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Top Ten epilepsy research priorities: A UK priority setting partnership

Anna C Norton [a,b,*], Caoimhe Twohig-Bennett [a,c], Maxine Smeaton [a], Anthony Marson [d,e], Jack Armstrong [a,f], Adam Kovac [a,f], Samantha Ashby [g], Hannah Cock [h], Anne Coxon [i], Jon M Dickson [j,k], Abbie Fearon [i], Alison Fuller [l], Michael Kinney [m], Andrée Mayne [n], Tom McLaughlan [i], James W Mitchell [d,e], Rosemarie Pardington [a,o], Angie Pullen [a,l], Rohit Shankar [p,q], Juliet Solomon [r], Phil Tittensor [s,t], Sukhvir Wright [u,v], Alice Yandle [i], Sameer Zuberi [w,x], Katherine Cowan [y], Rhys H Thomas [z,aa]

[a] *Epilepsy Research Institute, London, United Kingdom*
[b] *University of Manchester, Manchester, United Kingdom*
[c] *University of Oxford, Oxford, United Kingdom*
[d] *University of Liverpool, Liverpool, United Kingdom*
[e] *The Walton Centre NHS Foundation Trust, Liverpool, United Kingdom*
[f] *University of Edinburgh, Edinburgh, United Kingdom*
[g] *SUDEP Action, Wantage, United Kingdom*
[h] *St George's University Hospitals NHS Foundation Trust, St George's University of London, United Kingdom*
[i] *UK Epilepsy PSP Steering Group, London, United Kingdom*
[j] *University of Sheffield, Sheffield, United Kingdom*
[k] *Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom*
[l] *Epilepsy Action, Leeds, United Kingdom*
[m] *Belfast Health and Social Care Trust, Belfast, United Kingdom*
[n] *Epilepsy Society, Chalfont St Peter, United Kingdom*
[o] *Young Epilepsy, Lingfield, United Kingdom*
[p] *University of Plymouth, Plymouth, United Kingdom*
[q] *Cornwall Partnership NHS Foundation Trust, Bodmin, United Kingdom*
[r] *ILAE British Branch, London, United Kingdom*
[s] *Royal Wolverhampton Hospitals NHS Trust, Wolverhampton, United Kingdom*
[t] *Epilepsy Nurses Association (ESNA), Wolverhampton, United Kingdom*
[u] *Aston University, Birmingham, United Kingdom*
[v] *Birmingham Women and Children's Hospital, England, Birmingham, United Kingdom*
[w] *University of Glasgow, Glasgow, United Kingdom*
[x] *Royal Hospital for Sick Children, Glasgow, United Kingdom*
[y] *James Lind Alliance, Southampton, United Kingdom*
[z] *Translational and Clinical Research Institute, Newcastle University, Newcastle, United Kingdom*
[aa] *Royal Victoria Infirmary, Newcastle Hospitals, NHS Foundation Trust, Newcastle Upon Tyne, United Kingdom*

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ABSTRACT

Purpose: Research into epilepsy has experienced decades of chronic underfunding compared to other neurological conditions despite its prevalence and seriousness. To evidence the need for greater investment, the Epilepsy Research Institute (formerly Epilepsy Research UK) funded, led and managed a James Lind Alliance (JLA) Priority Setting Partnership (PSP). This "industry standard" methodology brings together healthcare professionals, patients, carers and patient group representatives to identify and prioritise research uncertainties within a defined area of health or care.

Methods: The UK Epilepsy PSP is a once-in-a-generation, national consensus that collated and ranked the research priorities of the UK epilepsy and associated condition community. Following JLA methodology, this 18-month

* Corresponding author at: UK Epilepsy PSP Coordinator and Research & Involvement Officer, Epilepsy Research Institute, Churchill House, 35 Red Lion Square, London WC1R 4SG, United Kingdom.
E-mail address: ukepilepsypsp@epilepsy-institute.org.uk (A.C. Norton).

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project engaged over 100 patient groups and 5000 people affected by and working in epilepsy, including medics and allied healthcare professionals, from across the UK.
Results: Over 5400 priorities were received, with anti-seizure medication, sudden unexpected death in epilepsy (SUDEP) and epilepsy in women among the most frequently reported themes. The responses received were categorised and translated into distinct, researchable questions. Questions were excluded if deemed to be "answered" following an evidence check, while research uncertainties (i.e. unanswered and partially answered questions) formed the basis of a second, shortlisting survey. The shortlisted questions were then discussed and debated at the final workshop by participants that broadly represented the UK epilepsy and associated condition community. The final ranking and Top Ten priorities for research into epilepsy were then agreed.
Conclusion: The aim of the UK Epilepsy PSP is to encourage and inspire researchers to investigate the research areas prioritised by those most affected by the condition and provide the evidence of need to aid future policy making discussions and support research funding applications.

1. Introduction

Epilepsy is one of the most prevalent, serious neurological conditions, with approximately 600,000 people in the UK living with epilepsy, costing the National Health Service (NHS) an estimated £2 billion annually [1,2]. Yet, despite this, there are stark inequalities in research funding for epilepsy in comparison to other neurological conditions. In 2018, epilepsy received just 0.3 % of the £4.8 billion funding spent on health-related research by the UK government [3]. Epilepsy is a compelling area for enhanced research support because there are preventable causes, and treatment paradigms that are ultra-precise (precision medicine strategies) and those that are agnostic to aetiology (such as neuromodulation) [4].

Epilepsy is not a single condition but rather a grouping of many disparate disorders, where seizures can be both seen as a primary feature as well as secondary to a recognised or a cryptic cause [5–7]. This results in significant variation in terms of presentation, treatment, management and severity. This variety creates a challenge when identifying strategic priorities for research into epilepsy.

The James Lind Alliance (JLA), founded in 2004, is a non-profit initiative which designed and developed the Priority Setting Partnership (PSP) methodology. This produces a true collaboration between patients, carers and health professionals to identify and prioritise unanswered questions, answerable through research for a distinct area of health and/or care [8]. Since the first PSP completed in 2007, over 100 partnerships have been successfully completed both in the UK and internationally for a broad range of health conditions [9]. Successful PSPs have led to strategic collaborations and increased research investment from institutional funders within the research areas prioritised by those living and working with the condition in question [10]. The JLA process is widely respected by major funders and acknowledged to be the gold standard in research prioritisation [8].

Prior to the formalisation of the JLA PSP methodology, a similar process, based on a focus group methodology, but supported by the JLA, was attempted in 2010 to establish the most important unanswered questions for research into epilepsy [11]. The remit was limited to unanswered research questions pertaining to treatments and clinicians' and patients' priorities were considered separately. This identified that patient priorities were more practical, focused on the here and now – such as "what to do when you miss a dose of medication?" – whereas clinician questions would need commissioned research to answer – such as "what are the neurodevelopmental effects of epilepsy medications in utero?" Consensus was seen around themes such as the cognitive impact of anti-seizure medication. Six years later, looking at which questions had been addressed by research, policy and guidance, showed that patient priorities were half as likely to be a research focus, and clinicians' questions were four times more likely to be in policy documents [12]. There was clearly a need for a *consensus* Top Ten of epilepsy research priorities in the UK.

2. Methods

2.1. Establishing the steering group and scope

The 2021 UK Epilepsy PSP was funded and led by the Epilepsy Research Institute (ERI; formerly Epilepsy Research UK) and undertaken in collaboration with the JLA and supported by the National Institute for Health and Care Research (NIHR), with involvement from the major UK epilepsy charities and over 100 partner organisations.

In September 2021, the Epilepsy Research Institute convened a steering group of 23 individuals with diverse professional and personal experience of epilepsy, including representatives from the Epilepsy Research Institute, each of the major collaborating charities (Epilepsy Action, Epilepsy Society, International League Against Epilepsy (ILAE) British Branch, SUDEP Action and Young Epilepsy), health professionals and people personally affected by epilepsy. Firstly, the scope of the UK Epilepsy PSP was defined. Due to the lifelong, variable nature of the condition, the causes, diagnosis, treatments and clinical management (including risk of epilepsy-related death) of epilepsy in children and adults was considered within scope, as well as the dissemination of research breakthroughs to influence epilepsy care, practice and policy. Health and social funding, social research and functional seizures were excluded from scope. The scope of the PSP was also limited to UK based participants. We followed the standard JLA method (Fig. 1) [8].

2.2. First survey

The steering-group designed a web-based survey (Supplementary I) which asked the epilepsy community – people with epilepsy, their parents, families, friends and carers, those bereaved by epilepsy, charity representatives and healthcare professionals – to list their top three research questions. Pure research scientists were excluded from the survey, as per the JLA principle of focusing on practitioners and people with lived experience. This was disseminated amongst the 100-plus partner organisations, across clinical networks and on social media. The survey was open for 4 months and was available in multiple formats and/or languages upon request.

Achieving representative engagement was essential to the success and validity of the UK Epilepsy PSP. To ensure responses received reflected the UK epilepsy community, several optional demographic questions were asked in the first survey (Supplementary I). To safeguard the privacy of survey participants, questions were carefully considered to avoid privacy concerns or ethical consent requirements [13]. Most participants voluntarily provided demographic information, enabling the monitoring of responses and subsequent engagement with underrepresented groups through targeted communications, including through direct email, social media and local radio networks.

2.3. Priority categorisation and summary research question development

Research priorities received in response to the first survey underwent data cleaning – out-of-scope submissions were removed, and in-scope

submissions anonymised. Each survey response was reviewed and categorised, with some priorities allocated to either one or multiple primary or secondary categories (Table 1; Supplementary II). Following categorisation, research priorities were translated into numerous, distinct summary research questions, which were reviewed and agreed by the steering group.

2.4. Evidence check

An evidence check was undertaken by two members of the research team with the skills and knowledge required to determine which of the summary research questions were "answered", "partially answered" or "unanswered" by the existing research literature. In September 2021, a Canadian Epilepsy PSP was published [14]. The Canadian PSP conducted a thorough evidence check, creating an evidence database in the process. This resource was shared with the UK Epilepsy PSP programme, expediting this stage of the priority setting process. The evidence database was updated (January 2020 to July 2022) and its scope expanded to include topics like data science. To ensure continuity of approach, the advanced search methodology employed in the Canadian Epilepsy PSP evidence check was used to search the following JLA-approved primary databases: Cochrane Epilepsy, Cochrane Reviews, NICE Guidelines and SIGN guidelines [14–16]. The steering group reviewed and verified the results of the evidence check. Summary research questions identified as "answered" were excluded from the remaining stages of priority setting process, and those "partially answered" or "unanswered" by the existing research literature (i.e. research uncertainties), were moved forward for shortlisting by the UK epilepsy and associated condition community. Research summary questions that had been nominated by 5 or fewer participants were excluded from the process at this stage, a pragmatic decision to ensure a manageable amount of data to take forward for prioritisation.

2.5. Shortlisting survey

The second shortlisting survey, designed and piloted by the steering group, launched 6 months after the first survey closed and used the same method of dissemination. We included 57 summary research questions following the evidence check (Supplementary III). Survey participants were asked to 'longlist' a maximum of 40 questions, from which they were subsequently asked to prioritise a maximum of 10 questions. As before, several optional demographic questions were asked, along with an explanation of their purpose (Supplementary I). Responses were monitored to ensure broad representation of the UK epilepsy community and to identify any underrepresented groups, who were again encouraged to participate in the shortlisting survey through targeted communications.

Table 1
Primary categories used to group the priorities submitted in response to the first survey.

Primary categories		
Causes	Management	Data
Diagnosis	Lifestyle	Health services
Prognosis	Support	Epilepsy in childhood
Prevention	Comorbidity	Out of scope
Treatment	Knowledge dissemination	

2.6. UK Epilepsy PSP Workshop

Following the second survey, the 25 most prioritised summary research questions were selected for the next stage of the process, an in-person workshop held in September 2022, led by JLA advisors (Fig. 1). Twenty-seven participants were invited, including people with epilepsy, parents, family, and carers of people with epilepsy, people bereaved by epilepsy, healthcare professionals and charity representatives. The participants were recruited through an open call, and majority were independent of the steering group and evidence checking process. Those expressing an interest in attending were grouped by their experience or area of expertise and participants were chosen at random from each group to ensure a broad representation of the epilepsy and associated conditions community and healthcare professional expertise. In line with the standard JLA method, the workshop took the format of a series

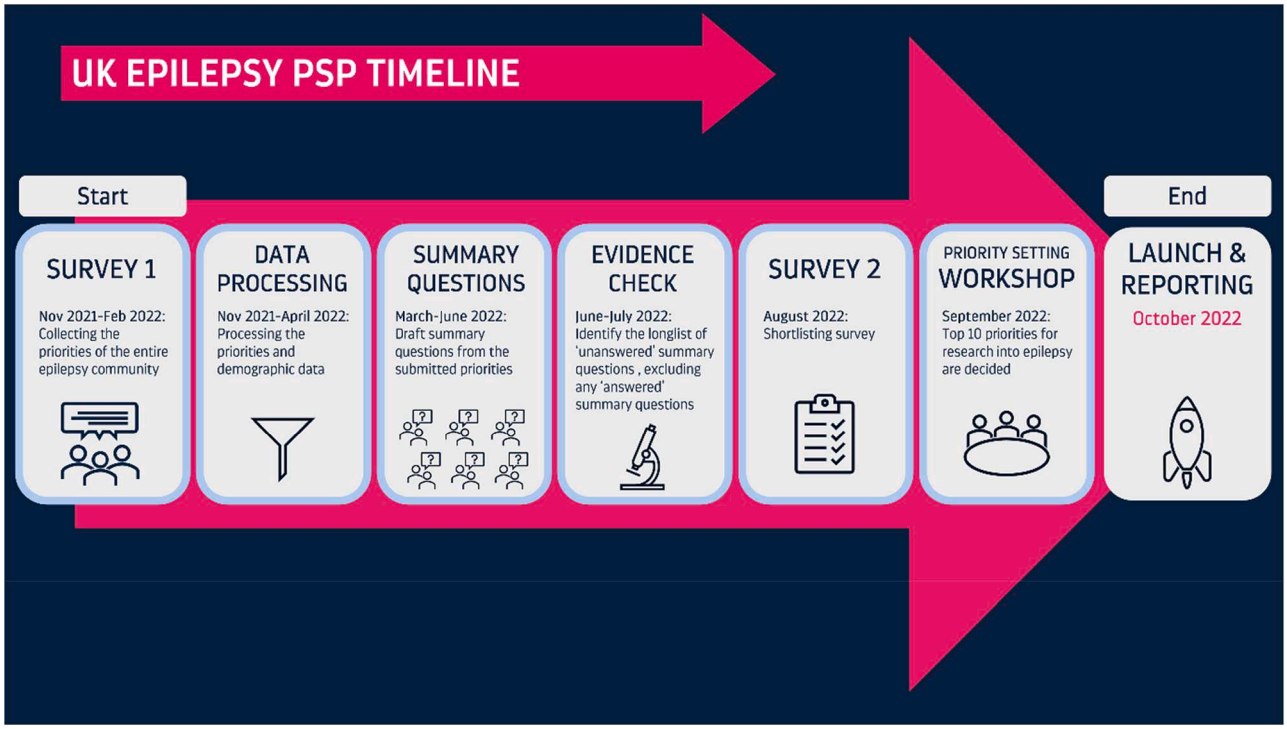


Fig. 1. UK Epilepsy Priority Setting Partnership (PSP) timeline illustrating the JLA methodology for the priority setting process.

of small group ranking sessions and large group plenary discussion, where a consensus was established through respectful debate and a deciding vote.

3. Results

The first survey received over 5400 research priorities from 2014 participants, including 1081 people with epilepsy, 464 parents of someone with epilepsy and 271 healthcare professionals. We achieved an equitable level of geographic engagement – participant demographic information can be found in Table 2 [17]. Questions about antiseizure medication, Sudden Unexpected Death in Epilepsy (SUDEP) and epilepsy in women were among the most frequently reported research priorities.

The cleaning and thematic categorisation of the 5400-plus priorities informed the drafting of 110 distinct, answerable research questions. Through the evidence-checking process, 89 of the summary research questions were identified as research uncertainties (i.e. questions "unanswered" or "partially answered" by the existing research literature). A total of 57 summary research questions, each suggested by more than 5 survey participants, were taken forward for prioritisation in the shortlisting survey. Questions proposed for exclusion were reviewed by the steering group before being withdrawn from the process [18].

Following the second survey, 25 summary research questions were shortlisted for discussion and debate at the UK Epilepsy PSP Workshop. 14 of the 25 questions were those featured most in the collective rankings received from each of the key stakeholder groups (Fig. 2; Table 3). In most cases, there was a consensus among stakeholder groups, with overlap in ranking observed across the most highly ranked questions. The ranking of the top 25 questions by each stakeholder group can be viewed in Supplementary IV. All 25 shortlisted research questions were ranked at the workshop, including the Top Ten priorities for research into epilepsy (Figs. 3; 4).

3.1. Priority 1: what are the causes and contributing factors of epilepsy-related deaths, including Sudden Unexpected Death in Epilepsy (SUDEP), and how can these deaths be prevented?

The number one epilepsy research priority is to prevent epilepsy-related death. This question was uncontroversial in the workshop and was championed by patients and clinicians alike. This priority being number one ranked was not a foregone conclusion; there is much that needs to be done to let all people living with epilepsy know about modifiable risks and SUDEP. There are 21 epilepsy-related deaths in the UK every week [19]. The priority asks us to look at direct and indirect causes of all epilepsy-related deaths, of which SUDEP is a significant proportion.

This summary research question was informed by 517 priorities - almost 10 % of all priorities received. Risk of SUDEP was ranked 4th in the Canadian Epilepsy PSP (Question 4: How can the risk of SUDEP (Sudden Unexpected Death in Epilepsy) be reduced in people with epilepsy?) [20]. Although up to 50 % of epilepsy-related deaths are thought to be avoidable [21] the underlying mechanisms of SUDEP are not yet known, making it difficult to determine who is most at risk. This question can be tackled in many different ways: by looking to modify known risk factors for death and SUDEP, such as inequalities and convulsive seizure frequency; identifying new risk factors and mechanisms; development of technological warning solutions. This was supported by the World Health Organisation (WHO) in their Intersectoral Global Action Plan (IGAP) and in the NICE guidelines published in April 2022 [22,23].

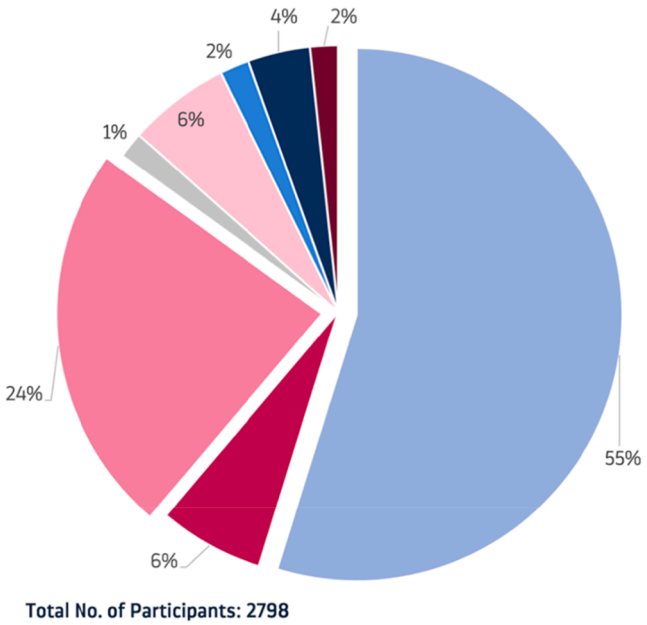
3.2. Priority 2. What underlying mechanisms cause epilepsy in children and in adults?

This is an essential, fundamental question; for an estimated 65 % of epilepsy cases, there is no known cause [19]. A comprehensive

Table 2
First survey participant characteristics – gathering research uncertainties.

	Number of submitted priorities	%
Total participants	**2014**	
Participant groups		
Total people with epilepsy	1081	45.8
Total parents, family, friends, carers and those bereaved	849	36.0
Total health and care professionals	271	11.5
Total epilepsy charity and organisation representatives	74	3.1
Other	79	3.4
Prefer not to say	5	0.2
Age		
0–15	18	0.9
16–25	183	9.2
26–35	268	13.5
36–45	413	20.8
46–55	470	23.7
56–65	372	18.7
66–75	210	10.6
76–85	40	2.0
Over 86	3	0.2
Prefer not to say	8	0.4
Gender		
Female	1431	72.4
Male	525	26.5
Prefer not to say	9	0.5
Prefer to self-describe	13	0.7
Ethnicity		
Asian/Asian British	77	3.9
Black/African/Caribbean/Black British	15	0.8
Mixed/Multiple Ethnicity	49	2.5
Other	28	1.4
White	1773	89.7
Prefer not to say	34	1.7
Location		
England	1673	84.0
Northern Ireland	46	2.3
Scotland	164	8.2
Wales	109	5.5
Type of healthcare professionals		
Adult neurologist	68	12.6
Paediatric neurologist	23	4.3
Epilepsy Specialist Nurse	73	13.5
General Practitioner (GP)	19	3.5
Neuropsychologist/psychologist	36	6.7
Neurosurgeon	7	1.3
Paediatrician	20	3.7
Neurophysiologist	13	2.4
Learning Disability Nurse Specialist	22	4.1
Social worker	14	2.6
Occupational or physical therapist	17	3.1
Dietician	5	0.9
Physician assistant	3	0.6
Pharmacist	3	0.6
Speech therapist	10	1.9
Prefer not to say	22	4.1
Other	186	34.4
Total number of original uncertainties submitted	**5418**	**100**

*Please note: the number of responses to Question 1: Which of the following best describes you? in the first survey [2359] is higher than the total number of responses received [2014] to reflect when more than one category was applicable to participants (e.g. healthcare professional and parent of someone with epilepsy).



Group	Response no.	% of response
Person with epilepsy	1560	54.81
Healthcare professional	182	6.39
Organisation representatives	45	1.58
Parent of someone with epilepsy	676	23.75
Family member or friend of someone with epilepsy	176	6.18
Caregiver or former caregiver of someone with epilepsy	51	1.79
Bereaved family member or friend of someone who had epilepsy	108	3.79
Other	48	1.69

Examples from 'Other':
- Had epilepsy
- Member of the public
- Health services data specialist

These 'Other' responses have been assigned to one of the main groups.

Fig. 2. Question 1: Which of the following best describes you? Demographics from the second, shortlisting survey.

understanding of the neurobiology of epilepsy will ensure we have the highest quality pipeline of novel and targeted treatments, not just aimed at seizure reduction but the holy grail of true anti-epileptogenesis, neuroprotection and preventative measures, like gene therapies. Despite generations of high-quality neuroscience there is much that we need to know about how and why seizures begin [7,19]. One factor limiting our insight is the reliability of pre-clinical epilepsy models employed in research; historically, these have not reflected the breadth of epilepsy syndromes or pathophysiology observed in humans [24,25].

This research uncertainty was informed by 229 priorities. This was highlighted as a research recommendation in the WHO IGAP, with a particular focus on increasing investment in drug development capacity, and featured as a Top Ten research priority in the Canadian Epilepsy PSP (Question 6: What are the brain changes, on a cellular level, that lead to seizure development?) [20,22].

3.3. Priority 3. What impact do epilepsy, seizures and anti-seizure medication (ASMs) have on brain health - including cognition, memory, learning, behaviour and mental health?

The impact of epilepsy, seizures and anti-seizure medication on brain health extends far beyond seizures. Patients with memory or mood disorders may be told that these symptoms may, to a greater or lesser extent, be subsequent to the underlying epilepsy biology, the seizures themselves, or medications [26]. This may be true, but this explanation is unsatisfactory and rarely leads to symptomatic improvement.

It was intended that the Top Ten reflected not only the diversity of the epilepsy community, but also the diversity of our ambition. Whereas some participants focused on the priorities that would ensure greatest transformation, others wished for a more immediate impact. Currently, living with epilepsy commonly means living with anti-seizure medications too, which are imperfect and, for some, bring with them unwanted side effects that are disproportionately likely to affect general brain health. It was felt by many that it was important that learning and mental health were specifically mentioned here, particularly for those people with intellectual disability and epilepsy. This research uncertainty was informed by 491 priorities - almost 10 % of all priorities received. The same was true for the Canadian Epilepsy PSP Top Ten, where several research uncertainties for epilepsy focus on this relationship [20].

3.4. Priority 4. How does epilepsy and epilepsy treatment impact neurodevelopment, and can this be managed or prevented?

Epilepsy is more common in people with an intellectual disability than in the general population; the more severe the intellectual disability, the more likely it will co-occur with epilepsy [27]. The same relationship is true for autism and attention-deficit/hyperactivity disorder (ADHD), with epilepsy being more prevalent in people with autism and ADHD than in the general population [28,29]. When epilepsy and a neurodevelopmental disorder co-occur, which is undoubtedly of greatest importance in children and young people, seizures can often be more difficult to control with existing treatments and anti-seizure medications. There are known genetic factors for both epilepsy and autism; however, the relationship between epilepsy, epilepsy treatment and neurodevelopment is largely unknown. A greater understanding of this neuropsychological relationship and the underlying mechanisms would enable the development of novel treatments and methods to manage epilepsy and neurodevelopmental disorders, broadly improving outcomes for children and beyond (e.g. the impact of foetal exposure to ASMs on developmental outcomes). This research priority overlaps with the recommendations published in the WHO IGAP and the research priorities identified by the British Paediatric Neurological Association (BPNA) Childhood Neurological Conditions PSP [22,30]. This research uncertainty was informed by 352 priorities - 7 % of all priorities received.

3.5. Priority 5. How can targeted, personalised medicine, such as gene therapy, be used to treat and/or prevent epilepsy?

This priority speaks of the community-wide ambition that personalised, cause-focused treatments, such as gene therapy, may offer hope for people with refractory epilepsy and the potential to prevent epilepsy. Research into gene therapies in animal models of epilepsy has shown promising results; however, to fully realise their potential and go beyond their current use in high-cost, high-complexity interventions, such as resective surgery and anti-sense oligonucleotide trials, more clinical research into targeted, personalised medicine is needed [4]. This was also recognised by the WHO IGAP, which highlights the need for increased investment in precision medicine and risk reduction as a research recommendation, as well as having overlap with the Canadian

Table 3
Shortlisting survey participant characteristics.

	Number of submitted responses	%
Total participants	**2798**	
Participant groups		
Total people with epilepsy	1560	54.8
Total parents, family, friends, carers and those bereaved	1011	35.5
Total health and care professionals	182	6.4
Total epilepsy charity and organisation representatives	45	1.6
Other	48	1.7
Age		
0–15	25	0.9
16–25	163	5.9
26–35	334	12.1
36–45	487	17.7
46–55	706	25.6
56–65	628	22.8
66–75	341	12.4
76–85	71	2.6
Over 86	4	0.1
Gender		
Female	2009	72.7
Male	724	26.2
Prefer not to say	20	0.7
Prefer to self-describe	11	0.4
Ethnicity		
Asian/Asian British	87	3.2
Black/African/Caribbean/Black British	33	1.2
Mixed/Multiple Ethnicity	47	1.7
Other	20	0.7
White	2518	91.4
Prefer not to say	50	1.8
Location		
England	2077	83.8
Northern Ireland	73	3.0
Scotland	190	7.7
Wales	138	5.6
Type of healthcare professionals		
Adult neurologist	66	13.1
Paediatric neurologist	27	5.4
Epilepsy Specialist Nurse	86	17.0
General Practitioner (GP)	20	4.0
Neuropsychiatrists/neuropsychologist/psychologist	22	4.4
Neurosurgeon	10	2.0
Paediatrician	20	4.0
Neurophysiologist	19	3.8
Learning Disability Nurse Specialist	10	2.0
Obstetrician/midwife/sonographer/other antenatal support	5	1.0
Social worker	9	1.8
Paramedic	2	0.4
Occupational or physical therapist	7	1.4
Dietician	5	1.0
Physician assistant	1	0.2
Pharmacist	5	1.0
Speech therapist	6	1.2
Prefer not to say	48	9.5
Other	137	27.1
Total number of survey responses submitted	**2798**	**100**

Epilepsy PSP Top Ten, which prioritised the prevention of treatment side-effects and the efficacy of drug combinations [20,22]. This research uncertainty was informed by 159 priorities.

3.6. Priority 6. How can tools, devices and biological markers be used to accurately predict and prevent seizures and the onset of epilepsy?

People living with and affected by epilepsy frequently report the unpredictability of seizures as the most worrying aspect of the condition, which contributes to the burden of disease on healthcare systems: there are over 1000 epilepsy-related emergency admissions every week in England [3]. Despite over three decades of research on seizure forecasting, there remains insufficient evidence to accurately predict seizures and the onset of epilepsy. While EEG is the most prominent biomarker for epilepsy, advances have been made in devices, big data, network theory and mathematical modelling; however, conclusive evidence for more tools, devices and biological markers is still required to make the prevention of seizures and the onset of epilepsy a reality.

This was echoed by the 2022 NICE guidelines, which recommends research into risk prediction tools for all-cause epilepsy-related deaths and second seizures, as well as digital health technologies [31,32]. The need for increased investment into the clinical implementation of diagnostic and prediction technologies was also highlighted as a research recommendation by the WHO IGAP and within the Canadian Epilepsy PSP Top Ten (Question 1: Can genetic markers be used to diagnose and treat epilepsy and seizure disorders?; Question 5: What is the most effective testing protocol for determining causes of seizures and/or a diagnosis of epilepsy or other seizure disorders and to reduce time to diagnosis?) [20,22]. This research uncertainty was informed by 489 priorities - just over 9 % of all priorities received.

3.7. Priority 7. How do hormonal changes in women throughout the lifespan (e.g. puberty, pregnancy, menopause) impact epilepsy, and how can this impact be addressed?

Hormonal changes experienced by women throughout their lifespan are thought to affect the underlying mechanisms of seizures, as well as the medications commonly used to control them [33]. In some cases, these changes can also lead to an increase in seizure frequency. Up to a third of women with epilepsy report catamenial exacerbation of their seizures; however, little research has been conducted on the mechanisms underlying this type of epilepsy [33]. Perimenopausal and pregnancy-related seizure aggravation is recognised; yet research and data on the relationship between epilepsy and the menopause remains limited. Tragically, women with epilepsy are ten times more likely to die during pregnancy than those without the condition [34]. This priority overlaps with the research recommendations published by the 2022 NICE guidelines, the WHO IGAP and the Canadian Epilepsy PSP (Question 13: Is there a relationship between hormonal changes (e.g. puberty, menopause, pregnancy) and seizure onset and/or frequency, and what are the effects of seizures during pregnancy?) [20,22,23] This research uncertainty was informed by 204 priorities.

3.8. Priority 8. How can quality of life be improved for people with epilepsy, their families and carers, including those bereaved by epilepsy?

The personal cost of having epilepsy is substantial, with 87 % of people with epilepsy reporting that the condition affects their day-to-day lives, interrupting their employment and impacting their independence and mental health, as well as that of their families and carers [3]. According to the 2019 National Patient Experience Survey, 48 % of people living with epilepsy were unable to continue their work as normal after their diagnosis.

The participants of the UK Epilepsy PSP Workshop felt that because many neglected areas contribute to quality of life, from exercise to sleep, that this question needed highlighted as part of the Top Ten. Research into the diagnosis, treatment, management and prevention of epilepsy is urgently needed to lower the impact of epilepsy on quality of life, which encompasses a broad range of topics, from exercise to sleep, and recognises the ramifications for parents, families, friends and carers of

Fig. 3. UK Epilepsy PSP Top Ten priorities for research into epilepsy.

those with epilepsy, as well as those bereaved by epilepsy. Quality of life is also an important outcome measure, as highlighted by the WHO IGAP, which recommends increased investment for the development and utilisation of core indicators [22,35]. This research uncertainty was informed by 65 priorities.

3.9. Priority 9. What causes drug-resistant (refractory) epilepsy, and how can it be best treated?

Evident by the response of the UK epilepsy community, as well as the 2022 NICE guidelines, the WHO IGAP and Canadian Epilepsy PSP, who all cited this as a research priority. For some people, breakthroughs in medication adherence will be needed to improve apparent drug-resistance; for others, it will be improvements in diagnosis that will allow us to prescribe the best possible drugs for the individual – and earlier. Other participants considered this question to address a more fundamental biological concept that could lead to either better drug delivery systems or a revolution in therapeutics. This research uncertainty was informed by 314 priorities – 6 % of all priorities received.

3.10. Priority 10. How can big data analysis, through artificial intelligence (AI) and machine learning, aid the diagnosis and management of epilepsy?

Big data research uses large, complex datasets, analysed using new technology, to provide robust and reliable answers that would otherwise be unobtainable. The exploitation of routinely collected data via cleaned, structured and coded hubs will allow us to ask and answer clinical questions about natural history and therapeutics. Work is currently under-way to develop a harmonised UK clinical record standard for epilepsy, led by the Professional Records Standards Body, the benefits of which could be employed for both rare and common epilepsies in the future [36]. Many of the clinical participants felt that the timelines for seeing the benefits of AI within the NHS are condensed and

Fig. 4. UK Epilepsy PSP priorities ranked 11–25 for research into epilepsy.

that decision-support tools and advanced diagnostics are nearer our grasp than previously thought.

Given the large population of people living with epilepsy, the use and analysis of routinely collected health data and new technology, such as AI and machine learning, has the potential to improve the accuracy of diagnosis, understanding of causes of epilepsy, informing seizure prediction and prevention, and guiding personalised treatment choices – as highlighted by the 2022 NICE guidelines and the WHO IGAP, which calls for increased investment in big data and population level research [22, 23]. Why do we need big data? If small data could have answered the questions, we would know it by now. This research uncertainty was informed by 25 priorities from the UK epilepsy community.

4. Discussion

We present the UK Epilepsy PSP research priorities. There is notable overlap between the UK Epilepsy PSP Top Ten and the evidence-based research recommendations provided by the World Health Organisation (WHO) in their Intersectoral Global Action Plan (IGAP) [22] and in the National Institute of Health and Care Excellence (NICE) guidelines [23], the research interests of the UK Department of Health and Social Care [37], and the Top Ten research priorities of the Canadian Epilepsy PSP, which concluded in September 2021 [20]. The research uncertainties presented here, including the Top Ten and priorities 11 to 25, reflect the diversity of the UK epilepsy and associated condition community who engaged with the PSP, with research themes ranging from the impact of hormones on epilepsy in women to the relationship between sleep, epilepsy and seizures; personalised medicine to improving existing and developing novel anti-seizure medications; big data to improving quality of life for those affected by epilepsy, including those bereaved by epilepsy.

We acknowledge several limitations typical of this style of research. In keeping with JLA methodology, basic scientists were not invited to participate. This ensures consistency across and maximum learning from

PSPs, while also addressing the power imbalance commonly seen in research, which is largely skewed toward the priorities of the pharmaceutical industry and interests of non-clinical researchers. Although the total number of responses received for the both the first survey (2014) and second, shortlisting survey (2987) were substantial, there was a paucity of responses from men, creating the potential for gender bias in the results of both surveys. Also, while postcode information (first 4 digits only) was collected to ensure UK-wide representation was achieved, these data were not analysed to provide a metric of the participants' socioeconomic background, but this will be analysed in future studies of these data. Furthermore, due to resource restrictions, we were unable to ensure that people with intellectual disability and children with epilepsy were able to respond independently. Instead, we relied upon the support of parents and carers to complete and submit the forms on their behalf. This was also a limitation of the Workshop, where the priorities of children with epilepsy and those with intellectual disability were represented through their parents and carers. Moreover, while there was representation within both surveys from individuals over 76 years individuals, due to limited resources, both surveys were available only online, resulting in a lack of involvement from individuals over 76 years. We aimed to overcome this limitation by offering the opportunity for individuals who lacked confidence completing the survey online to call a member of the research team, where they could provide their responses to both surveys over the phone. We also provided an email address that could be contacted at all times with any questions or requests for help. As a result, and despite these limitations, we were able to achieve a consensus and receive representation from a large proportion of the UK epilepsy and associated condition community throughout the priority setting process.

While the UK Epilepsy PSP was funded, led and managed by the Epilepsy Research Institute UK (formerly Epilepsy Research UK), decisions throughout the priority setting process were independent from the Institute and its research team. Given the breadth of involvement throughout the 18-month project – from the Steering Group, comprised of individuals from various institutions and organisations, to the UK epilepsy community, who provided the priorities, shortlisted the resulting questions and ranked the Top Ten during the Workshop – all possible conflicts of interest arising from any individuals or organisations involved were sought, logged, and managed.

Research to address the Top Ten research priorities will have both immediate impact and ensure long-term transformation of the diagnosis, treatment, management and prevention of epilepsy, both locally and globally. We know that PSPs can lead to increased research funding, which is so urgently needed for epilepsy in light of research funding inequalities. Here, we provide the evidence needed to convince government and institutional funders to invest more in epilepsy research and a Top Ten that will encourage researchers to develop studies in response to the priorities of people living with epilepsy. It is our ambition that this PSP will provide the evidence of need and priorities to support research development, shaping the research agenda and affecting change for research into epilepsy.

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*The Epilepsy Research Institute is a company registered in England and Wales with company number 4873718. Registered Office: Epilepsy Research Institute, Churchill House, 35 Red Lion Square, London, WC1R 4SG.

Conflicts of interest

RHT (Clinical Lead) has received honoraria from Angelini, Bial, Eisai, GW Pharma, Paladin, NeuraxPharm, Sanofi, Takeda, UCB Pharma, UNEEG, Zogenix, and unrestricted research funding from Angelini/Arvelle and UCB Pharma, independent of this project.

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Data availability statement

The 25 research uncertainties taken to the final workshop, engagement summary, question verification form and data management spread sheet are available to view on the James Lind Alliance website at the following address: https://www.jla.nihr.ac.uk/priority-setting-partnerships/epilepsy/

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Collaborating UK-wide epilepsy charities:
Epilepsy Action
Epilepsy Society
International League Against Epilepsy (ILAE) British Branch
SUDEP Action
Young Epilepsy

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.seizure.2024.12.008.

References

[1] Wigglesworth S, et al. The incidence and prevalence of epilepsy in the United Kingdom 2013-2018: a retrospective cohort study of UK primary care data. Seizure Eur J Epilepsy. 2023;105:37–42. https://doi.org/10.1016/j.seizure.2023.01.003.
[2] GBD 2021 Nervous System Disorders Collaborators. Global, regional, and national burden of disorders affecting the nervous system, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021 [published correction appears in

Lancet Neurol. 2024 Mar 18]. Lancet Neurol 2024;23(4):344–81. https://doi.org/10.1016/S1474-4422(24)00038-3.
[3] Epilepsy Research Institute. #ALifeInterupted campaign and report, https://epilepsy-institute.org.uk/eri/about-us/alifeinterrupted/; 07 October 2020 [accessed 08 April 2024].
[4] EpiPM Consortium. A roadmap for precision medicine in the epilepsies. Lancet Neurol 2015;14(12):1219–28. https://doi.org/10.1016/S1474-4422(15)00199-4.
[5] Epilepsy Foundation. Types of seizure, https://www.epilepsy.com/what-is-epilepsy/seizure-types; 20 March 2014 [accessed 08 April 2024].
[6] International League Against Epilepsy (ILAE). Classification and definition of epilepsy syndromes, https://www.ilae.org/guidelines/definition-and-classification/classification-and-definition-of-epilepsy-syndromes; 03 May 2022 [accessed 08 April 2024].
[7] NICE Guidelines. Epilepsy diagnosis and management, https://www.nice.org.uk/guidance/cg137; 11 January 2012 [accessed 08 April 2024].
[8] Partridge N., Scadding J. The James Lind Alliance: patients and clinicians should jointly identify their priorities for clinical trials. 2004;364(9449):1911–9210.1016/S0140-6736(04)17494-1.
[9] James Lind Alliance. The PSPs, https://www.jla.nihr.ac.uk/priority-setting-partnerships/; 02 September 2015 [accessed 08 April 2024].
[10] National Institute for Health and Care Research. Identify research needs, https://www.nihr.ac.uk/partners-and-industry/charities/identify-research-needs.htm; 10 December 2019 [accessed 08 April 2024].
[11] Thomas RH, et al. Identifying and prioritising epilepsy treatment uncertainties. J Neurol Neurosurg Psychiatry 2010;81(8):918–21. https://doi.org/10.1136/jnnp.2009.192716.
[12] Hughes EG, Thomas RH. Epilepsy treatment priorities: answering the questions that matter. J Neurol Neurosurg Psychiatry 2017;88:999–1001. https://doi.org/10.1136/jnnp-2016-315135.
[13] UKRI Medical Research Council. HRA NHS research ethnics committee (REC) decision tool, https://www.hra-decisiontools.org.uk/ethics/; 10 April 2020 [accessed 08 April 2024].
[14] Singh A, et al. Canadian epilepsy priority-setting partnership: toward a new national research agenda. Epilepsy Behav 2022;130:108673. https://doi.org/10.1016/j.yebeh.2022.108673.
[15] James Lind Alliance. Epilepsy (Canada) quantitative question verification form, https://www.jla.nihr.ac.uk/documents/epilepsy-canada-quantitative-question-verification-form/28658; 15 September 2021 [accessed 08 April 2024].
[16] James Lind Alliance. Epilepsy (Canada) qualitative question verification form, https://www.jla.nihr.ac.uk/documents/epilepsy-canada-qualitative-question-verification-form/28654; 15 September 2021 [accessed 08 April 2024].
[17] Gov.UK. Population of England and Wales, https://www.ethnicity-facts-figures.service.gov.uk/uk-population-by-ethnicity/national-and-regional-populations/population-of-england-and-wales/latest; 22 December 2022 [accessed 08 April 2024].
[18] Gargon E, et al. Higher number of items associated with significantly lower response rates in COS Delphi surveys. J Clin Epidemiol 2019;108:110–20. https://doi.org/10.1016/j.jclinepi.2018.12.010.
[19] Epilepsy Research Institute. Epilepsy statistics, https://epilepsy-institute.org.uk/eri/about-epilepsy/epilepsy-statistics/; 05 March 2020 [accessed 08 April 2024].
[20] Ontario Brain Institute. Epilepsy priority setting, https://braininstitute.ca/programs-opportunities/setting-research-priorities/epilepsy-psp; 15 April 2021 [accessed 08 April 2024].
[21] Mbizvo GK, et al. Epilepsy-related and other causes of mortality in people with epilepsy: a systematic review of systematic reviews. Epilepsy Res 2019;157:106192. https://doi.org/10.1016/j.eplepsyres.2019.106192.
[22] World Health Organisation. Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031, https://www.who.int/publications/i/item/9789240076624 20 July 2023 [accessed 08 April 2024].
[23] National Institute of Health and Care Excellence (NICE). Epilepsies in children, young people and adults, https://www.nice.org.uk/guidance/ng217; 27 April 2022 [accessed 08 April 2024].
[24] Kandratavicius L, et al. Animal models of epilepsy: use and limitations. Neuropsychiatr Dis Treat 2014;10:1693–705. 10.2147%2FNDT.S50371.
[25] Javaid MS, et al. Human *in vitro* models of epilepsy using embryonic and induced pluripotent stem cells. Cells 2022;11(24):3957. https://doi.org/10.3390/cells11243957.
[26] Josephson CB, Jetté N. Psychiatric comorbidities in epilepsy. Int Rev Psychiatry 2017;29(5):409–24. https://doi.org/10.1080/09540261.2017.1302412.
[27] Epilepsy Society. Learning disabilities, https://epilepsysociety.org.uk/learning-disabilities; 16 February 2020 [accessed 08 April 2024].
[28] Autistica. Epilepsy and autism, https://www.autistica.org.uk/what-is-autism/signs-and-symptoms/epilepsy-and-autism; 11 September 2017 [accessed 08 April 2024].
[29] Epilepsy Foundation. Epilepsy and ADHD, https://w.w.w.epilepsy.com/complications-risks/moods-behavior/adhd#:~:text=Attention-deficit%2Fhyperactivity%20disorder%20(,disorder%20in%20children%20with%20epilepsy; 29 July 2018 [accessed 08 April 2024].
[30] British Paediatric Neurological Association. Childhood neurological conditions priority setting partnership, https://bpna.org.uk/?page=childhood-neurology-priority-setting-project; 16 June 2012 [accessed 08 April 2024].
[31] Jha A, et al. Sudden unexpected death in epilepsy: a personalized prediction tool. Neurology 2021;96(21):e2627–38. https://doi.org/10.1212/WNL.0000000000011849.
[32] National Institute for Health and Care Excellence (NICE). Quality and outcomes framework (QOF) indicator development programme: epilepsy briefing paper, https://w.w.w.nice.org.uk/Media/Default/standards-and-indicators/qof%20indicator%20key%20documents/NM03%20Briefing%20paper%20to%20the%20committee%20on%20Epilepsy.pdf; 16 June 2009 [accessed 08 April 2024].
[33] Stephen LJ, et al. Management of epilepsy in women. Lancet Neurol 2019;18(5):481–91. https://doi.org/10.1016/s1474-4422(18)30495-2.
[34] Edey S, Moran N, Nashef L. SUDEP and epilepsy-related mortality in pregnancy. Epilepsia 2014;55(7):e72–4. https://doi.org/10.1111/epi.12621.
[35] Mitchell JW, et al. Development of an international standard set of outcomes and measurement methods for routine practice for adults with epilepsy: the international consortium for health outcomes measurement consensus recommendations. Epilepsia 2024;65(7):1916–37. https://doi.org/10.1111/epi.17971 (Copenhagen).
[36] Professional Record Standards Body (PRSB). Epilepsy discovery report May 2023, https://theprsb.org/wp-content/uploads/2023/08/Discovery-Report-Epilepsy-Information-Standard.pdf; 16 May 2023 [accessed 04 September 2024].
[37] Department of Health and Social Care (DHSC). DHSC's areas of research interest, https://www.gov.uk/government/publications/department-of-health-areas-of-research-interest/department-of-health-areas-of-research-interest; 25 January 2023 [accessed 08 April 2024].