthen nerve signals in the hippocampus, which could lead to seizures. The study has also suggested that LPI weakens signals that stop seizures. This may explain why CBD blocking this molecule helps to reduce seizures. The full study is available on the Neuron website at: ***cell.com/neuron/home.***

Meanwhile, in Argentina researchers found a "significant improvement" in the quality of life of focal epilepsy patients who received CBD as an additional treatment.

Of the 44 patients who completed the trial, 5% were seizure-free, 32% reduced more than 80% of their seizures and 87% reduced their monthly seizures by half. Only 11% presented a decrease of less than half.

The team studied 55 patients between 18 and 60 years old with drug-resistant focal epilepsy.

The study was reported in the journal Epilepsy & Behavior and is available at: ***bit.ly/42jV2RQ***

Study reveals potential improvements to epilepsy surgery

Disconnecting pathways in the frontal lobe could be the key to improving epilepsy surgery, according to research from the UCL Queen Square Institute of Neurology.

The research, published in the journal Brain, suggests longer-lasting seizure freedom could be possible after brain surgery.

Currently, of those with frontal lobe epilepsy, only about a third (30%) remain seizure free in the long term after surgery.

The networks of connections that the researchers identified link the frontal lobe to structures such as the thalamus and striatum.

In their research, 47 people with damage to their frontal lobe had these networks disconnected. The results suggested nearly nine in 10 people stayed seizure free three years after the surgery, and between seven and eight in 10 were seizure free after five years.

The research found the surgery did not have negative effects on language or executive functions such as planning, self-control and focus. However, functions such as mood or emotions still need to be studied.

Neurosurgeon at UCL and lead author of the study, Mr Davide Giampiccolo, said: "In some patients, seizures recur years after neurosurgery and, until now, it has not been clear why this happens.

"This might be related to connections in the brain that form a network that gives rise to seizures. If this is correct, disconnecting this frontal lobe network with surgery could prevent seizures recurring years later. This will allow us to redesign neurosurgical operations and personalise the operations for each patient, ensuring the right connections are cut. We hope this will lead to a great improvement in the long-term results of epilepsy surgery."

Tom Shillito, health improvement and research manager at Epilepsy Action, said: "It is exciting that these findings have seen improved results in giving people long-term freedom from seizures and it is a promising development. We hope this can empower more people to make informed and confident decisions about their treatment."

The researchers said the results need to be confirmed by a larger study.

ILAE's first female president given Lord Hastings Award

Professor J Helen Cross OBE has received the 2022 Lord Hastings Award from Epilepsy Action. The award recognises "outstanding personal contribution" to the field of epilepsy.

Prof Cross (pictured right with Epilepsy Action deputy chief executive Rebekah Smith) was elected as the first female president of the International League Against Epilepsy (ILAE) in 2021. She is also the Prince of Wales's chair of childhood epilepsy and an honorary consultant in paediatric neurology at Great Ormond Street Hospital for children.

Over the years, Prof Cross' research has focused on improving outcomes for children with early onset epilepsy. She initially worked on improving imaging techniques to identify areas where seizures start in children with drug-resistant focal epilepsy. Following this, she developed an epilepsy surgery programme.

Prof Cross conducted the first randomised controlled trial of the ketogenic diet in the treatment of children with drug-resistant focal epilepsy.

She is the 16th recipient of the Lord Hastings Award, which is in its 33rd year.

Smith said: "It was an honour to present Professor Cross with the Lord Hastings Award at our recent Let's Talk About Epilepsy event in London. The award is an important opportunity for us to recognise and celebrate individuals who have made a huge impact in the field of epilepsy.

"Professor Cross has worked tirelessly to research and improve outcomes for children with early onset epilepsy. The impact of her work has been huge for children with drug-resistant epilepsy and her dedication to the field offers hope for the families of these children."

The Lord Hastings Award was established in 1990 and recognises individuals who have made an outstanding contribution to improving the lives of people with epilepsy.

Better communication needed about epilepsy medicine risks in pregnancy – survey

More than half of women with epilepsy under the age of 24 in the UK are not aware of the risks of some epilepsy medicines in pregnancy, a survey by three epilepsy charities has found.

Epilepsy Action, Epilepsy Society and Young Epilepsy conducted a survey of more than 1,200 women and girls with epilepsy across the UK in November and December 2022, to gauge awareness about the risks of some epilepsy medicines if taken in pregnancy.

The Epilepsy Medication in Pregnancy survey showed that 53% of women under 24 were not aware of the potential risks of taking some epilepsy medicines, such as topiramate, carbamazepine, phenobarbital, phenytoin or pregabalin, in pregnancy.

These medicines, alongside sodium valproate, can increase the risk of babies being born with physical birth abnormalities if taken during pregnancy.

Nearly two fifths (39%) of respondents under 24 years old said they were not satisfied with the information they received about these risks.

Overall, a third (33%) of women taking these medicines were not aware of the risks they carry in pregnancy.

The survey did show that awareness around the risks of taking sodium valproate in pregnancy is improving, with only 9% of respondents unaware. However, the level of awareness was different between age groups, with a fifth (20%) of those over 45 unaware of the risks, compared to just 2% of 25 to 44 year olds.

The charities say the overall results show that communication around epilepsy medicines and pregnancy must be improved.

Over a third of the responders (36%) said the information they received about the risks of their medicines was not adequate, including 17% who said they weren't at all satisfied.

Alison Fuller, director of Health Improvement and Influencing at Epilepsy Action, said: "While it is encouraging that there has been an increase in the proportion of people who are aware of the risks of valproate medicines, it is very concerning that a significant number of women and girls were unaware of the risks of other epilepsy medicines.

"We have received multiple testimonies from women with epilepsy saying no discussions were ever held with them about the risks of taking certain medications while pregnant, some of which were really upsetting.

"Our report on the survey results outlines recommendations for key stakeholders on how to address safety by communicating the risks of these medications, and ensure the historic mistakes made with sodium valproate are not repeated.

"These include a national review of pre-conception counselling services to ensure that all women and girls with epilepsy are provided with the right information, at the right time and by the right healthcare professional.

"We will actively be pursuing and monitoring their implementation.

"We would also encourage all women and girls affected to raise this issue with their MPs, asking them to support our call for a national commitment to fund research on the effects of taking anti-seizure medication while pregnant."

The charities are calling for better communication, more information from healthcare professionals, and more research.

Blood tests could aid diagnosis

A blood test could help identify epilepsy, according to research from scientists at Lund University in Sweden.

Matilda Ahl and colleagues found there were higher rates of protein IL-6 in the blood in people with epilepsy. The research was published in Heliyon.

The study investigated 56 people with epilepsy, split into four groups: those with temporal lobe epilepsy (TLE), frontal lobe epilepsy (FLE), psychogenic non-epileptic seizures (PNES), and combined TLE and PNES.

The researchers confirmed patients' seizures using video EEG and knew if they were taking blood samples before or after seizures.

The study found levels of IL-6 in the blood were higher in people with FLE and TLE, including in the group of people who had both TLE and PNES, compared to people without epilepsy or PNES. After a seizure, the levels of the protein increased in people with TLE, but not in people with FLE.

The results also showed IL-6 levels did not increased in people with PNES.

Marie Taylor, part of the research team, said investigating whether someone has epilepsy or PNES takes a lot of resource.

She said: "It may require the patient to be admitted to hospital for several days with constant video and EEG surveillance, with medical staff on hand around the clock."

The researchers said the next step would be to repeat the research in a broader group of people.

The full research is available on the Heliyon website: ***cell.com/heliyon/home***

Epilepsy Research UK awarded institute status

Medical research charity Epilepsy Research UK has announced it will become an institute, aiming to "radically advance research into epilepsy". It will also change its name to Epilepsy Research Institute UK.

The announcement was made on May 16, at the Francis Crick Institute in London, by minister for science, research and innovation George Freeman. The change will be made later in the year.

The group said it would focus on driving "strategic investment and building the research ecosystem to advance the treatment and prevention of epilepsy".

Epilepsy Research UK CEO Maxine Smeaton said: "We are delighted to receive the approval from government to become the Epilepsy Research Institute UK. Forming the institute later this year will enable us to provide a solid foundation for the development of the epilepsy research ecosystem and bring together key epilepsy charities as founding partners."

Epilepsy Action is among the institute's founding partners.

Chief executive Philip Lee said: "We're delighted to be involved in the Epilepsy Research Institute UK. The institute will drive much-needed investment into research, putting the voices of people with the condition right at the heart of that work."

Other partners include the International League Against Epilepsy (ILAE) British branch, Young Epilepsy and Epilepsy Scotland.

Trileptal out of stock

Novartis, the manufacturer of Trileptal (oxcarbazepine), has told Epilepsy Action that Trileptal 150mg tablets are out of stock. It was not able to confirm when they will be back in stock.

Novartis has confirmed that other strengths and formulations remain in stock. Other manufacturers' versions of oxcarbazepine are also available. The situation will be updated at: ***epilepsy.org.uk/trileptal-oxcarbazepine-stock***

Teva zonisamide unavailable until July

Teva, the manufacturer of Teva zonisamide, has told Epilepsy Action that all strengths of Teva zonisamide capsules are now out of stock until the beginning of July 2023.

Frisium back in supply

Frisium (clobazam) 10mg tablets are now back in stock, according to Sanofi, its manufacturer.

In April, the company said a delay to the renewal of the controlled drug licence for the medicine had forced it to stop supplying in the UK.

Population health

Monitoring population health in epilepsy: a data dashboard for NHS Wales

Dr Anderson and Dr Martin describe the way the epilepsy data dashboard in Wales can help monitor epilepsy population health in real time and the benefits this could bring.

Summary
Epilepsy teams in Wales have worked in collaboration with information technology specialists to create a 'live' epilepsy data dashboard that monitors metrics of population health across Wales, in relation to epilepsy and seizures. The dashboard provides valuable data on epilepsy outcomes across all of Wales in real time, and this article outlines the background and processes that led to this development, as well as demonstrating the functionality of the dashboard.

Introduction
In recent years, policy documents setting out aspirations for the continued development of neurological services in Wales have been supported by Implementation Groups for the major disease areas. The Neurological Conditions Implementation Groups (NCIGs) comprise of members from all NHS health boards in Wales (and are a mix of a range of clinicians and stakeholders). One such sub-group has been an epilepsy group, made up predominantly of consultant neurologists and epilepsy nurse specialists from epilepsy teams across Wales. In previous years, the epilepsy group has created an all-Wales referral pathway for seizures from primary and secondary care. A later project saw health boards work together on unifying approaches and avoiding duplication in the work to implement the MHRA PREVENT programme for women taking sodium valproate, for example.

The National Epilepsy Dashboard is a project between the Epilepsy NCIG, the Welsh Value in Health Centre, and Digital Health and Care Wales, bringing together three national workstreams in NHS Wales to work collaboratively.

We sought to use already existing national data sources to create a 'live' data dashboard related to epilepsy

Epilepsy is a common and unpredictable neurological disorder, which causes significant morbidity and mortality, and accounts for a large proportion of acute hospital admissions for neurological conditions. We sought to use already existing national data sources to create a 'live' data dashboard related to epilepsy. The goal of this was threefold:

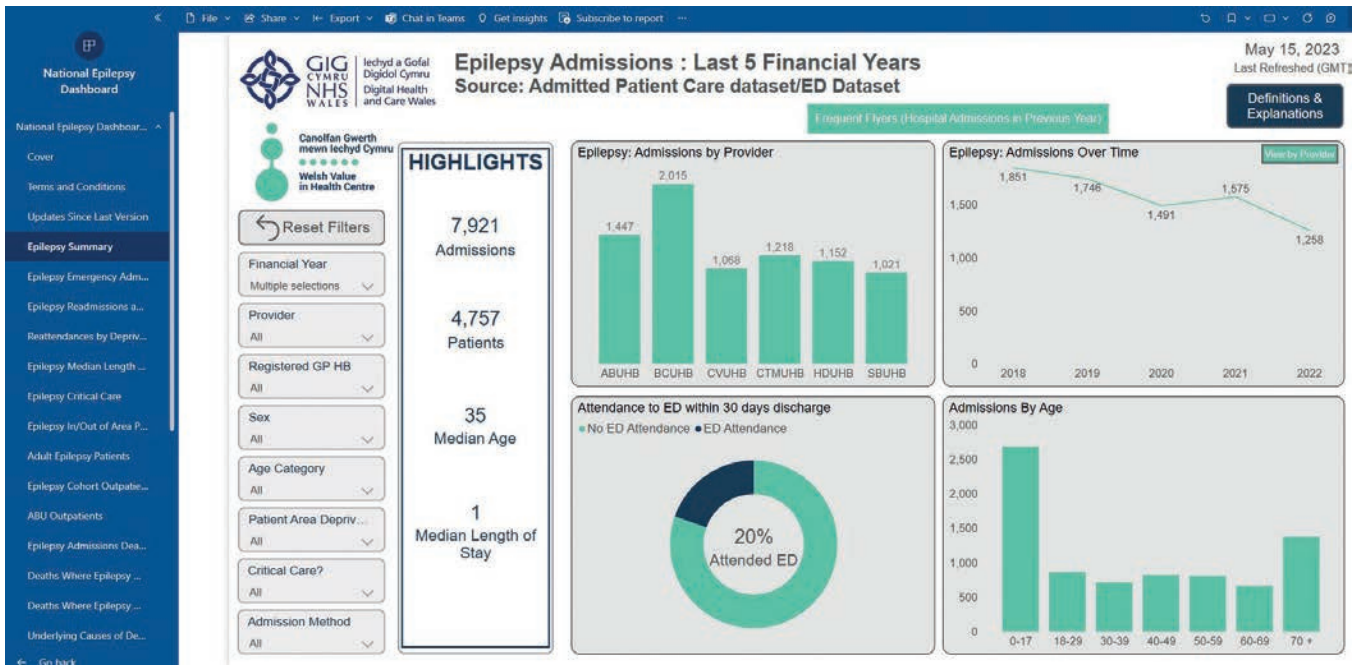
1. To help us understand the national picture, particularly around hospital admissions and unscheduled care, for people with epilepsy. This would help us understand the resources being used and how this has changed over time.
2. To provide an easily accessible source of accurate and up-to-date data on epilepsy that can be used in preparing business cases to develop epilepsy services, to respond to Freedom of Information requests, and to explore variance in services and outcomes between different Health Board regions in Wales.
3. To try to further understand the critical issue of epilepsy-related deaths.

Method
The relevant data sources available for the data dashboard included:

1. Admitted Patient Care Data Set (i.e. hospital episode data on admissions, length of stay, critical care stay etc. known as 'Hospital Episode Statistics' in NHS England)
2. Emergency department data
3. ONS Data (deaths due to, or involving, epilepsy)
4. Primary care data (diagnostic coding from QOF and QAIF data)
5. Welsh Ambulance (WAST) data for calls related to 'fit' or 'convulsion'.

All of these data sources have their limitations, and it can be difficult to interpret the data without an understanding of how and why each data source is collected.

Figure 1. Admissions including a primary diagnosis of epilepsy (all Wales, 2017-22)



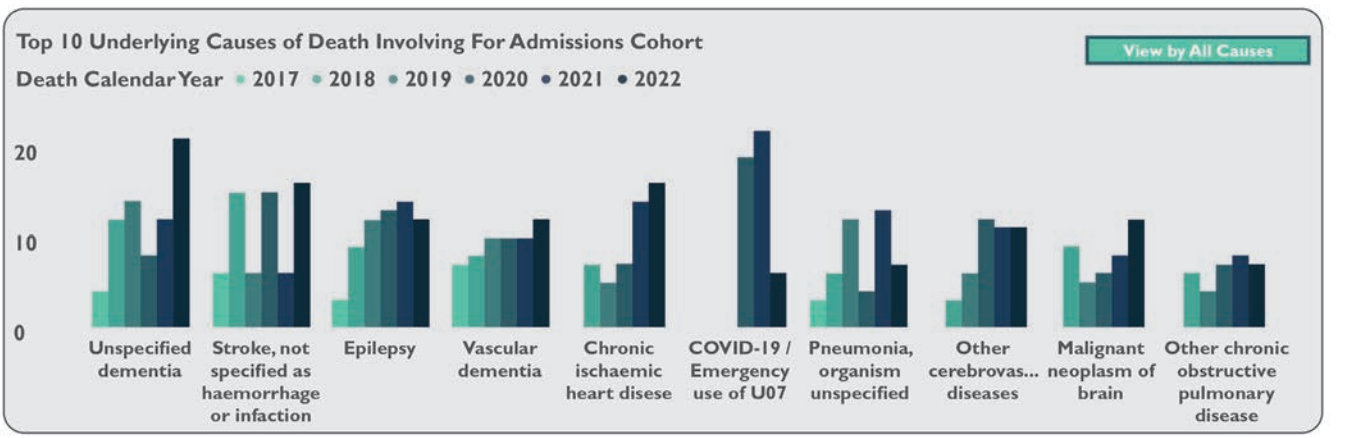
Clinicians and data scientists on the project would meet monthly to generate ideas and questions for the dashboard. As a consequence, these developed into discussions about what data to display and how to display it. Between meetings, these ideas would be implemented, and iterative cycles of development over around 12 months led to the finished product. Partway through the project it was decided to duplicate some of the pages for 'non-epileptic attack disorder' as opposed to epilepsy. The dashboard is available for use by all on the NHS Wales IT network, and is hosted at ***vbhc.nhs.wales***.

Results

The data dashboard was launched on 6 February 2023. It is built in Microsoft Power BI (***powerbi.microsoft.com***) and displayed in the user's internet browser. It contains important disclaimers about appropriate use of the data, as well as a glossary, definitions and explanations of the data sources. The dashboard consists of multiple 'pages' displaying different categories of data (usually for the last five years), and importantly this data can be filtered by multiple variables in real time. These filter variables include resident health board and age, for example, meaning individual adult or paediatric teams from respective centres can extract data relevant to just their patient cohort. There is also the ability to filter data by the socioeconomic status of patients based on their home postcode, which correlates with their Welsh Index of Multiple Deprivation (***gov.wales/welsh-index-multiple-deprivation***). *Figure 1* illustrates a typical page, including filters.

While most of this data will display large numbers that examine trends, for example number of admissions per year for 'epilepsy', the dashboard can

Figure 2. Primary cause of death (ONS data) in the cohort of patients who had an epilepsy-related admission to hospital and died soon after (all Wales, 2017-22)

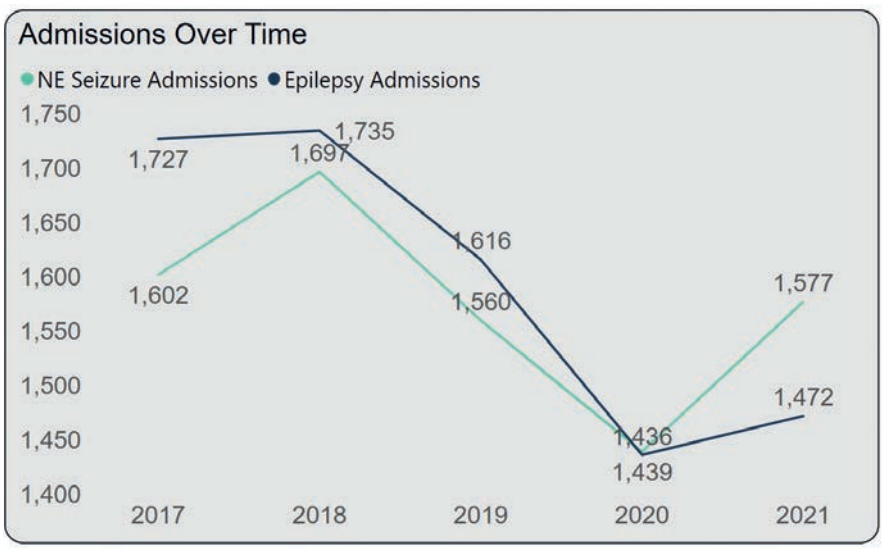


also be used to explore smaller, patient-level data, such as 'frequent flyers'. Through this function, the numbers of patients being admitted three or more times in a year can be calculated, and individual epilepsy teams can then request the NHS numbers for those patients, in order to explore the reasons for frequent admission. This is valuable to epilepsy teams as they may not otherwise be aware of these patients if they do not access out-patient services appropriately. This provides an opportunity to work with acute inpatient services and the emergency department to promote better management of these patients. This could be, for example, ensuring they receive neurology input while they are in hospital if there are barriers to their appropriate use of outpatient services. Importantly, unlike the wider dashboard, this patient-level data would only be available on request to appropriate clinicians with responsibility for those patients.

The numbers of patients being admitted three or more times in a year can be calculated and individual epilepsy teams can then request the NHS numbers for those patients

Data on epilepsy-related deaths is available on the dashboard, but as this anonymised data is provided by the Office for National Statistics (ONS) and not the NHS, UK law does not allow epilepsy teams to request the patient-level data. This remains an important dip in learning for epilepsy teams, especially in relation to supporting families and being able to learn lessons from instances of sudden unexpected death in epilepsy (SUDEP). Despite this dashboard, we remain dependent on being directly informed of any potential SUDEP in order to support the family and explore what happened. We can, however, have a much better understanding of numbers of epilepsy-related deaths in patients who have had an epilepsy-related admission to hospital, and also

Figure 3. Number of emergency admissions for epilepsy compared with non-epileptic attacks (all Wales, 2017-21)



of the underlying primary pathology (e.g. stroke, dementia, tumours) in those patients (*Figure 2*).

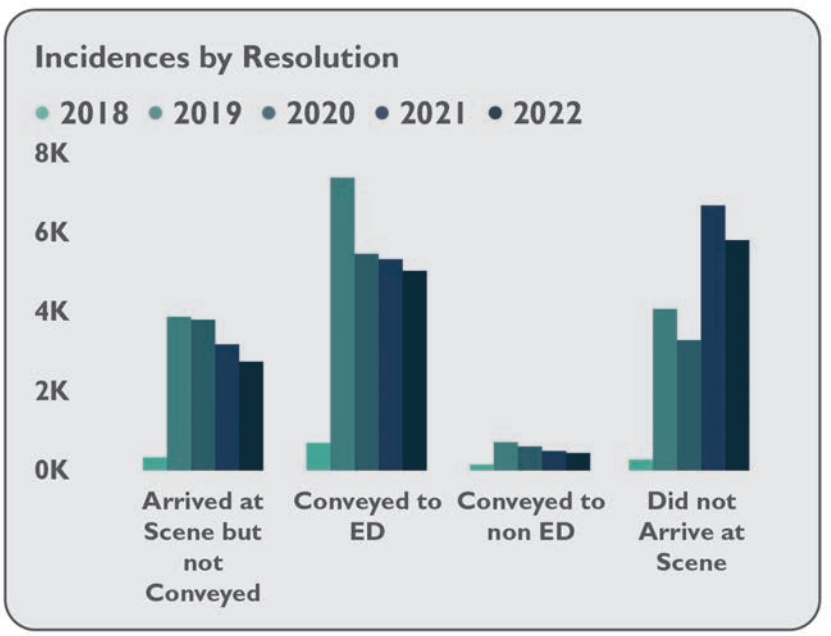
Outpatient data is typically not coded well in NHS organisations within Wales, and there is no standardised method of running clinics and setting clinic codes for epilepsy across organisations (unlike inpatient admissions). Moreover, individual epilepsy clinics invariably contain patients with conditions other than epilepsy. As such, trying to incorporate data on outpatient clinic performance in the dashboard has not been successful or reliable.

Other areas where the dashboard has provided valuable insights into epilepsy-related use of resources has included looking at 'out-of-area' patients, and admissions for non-epileptic attack disorder. The dashboard identifies and quantifies geographical scenarios where large volumes of patients are being conveyed or self-presenting to emergency departments outside of their resident health board, due to the proximity to their home address. This is an important consideration for services, as good lines of communication (and referral pathways) are needed between epilepsy teams and their neighbouring emergency departments. This is key, for example in prompt referral for suspected first seizures. A patient should not suffer delays in their specialist outpatient assessment due to the choice of hospital they presented to. There are, of course, important financial considerations to this data also.

A major insight provided by the dashboard has been the number of inpatient bed-days used for non-epileptic seizures. We used the same setup for emergency admissions involving a primary diagnosis of 'dissociative seizures' (ICD-10 F44.5 and R56.8) as we did for epilepsy (G40 & G41), combined with length of stay. With this, we have been able to calculate the number of bed-days used for both conditions across all of Wales in the last five years (*Figure 3*); approximately 58,700 bed-days a year across Wales for epilepsy, and 45,100 for non-epileptic seizures. This information demonstrates very clearly that in terms of seizure disorders and use of acute resources, non-epileptic attack disorder needs to be considered alongside epilepsy. Most epilepsy teams will already be aware that diagnosing and managing non-epileptic attack disorder takes a considerable amount of their time. We have been able to demonstrate that for acute medical teams, it is almost on a par with epilepsy. This again is important for Health Boards when

The dashboard has provided valuable insights into 'out-of-area' patients and admissions for non-epileptic attack disorder

Figure 4. Outcome for 999 calls for 'fit' or 'convulsion' (all Wales, 2018-22, 2018 data incomplete)



considering what specialist services to develop and commission.

Finally, ambulance data demonstrates the volume of seizure-related calls that are dealt with by paramedics and 999 call handlers, but not brought to hospital. *Figure 4* demonstrates that these incidents ('arrived at scene but not conveyed' and 'did not arrive at scene' respectively) outnumber those where the patient is brought to hospital. Epilepsy teams will not be aware of these incidents unless the patient or GP contacts them retrospectively. In many cases, this doesn't happen, and an opportunity to address seizure control and seizure-related risks (including SUDEP) is missed. This gives a clear indicator of a need to develop links between epilepsy services and local ambulance services.

Conclusion

A collaborative approach between clinicians and information technology specialists can drive rapid developments in data visualisation tools. Data dashboards for epilepsy can be a useful tool to examine regional and national trends in important epilepsy outcomes, ultimately improving patient care. The dashboard also saves clinician time, as data is 'live' (weekly refreshed) and easily accessed. We hope the dashboard will play a pivotal role in making the case for further development of epilepsy services across Wales, as well as for non-epileptic attack disorder.

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Diagnosis and treatment

Not always hand in hand

Dr Sharma, Dr Lawn, Dr Chen and Prof Kwan share some background and their own research into the causes of delay in initiating treatment for epilepsy and patients' self discontinuation of anti-seizure medicines, and suggest ways to help combat this and work with patients on appropriate management

The last two decades have seen a significant expansion in the diagnostic definitions of epilepsy. In the 1990s and prior, major epidemiological studies explicitly required two or more unprovoked seizures to fulfil a diagnosis of epilepsy [Hauser *et al*, 1991]. In 2005, the International League Against Epilepsy (ILAE) conceptually defined epilepsy as a neurological disorder with enduring predisposition towards the generation of epileptic seizures [Fisher *et al*, 2005].

In 2014, a practical clinical definition of this theoretical construct was developed, with a diagnosis of epilepsy requiring two or more unprovoked seizures occurring more than 24 hours apart, or the occurrence of at least one unprovoked seizure in the presence of evidence of an enduring risk of further seizures. The qualification of the latter definition is based on the recurrence risk (at least 60% over 10 years) after two unprovoked seizures [Fisher *et al*, 2014]. Prior to this, many patients with a single unprovoked seizure who had risk factors for further events remained in a state of diagnostic and treatment uncertainty.

Several studies attempted to answer the question of whether patients with a single unprovoked seizure required treatment. The most important were two large non-blinded randomised controlled trials – First Seizure Trial Group (FIRST) [Musicco *et al*, 1997] and MESS [Marson *et al*, 2005]. These trials found that immediate treatment after a first seizure modestly reduced the short-term risk of recurrence, particularly if risk factors for further events were present, but did not alter the long-term outcomes [Kim *et al*, 2007]. They additionally highlighted that there was no impact on quality of life with any benefit in terms of short-term seizure reduction with immediate treatment being offset by side effects of anti-seizure medications (ASMs), as well as the psychological toll of being diagnosed with epilepsy and being required to take medication [Jacoby *et al*, 2007]. Although a proportion of patients in met current ILAE criteria for diagnosis of epilepsy after a single seizure, the outcomes of these patients were not specially analysed.

In our cohort of more than 600 patients, more than 30% were not treated with ASMs at the time of diagnosis

Using a prospectively maintained patient registry in Western Australia, we explored the real-world treatment pathways that clinicians and patients embark on after a new diagnosis of epilepsy. Our aims were to identify which types of patients tended to not be treated despite diagnosis and whether this affected short-term or long-term outcomes. We also explored patient self-discontinuation of ASMs, with the broader goal of identifying key areas for improved communication and patient education.

Factors leading to treatment

Many of the factors contributing to the 'treatment gap' in epilepsy in developing countries, such as lack of education, access to trained clinicians/medications, financial pressures and superstition [Mbuba *et al*, 2008] are less applicable in a well-resourced urban setting. Despite this, we found in our cohort of more than 600 patients, that more than 30% were not treated with ASMs at the time of diagnosis, and one in nine remained untreated

at the end of five years' follow-up, at times, despite further seizures [Sharma *et al*, 2020].

An epileptogenic lesion on neuroimaging was associated with treatment commencement at diagnosis, whereas on multivariable analysis, epileptiform EEG findings did not influence the decision to treat.

Other factors associated with a higher likelihood of treatment included older age, increased frequency of seizures and lower socio-economic status. These results are broadly consistent with studies that audited national hospital and pharmaceutical databases in New Zealand [Hamilton *et al*, 2020] and larger insurance claims database assessments in the United States [Faught *et al*, 2018].

In our cohort, half of those not treated at diagnosis were not offered treatment (usually due to having had a single seizure, awaiting EEG or MRI, or the presence of modifiable lifestyle/external factors thought to precipitate seizures). However, among the 90 patients who declined treatment, this was overwhelmingly due to not being convinced of the necessity of treatment, or the diagnosis. This latter group is more concerning, given 64% of these patients commenced therapy later after having had further seizures.

Investigating the outcomes of these treatment decisions essentially supported older trial data. Immediate treatment in those patients with a single seizure but a diagnosis of epilepsy supported by EEG, CT/MRI findings or known remote aetiology, was less likely to reduce seizure recurrence in the short term. In this group, the number of patients needed to treat to prevent someone experiencing a seizure recurrence was eight, compared to four among those diagnosed after two or more seizures [Sharma *et al*, 2021]. Similar to the FIRST and MESS trials, treatment did not significantly alter long-term outcomes, and supporting the ILAE definition, single and multiple seizure diagnostic groups had similar overall long-term outcomes.

A higher number of patients than expected self-discontinued treatment during follow-up

The lack of impact of immediate treatment was not surprising – although their effect in seizure suppression is appreciated, recent nomenclature changes from 'anti-epileptic' to 'anti-seizure' medications was in part a recognition of the lack of their disease-modifying properties [French *et al*, 2020]. However, they do remain the mainstay of management for most newly diagnosed patients.

Self-discontinution

A higher number of patients than expected self-discontinued treatment during follow-up. Physician-directed treatment discontinuation is typically considered in patients who have been seizure free for more than two years. This follows a careful consideration of the risks of seizures and related consequences, such as injuries or driving restrictions against the medical and psychological (or sometimes financial) side effects of ongoing treatment [Beghi *et al*, 2013]. Patient-initiated cessation of treatment has rarely been studied.

In our cohort, 16% of treated patients self-discontinued treatment after a median duration of 1.4 years, and with a median period of seizure freedom of less than a year [Sharma *et al*, 2022]. Although most patients ceased their first tried monotherapy,

a minority stopped their second or third trialed therapy, with some of these patients stopping multiple ASMs at once. No single monotherapy option predominated among those who self-ceased therapy.

The most common reason for discontinuation was adverse effects

The most common reason for discontinuation was the presence of adverse effects, with these patients discontinuing therapy after a median of less than nine months of therapy, and less than six months of seizure freedom. The next most common group was patients who thought treatment was no longer necessary, after achieving a median seizure freedom period of 1.6 years.

Other reasons for self-discontinuing included pregnancy-related concerns or the culmination of chronic non-adherence. Of these patients, 65% experienced further seizures after discontinuation of therapy and overall 55% restarted treatment, sometimes after a significant seizure-related injury, with those who had stopped treatment due to side effects most at risk of seizure recurrence.

Those patients with epileptogenic neuroimaging lesions, tonic-clonic seizures or seizure clusters at presentation were less likely to stop treatment. However, those with significant alcohol or illicit substance use or sleep deprivation in association with seizures leading to diagnosis were more likely to cease therapy. Compared to previous assessments of non-adherence to ASMs, youth, male gender and psychiatric comorbidity were not significant factors [Henning *et al*, 2019].

Based on these real-world observations of epilepsy care, there seem to be discrepancies in the perception of epilepsy diagnosis and treatment between professional guidelines, clinicians and patients. The ILAE makes no specific recommendation for the patient with a single seizure on how to assess the magnitude of the contribution from EEG and neuroimaging findings or other factors when assessing the risk of subsequent seizures.

In our study, compared to EEG, neuroimaging findings appeared to play a bigger role, favouring treatment commencement and continuation, despite data showing the presence of epileptiform abnormalities on EEG is associated with an increased risk of recurrence after a first seizure, similar to that seen when an epileptogenic lesion is identified on neuroimaging (Lawn *et al*, 2015). This may represent different weights ascribed by neurologists to different investigations in the diagnostic pathway for epilepsy [Askamp *et al*, 2013].

Patients were also less likely to accept the recommendation for treatment if epileptiform EEG findings were the predominant supporting evidence behind diagnosis. Likewise, patients with epileptogenic neuroimaging lesions were less likely to self-discontinue treatment, whereas epileptiform EEG made little difference. Although a meta-analysis of physician-initiated discontinuation found a weaker association between EEG findings and seizure recurrence than that of neuroimaging [Lamberink *et al*, 2017], it does highlight a difference in perception.

Beyond evidence underlying recurrence risks, the focus on neuroimaging likely derives from the

most common lesions of stroke, trauma and tumours, which have significant effects outside of their epileptogenic potential. Patients may already be taking treatment for these conditions. There is likely room for focused education among clinicians and patients as to the importance of different investigation results. This should explore their utility in risk prediction specifically for seizures, outside of the significant broader life events they might be.

Most patients who self-ceased treatment due to side effects did so before six months of seizure freedom

The discontinuation study highlighted the patient experience of side effects, as well as their belief in the diagnosis and necessity for treatment of newly diagnosed epilepsy. Most patients who self-ceased treatment due to side effects did so before six months of seizure freedom, placing them at significant risk of recurrence (most had recurrent seizures within six months of cessation).

We did not find a statistical relationship between time to first follow-up clinic appointment or follow-up frequency in general with self-ceasing treatment, but it is not unreasonable to suppose that rapid focused follow-up may help maintain adherence to ASMs. Nurse practitioners or epilepsy nurses enquiring for side effects and providing advice on managing and, where appropriate, altering treatment may be able to mitigate the risk of discontinuation [Duncan, 2022]. Most patients were agreeable to recommence therapy after recurrent seizures, highlighting a lack of objection to treatment once deemed tolerable.

A minority of patients declined treatment due to not believing in its necessity or the diagnosis, or later discontinued treatment after a short period of seizure freedom. This group is likely much more sizable outside of those followed up in clinic – many patients never attended follow-up, and reticence to accept the diagnosis of epilepsy or undertake treatment may account for some proportion of this.

Starting treatment

Decisions to commence treatment are collaborative – certainly some patients who declined therapy and opted for lifestyle optimisation initially had good seizure outcomes, and some patients who self-discontinued ASMs, preferring to avoid alcohol, illicit substances or sleep deprivation, were seizure free during follow-up. Early and ongoing education in a multidisciplinary setting regarding the nature of an epilepsy diagnosis and risks and benefits of treatment is a key and probably underutilised component of epilepsy management [Foley *et al*, 2000].

The psychological effects of diagnosis are well documented. The ILAE 2014 definition of epilepsy highlighted that epilepsy can "resolve". This is, for example, in children who outgrow paediatric syndromes, or in adults who are able to spend time off treatment and without seizures. The authors contend however this is not the same as being "cured".

The 2014 definition also highlighted that a diagnosis of epilepsy did not universally infer a need for treatment, recognising the role of non-pharmacological management. Although not necessarily achievable in all cases, it is important for clinicians to recognise patients' aspiration for seizure remission off treatment, and

that patients may not want to wait years, while taking medication, to attempt a treatment withdrawal trial. Multidisciplinary engagement may also reduce the risk of premature self-discontinuation [Al-Aqeel *et al*, 2020].

Clinicians and researchers should identify areas to improve these 'gaps' in well-resourced settings, both at diagnosis and follow up. Epilepsy clinics in close collaboration with primary care are a key component to epilepsy management, allowing discussions about diagnosis and necessity for individualtreatment, minimising self-discontinuation and improving outcomes.

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Melissa Maguire

Music and sound

Could it set the tone for treating epilepsy?

Dr Melissa Maguire describes the evidence around infrasound, audible sound and ultrasound in affecting brain waves and the potential of sound to impact seizure activity.

There is an increasing body of evidence that sound, both audible and inaudible, may benefit people with epilepsy. Research into the anti-seizure effect of sound has largely focussed on the famous K448 Mozart piano sonata [Maguire, 2015]. This follows on from the published 'Mozart effect', reporting on enhanced cognitive ability following exposure to the sonata in animal and human studies Rauscher *et al*, 1998]. However, other pieces from the same composer and other composers of classical music have also been studied [Maguire, 2017].

Sound has a frequency spectrum ranging from infrasound (<20 Hertz

(Hz)), audible sound (20-20,000 Hz) and ultrasound (>20,000 Hz) [Heffner, 2004]. Sound can take on the form of simple audible tones or a part of a complex ensemble of tones in creating music. Infrasound, under usual exposure conditions, is not detected by the human auditory apparatus [Watanabe and Møller, 1990]. It is created artificially by wind turbines, low speed fans and supersonic aircraft. It is also created naturally from lightning, earthquakes and other severe weather conditions [Hanson, 2010]. The human ear perceives sound between 20-20000Hz either as simple tones or as part of orchestrated music [Purves *et al*, 2001]. Ultrasound is similarly inaudible to humans, however bats and porpoises use it to locate prey and navigate obstacles. Ultrasound is also used in medical ultrasonography and in cleaning and chemical industries [Escoffre and Avache, 2016; Mason, 2007].

Transference of sound typically occurs through the process of air conduction. Sound waves vibrate the ear drum and are then subsequently amplified by the ossicles in the middle ear and from there waves are transmitted from air to liquid within the inner ear. These vibrations are then analysed within the basal membrane of the cochlea according to their frequency and converted to electrical impulses. These electrical impulses relay from the auditory nerve to the brain stem and subsequently to the primary auditory cortex where they are perceived as sounds [Yost, 2007]. To analyse music, the brain activates a complex network of neurons within auditory, limbic and multisensory cortices, with this processing lateralising to the right brain hemisphere [Stewart *et al*, 2006].

Waves are constantly being generated by the brain at a frequency depending on the level of alertness and activity. From slow delta waves, typically occurring in deep sleep, to beta and gamma waves associated with active concentration and feedforward connectivity across different brain regions [Barker and Burgwin, 1948; van Kerkoerle *et al*, 2014; Foster *et al*, 2017].

The encounter of two or more waves through superposition is well described in physics. Superposition is where waves can super impose themselves onto one another in a constructive or destructive interference pattern. If interference is constructive, then superposition will create a cumulatively higher amplitude. If interference is destructive, the waves' amplitudes may cancel one another out [Radi and Rasmussen, 2013]. More commonly, wave forms are not precisely aligned so there may be periods of constructive and destructive interference and if waves are only very slightly different in frequency, there is a resultant beat frequency [Campbell *et al*, 2004].

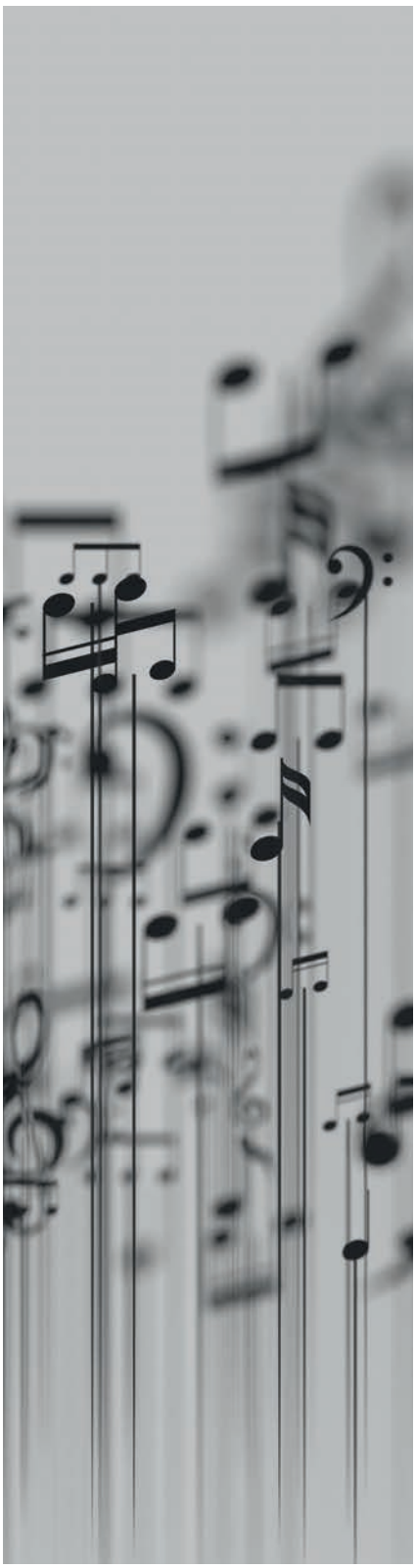
Could sound waves influence brain waves by constructive or destructive interference to a pattern of brain wave activity associated with a non-seizure state?

Given the known physiological interactions between waves, could sound waves therefore influence brain waves by constructive or destructive interference to a pattern of brain wave activity associated with a non-seizure state?

Audible sound

One area in which this question has been explored is brain wave entrainment using binaural beats. Binaural beats occur when two sounds of slightly different frequencies are played in each ear with the net frequency entrainment being the difference between the two frequency exposures [Oster, 1973]. In children with anxiety, inducing a lower entrainment frequency improved symptoms, while entrainment to frequencies within the alpha or beta region improved attention [Kennel *et al*, 2010]. Binaural beats have also been examined in patients undergoing stereotactic EEG for epilepsy. It was noted that induced lower frequencies resulted in loss of synchronisation and power at the frequency of the beat, while beat frequencies within 10-40Hz showed an increase in power with entrainment [Becher *et al*, 2015]. These experimental results may happen naturally, as evidenced in one study by the production of alpha and beta brain wave activity in sites remote from interictal discharges in people with epilepsy. These alpha-beta oscillations were associated with better cognitive profiles, prompting researchers to speculate that this was the brain's way of protecting unaffected cortical regions from epileptiform activity [Pellegrino *et al*, 2021]. Furthermore, monoaural gamma entrainment at 40Hz has not only shown to improve condition states in patients with stroke and Alzheimer's disease, but was also found to reduce inter-ictal discharges in subjects with refractory epilepsy [Quon *et al*, 2021].

The utility of binaural or monaural beats as a neuromodulatory treatment may be limited however, since patients who listened to pure tones for any prolonged period did not find this experience particularly pleasant. Investigators have therefore looked to



music as a potential therapy providing a more realistic and tolerable option for patients.

Potential of music

Most studies examining music have focussed on the K448 Mozart piano Sonata [Maguire, 2012]. The historical landmark studies by Hughes *et al* in 1998 reported impressive reductions in focal and generalised interictal discharges (IED) in 23 out of 29 people with epilepsy, three of whom were in status epilepticus at the time [Hughes *et al*, 1998]. Similar IED reductions by 44% and a reduction in drop attacks was seen in a child with Lennox Gastaut syndrome exposed to 10 minutes of the Sonata on the hour every hour whilst awake [Hughes *et al*, 1999]. Hughes examined the effect of Mozart K448 by looking at musical parameters and comparing them to other composers' works. Longer periodicities and repeating notes within the melodic line were more evident in the musical piece when compared to other works by JS Bach, JC Bach, Chopin, Beethoven, Wagner and Haydn [Hughes, 2001].

Regions of the brain involved in emotion and cognition were also shown to recruit early in musicogenic seizures, suggesting a learnt response to the seizure-provoking exposure

There have been sixteen studies (4 RCTs and 12 prospective studies) published comparing K448 to an active control (alternative composer piece) or no musical intervention [Maguire, 2022]. Most studies report on the impact on IEDs and six studies report the impact on seizure events in people with mainly focal epilepsy. Overall, the studies report a mean reduction in IEDs by 80% and seizure reduction by 30% on exposure to K448. The studies vary in methodology, particularly in relation to exposure times, control groups, exposure frequencies and duration of treatment. There is also significant clinical heterogeneity across study populations which creates a challenge in synthesising the data across the cohorts. There is also a reliance of scalp EEG in measuring treatment effect which may lack robust accuracy in data capture.

Two more recent studies, however, have examined patient responses using stereotactic EEG as part of work up for epilepsy surgery [Quon *et al*, 2021; Štillová *et al*, 2021]. One study observed the effect of different exposure times of K448 compared to Wagner's Lohengrin on IEDs within seizure and non-seizure onset zones. An average 66% reduction in IEDs across all zones was seen for exposures 30 seconds or longer. The maximum exposure group was 90 seconds. However, the response was not sustained beyond the exposure suggesting that longer periods of time are required for a neuromodulatory effect [Quon *et al*, 2021]. The second stereotactic EEG study used a different comparator, Haydn Symphony No94. This composer produced music of a similar structure to Mozart, with repetitive melodies providing a more comparable active control. Baseline IEDs were recorded for two days followed by a 10-minute exposure of Mozart or Haydn selected at random. This was followed by a 10-minute break, similar to a washout period followed by a further 10-minute

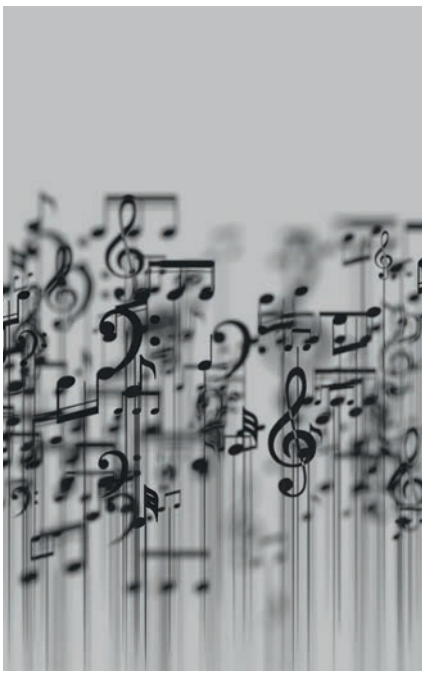
exposure again selected at random. The study reported a 32% reduction in IEDs on listening to K448 but an increase in IEDs by 45% with Haydn relative to the baseline IEDs. This divergence in response was more evident in men than women. This was a surprising result which could not be explained by a difference in emotive responses. Further analysis of musical parameters suggest that the harmonic spectrum of K448 appeared relevant to its anti-seizure effect [Štillová *et al*, 2021].

Music as seen with the Haydn symphony No 94 has been described as a trigger for seizures in some patients. These patients are described as having 'musicogenic epilepsy', a term coined by Critchley in 1937. In a review of 126 cases, musical exposure was shown to vary significantly and was not limited to a certain type of music or composer. Regions of the brain involved in emotion and cognition were also shown to recruit early in musicogenic seizures, suggesting a learnt response to the seizure-provoking exposure [Garcia-Casares *et al*, 2019].

In day-to-day listening, a novel musical piece may provoke an emotive or pleasant experience, but this effect doesn't last as continued exposure occurs over time

The exact mechanism by which Mozart exerts its anti-seizure effect is currently unknown. Earlier, researchers hypothesised that the highly organised structure of the music (comparing it to the architectural order of a cathedral) might have the ability to 'resonate' with the columnar and connectivity patterns of the cerebral cortex as described by Mountcastle [1997]. Resonating in tune with innate columnar cortices might entrain other areas of suboptimal functioning. Mozart's music has been mathematically modelled based on the 'Trion model' of this columnar arrangement [Leng *et al*, 1990]. More recent work using the Trion model has examined the impact of musical rhythm predictability. This work postulates that unpredictable music patterns have a greater ability to shift the brain waves from a highly predictable and synchronous state (i.e. during a seizure) to one that is able to track the scale free rhythm of the sensory world. The research examined 558 compositions, reporting that, for example, Beethoven had a significantly higher rhythm predictability than Mozart [Rafiee *et al*, 2021]. Further work is needed in this area to form any robust conclusions in relation to this observation and its anti-seizure effect.

Other researchers have looked at the ability of music to flood the brain with dopamine, in particular brain reward pathways [Blood and Zatorre, 2001]. A lack of dopamine within the striatum is linked to several epilepsies, with a subsequent knock-on effect in dopamine's ability to control thalamocortical excitation [Fedi *et al*, 2008]. Unpredictable music has a greater ability for dopamine flooding which may link with the rhythm predictability work described earlier [Montag *et al*, 2011]. In day-to-day listening, a novel musical piece may provoke an emotive or pleasant experience, but this effect doesn't last as continued exposure occurs over time. Studies have also examined the effect of music on parasympathetic



tone which is known to be lower in people with epilepsy. Mozart K448 has been shown to elevate parasympathetic tone and may modulate thalamocortical excitation involved in reducing epileptic activity [Lin *et al*, 2013].

A recent meta-analysis by Oberleiter and Pietschnig [2023] has questioned the findings from a number of past studies looking at the Mozart effect. The authors conclude that present evidence "shows that there is only little evidence for any meaningful beneficial effect of listening to Mozart's sonata KV448 (or any other music) on epilepsy in particular or other medically relevant conditions in general". They say studies in this arena suffer from "unfounded authority, underpowered studies and non-transparent reporting".

Ultimately, at the moment, there is not enough robust data to recommend music as a treatment strategy. We do not yet understand the fundamentals of how music could interact with epilepsy to effect change in EEG and seizure activity.

Infrasound and ultrasound

Finally, we turn to infrasound and ultrasound as potential therapies for epilepsy. Infrasound as a therapy has not been investigated to date. There are exposure studies which have demonstrated living close to wind turbines, for example, may activate a stress response [Ascone *et al*, 2021]. But there are no clinical studies examining risks or benefits in epilepsy. Rat studies, however, have shown that exposure to infrasound may increase

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Three studies, to date, report on fifteen people exposed to ultrasound as a neuromodulatory treatment [Lee *et al*, 2022; Stern *et al*, 2021; Brinker *et al*, 2020]. Only one study of six patients reported the effect of low intensity ultrasound on seizures. The study reported an overall reduction in seizures by 33% [Lee *et al*, 2022]. The other two studies either reported on the safety of low intensity ultrasound, examining for histological tissue damage within planned resection tissue (and concluding no damage), or validated a platform technology [Stern *et al*, 2021; Brinker *et al*, 2020]. While there is some limited evidence of an effect on seizures, large scale trials are yet to be reported on.

In summary, we do not reliably know whether sound beyond the audible spectrum has any viable treatment potential in epilepsy.

Conclusions

Current evidence reports an anti-seizure effect with the K448 Mozart sonata, demonstrating an average reduction in seizures by one third and an 80% reduction in IEDs. Beyond audible sound, the data on any therapeutic effect or risk in epilepsy is either unavailable (infrasound) or very limited (neuromodulatory ultrasound). The anti-seizure effect of Mozart K448 is shared with another Mozart sonata K545 [Lin *et al*, 2012], but not other composer compositions. Researchers have tried to explain why this anti-seizure effect is specific to Mozart's music, with several theories posed but no definitive answer. An interaction between musical resonance, predictability of rhythmic structure and brain wave modulation has been implicated. Computational analysis of acoustic parameters may enable further exploration of sound neuromodulation in the treatment of epilepsy. For now, we will need to stay tuned.

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Tom Shillito

Research update

Epilepsy Action health improvement and research manager, Tom Shillito shares updates from Epilepsy Action's research work

Step Together: Benchmarking services for people with epilepsy and a learning disability

The Step Together benchmarking toolkit allows providers to self-assess the care they offer to people with epilepsy and a learning disability. It can be used by services, trusts, systems and regions across the UK to understand and evaluate the care they provide to this vulnerable group.

The toolkit is based on the Step Together Integrating Care for People with Epilepsy and a Learning Disability led by Professor Rohit Shankar of the University of Plymouth, and has been created as a partnership between Prof Shankar and Epilepsy Action.

Creation of the toolkit

Engagement with service users and key stakeholders was central to the creation of the toolkit. This has ensured it focuses on the things that are most important for providing quality care to this group, and lends the tool a high level of validity.

Workshops were held with people with epilepsy and a learning disability, their carers and families, and with four multidisciplinary teams from across the UK.

Engagement with service users and key stakeholders was central to the creation of the toolkit

These teams included nurses, neurologists, psychiatrists, commissioners and many other health and social care professionals. The outcomes of these workshops, including the priorities and challenges faced by each group, were used to create the toolkit.

Eight key domains were identified, which were: workforce, local planning, key service provision, diversity of provision, care planning, transition, sharing of information between providers, and user and carer participation. The toolkit assesses services in each of these domains and can show strengths and weaknesses in each area.

Outside of the specific domains, the toolkit prioritises three areas: safety, management and quality of life. The highest priority must always be patient safety, ensuring that patients' risk of harm is minimised in all possible ways. By completing the toolkit, systems will have better visibility of, and be able to, resolve potential safety concerns.

Another area of focus is management of the patient's conditions, ensuring their symptoms are controlled as well as possible and that they are treated in a holistic way with appropriate wrap-around care.

The final focus is quality of life, ensuring that people with epilepsy and a learning disability have access to all opportunities for living with their seizures and other symptoms, and there is a good understanding of the enablers and challenges for them to participate in society and find enjoyment in their activities to the greatest extent.

A regional analysis

The toolkit has recently been completed by the Midlands region, with 10 of the 11 integrated care systems in the region completing the toolkit. We have used this data to create a 50-page report that lays out the regional strengths and weaknesses, and breaks down the results by system, and for some areas by trust, and by children's or adults' services. These results were presented at a feedback event at the end of March this year.

Improvements began to be seen before the toolkits had even been completed

The results of the Step Together benchmarking exercise have allowed the region to discover areas where cross-system and cross-service collaboration can occur to improve

services, and where best practice can be shared and built on across the region.

Feedback from the Midlands' systems has been overwhelmingly positive, with participants praising the depth of the data the toolkit creates, its power in finding gaps in care, and how useful the results have been in driving quality improvement in their service.

Improvements began to be seen before the toolkits had even been completed, as the process of completing them encourages cross-departmental and cross-service conversations that may not otherwise have happened. These often led to new ideas and learning.

How you can take part

The next step for the Step Together toolkit is a nationwide rollout. Our ambition is for every service to complete the toolkit and share their results with us, so that we can have a nationwide picture of the quality of care and can facilitate sharing best practice and quality improvement. We can also track the changes over time for individual services and the nation as a whole.

Further reading

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If you are interested in completing the toolkit for your service, trust or system, all of the details can be found here: www.epilepsy.org.uk/professional/step-together

If you would like to complete the toolkit across a whole region, we will be hosting an information session in June with more information and advice on how to do this. For more details and to reserve a place, please email researchadmin@epilepsy.org.uk.

Markus Reuber

Highlights

Top picks from *Seizure*

Editor of the journal *Seizure*, Professor Markus Reuber highlights his key papers from the latest editions

Climate change – and the profligate, inequitable, fossil fuel-driven consumption that causes it – is everyone's problem.

My editor's choice from volume 106 of *Seizure* is an article with testimonies from members of the International League Against Epilepsy (ILAE) Climate Change Commission (CCC) [Aledo-Serrano, 2023], which makes clear how climate change affects all of those living and working with epilepsy and other seizure disorders.

Climate change affects health in myriad ways – through its direct effects on heat waves and extreme weather events; its indirect effects on natural systems, such as changing land use, and distribution of infectious diseases and their vectors; and through disruption of social dynamics – intersecting with other political, social and economic determinants of health to exacerbate food and water insecurity, political instability and forced migration [Pörtner *et al*, 2022], [Watts *et al*, 2015]. The fossil fuel dependence that overwhelmingly causes climate change also affects health directly – from environmental degradation and community disruption, to the 3.6 million annual deaths attributable to ambient air pollution from fossil fuels [Beagley *et al*, 2023].

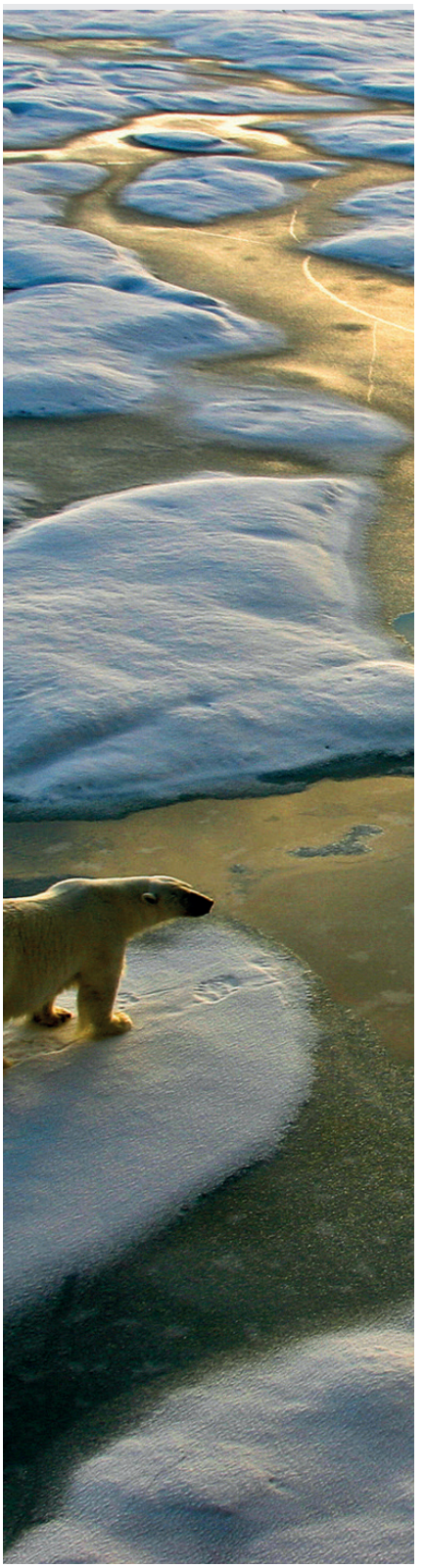
Climate change is everyone's problem. That can make it seem like no one's problem. The tools of healthcare ethics are equipped for dealing with decisions between clinician and patient. They are less able to engage with problems caused by the cumulative effects of many people's actions, whose consequences may be felt by people miles – or years – away. Protecting human health from climate and environmental crisis demands that we do not just ask what we are responsible for – it requires seeing that our usual mechanisms for distributing responsibilities are failing and asking how we, collectively, can rectify these failures [Wardrope *et al*, 2016]. The accounts of the ILAE CCC invite us all to take action.

Climate and environmental crises affect people with epilepsy at every point. The fossil-fuel-driven economy has negative impacts on the biggest causes of epilepsy worldwide: 20.1% of stroke risk is attributable to ambient air pollution [Feigin *et al*, 2021], motor vehicle road injuries are the second most common cause of traumatic brain injury globally [James *et al*, 2019], and increasing temperature variability and aridity is increasing the incidence and spread of meningitis [Akanwake *et al*, 2022], [Chen *et al*, 2023], and potentially other infectious precipitants of epilepsy [Gulcebi *et al*, 2021]. Those already living with epilepsy may have vulnerabilities such as heat-sensitive seizures [Gulcebi *et al*, 2021]. Less directly, climatic disruption of social systems is liable to have damaging impacts on epilepsy prevention and management, from disruption of supply and storage of medications [Gulcebi *et al*, 2021], to drought or conflict-driven forced migration [Abel *et al*, 2019], which poses high risks of developing epilepsy – seizures are the leading cause for medical referral in camps for forcibly displaced persons [Hallab and Sen, 2021].

Climate and environmental crises affect people with epilepsy at every point

The causes of these environmental determinants of brain health and their effects are unevenly distributed, in ways that exacerbate inequities affecting people with epilepsy. Wealthy consumers and large industries in the global north overwhelmingly drive climate change, while small island nations and Sub-Saharan African populations are more vulnerable to the direct and indirect health effects of climate change [Ritchie *et al*, 2023], [Edmonds *et al*, 2020]. Countries most vulnerable to the health effects of climate change are those where people with epilepsy are already most vulnerable, with the proportion of people in low-income countries not receiving basic epilepsy treatment estimated at 86.9% [Kwon *et al*, 2022].

No individual action can begin to mitigate the scale and complexity of these health threats. Responding to climate change requires institutional and political action. However, existing political actions are insufficient to address the threat adequately, with



current policies leaving the world on track to surface temperature rises of 2.7C by 2100 [Romanello *et al*, 2022]. Those entrusted with working for the health of people with seizure disorders cannot be complacent. The formation of groups such as the ILAE CCC provide opportunities for health workers to take collective action.

CCC members highlighted the health and planetary benefits of plant-based diets. Such a shift not only reduces the carbon intensity of food; it could also avert more than 10 million diseases per year from non-communicable diseases and reduce causes of epilepsy such as stroke [Willet *et al*, 2019]. But reaping these benefits requires not just individual change, but also shifting food systems from intensive industrial agriculture to diversified, agroecological methods. Health workers can support this transition by creating alternative spaces for food production and sharing in their communities [Jochelson, 2005].

Similarly, fossil-fuel-powered transport comprises a large portion of individual and global carbon emissions, but framing transport modes as an issue of individual choice neglects situational factors that support or discourage choices – and which health workers can influence. The pandemic has demonstrated the availability of alternatives to the academic norm of frequent long-haul flights for international conferences; more resources are available than ever to facilitate low-carbon information sharing in ways that are also more accessible to poorer and marginalised communities [Willett *et al*, 2019]. Context-sensitive use of telemedicine can also reduce emissions from healthcare attendances [Jochelson, 2005], [https://flyingless.de/en], [Blenkinsop *et al*, 2021].

Health professionals can use existing forms of collective organisation to support a just transition to a more sustainable society – this editor's choice gives just a small sample of reasons why they should, and how they could.

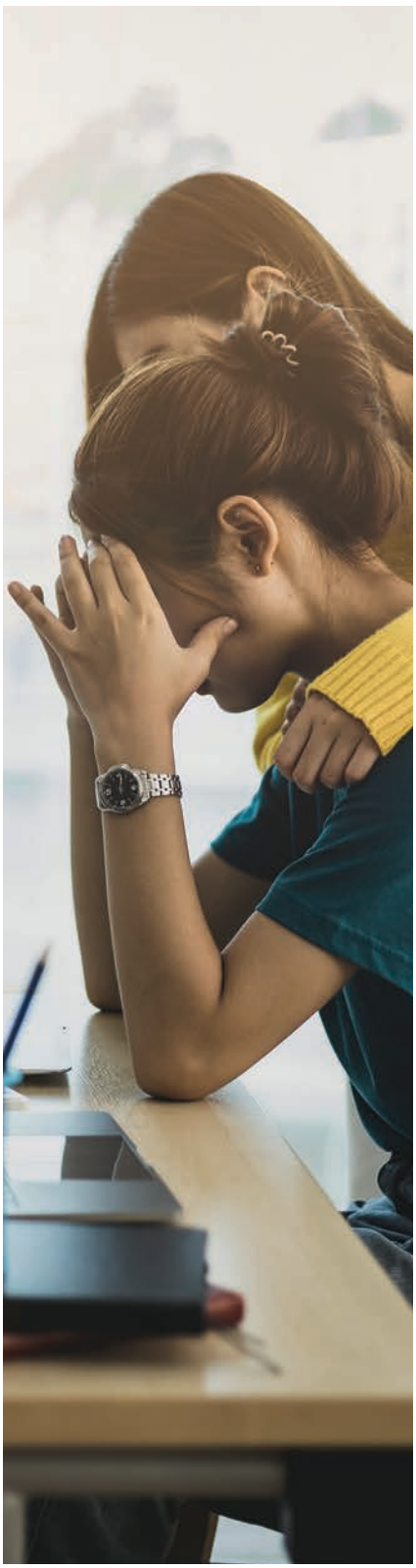
Suicide prevalence

Suicide and other forms of self-injurious behaviours are complex issues that may be related to a range of factors, including mental health, social support and healthcare access.

In individuals with epilepsy, the list of potentially relevant factors is even longer – and includes seizures, the impact of seizures on mood and quality of life, social isolation, stigma and anti-seizure medications (ASMs).

The prevalence of suicide attempts is not only increased after people receive a diagnosis, i.e. as a potential consequence of having epilepsy. Large epidemiological studies have shown that, in individuals subsequently diagnosed with epilepsy, the increased risk of suicidal ideation and suicide attempts (as well as an increased prevalence of depression and anxiety disorders) predates the onset of epilepsy and commencement of ASMs [Hesdorffer *et al*, 2012], [Hesdorffer *et al*, 2016]. This observation is one of the reasons why the possible association of ASMs with an increased risk of suicide, which was based on a meta-analysis of randomised controlled studies involving these drugs, has been called into question [Mula, 2022].

My editor's choice article from volume 107 of *Seizure*, is an original research paper by M Zinchuk *et al*, which adds to our understanding of the risk factors for suicide and other self-injurious behaviours in people with epilepsy [Zinchuk *et al*, 2023]. In this study of 456 patients, the one-year prevalence of suicide attempts was 0.7% and that of non-suicidal self-injury (NSSI) was 2.8%. The lifetime



This study highlights the importance of a greater awareness of the heightened suicide risk associated with epilepsy

risk of a suicide attempt was 8.3% and that of NSSI was 15.3%. Higher seizure frequency, lifetime NSSI and lifetime diagnosis of mental disorder were associated with suicidal ideation, whereas traumatic brain injury, substance abuse and NSSI were associated with suicide attempts.

This study highlights the importance of a greater awareness of the heightened suicide risk associated with epilepsy. It also demonstrates the importance of screening for suicidal ideation and NSSI in order to identify individuals at particular risk. Clinicians who want to introduce suicidality screening are advised to consider the Neurological Disorders Depression Inventory for Epilepsy screening instrument for depression [Mula *et al*, 2016].

Epilepsy and gut disorders

Over the last few centuries, much progress in medicine has depended on the clinicopathological method – an approach linking manifestations of illness with specific structural and pathophysiological processes. The better differentiation of medical disorders and recognition of specific causes continues to inspire the development of new and more effective treatments.

However, there are limits to the progress that can be made by distinguishing diseases from each other. It is becoming increasingly clear that it is as important to study the links between "separate" disease entities to gain a fuller understanding of their pathology and how they affect individual sufferers [Gaitatzis, *et al*].

The risks of illness or chronic disease are not distributed randomly. While the causes of multimorbidity encompass complex and interacting medical, socioecomomic, environmental, behavioural and experiential factors, the fact that there are societal clusters at greater and lower risk of all kinds of ill health is well-recognised [Zhu, *et al*]. Beyond non-specific factors mediating an increased risk of disease in general, there are more direct connections between some diseases.

In the case of epilepsy, the bidirectional relationship with mental health disorders is well-established [Zhu, *et al*]. In contrast, the understanding of links between epilepsy and cardiovascular disorders or between epilepsy and gut disorders – albeit recognised – is less well-developed. My editor's choice article from volume 108 of *Seizure* is a systematic scoping review by Alexandra Gabrielsson *et al*. It makes an important contribution to the field by summarising eight previous studies exploring the clinically important but widely neglected topic of links between constipation and epilepsy [Hesdorffer, *et al*].

The key findings of the review are that up to five times as many people with epilepsy (PWE) have symptoms of irritable bowel syndrome (including constipation) and that more than one third of PWE complain of functional constipation. Constipation was reported to be the second most common comorbidity in children with epilepsy. It has also been shown to be a common side effect of ASMs. The links between functional bowel disorders and epilepsy may be bidirectional: two

studies documented a higher risk of constipation prior to the manifestation of seizures.

While these studies should prompt clinicians working with PWE to ask patients about their bowel habits and to consider treatment modifications to those troubled by constipation, they should also encourage researchers to investigate the links between the two anatomically and developmentally distinct organ systems of gut and brain. There are many reasons to think epilepsy and functional bowel disorders are not merely connected by non-specific factors mediating an increased multimorbidity risk.

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Reducing readmission rates

I am sure most clinicians working in busy district general or tertiary teaching hospitals often encounter ward referral requests for specialist input, or receive a request for an in-patient review of patients known to a neurologist with an interest in epilepsy or to the nurse specialist team.

As I go on my district general hospital rounds, I frequently encounter such patients. Often they have epilepsy and are already under my long-term follow-up. This has caused me to consider and reflect on the reasons for readmission in epilepsy patients and what can we do about it.

There is some, but not a wealth of literature on this, with different factors proposed in different patient cohorts. Generally, individuals who have comorbid conditions and those who come from areas of social deprivation are more likely to be readmitted. Intellectual disability, psychiatric comorbidity, dissociative seizures and those with alcohol and drug misuse also seem to represent clear risk factors for readmission.

In paediatric populations, ongoing seizures and problems with medication or with discharge plan documentation are reported, while in older patients with epilepsy, ongoing seizures and sepsis, which in turn may trigger further seizures, are reported as reasons for readmission. In postpartum women with epilepsy, psychiatric symptoms and conditions are cited as reasons for readmission.

However, overall ongoing and recurrent uncontrolled seizures are still a major factor in readmission to hospital, as are adverse events from previous hospital admissions.

In light of this, especially given the pressure on our health service, and knowing the risk that hospital readmission can place on certain vulnerable patients, it's worth thinking about what we can do to prevent or limit readmissions.

Firstly, we still need to focus on controlling seizures and in optimising anti-seizure medications (ASMs). Although ward referrals and liaison work are arduous – as we often know a lot of these patients well – we are probably best placed to tweak ASMs and are best able to deal with adverse events.

Given the special populations of patients who can be readmitted, such as those with intellectual disability and the post-partum group, time spent in advance working on patient pathways and care plans may pay dividends, either in keeping people at home or in assisting the medical teams to look after them in our absence or in advance of our review.

Other aspects worth considering are: exploring and maintaining joint clinics with learning disability and psychiatry (to keep common dialogue), to have joint decision making and to facilitate care plans and pathways.

Specific targeted interventions by learning disability, psychiatry teams and/or by community epilepsy nurses, might also enable care closer to home and abort hospital admission. This might be appropriate if some medical problems and comorbidities need closer attention.

But maybe a key area to focus on, and develop further, is the ambulance service. It would need an investment in technology and other adequate resourcing, staffing and training, but we could create more established links and dialogue between paramedics and clinical nurse specialists.

Maybe the future is an integrated, bi-directional system between the home and tertiary epilepsy centres that engages families and carers in real time – allowing emergency care, triaging the need for hospital admission and providing a real-time opportunity to adjust medication and arrange further follow-up as needed.

Dates for the diary

Dates and events may be subject to change – please check on the relevant websites.

2023

20-24 June
15th European Paediatric Neurology Society Congress (EPNS)
Prague, Czech Republic
epns.info/epns-congress-2023

24-26 August
13th ILAE School for Neuropathology and Epilepsy Surgery (INES)
Vienna, Austria
bit.ly/30Spwk8

2-6 September
35th International Epilepsy Congress
Dublin, Ireland
bit.ly/30Spwk8

2-4 October
ILAE British Branch Annual Scientific Meeting
Gateshead, UK
ilaebritishconference.org.uk

8-13 October
10th Eilat Educational Course: Pharmacological treatment of epilepsy
Jerusalem, Israel
eilatedu.com

11 November
ILAE British Branch Clinical Epilepsy Course for Doctors in Training
Birmingham, UK
https://bit.ly/3OyJ0kw

2024

3-8 March
4th International Training Course on Neuropsychology in Epilepsy
Lyon, France
bit.ly/3gLFWD4

5-8 May
Seventeenth Eilat Conference on new Antiepileptic Drugs and Devices (EILAT XVII)
Madrid, Spain
bit.ly/3u7Mzm6

Next issues:

Dr Kathryn Bush

Dr Bush discusses the link between socioeconomic deprivation and epilepsy and helping address the imbalance in healthcare.

Dr Pablo Casillas-Espinosa

Dr Casillas-Espinosa discusses the potential use of sodium selenate in epilepsy

If you are interested in submitting a research paper for inclusion in *Epilepsy Professional,* please contact the Editor:

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