

Socioeconomic inequality How does deprivation affect epilepsy?

Dr Kathryn Bush

Sodium selenate – Dr Pablo Casillas-Espinosa

Opinion: climate change – Alistair Wardrope

Sodium valproate update – Grace Wood

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The first sign of summer from my window is the arrival of the swifts in late April/early May. They come from south of the Sahara and yet they have already, as I write in early August, begun their autumn migration south. And so, I welcome you to our autumn edition of *Epilepsy Professional*.

I hope everyone managed to take some time out over the last few months to rest, maybe travel, see family and friends and, even if only lately, enjoy this surprisingly tropical spell of weather, spend time outdoors, feel recharged, engaged and ready for the months ahead.

The weather extremes over the last few months and the emerging storm seasons of recent years in the UK certainly tuned my attention to Alistair Wardrope's article 'The world is on fire'. This really stresses the global dependence on fossil fuels, which are fuelling air pollution and in turn contributing to increased incidence of stroke, traumatic brain injury, brain infections and epilepsy.

Alistair comments on the unjust nature of climate change. Communities facing the greatest health risks from climate change have probably done the least to cause it. These populations are often in low-income countries and already face harsh challenges in managing their epilepsy. Therein are many challenges, but maybe we can reflect and consider altering some of our choices at an individual and professional level – in terms of transport, food and consumer goods.

There is still a lot of work to be done on navigating what is best for our patients

Thinking of the future in epilepsy, Pablo Casillas-Espinosa peaks my interest with his article on the novel phase 2 clinical trial of sodium selenate in patients with drug-resistant temporal lobe epilepsy. This is another repurposing drug trial, after an initial study in animal models that showed long-lasting effects after stopping the drug, reduced seizure frequency and improved memory, learning and sensor-motor functioning. This is an exciting clinical trail labelled as potentially disease modifying, so let's see.

Dr Kathryn Bush appends a topical article on socioeconomic deprivation in epilepsy. She highlights that people living in the most deprived areas of the UK are at a higher risk of developing epilepsy than those living in the least deprived. She argues that we need a systems-level approach that recognises the social determinates of health. With this in mind, it's worth considering what needs to be done to help the most vulnerable in our society access the care they need. Kathryn makes some suggestions with regard to patients with epilepsy and maybe it's worth considering how we can alter our practices accordingly.

So, if you have any down time on returning from annual leave – although I am quite sure the inbox is bulging – I do hope this edition provides something to chew on. Autumn is often an industrious time and certainly 'Valproate so far' by Grace Wood reminds us that there is still a lot of work to be done by clinicians and the MRHA on navigating what is best for our patients.

Ann Johnston
Consultant neurologist
Executive medical adviser
Epilepsy Professional

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Dr Casillas-Espinosa from Monash University and Alfred Health in Melbourne, Australia, explains why sodium selenate treatment could be the first-in-class disease-modifying therapy for drug-resistant temporal lobe epilepsy



This month I attended the International League Against Epilepsy's annual congress in Dublin. Clinicians, researchers and patients met to discuss developments in the treatment of epilepsy.

There is exciting research going on. I heard from a Swiss epileptologist looking at whether South American plants hold a treatment for drug-resistant epilepsies (Siegward Elsas p12) and a Canadian researcher who is using AI to predict neurosurgery outcomes (p10). There is also work around new drugs, as Pablo Casillas-Espinosa discusses (p22). But, as Kathryn Bush (p16) points out in her article about deprivation, many people are still not getting basic care.

Dr Bush reminded me of two people I spoke to recently. Bradley had a seizure after surgery for a glioma 18 months ago, but he's yet to see an epilepsy neurologist. He's confused and frustrated. Dave has been waiting for a neurology appointment since before the Covid pandemic.

Neurology and neurosurgery services have some of the longest waiting times in the UK. As healthcare professionals, we want better for people with epilepsy.

Of course, there is hope. As Tom Shillito (p28) says, there are projects working to improve healthcare services and an increased move towards personalised treatments. So, while there should be much to make you excited in this edition of *Epilepsy Professional*, I think we all hope that this research will serve people with epilepsy and that our healthcare services are resourced enough to be able to pass it on to them.

Grace Wood
Editor

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Epilepsy ignored in government's Major Conditions Strategy

The government has left epilepsy out of its strategy for major health conditions.

The Department of Health and Social Care's Major Conditions Strategy is a five-year plan for the main causes of ill health and early mortality.

The government has selected six conditions to focus on: cancer, chronic respiratory disease, dementia, cardiovascular disease, musculoskeletal disorders and mental ill health.

It claims that together these six groups drive more than 60% of mortality and morbidity in England.

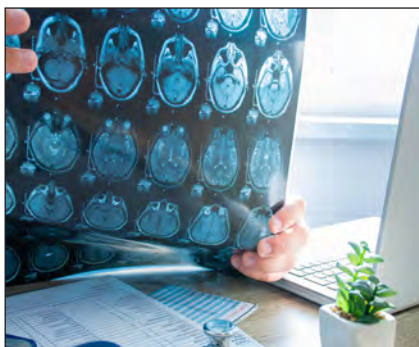
With epilepsy affecting 1 in 103 people, and about 1,000 people dying every year in the UK from causes related to epilepsy, Epilepsy Action is disappointed that the condition has been ignored.

Senior policy and campaigns manager Daniel Jennings said: "The government has ignored pleas from various epilepsy charities to include epilepsy in the Major Conditions Strategy. This is despite it being one of the most common and serious neurological conditions.

"With epilepsy not being included in the strategy, it is likely that epilepsy services will not get the same level of input or improvement as those that are included in the strategy. This comes as existing epilepsy services are already understaffed and under-resourced.

"This is yet another shocking example of people with epilepsy being left behind by the government and Department of Health."

Led by Epilepsy Action, a number of charities wrote to health secretary Steve Barclay to request it be



amended "to include neurology as a seventh priority, with a particular focus on epilepsy".

The letter said: "Given the unique and specific challenges facing epilepsy services, and people with epilepsy, it is an opportunity to revisit the Major Conditions Strategy and include epilepsy as a focus within a neurological priority."

The charities included Epilepsy Action, Epilepsy Research UK, Young Epilepsy, the Epilepsy Society, SUDEP Action, Behçet's UK, Roald Dahl's Marvelous Children's Charity and more.

In response, health minister Will Quince said: "The strategy focuses on dementia, rather than neurological conditions more broadly, because it is the leading cause of death in women and the second biggest cause of death for men.

"Focusing on these groups of conditions will allow us to identify the key actions that are needed to achieve our ambitions to increase healthy life expectancy, reduce pressures on the NHS and tackle labour market inactivity. The actions we take have the potential to benefit patients living with other conditions beyond the scope of this strategy."

EMA updates topiramate guidance

The European Medicines Agency's safety committee has recommended new guidelines around prescribing topiramate to pregnant women.

The safety committee's new measures have been put in place to "avoid exposure of children to topiramate-containing medicines in the womb".

The organisation said "the medicine may increase the risk of neurodevelopmental problems after exposure during pregnancy".

Epilepsy Action is expecting an update from the UK government's Medicines and Healthcare products Regulatory Agency (MHRA) on the outcome of this safety review.

The drug is already known to cause serious birth defects when used during pregnancy.

In July 2022, the MHRA launched a safety review into topiramate. The review was triggered by a study in the journal *JAMA Neurology*, which suggested that topiramate may increase the risk of autism and problems with learning and development in children whose mothers took it during pregnancy.

In the study, Marte-Helene Bjørk and colleagues found that topiramate and valproate, when taken on their own, were associated with a 2-4 times higher risk of autism and learning and development problems.

In 2019, a study in *Neurology* suggested an increased risk of birth defects in babies born to mothers taking topiramate.

Topiramate was also linked to an increased risk of cleft lip.

NHS updates medicine guidance for trusts

The NHS has released updated guidance for trusts around optimising medicine use, including advice on sodium valproate, anti-depressants and polypharmacy.

The “optimisation opportunities” ask integrated care boards (ICBs) to focus on 16 priorities.

It asks ICBs to choose at least five “medicine optimisation opportunities” to focus on.

Valproate

One “optimisation opportunity” is around improving the safety of sodium valproate.

Last year, the MHRA updated its safety measures and policy relating to sodium valproate. It stated that all people under 55 (including boys and men for the first time) who were prescribed sodium valproate were to have two signatures from specialists documenting that no other suitable alternative medication had been effective or tolerated.

Taking valproate during pregnancy can cause problems with a child’s learning and development. However, the change caused some concern among patients and epilepsy charities because valproate remains the most effective medicine for some people.

The guidance asked ICBs to ensure people only take valproate in line with a Pregnancy Prevention Programme, and to reduce in-utero exposure to valproate causing harm to babies.

Epilepsy Action’s health improvement and influencing research manager Tom Shillito said: “The guidance around sodium valproate could raise a few questions. For some patients, this is the most effective medication overall to control their seizures. If they were to come off



sodium valproate, they might have to be prescribed multiple anti-seizure medications to have the same effect, which could work against the aim to reduce polypharmacy.”

Polypharmacy

The guidance also asked ICBs to consider identifying and reviewing patients with “problematic polypharmacy” and support “cultural and behavioural changes”.

Shillito added: “It’s encouraging to see action being taken to optimise prescription of some medications in NHS trusts across the country.

“Implementing measures to reduce polypharmacy where appropriate is especially important to lower the risk of adverse side effects and the likelihood of medication interaction, which can increase when patients take multiple prescriptions at once.”

Anti-depressants

The guidance calls on ICBs to “reduce inappropriate long-term prescribing” and “reduce inappropriate spend on anti-depressants”.

Around 1 in 3 people with epilepsy experience depression and many are prescribed anti-depressants.

The NHS guidance said: “In 2020/21, almost 80 million prescriptions for anti-depressants were issued to 7.8 million patients.”

Shillito added: “When it comes to anti-depressants, some studies show there is limited evidence they decrease depressive symptoms more than other treatments, placebo, or no treatment in people with epilepsy. Some patients are prescribed both anti-seizure medications and anti-depressants when the latter aren’t really justified, which could potentially be causing harm.

“Reducing prescription of these medications where appropriate, and aiming to decrease polypharmacy overall, could massively lower the associated risks and improve patients’ quality of life.

“Overall, we welcome measures aimed at improving the quality of life of people with epilepsy, and hope these can improve patient access to the most effective treatments.”

Other opportunities

The NHS said its medicines guidelines for 2023/24 had four key objectives: to improve outcomes in population health and healthcare; to tackle inequalities in outcomes, experience and access; to enhance productivity and value for money; and to help the NHS support broader social and economic development.

Other “optimisation opportunities” included: addressing low priority prescribing; improving the uptake of the most clinically and cost-effective medicines; reducing opioid use in chronic non-cancer pain and switching intravenous antibiotics to oral.

Wearable brain scanner developed at the University of Nottingham

A wearable brain scanner that can measure brain function while the patient is moving has been developed at the University of Nottingham.

The first wearable brain scanner was developed in 2018, but researchers have now demonstrated that the system can be used while the patient is moving.

The technology uses optically pumped magnetometers (OPM) to measure magnetic fields in the brain – a technique called magnetoencephalography (MEG).

The lightweight helmet, which is 3D-printed, also means the scan is more comfortable for the patient.

Epilepsy Action's health improvement and research manager Tom Shillito said: "This is an exciting advancement with the potential to improve epilepsy testing for many patients. MEG scans can be used in addition to EEG tests to obtain more detailed data about a patient's epilepsy, which can result in better treatment."

Patients can access MEG scans through the NHS currently, but the testing process doesn't allow them to stand or walk around.

Young Epilepsy's Health and Research Centre installed the first scanner in the UK. It believes the technology can be used for earlier epilepsy diagnosis and interventions, and better management and treatments for patients.

Cerca Magnetics is the commercial company that produces and sells the scanners. It is working towards gaining clinical approval to allow them to be used in clinical settings.

The University of Nottingham's study lead Niall Holmes said: "We can, for the first time, realise many



scanning scenarios that would have previously been considered impossible, but that have the potential to significantly expand our understanding of exactly what is happening in the brain during movement, neurodevelopment and in a range of neurological issues."

The Nottingham team designed a 'matrix coil' system, which is formed of 48 simple square coils.

Professor Matt Brookes, who leads MEG research at Nottingham University, said: "Just five years ago, the idea of acquiring high resolution images of human brain electrophysiology while people walk around a room would have seemed like something from science fiction."

In a research paper outlining the development, the authors said: "As systems continue to develop, and the range of allowed experiments continues to expand, OPM-MEG has significant potential to become the method of choice for functional neuroimaging."

Shillito added: "A wearable device that gives the patient freedom to move around while the test is being carried out would make the whole process much more comfortable."

Inhaling scents could lead to better memory

Researchers studying the effect of essential oils on the brain have found that inhaling certain scents during sleep could lead to a boost in memory.

The study at the University of California followed 43 healthy men and women aged between 60 and 85. They were split into an exposed group and a control group. The exposed group was given seven different scents a week, one per night, for two hours, using an essential oil diffuser.

The results showed a 226% improvement in the group inhaling scents compared to the control group. Other measures of learning and thinking showed no improvement.

The researchers concluded that introducing a small amount of scent at night led to improvements in brain functioning. They added that this may provide an effective and low-effort way to improve memory.

They suggest the reasoning behind the results could be because the olfactory system has direct links to the limbic system.

Speaking to Medscape, Donald Wilson, professor of child and adolescent psychiatry and of neuroscience and physiology in New York, said it was "a very exciting, though relatively preliminary, finding".

The paper's authors said they hoped the findings would lead to large-scale clinical trials.

People with epilepsy are at a higher risk of memory problems. The study did not consider people with specific neurological conditions.

Some essential oils are not recommended for people with epilepsy.

Epilepsy patients aid memory study

A group of epilepsy patients in Arizona, USA, have helped researchers better understand the function of memory.

The study followed 13 patients who were about to undergo epilepsy surgery.

It is hoped the research will have implications for treating patients with brain damage and cognitive impairments, including patients who have experienced seizures.

Many people with epilepsy report problems with their memory.

The research looked into theta oscillations, which are rhythmic patterns of electrical activity in the brain. These patterns are usually active

in the brain's hippocampus during activities such as exploration, navigation and sleep.

Electrodes were implanted in the patients' brains for detecting seizures.

It was previously believed that movement was a driver for theta oscillations, but this study has concluded that "memory is a more potent driver of human hippocampal theta oscillations than navigation".

The results suggest that memory is improved by focusing on memory-improvement techniques rather than other, previously suggested, navigation and movement exercises.

The patients participated in a

virtual reality experiment, in which they were given a joystick to navigate a virtual city on a computer. While using the joystick, researchers found the oscillations were less frequent and shorter compared to oscillations that occurred when participants were just imagining or remembering the route.

Lead study author Sarah Seger said: "This is a huge step forward in the field in terms of designing new experiments and understanding the neural basis of memory."

For more information:

news.arizona.edu/story/news-arizona-study-links-brain-waves-directly-memory

Children's care improved but inconsistent – Epilepsy12

Epilepsy care for children has improved but remains inconsistent, according to the latest Epilepsy12 annual report.

The report into paediatric epilepsy care showed wide regional variations of care provision, with the most deprived areas having the highest prevalence and incidence of epilepsy.

According to the report:

- 99% of diagnoses among children were accurate.
- 91% of children received input from a paediatrician with expertise in the first year since diagnosis – an improvement of 2%. Only 21% were seen within two weeks of referral.
- 77% received input from an epilepsy specialist nurse – a 1% improvement.
- 70% underwent an ECG.
- 79% had comprehensive care plans.
- 37% had individual healthcare plans in schools.



However, the percentage of children who received input from tertiary care providers, were referred for surgery or had an MRI, decreased.

Established in 2009, the 'National Clinical Audit of Seizures and Epilepsies for Children and Young People (Epilepsy12)' focuses on improving care for children. This is its fourth auditing round.

While epilepsy and mental health conditions are commonly linked, the

report said 80% were not being screened for these conditions and more than a third of trusts did not have referral pathways for depression, anxiety or mood disorders.

The report also showed an increase in the number of girls aged nine or over taking sodium valproate, which has been linked to risks in pregnancy, but only 86% had those risks explained to them.

No trusts reported having conversations about Sudden Unexpected Death in Epilepsy (SUDEP) with 100% of children. Overall, 56% of children or families had been warned about SUDEP.

The reports recommendations included providing holistic support from a network of professionals, and exploring with education services ways to improve the number of children with effective ongoing care plans.



What's new in research?

Grace Wood reports from the International League Against Epilepsy's annual congress in Dublin

The International League Against Epilepsy held its annual international congress from September 2-6, in Dublin.

Epileptologists, patient groups and academics met to discuss the future of epilepsy research, patient care, treatment and diagnosis. The event was chaired by ILAE president J Helen Cross and International Bureau for Epilepsy president Francesca Sofia.

Presidential Symposium

Opening the symposium was Amber Freed, the founder of SLC6A1 Connect – a patient organisation she set up to find a cure for her son Maxwell's rare epilepsy caused by a de novo SLC6A1 gene variant.

She explained how the organisation had grown into a national body in the USA that supports researchers with genetic testing and patient registries.

James Mitchell from the University of Liverpool spoke about outcome measures in research. He explained how the outcome measures researchers want from trials can differ from those that patients want.

He asked: what outcome should we be measuring? He said only 11% of the trials he had studied included unplanned hospital admissions, while 14% measured feelings of anxiety.

His research also showed that the outcomes stakeholders deemed critical were sleep quality, impact on driving and fertility.

Next to speak was Scott Demarest, professor of Pediatrics and Neurology at Colorado University, he covered the topic: are all epilepsies the same?

"Of course not!" he said, adding that because of this, our aims from research and trials need not be the same. He discussed the differences between anti-seizure medication (ASM)

trials and disease modifying treatment (DMT) trials adding that seizure frequency need not always be the top measure and that the "trial design has to fit the purpose of the trial".

Colin Josephson from the University of Calgary, Canada, joined the congress online, to discuss how machine learning can help predict the outcomes of epilepsy surgery.

He discussed whether artificial intelligence could replace or assist clinicians with deciding whether to send patients with temporal lobe epilepsies for surgery. Josephson concluded that while the computer program was about as good as an epileptologist at predicting outcomes, we would not be seeing it replace experts any time soon.

The last person to speak was Action Amos, who asked: will the Intersectoral Global Action Plan on epilepsy (IGAP) improve outcomes for

people with epilepsy (PWE)? IGAP was set up to “provide care and services for people with epilepsy and other neurological disorders that exist worldwide”.

Having travelled from Ghana, Amos spoke about the difficulties of engaging national governments and healthcare providers with epilepsy professionals, adding there was a need to have good monitoring tools to hold governments to account. He said just 2.5% of research budgets globally went to low and medium-budget countries.

Could AI diagnose and treat epilepsy?

“Artificial intelligence is a tool for epilepsy professionals, it’s all about using it with regulation”, according to a panel of experts.

The panel included Sandor Beniczky from Aarhus University in Denmark, Stefan Wolking from Aachen University Hospital, Germany, Katia Lin from the University of Santa Catarina in Brazil, and Jacqueline French from New York University.

The first topic of debate was artificial intelligence, with Lin taking the view that clinical decisions systems will improve the doctor and patient experience. She argued that artificial intelligence in neurology could lead to reduced costs and higher efficiency.

She cited the tool EpiPick, an ASM selection tool. She said that in one study ASM choices from EpiPick had higher retention rates.

She added that machine learning tools were able to give accurate classifications of seizure types, and that in some instances AI had managed to interpret EEGs with 80% accuracy – a similar rate to trained clinicians.

French then countered her argument, claiming that clinical decision systems are not suitable for use in day-to-day clinical practice.

She said that while decision

support tools might work for many patients, they don’t account for anomalies, adding that while an algorithm might work on one data set, this did not mean it would definitely be generalizable to a wider population.

Both French and Lin agreed that artificial intelligence needed to be overseen by humans.

Wolking and Beniczky then debated seizure detection systems.

They considered the increased use of seizure detection devices, with Wolking arguing that they could be more reliable than patient evidence – especially where the seizure left a patient with poor memory.

However, Beniczky added, these devices often have high false alarm rates. They agreed there was potential in these systems but that more work was needed for them to be reliable.

Epilepsy and exercise

Should epilepsy specialists be prescribing exercise? This was the question debated by an expert panel.

Ricardo Arida from the University of Sao Paulo in Brazil presented his research in animal models, which suggested that exercise could be a protective factor against seizures.

He added that treadmill exercise in rats increased neuroplasticity and prevented GABA neuron loss.

Elinor Ben-Menachem from the University of Gothenburg in Sweden discussed exercise self-management programmes. Her work has focused on men in Sweden born between 1987 and 1992. It found that low-cardiovascular fitness in childhood was

Should epilepsy specialists be prescribing exercise?

associated with an increased risk of epilepsy in later life. The work also considered a brother model, in which men who had exercised as children had higher IQs and lower risk of epilepsy than their genetic brothers.

She concluded that “everybody should be making sure their kids are out and not just playing video games”.

Ben-Menachem also cited studies in South Korea and Turkey that suggested children with epilepsy exercise less than their peers – even if they are seizure free. But, only 2% of adults had seizures during exercise.

She reiterated the importance of educating patients about the value of low-risk exercise such as indoor bikes and walking.

Halley Alexander from Wake Forest University in North Carolina, USA, talked about how PWE can optimize the effects of exercise.

“Physical medicine is medicine,” she said, citing studies that suggested weight-resistance training may reduce seizure frequency. She also suggested that programmes of combined cardiovascular and strength training might be the best way forward.

“Some activity is better than nothing”, she said, adding “it is partially true that sitting is the new smoking”.

Finally Jane Allendorfer from the University of Alabama, USA, discussed how to improve patient engagement with exercise. She said stigma was a major factor for PWE as well as travel and safety fears.

Allendorfer’s research showed that 74% of clinicians didn’t know about the benefits of exercise and 86% agreed there needed to be more knowledge among healthcare providers.

When the researchers asked PWE what stopped them from exercising, 90% said their families were overprotective and 75% said it was because they feared having seizures while exercising.

Plant-based therapies

Patients need the same access to medical cannabis as any other ASM, according to Yvonne Cahalane, the mother of Tristan Forde, the first person in Ireland to be legally allowed access to medicinal cannabis.

Cahalane was speaking on a panel discussing the benefits of plant-based therapies for epilepsy.

Tristan, who has Dravet syndrome, had his first seizure aged five months and Cahalane said none of the prescribed ASMs would work. He was first given access to cannabis in 2016 after spending time on a research project in Colorado, USA.

The family saw improvements in weeks. After three months of treatment, his seizures were greatly reduced and the family were able to remove seven ASMs. However, the family faced stigma, with schools refusing to administer the drug and many doctors unwilling to prescribe.

The panel also included Elizabeth Thiele, a neurologist and epileptologist at Massachusetts General Hospital, USA; Cecilie Johannessen Landmark, a senior researcher from Oslo University Hospital; Finbar O’Callaghan from University College London and Great Ormond Street Hospital; KP Vinayan from the Amrita Advanced Center for Epilepsy in Kerala, India, and neurologist Siegwald Elsas from Arlesheim, Switzerland.

Thiele considered why there was a high demand for medical cannabis among patients, arguing that PWE were struggling with the low efficacy of ASMs, that there is a growing interest in natural treatments and that there was good anecdotal evidence for cannabis-based medicines. She argued that other plant-based therapies had become common medicines, such as Aspirin, which was found in the bark of the willow tree, and morphine, which is based on the poppy plant.

‘Patients need the same access to medical cannabis as any other ASM’

Landmark considered the limitations of medical cannabis – its poor absorption, that it is affected by food intake and that it has a high potential for drug interactions.

O’Callaghan – who was a member of the UK Home Office expert panel on cannabis-based medicines in 2019 – said cannabis-based medicine had been effective against a range of seizure types and could be used for more than the treatment of Dravet Syndrome, for which it is permitted in the UK. However, he said that researchers needed to be wary of the high placebo effect in CBD trials. He emphasized that more randomized control trials were needed.

Vinayan discussed traditional Asian medicine, with a focus on Ayurveda. He said 70% of people in India prefer natural systems for treating epilepsy.

He added that while it was difficult to translate Ayurvedic treatments into clinical settings, clinicians should be aware that many patients are using it.

Finally, Elsas discussed his research into plant-based medicines. He explained how valproate had come from the valerian root and looked at the Madagascan plant *mallothus oppositifolius*, the orchid *gastrodia elata* and the flower *passiflora incarnata*.

He said the difficulties of plant-based treatments included that the concentration of ingredients changes seasonally, the differing methods of extraction, and that natural compounds cannot be patented.

All the panelists emphasized the gap between research, clinicians and what’s available on the market.



Epilepsy and anxiety

“People with anxiety are at an increased risk of developing epilepsy” and PWE are at an increased risk of developing anxiety, according to researchers.

The panel, led by the ILAE Integrated Mental Health Care Pathways taskforce, discussed the links between anxiety and epilepsy, pre and post diagnosis.

The taskforce comprised an interdisciplinary team of psychologists and neurologists, chaired by Milena Gandy from Macquarie University, Sydney, Australia, and Heidi Munger Clary from Wake Forest School of Medicine in North Carolina, USA.

Munger Clary discussed how in people diagnosed with an anxiety disorder before their epilepsy diagnosis, epilepsy caused a change in their anxiety symptoms.

She added that in patients who presented anxiety symptoms after their epilepsy diagnosis, often anxiety was caused by a fear of seizures. She stressed that it is vital that clinicians listen to their patients’ fears.

Gandy discussed tools for differentiating between normal anxiousness and an anxiety disorder. She said “anxiety becomes a disorder when it affects day-to-day functioning”, is disproportionate to the situation a patient is fearful of, and becomes a challenge for the patient to manage.

She stressed the need for clinicians to use structured tools when diagnosing anxiety. She said that when PWE were assessed using a structured interview, 27% came away with a diagnosis, but when the patient was assessed using just clinician judgment, that figure fell to 8%.

Coraline Hingray from the Centre Hospitalier Universitaire de Nancy, France, discussed the increased risk of people with pre-existing mental health conditions developing epilepsy,

including anxiety and post-traumatic stress disorder. She said ASMs and anxiety have a bidirectional impact.

Hingray spoke about how psychological factors, such as intentional bias, avoidance and intolerance of uncertainty, can lead to anxiety in PWE, adding that while some avoidance may be seen as useful – for instance avoiding situations in which they had previously had seizures – in the long term it did not lead to healthy patterns.

Gaston Baslet from the University of Illinois, Chicago, USA, discussed how anxiety can lead to worse seizure control and impact a patient’s quality of life. He added it was important clinicians gain a thorough history from patients when considering anxiety.

He went on to compare seizures with panic disorders, describing how ictal-fear can present similarly to a panic attack, but there were key differences such as the length of the event (ictal fear tends to last 1-2 minutes, whereas panic attacks can last up to 20 minutes), that ictal fear has a sudden onset but panic attacks build up to a crescendo, and the post-event symptoms – for instance people are often left confused after a panic attack.

Sophie Bennett from Great Ormond Street Hospital, London, then discussed anxiety in children with epilepsy. She presented findings from Epilepsy12 and the MICE project.

She added that there was a high comorbidity between anxiety and epilepsy in children and reiterated the importance of personalisation when treating these patients.

Finally, the panel discussed medication and anxiety. They spoke about how anti-depressants and ASMs impact one another and emphasised how understudied the field was, adding there had been “no randomised controlled trials in the treatment of anxiety disorders in epilepsy”.

Epilepsia Prizes for research announced

Brad Kamitaki and Riccardo DeFeo have been awarded the annual prizes for best paper in *Epilepsia*, the International League Against Epilepsy’s scientific journal.

Kamitaki, from Robert Wood Johnson University, New Jersey, USA, was awarded the Epilepsia Prize for his article ‘Clinical and EEG factors associated with anti-seizure medication resistance in idiopathic generalized epilepsy’.

Accepting his prize at a ceremony at the annual congress, Kamitaki said: “Anyone who publishes a paper just wants someone to read it”.

His paper looked into drug-resistant catamenial epilepsy and worked with researchers from Columbia University, New York; Cornell University, New York; Rutgers University, New Jersey, and Monash University, Melbourne, Australia.

Kamitaki said: “I came into research late, after I completed fellowship, so I want to encourage you, even if you have an unfinished project, it’s never too late.”

De Feo, from the University of Eastern Finland, was awarded the Epilepsia Prize for his article ‘Hippocampal position and orientation as prognostic biomarkers for posttraumatic epileptogenesis: An experimental study in a rat lateral fluid percussion model’.

De Feo’s study found that at five months post-surgery, epileptic and non-epileptic rats could be distinguished based on hippocampal geometry with 80% accuracy. He said he hoped the research could develop into studies on human brains.



Sodium valproate

A timeline of the situation so far

With the MHRA changing its guidance around the controversial drug, and charities and patient bodies up in arms, Grace Wood takes a look at what's happened so far

Sodium valproate was first used for treating epilepsy in France in 1967. It is cheap and, for many patients it is the only medication that controls their seizures. However, it has been associated with abnormalities in foetal exposure.

The effects of taking anti-seizure medications (ASMs) during pregnancy have been studied for some time. According to the MHRA, about 10 of 100 babies born to mothers taking sodium valproate will have a physical birth abnormality. It adds that “about

30 to 40 of the 100 children will go on to have disorders affecting their learning and thinking abilities, including autism”.

Until December 2022, in the UK only women of childbearing age were advised against taking valproate, unless they were under a pregnancy prevention programme – but there was no particular guidance for men. Then, the MHRA said no one under the age of 55 should be initiated on valproate unless two specialists independently find there is no other

effective or tolerated treatment.

We are not sure what research the MHRA has used to base its decision on, but it has said that some research suggests there may be a risk of reduced fertility in men and boys. It says animal studies also suggest there may be effects passed from animals taking valproate to their offspring and future generations, but researchers are not sure if this would be the same in humans as it is in animals.

Ahead of the expected change, here is a timeline of events so far.

12 December 2022

The MHRA issues an update into safe use of valproate’.

It says it has conducted a review of the available data and asked for advice from the independent Commission on Human Medicines (CHM).

The CHM advises that “no one under the age of 55 should be initiated on valproate unless two specialists independently consider and document that there is no other effective or tolerated treatment. Where possible, existing patients should be switched to another treatment unless two specialists independently consider and document that there is no other effective or tolerated treatment or the risks do not apply”.

For the first time the advice includes men. The MHRA says the changes are due to come into effect in 2023.

27 March 2023

A number of UK epilepsy organisations call for the MHRA decision to be paused immediately.

The group includes: Epilepsy Action, the Epilepsy Society, SUDEP Action, Epilepsy Research UK, Young Epilepsy, the British chapter of the International League Against Epilepsy, Epilepsy Cymru, the Epilepsy Nurses Association, Epilepsy Scotland, Epilepsy Connections and Quarriers.

The charities say they are concerned about the lack of patient consultation, and that patients might be left unable to use a medicine that has given them seizure control and lowered their risk of death.

Concerns are also raised about how the measures might be implemented in practice, with the measures requiring two specialists to review an individual case when waiting times for patients with epilepsy, and demands on neurologists and epilepsy specialist nurses, are already high.

A statement says: “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.”

They call for an urgent review and scrutiny of the policy.

31 March 2023

The coalition says the rule changes are “out of proportion” and writes an open letter to health secretary Steve Barclay. In their open letter, the organisations warn 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)”.

16 June 2023

The maker of Depakine (sodium valproate), Sanofi, releases a statement claiming an earlier study it had undertaken has limitations.

The original post-authorisation safety study assessed the potential risk of neurodevelopmental disorders in children whose fathers were treated with valproate monotherapy in the three months before conception. It says the “retrospective observational study based on electronic medical records from three Nordic countries” has limitations and that “new analyses need to be performed before final conclusions can be drawn”.

It says the original study had been requested by the European Medicines Agency (EMA) and results had been shared with the EMA. The study was not made public.

21 June 2023

The coalition of epilepsy charities expresses a loss of confidence in the MHRA over the proposed changes – the same day that the health body is meeting to discuss the changes.

14 July 2023

The coalition of charities releases a statement following a meeting with the MHRA.

It says: “The coalition does not support the MHRA’s current position and believes the proposed regulations are fundamentally flawed without an adequate comprehensive risk/benefit assessment. The coalition considers the overall impact and consequences of the new regulations, as currently proposed, to be unsafe for people with epilepsy and will increase risks to life.”

However, the charities add that they “wish to explore conditions for future engagement with the MHRA but need assurances that there will be transparency and meaningful engagement”.

Despite the concerns raised by charities and patient groups, the MHRA has confirmed it is moving ahead with plans for the new regulations, but it has not provided any timescale for when this might happen. It has, however, indicated that the measures will be phased in, with new prescriptions for valproate subject to the regulations initially, followed by existing prescriptions in the future. The MHRA has also indicated that nobody currently taking valproate will have their prescription taken away against their wishes.

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Epilepsy and deprivation

How does socioeconomic inequality affect epilepsy?

Dr Kathryn Bush is funded by Epilepsy Research UK and based at Newcastle University in the Population Health Sciences Institute. She discusses the prevalence and incidence of epilepsy among socioeconomically deprived groups



What do we know?

Most professionals reading this will be aware that epilepsy has a prevalence of about 0.8% in the UK; with about 80 people in every 10,000 having an epilepsy diagnosis [Public Health Profiles, 2023]. However, what is less often considered is that epilepsy does not affect people in society equally. People living in the most deprived areas of the UK are at higher risk than those living in the least deprived.

A recent study of epilepsy incidence in the UK using CPRD Gold data, showed epilepsy incidence rates of 35.60 (32.88-38.48) per 100,000 person years in the least deprived populations, compared to 58.35 (55.32-61.50) per 100,000 person years in the most deprived populations [Wigglesworth *et al*, 2023]. This means that the rate of epilepsy in the most deprived population is 1.64 times that in the least deprived populations (known as the incidence rate ratio). Put simply, people in the most deprived populations are 64% more likely to develop epilepsy.

This difference in the rates of epilepsy, according to levels of socioeconomic deprivation, is known as a socioeconomic inequality. Inequalities are defined by NHS England as 'unfair and avoidable differences in health across the population...' [NHS England, 2023]. To date, the association between

socioeconomic deprivation and epilepsy has received little attention from a strategic public health or NHS perspective in the UK.

In order to improve health and wellbeing we cannot rely on health services alone

Socioeconomic inequalities are not just seen in epilepsy. The Marmot Reports highlight and explain the wider relationship between socioeconomic deprivation and ill health [Marmot and Marmot, 2022, 2013]. In order to improve health and wellbeing we cannot rely on health services alone. Instead, we need to consider the wider social determinants of health, which include material circumstances, the social environment, psychosocial factors, behaviours and biological factors. These factors are sitting within the wider sociopolitical, cultural and social context, which means that to improve population health, we need to consider a 'systems level' approach.

A systems-level approach recognises that the whole spectrum of the social determinants of health need addressing to improve health – and

that action from the NHS and Department of Health alone will not be sufficient to reduce health inequalities.

Unfortunately, inequalities in epilepsy are not limited to who gets epilepsy in the first place. There are also significant inequalities in outcomes for people with epilepsy according to socioeconomic factors that stretch across the life-course:

- The most deprived people in your epilepsy clinic are more likely to be admitted to hospital, less likely to persist with anti-seizure medications and less likely to achieve seizure freedom [Jackson *et al*, 2022; Marshall *et al*, 2022; Ashworth *et al*, 2007].
- Women from the most deprived areas are less likely to be taking pre-conceptual folic acid, more likely to have seizures in pregnancy and more likely to be prescribed multiple anti-seizure medications during pregnancy [Campbell *et al*, 2013].
- People from the most deprived areas are more likely to have poor quality

Inequalities in epilepsy are not limited to who gets epilepsy in the first place



of life and have multiple health problems, including depression and cardiovascular disease [Taylor *et al* 2011; Josephson *et al*, 2021; Weatherburn *et al*, 2017].

- They are also more likely to die from an ‘epilepsy related death’, which is a death where epilepsy, seizures or status epilepticus are considered to be the underlying cause of death. [Mbizvo *et al*, 2022; Public Health England, 2018].

Inequalities also matter because they dictate who clinicians will see in clinic, and possibly more importantly, who doesn’t turn up to their appointment or get treatment at all.

Understanding the situation and having evidence is the first step in enacting change

Why do health inequalities matter?

Health inequalities matter because they represent an opportunity for intervention and change, particularly in those with greater risks of disease. Whenever we observe differences in health between groups of people, it represents the opportunity to improve the health of the ‘sickest’ group, up to (or beyond) that of the ‘healthiest’. Therefore, in the case of epilepsy, we would be looking to reduce the numbers of people living in the most deprived areas who develop epilepsy and then improve the treatment, outcomes and survival for those who do develop epilepsy.

However, this change is only possible if we are not willing to accept that the most deprived people in our society should have the poorest

health. To bring about change we need to recognise the factors underlying the inequalities, consider our options and advocate for action.

What needs to be done?

Change is needed at a system level to recognise and reduce socioeconomic inequalities in epilepsy. To achieve this change we will need a collective effort to influence local and national priorities and policies. The first step in this process is bringing together all of the published information on the topic of socioeconomic inequalities in epilepsy, so that we understand the breadth and extent of the issues.

I am currently working on a systematic review of the evidence, with topic experts including Owen Pickrell (consultant neurologist and honorary clinical associate professor) at Swansea University, Sheena Ramsay (Professor of Public Health and Epidemiology) and Rhys Thomas (consultant neurologist and clinical senior lecturer) from Newcastle University. We aim to have this work published later this year.

The next stage of our work is to try to understand the factors that are driving inequalities in the UK. The World Health Organisation predicts that 25% of all epilepsies in high-income countries are preventable [World Health Organization 2019]. But to know whether this is true for the UK, we need to try to understand and quantify the underlying factors causing epilepsy at a population level.

We will use national linked data sets to explore factors underlying inequalities and their impact. Once we understand these factors, we can start to consider what change is needed to improve the health of our most deprived populations. Some of these factors will be within our own

We need to recognise that some of the most deprived and vulnerable groups may need more to get the same outcomes

professional spheres of influence, others will doubtless lie outside in the wider political system. Nevertheless, understanding the situation and having evidence is the first step in enacting change.

We also know there are inequalities in service provision across the UK, with some areas having lower levels of neurology service provision than others. While we advocate for equality in this area, the problem is that simply increasing the number of clinics does not always equate to reducing inequalities. In fact, just putting in more of the same provision is likely to widen inequalities further – as the most deprived people with epilepsy are the least likely to be able to access it.

To achieve a reduction in inequalities, we need to recognise that some of the most deprived and vulnerable groups may need more to get the same outcomes; whether that is more time, more resources or different ways to access care. This is what equity and justice in the health service looks like: appropriate levels of care, varied according to need – a concept that is referred to as ‘proportionate universalism’ [Marmot *et al*, 2013].

Finally, we need to advocate for change and improvement. Epilepsy health professionals need to engage with the wider health systems and

groups working to reduce inequalities and improve population health.

What can I do right now to make a difference?

Be an advocate for the most vulnerable populations:

- Despite the well-recognised impact of epilepsy on the lives of people who have it, epilepsy in adults has not featured in any major UK, NHS or government commissioning priorities.
- The NHS Core20PLUS5 is an NHS England approach that aims to support the reduction of health inequalities. The ‘Core20’ refers to the most deprived 20% of the population, according to the Index of Multiple Deprivation (IMD) score. Many people with epilepsy will therefore fall into this category by virtue of the fact that they live in the most deprived areas. This represents an opportunity to bring epilepsy to the attention of local commissioning groups, which will have multiple competing priorities. Epilepsy professionals need to ensure that people with epilepsy are represented during commissioning and prioritisation discussions. These discussions will be occurring now, at a local level across England, within Integrated Care Board or Population Health Management groups.
- The ‘PLUS5’ refers to vulnerable inclusion health groups and ‘5’ clinical priorities. Epilepsy in children

Epilepsy health professionals need to engage with the wider health systems





Healthcare professionals need to advocate for people with epilepsy and improvements in their care at a systems level to achieve change

and young people has been recognised as a clinical priority, with an aim to increase access to epilepsy specialist nurses and ensure access in the first year of care for those with a learning disability or autism. This is great news and will help support the new Integrated Care Systems in England to drive targeted action in this area, but it will need clinical engagement by epilepsy professionals to be implemented effectively.

- Adults with epilepsy also require access to epilepsy specialist nurses and expert care. We need to work towards epilepsy in adults being recognised by the NHS as a priority across the life-course. Clinical teams should consider engaging with their local Integrated Care Board or Population Health Management groups in England, or the equivalent Population Health/Public Health teams in your country.

Epilepsy and its impact are often poorly understood outside of the community. Epilepsy healthcare professionals need to advocate for people with epilepsy and improvements in their care at a systems level to achieve change. If people advocating for people with epilepsy are not contributing to the discussions, it will continue to be missed from inequalities work, commissioning and public health priorities.

Consider what you tell people and how:

- 1 in 7 adults in England have literacy skills at or below the UK government's entry level 3. This means that they may not be able to read food packaging labels or read bus/train timetables. Depending on the area that your clinic serves, overall literacy rates in clinic attendees are likely to be lower than this.
- If you are asking the person with epilepsy to take some form of action by letter, for example, to change a regular medication, consider the language used and the reading age of the content.
- Remember that written consent to investigations and procedures is only valid if the person can read what is written on the page.
- Consider the content of any education sessions that you run (and the invite to attend). What is the reading age of the content that you are using?
- Remember the clinical value of taking a 'social history' as part of the assessment of a new person in clinic. The person's occupation and living arrangements may help you to better understand their potential needs.

Recognise the whole person and the whole context. Now, more than ever, financial concerns are impacting on the choices that people make every day.

Now, more than ever, financial concerns are impacting on the choices that people make every day

- Ensure that newly diagnosed people with epilepsy know that they will not have to pay for anti-seizure medications, or any other prescriptions they receive.
- Make sure they are aware of access to free bus travel if driving is restricted by their epilepsy, and where to get further advice if needed (e.g. Epilepsy Action, Citizen's Advice or Turn2Us).
- Consider the fact that some government benefits are based on the frequency and types of seizures occurring and that your letters may be used in evidence for claims.
- Consider where clinics are located and how easy (and costly) they are to access.
- Consider whether telephone follow up could be used to limit travel costs – but remember, mobile phones cost money to charge and put credit on.
- Consider if you have people with epilepsy under your care who could be better served with a different system or set up. What could be done differently and why isn't it?
- Consider the fact that if the person with epilepsy is socioeconomically deprived, it is likely that they will have other health comorbidities both diagnosed and undiagnosed. Remember that you might be the only team seeing the person on a regular basis (or at all) and be best placed to recognise new comorbidities such as low mood, dietary deficiencies or hypertension.

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Sodium selenate

Disease-modifying therapy for drug-resistant epilepsy

From bench to bedside: Dr Pablo Casillas-Espinosa MD, PhD, from Monash University and Alfred Health in Melbourne, Australia, explains why sodium selenate treatment could be the first-in-class disease-modifying therapy for drug-resistant temporal lobe epilepsy

Epilepsy affects more than 600,000 Brits, 150,000 Australians, and 50 million globally, with one-third struggling to control their condition with the currently available anti-seizure medications. People with drug-resistant epilepsy have high rates of disability, mental health, memory and learning problems, injury and death rates.

Now, a drug has been discovered that is the first potentially curative drug for people with epilepsy who are resistant to control with current anti-seizure medications (ASMs).

All currently available medications used to treat people with epilepsy are symptomatic (only reducing seizure frequency in <70% of cases), but without a sustained effect to mitigate or cure

epilepsy, or its associated conditions. Disease modification in epilepsy indicates the ability to reverse the severity of the underlying disease in an enduring manner and therefore potentially drug resistance.

Surgical resection of the epileptogenic zone is the only disease-modifying treatment currently available and can render drug-resistant epilepsy

drug-responsive in highly selected patients. However, only a minority of patients (<5%) are suitable for epilepsy surgery, which has significant risks. Therefore, the key challenge for translational epilepsy therapy research is to develop pharmacological disease-modifying treatments for drug-resistant epilepsy that have the disease-modifying benefits of epilepsy surgery – but would be applicable to many more patients.

In a study published in the scientific journal *eLife* [Casillas-Espinosa *et al*, 2023], researchers reported that sodium selenate could be the first medical disease-modifying therapy for drug-resistant temporal lobe epilepsy (TLE). Drug-resistant epilepsy is associated with significantly increased morbidity, mortality and cost of care.

The study, published in March 2023, done in an animal model of drug-resistant epilepsy, revealed sodium selenate to have a long-lasting effect (after months of stopping the medication) in reducing the frequency of seizures (and in 30% of cases stopping them altogether) and improving other aspects of epilepsy such as memory, learning and sensor-motor functioning.

The research studied Wistar rats, which underwent kainic acid-induced seizures, and eventually develop pharmacoresistant temporal lobe epilepsy. Ten-weeks after this, the animals received sodium selenate, levetiracetam, or vehicle subcutaneous infusion continuously for four weeks.

To evaluate the effects of the treatments, the team acquired one week of continuous video-EEG before, during, and at four and eight weeks post-treatment, and then performed behavioural tests. The results showed that sodium selenate

treatment was associated with mitigation of measures of disease. These included a reduction in seizures, an improvement of cognitive deficits, and modification of pathological changes at the molecular level.

On the strength of these findings, the team was awarded a \$3 million Medical Research Future Fund grant to start a clinical trial of sodium selenate as a first-in-class disease-modifying treatment in people with drug-resistant epilepsy.

The trial – lead by Dr Lucy Vivash, Prof Terry O'Brien and Dr Casillas-Espinosa – will start later this year and will be the world's first to investigate the effect of six months of treatment with sodium selenate in patients with drug-resistant TLE – to see whether, as in the pre-clinical animal studies, there is a sustained beneficial effect to reduce seizure frequency and neuropsychiatric comorbidities. 124 patients will be enrolled across Australia.

Following screening assessments, participants will be randomised to receive either sodium selenate or placebo for six months, and then followed for another six months and assessed for effects on: the number of seizures experienced, measures of quality of life, and presence and severity of adverse events, using a novel patient-designed desirability of outcome ranking (DOOR) scale.

Sodium selenate treatment was associated with reduction in seizures, and an improvement of cognitive deficits

Secondary outcomes measure other epilepsy-related outcomes, including cognitive deficits and depression and anxiety.

Despite the cost of the drug-resistant TLE, estimated at \$12.3 billion/annum in Australia, and the enormous amount of research into it, there has not been a single therapy developed to prevent the progression of epilepsy, nor to mitigate its severity once established. Until now.

This phase 2 clinical trial, if effective, has the potential to tackle a disease that is an enormous global burden and truly transformative for people impacted by often daily seizures, with no respite.

The clinical trial uses a patient-centre DOOR scale, adapted for use in the trial by a focus group of people with epilepsy. The group from multiple Australian states (New South Wales, Victoria, South Australia and Queensland) developed the scale according to the outcomes most important to the people with epilepsy when trialling a new treatment for epilepsy.

Dr Pablo Casillas-Espinosa MD, PhD from Monash University and Alfred Health, Melbourne, Australia

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Climate change

Forest fires, floods and fossil fuels

Following a summer plagued by extreme weather events, Alistair Wardrope discusses how the climate emergency is impacting people with epilepsy

The world is on fire. Previously I have used this expression figuratively, if only slightly hyperbolically, to convey the urgency of action on the intersecting climate, environmental and biodiversity emergencies that confront us. This summer, though, has demonstrated the increasingly literal truth of this statement, with wildfires across the

Mediterranean, US and China. Heat records have fallen like dominoes across the globe. Antarctic sea ice extent is lower than it has ever been – more than six standard deviations below the long-term moving average (a one in 7.5 million year event) [British Antarctic Survey, 2023]. Health impacts are being felt globally, with increased hospitalisations for heat-related illness

reported across continents. Epilepsy communities are no exception.

The world is on fire and yet we – as individuals, communities, nations and globally – are failing to act. As recently as 2021, the UK government boasted it was ‘leading the way’ to a net-zero future; action then fell far short of rhetoric, and since then both Rishi Sunak and Keir Starmer have

signalled their willingness to sacrifice our collective future to the altar of short-term political gain [GOV.UK 2022]. Globally, current environmental policies and actions commit us to an expected 2.7c surface temperature rise by 2100, vastly exceeding the 1.5c target set in the 2015 Paris Agreement. To achieve this target, 90% of already listed fossil fuel reserves must remain unused – yet governments continue to license new developments aiming to extract yet more unburnable carbon [Romanello *et al*, 2022].

The world is on fire – and this matters for everyone working or living with epilepsy. Among the diverse range of effects climate change and the processes driving it have on human health, many are specifically relevant to epilepsy. Acting to mitigate climate change, and its threats to human and planetary health, is everyone's responsibility, and the epilepsy community is mobilising to meet it.

Epilepsy and fossil fuel dependence

Climate change is overwhelmingly driven by a continued global dependence on fossil fuels. This dependence is a political choice, not a physical necessity. Present energy needs could readily be met in the UK and internationally by a sustainable transition to zero-carbon renewable energy systems. The ongoing political fixation on economic growth, at the expense of all other considerations, drives human and environmental exploitation without significantly furthering human wellbeing.

This fossil fuel economy also drives the causes of epilepsy as diverse as stroke, brain injuries and infections of the central nervous system, are all made worse by fossil fuel use. Outdoor air pollution from burning

fossil fuels leads to about 3.6 million deaths annually [Beagley 2022].

Air pollution from fossil fuels is a major cause of stroke, accounting for more than 20% of all strokes worldwide [Feigin *et al*, 2021]. Motor vehicle road accidents are the second most common cause of traumatic brain injury [James *et al*, 2019], and limiting their use and increasing walking and cycling reduces accident rates [Buck *et al*, 2023]. Climate change is causing alterations in temperature and aridity in large regions of the globe in ways that affect the spread of infectious diseases; rates of meningitis, and potentially other infectious causes of epilepsy, appear to be rising and spreading to different regions [Gulcebi *et al*, 2021].

Climate change also poses risks for those already living with epilepsy. The most direct effects relate to increased heat. Seizure incidence in many parts of the world varies with temperature, and many people with epilepsy report that extremes of heat makes their seizure control worse [Gulcebi *et al*, 2021]. This may be exacerbated by difficulties with storage of anti-seizure medications, the stability of which may depend on stable temperatures.

However, while the effects of heat may be the easiest to visualise and relate directly to climate change, its greatest significance for those with epilepsy is likely to be through its secondary effects on natural and social systems – whether through lack of secure food, water or medication supply, or drought or conflict-driven forced migration. Seizures are one of the leading causes for medical referral in camps for forcibly displaced persons [Hallab *et al*, 2021].

Climate change is also deeply unjust. The communities facing the greatest health risks from climate change are those who have done least to cause it. Average carbon dioxide

Climate change poses risks for those living with epilepsy

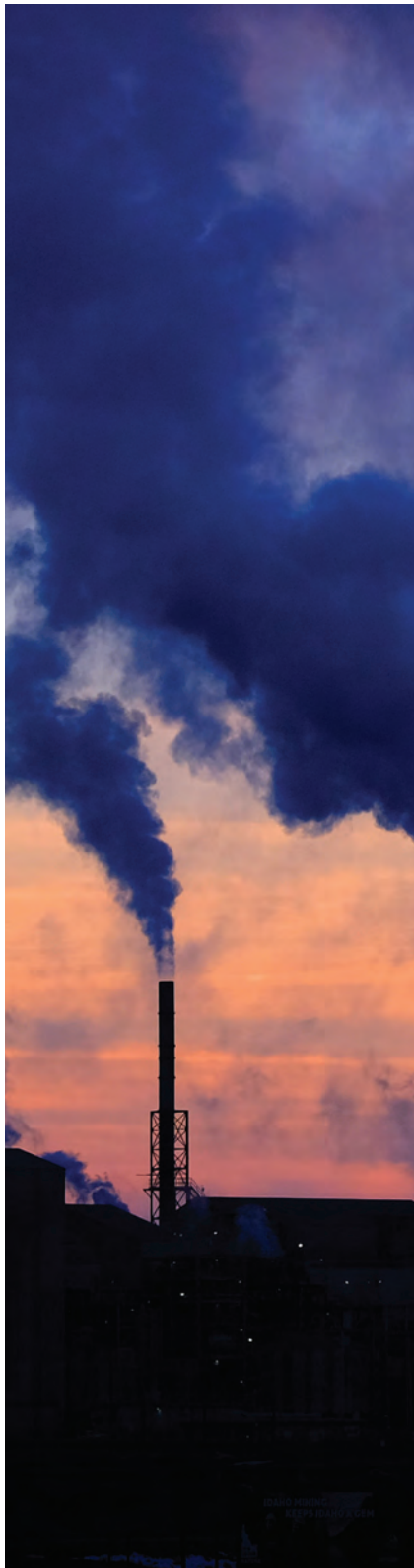
emissions per person in Australia and the USA are more than 160 times higher than in some Sub-Saharan African nations, which are most exposed to the risks of heat, drought, and conflict [Ritchie *et al*, 2023]. Nonetheless, these wealthy nations continue to prop up the fossil fuel industry. Each dollar of the US\$584 billion given in subsidies to fossil fuel companies between 2017 and 2019 is estimated to have caused six dollars of health costs [Beagley 2022]. For people with epilepsy, this adds to existing inequities. People in low-income countries already face extreme challenges in managing their epilepsy, with more than 86% not receiving basic epilepsy treatment [Kwon *et al*, 2022].

The role of the epilepsy professional

It is easy to feel despairing or powerless at the scale of the challenge confronting us. However, action at individual, institutional and political levels is already taking place, and can help to bring about the necessary transition to a zero-carbon society.

As an individual

Individual behaviour change offers the most immediate and direct way for many people to take action on climate change. The overall change from a single person's decision to fly less or eat a plant-based diet is not going to stop global heating. Its importance comes from changing social norms – such behaviours become contagious, until a social “tipping point” is reached



where sustainable lifestyles become the new normal [Howard *et al*, 2023]. This is particularly important for health workers, with doctors and nurses regularly rated as the most trusted professionals.

Not everyone will be able to make every low-carbon choice, but everyone can take steps to make their lifestyles more sustainable. Even better, the majority of these changes provide health benefits of their own.

Reducing private car usage and replacing with walking or cycling saves money, carbon and improves health – relative to driving, cycling to work reduces risk of death by nearly 40% [Buck *et al*, 2023]. The more people who cycle, the safer it becomes [Aldred *et al*, 2018]. Decisions about long journeys also matter – for the average person living in the UK, a single long-haul return flight would increase their carbon footprint by nearly half [Timperley 2023].

Industrial animal farming accounts for nearly one fifth of all greenhouse gas emissions (more than all forms of transportation combined) [Sandler, 2023]. Diets that are lower in dairy and animal protein and higher in plants produce 40-50% less carbon than the standard western meat-based diet [Maslin, 2023]. They are also better for many people – a largely plant-based ‘planetary health diet’ (that still allows for some meat and dairy) could prevent more than 10 million adult deaths per year from conditions such as heart disease and diabetes [Knuppel *et al*, 2019]. Moreover, such a diet could be sustainably produced to feed

**Many health workers
have made the decision
to divest from fossil fuels**

a growing global population, in contrast to the current situation in which more than 2.3 billion people are malnourished [Abrams *et al*, 2021].

We can move our money away from the companies that are funding the climate crisis and towards those working for a sustainable future. The fossil fuel industry continues to invest in unburnable carbon, and works to undermine science on climate change and health – just as the tobacco industry did to oppose smoking. Many banks and building societies now help individuals to avoid being complicit in this, by not investing in these companies. Many health workers have made this decision to divest from fossil fuels, as have institutions including several medical royal colleges, and the British, Canadian and American medical associations [Abbasi *et al*, 2020].

As a professional

Organisations such as the Centre for Sustainable Healthcare and the Greener NHS programme provide a host of resources to enable health workers to make their practices fit for the future. The Green Impact for Health Toolkit, designed for GP surgeries, helps to explore the sustainability of workplaces and healthcare practice.

Sustainable healthcare practice emphasises prevention, patient self-care, lean service delivery and lower-carbon alternatives. Community epilepsy services can empower patients with this, minimising intensive inpatient care. Where specialist medical input is needed, for many patients telemedicine is able to provide care more accessibly, while reducing healthcare-associated transport emissions.

Researchers can work to share their outputs in lower-carbon ways that are more accessible to workers in more marginalised situations – the

Covid-19 pandemic has shown us all that frequent long-haul flights are not necessary for effective international research collaboration.

As a citizen

People living and working with epilepsy are uniquely positioned to speak to the effects of climate change on their health. Health workers are highly trusted voices within communities. This gives both health workers and patients powerful voices for political action. This action can come in many forms. As individuals or groups, we can lobby

local representatives for climate action – or specific local policies that affect environmental health. Other health groups work to influence policy at national and international levels, making the health case for sustainable energy, food and transport policy. Groups such as Doctors for Extinction Rebellion have taken still more direct action, putting their bodies on the line to stop the industries driving the climate crisis.

Taking political action requires organisation. Epilepsy professionals' groups have formed to help clinicians collaborate for action to protect brain

health from climate change. The ILAE's Climate Change Commission and the Epilepsy Climate Change Consortium (EpiCC) represent two such groups.

Conclusion

The climate crisis is everyone's problem. The effects of climate change on epilepsy make it an issue of particular concern for epilepsy professionals. But, as individuals, professionals or citizens of the world there actions we can take to work for a future with better human and planetary health.

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Research update

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

The Royal College of Paediatrics and Child Health is preparing to launch its highly acclaimed Epilepsy Quality Improvement Programme (EQIP) for the 2023/24 term. Epilepsy Action's director of health improvement and influencing Alison Fuller is a member of the EQIP steering group and she is delighted to be involved again this year, and excited to see what projects come from the teams involved.

EQIP offers a platform for paediatric epilepsy teams to undertake quality improvement projects alongside experienced quality improvement coaches and receive ongoing training to improve their skills. The programme guides participating teams through projects in the areas they feel need attention. This

approach empowers teams to identify areas in need of improvement, experiment with a range of quality improvement methodologies and make decisions on changes based on real-world data. The ultimate goal of this programme, for those running it and the teams taking part, is to elevate the standard of care given to children with epilepsy and their families.

The diversity of projects undertaken each year stands as a testament to the programme's adaptability and far-reaching influence. Examples of past projects span a wide spectrum, from streamlining transition processes for patients to enhancing the accessibility of care plans within electronic health records, optimising care pathways and reducing waiting times for critical investigations such as EEGs.

This programme is an excellent opportunity for professionals looking to not only improve the quality of their service but also cultivate a new skillset and gain invaluable experience in quality improvement and associated methodologies. As 2024 approaches, EQIP once again takes centre stage, promising a renewed wave of positive transformation in the landscape of paediatric epilepsy care.

For more information, or to sign up, visit: eqip.rcpch.ac.uk

Quality of life

Epilepsy Action was honoured to be invited to write a guest blog for Epilepsy Research UK in July. Fuller wrote about the importance of quality of life for people with epilepsy and shared her dedication to improving

quality of life through the work that we undertake at Epilepsy Action. She identified two key areas where research could make a real impact on quality of life: mental health and personalised treatments.

Mental health

People with epilepsy are at an increased risk of developing depression and anxiety disorders. Understanding the link between epilepsy and mental health is vitally important for improving the overall wellbeing and quality of life for people living with epilepsy.

These disorders can have a significant impact on a person's emotional wellbeing, social interactions and daily life. By identifying and addressing this link, healthcare providers can ensure the delivery of comprehensive care encompasses both the physical and mental health aspects of epilepsy. Additionally, depression and anxiety can have a reciprocal relationship with epilepsy, where one condition exacerbates the other. For instance, the psychological distress caused by seizures and the challenges of living with epilepsy can contribute to the development or worsening of depression and anxiety. Conversely, the presence of these mental health conditions may negatively affect seizure control and overall treatment outcomes. Research that helps healthcare professionals to better recognise and manage this complex interplay could lead to more effective treatment strategies and better seizure management, which would improve many people's quality of life.

Depression and anxiety can have a reciprocal relationship with epilepsy

Personalised treatments

Drug-resistant epilepsy can severely impact an individual's quality of life, leading to distressing and disruptive seizures, limitations to daily activities

and psychological distress. By identifying and developing treatments that specifically target drug-resistant epilepsy, researchers and healthcare providers can offer hope for those who have exhausted conventional treatment options.

The search for treatments with fewer and less serious side effects is essential. Many people with epilepsy experience side effects from anti-seizure medications, such as fatigue, memory problems, brain fog and mood disturbances. Finding treatments that effectively control seizures while minimising side effects would greatly enhance the overall treatment experience for people with epilepsy and improve their quality of life.

Personalised treatments offer real promise in both these areas. Epilepsy is a diverse condition, with many underlying causes, seizure types and responses to treatments, all of which can greatly vary. What works for one person may not be effective for another. This individual variability poses a significant challenge in epilepsy management but also presents an opportunity for personalised treatment approaches in genetics, pharmacology and neuroimaging. By studying an individual's genetic makeup, researchers can identify specific variations or biomarkers associated with drug response or treatment resistance. This knowledge can guide treatment decisions and

help healthcare providers choose the most appropriate medication or intervention for each person.

Developments in pharmacology can contribute to more targeted and effective medications. By understanding the intricate causes of epilepsy and the pathways involved in seizure generation, researchers can design medications that target these pathways. Overall, personalised treatment options could maximise efficacy, minimise side effects, improve outcomes and have the potential to revolutionise epilepsy management.

We hope that by highlighting these opportunities to the research community we can ensure quality of life is prioritised in epilepsy research.

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Highlights

Top picks from *Seizure*

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

Clinicians working to treat seizure disorders will be familiar with uncertainty in all its forms: in this medical field, most advice about diagnosis, treatment, lifestyle and personal choices, and prognosis will be characterised by uncertainty [Han *et al*, 2019].

Clinical encounters in seizure clinics will regularly expose clinicians and patients to “epistemic uncertainty” (due to lack of knowledge at the individual patient level, in general or even unknown unknowns), “aleatory uncertainty” (related to inter-individual biological, psychological or social variability) and “Knightian uncertainty” (where a lack of quantifiable knowledge means risks cannot be quantified). Uncertainties will be related to the unpredictability

of outcomes at the individual patient level, imprecision of evidence, conflict of opinion, lack of information and complexity of available data [Han *et al*, 2011].

Good advice on how to deal with uncertainty in practice is available [Berger *et al*, 2015], but there are times when clinical scenarios force patients and clinicians to face binary choices – such as: “Is this epilepsy?” “Do we start anti-seizure medication?” “Shall we operate?”, “Shall we stop medication?”. Occasionally there may be a third way such as seeking more information or deferring a decision while reflecting on its consequences, but often choices have to be made despite uncertainty.

One of the most consequential sources of uncertainty in clinical epileptology relates to the nature of the patient’s seizures. This uncertainty is particularly acute when seizures include loss of consciousness – limiting the information available about seizures from patients.

Of the three most common causes of transient loss of consciousness – syncope, epilepsy and functional/dissociative seizures (FDS) – the first is relatively easy to distinguish from the other two based on the symptoms before and immediately after the period of loss of awareness [Chen *et al*, 2019]. The differentiation between epilepsy and FDS based on the patient’s history alone is much harder [Wardrop *et al*, 2018].

Arguably the most important development in the differentiation of epileptic and FDS disorders, which I have gained personal experience of over the last three decades, is the greater availability of home video recordings of seizures.

My editor’s choice from volume

There are times when clinical scenarios force patients and clinicians to face binary choices

110 of *Seizure*, a meta-analysis by Cemal Karakas *et al*., documents that, in optimal circumstances, such video recordings have a sensitivity for the identification of epilepsy of 82%, a specificity of 84%, and yield diagnoses of epilepsy with an odds ratio of 24.7 [Karakas *et al*, 2023]. The area under the receiver operating curve for video-based diagnoses was excellent.

Of course, there are several limitations: experts (epileptologists) were considerably better than non-experts (including general neurologists) at differentiating correctly between videos of the two different types of seizures.

What is more, not all studies included in the meta-analysis were prospective, and it could be argued that prospective and retrospective studies should not be combined. It is also unclear how representative study populations of patients with video-EEG based “gold standard” diagnoses are of the whole patient populations encountered in a seizure clinic.

Nevertheless, as home video recordings have become an essential part of the epileptologist’s toolkit and there is increasing access to commercial and semi-automatic video monitoring systems, this meta-analysis removes some uncertainty about the level of uncertainty of what has become one of the most important diagnostic tools in epileptology.

Premature deaths

In 1520, in his last major work before his death, the Italian renaissance artist Raphael depicted the transfiguration of Christ on Mount Tabor and the epileptic seizure of a young boy at the foot of the mountain in the same painting. Raphael's combination of these two scenes creates a graphic link between two stories that are told successively in the Bible in three of the gospels, as if they had taken place at the same time (Matthew 17:14-21; Mark 9:17-29; Luke 9:38-43). In this way, the transitory "death" of the boy associated with his epileptic seizure becomes a visual metaphor for the temporary death of Jesus after his crucifixion and before his ascendance to heaven, which is a central tenet of Christian belief [Janz, 1986].

While an epileptic seizure is used as a narrative tool to communicate the idea of resurrection and life after death in these biblical stories, it has been recognised for a long time that epilepsy is associated with a significantly increased risk of premature death.

Standardised mortality ratios associated with epilepsy range from 1.6 to 3.0 in high-income countries [Thurman *et al*, 2017] to 19.8 in low and middle-income countries [Levira *et al*, 2017]. Male patients with epilepsy, children and adolescents, as well as those without access to health care are at particular risk of premature death [Trinka *et al*, 2023].

Home video recordings have become an essential part of the epileptologist's toolkit

While epilepsy may simply be a marker of other diseases with their own excess mortality, of disease severity or of socioeconomic risk factors associated with early death, epilepsy-related deaths (including avoidable epilepsy-related deaths) have been thought to explain up to 50% of the excess mortality in young people [Sidebotham *et al*, 2015; Hanna *et al*, 2002]. Sudden unexpected death in epilepsy (SUDEP) is recognised as the most common cause of death in young people with epilepsy [Trinka *et al*, 2023].

Although numerous studies of the mortality associated with epilepsy in childhood have been published previously, many questions remain unanswered and some questions that have been answered for some populations at particular points in time need to be addressed again because health risks, treatments and the management of risk factors have changed.

My editor's choice from the current volume of *Seizure* is a cohort study of 1,191,304 children living in the UK by Christian Schnier and Robert Chin, which makes a further contribution to the literature on the mortality associated with epilepsy in childhood and adolescence [Schnier *et al*, 2023].

The study captured mortality data from 13,994,916 person-years. Just over 3% of children in the cohort died during the study period. The all-cause mortality rate was 4/1,000 children per year. After adjustment for sex and socioeconomic status, compared to children of the same age without epilepsy, the all-cause mortality risk was increased by a factor of 50 in young people with epilepsy. Unlike in middle age, when suicide is the most common cause of death associated with epilepsy, almost all of the deaths in children were





classified as ‘natural’ – one quarter were directly attributed to epilepsy.

The increased mortality risk in young people documented in this study should give cause to serious concern and be sufficient to prompt the development and maintenance of responsive and capable health services for children and young people with epilepsy.

However, it has been argued that studies such as the one by Schnier and Chin may still underestimate the true number of epilepsy-related deaths because of inaccuracies of the

coded causes of death. It has been suggested that, especially in young children, labels of sudden infant death syndrome (SIDS) or sudden unexpected death in childhood (SUDEC) may have been applied when SUDEP may actually have been a more appropriate or likely as a cause of death [Harowitz *et al*, 2021].

Seizure is the European Journal of Epilepsy. It is the official journal of Epilepsy Action. For more information: www.seizure-journal.com

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Epilepsy Action is here for you



helpline

Epilepsy can be very confusing. Our **Helpline team** are ready to answer any questions you might have on the phone, via live chat or email.



counselling

Counselling can be really helpful when things get tough – we're ready to help in Wales and Northern Ireland. Our professional **Counselling** team can provide the support you need online or over the phone.



talk and support

If you want to talk to other people about life with epilepsy, you're welcome to come to one of our **Talk and support** groups to meet and share your experiences either on line or face-to-face.



family support
Northern Ireland

Epilepsy doesn't just affect the person with the diagnosis – that's why our **Family support** service is there for family members and carers in Northern Ireland.



befriending

Not everyone's ready for a group, though – one-to-one support through **Befriending** might be better for you. We'll connect you to a volunteer who will offer you a friendly listening ear either on the phone or online.



epilepsy.org.uk/support

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Remembering epilepsy nurse Ena Bingham

We were saddened to hear of the passing of Ena Bingham on May 5, retired epilepsy specialist nurse, former Epilepsy Action council member and unparalleled champion of people with epilepsy in Northern Ireland.

Born on November 17, 1945, Ena became a nurse at the Royal Victoria Hospital, Belfast.

Some will remember her as the 'red' or senior sister on the neurology ward, which she ran with

military precision. The staff were always well turned out, the ward immaculate, yet always the patients came first – woe betide any medical student or junior doctor who dared to sit down on a bed to talk to a patient.

At the height of her career, Ena became the first ever epilepsy specialist nurse in Northern Ireland – a post so different from her previous position that some initially wondered if she could adapt to it.

One need not have worried. Ena quickly became a model to others and made a huge difference to many thousands of lives directly or indirectly affected by epilepsy in Northern Ireland.

She was committed to helping people, through volunteering with Epilepsy Action for more than 25 years, running local support groups, and giving talks and presentations to raise epilepsy awareness. She was an advocate for all those with epilepsy and their families (yet she still found time to keep the doctors on their toes).

Ena served on Epilepsy Action's Council of Management between 2007 and 2013 and on Epilepsy Action's Northern Ireland advisory council from the beginning of 2010 until her health began to fail in 2021. She was awarded an MBE for services to epilepsy in 2012.

Ena made an immense contribution to epilepsy services and her legacy will be the motivation, dedication and enthusiasm she demonstrated throughout her life, which she has undoubtedly passed on to the many others who now follow her lead and continue her work.

She will be greatly missed.

Dr Jim Morrow
Neurologist
Belfast

Support for professionals

Epilepsy Action supports a wide range of medical and non-medical professionals.

Epilepsy specialist nurses

We can provide resources for you and your patients, as well as access to our nationwide network of other professionals.

<https://bit.ly/3YTWtXa>

Primary care staff

Find resources and information for GPs and practice nurses.

<https://bit.ly/47TJGYD>

The care sector

We have a course designed for people who support or care for people with epilepsy.

<https://bit.ly/3L47YWl>

Education providers

We have online training for teachers and school staff, as well as extensive information to help you support pupils with epilepsy.

<https://bit.ly/3YYbxmp>

Support for researchers

There are a number of ways in which Epilepsy Action can support researchers and people working in quality improvement.

<https://bit.ly/45vbEsm>

Maternity services

Find support for midwives and obstetricians.

<https://bit.ly/3R10Spb>

Dates for the diary

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

2023

13-16 September
20th International Congress
of Neuropathology
Berlin, Germany
<https://bit.ly/3Peovt4>

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

29 June-2 July
10th Congress of the European
Academy of Neurology
Helsinki, Finland
<https://bit.ly/47LSi3L>

7-15 September
15th European Epilepsy Congress
Rome, Italy
<https://bit.ly/45p17Pg>

Next issues:

Dr Louise Spiers

Dr Spiers discusses her research into people with epilepsy who may have what might be considered exceptional, anomalous and spiritual experiences.

Rozalia Valentine

The research assistant at Boston Children's Hospital discusses genome sequencing in infantile epilepsy.

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

gwood@epilepsy.org.uk

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