Priorities for epilepsy research:

A briefing report

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No one should go it alone

Table of Contents

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1.0 – Introduction

1.1 - Executive Summary

In summary, the major challenges reported by key experts in epilepsy research included understanding the causes of epilepsy, recognising the urgent need to change the approach in generating new drugs, the difficulty in diagnosing and treating comorbidities, the lack of funding and community attitudes, ensuring there is a next generation of leaders, engaging patients to take part in research, and breaking down the divide between community service organisations and the epilepsy research community.

Overall, there were 10 aspects across 4 different types of epilepsy research areas identified with high priority (in no particular order) –

Pre-clinical research

1. Understanding the causes, risk factors and genetic basis of epilepsy
2. Prevention and/or cure of epilepsy

Applied/Translational research

3. Translating progress made in research into treatments in clinical practice, and improving research infrastructure to facilitate translation

Clinical research

4. To improve health care, including access to health services and treatments
5. Risk factors for injuries, status epilepticus, avoidable death, SUDEP and suicide
6. Understanding the experience of patients undergoing genetic testing
7. Limit or prevent adverse consequences of seizures and their treatment across the lifespan (e.g. Avoidable death, SUDEP, comorbidities)

Social/community

8. Improving public knowledge, awareness, and attitudes towards epilepsy
9. Improving education for patients and family and for health professionals (social/community research)
10. Mobility issues, e.g. inability to drive

There was agreement by professionals and consumers that 3 groups of people with other established conditions and epilepsy should be considered with high priority –

- People who have had an acquired brain injury, e.g. a stroke or traumatic brain injury
- People with autism
- People with intellectual disabilities.

1.2 - Epilepsy in Australia

Epilepsy is a lifelong neurological condition estimated to affect over 65 million people worldwide (Ngugi et al, 2011 and Bell, Neligan and Sander, 2014). The formal definition of epilepsy endorsed by the International League Against Epilepsy (ILAE, the organisation for medical professionals worldwide) is having at least two unprovoked seizures, or with at least one unprovoked seizure followed by at least two over the next ten years, and/or having a diagnosis of epilepsy (Fisher et al, 2014). Currently in Australia, it is still not known exactly how many people are newly diagnosed with epilepsy each year (incidence), or how many people are living with epilepsy amongst the general population (prevalence). However, there are some estimates available that provide some insight into how many people are affected by epilepsy (in Australia).

- In 2006, the prevalence of epilepsy in Australia was estimated at **268,473 people** or **1 in every 73 Australians** using data from the 2004 - 2005 National Health Survey (when underreporting was taken into consideration, i.e. not disclosed or known to have the condition) (Brown, 2011). More recent estimates report that approximately **99,800 people** in Australia have epilepsy or **4.4 cases per 1000 people** are affected using specific population data (from a Tasmanian epilepsy register) (D'Souza et al, 2012).
- Data from the Australian Institute of Health and Welfare (AIHW) in 2011 reported that epilepsy was rated as the second highest neurological condition contributing to 7% of the total burden of disease in Australia (AIHW, 2016a, b). The total burden rate for epilepsy was reported as **1.9 per 1,000 people** for non-indigenous Australians and even higher in indigenous Australians at **5.3 per 1,000 people**.
- Epilepsy contributed to the highest proportion of disability adjusted life years (DALYs) in children aged under 15 (46%), adolescents and young adults aged 15–24 (45%) and in adults aged 25–44 (40%). DALYs are defined as a 'measure (in years) of healthy life lost, either through premature death defined as dying before the ideal life span (YLL) or, equivalently, through living with ill health due to illness or injury (YLD)'.

1.3 – The relevance of research in epilepsy

Outcomes for people with epilepsy, both short and long-term, are important to ensure full and meaningful lives and a reduced burden to the healthcare system and society. Health professionals and community service providers work hard to enable these outcomes to be optimal for each individual using good clinical practice. It is well known that good clinical practice and policy is based on evidence derived from high quality and high impact research.

The management of epilepsy has for the most part focused on controlling or eliminating seizures so a person's quality of life is improved. A significant number of research studies have therefore explored potential targets for drug treatment for seizure control. There are a small proportion of people with epilepsy who cannot achieve any control or freedom from their seizures as drug treatment has failed (approximately 30 – 40%). This can be due to having the wrong diagnosis, wrong drug, or wrong dose provided, or lifestyle issues, e.g. poor drug compliance, or alcohol or drug abuse (Kwan, Schachter and Brodie, 2011). It can also be due to the limited range of drugs available for treatment. Over the last couple of decades there have been about 26 new targets discovered as possible drugs for treatment. Unfortunately, most of them did not enter the market

and those that did were only effective for certain types of epilepsy. Further, there was no major improvement in prognosis for people with these new drugs compared to those already available. Due to these findings, it is very important to carry out research to discover better treatments which will improve outcomes for people living with this chronic condition.

1.3.1 - Epilepsy Research

Epilepsy management first began **in Victoria** in 1907 with a colony-farm for people with epilepsy in Melbourne. The farm relocated in the 1960s to the grounds of the current Austin Hospital in Heidelberg. In the 1970s, a Comprehensive Epilepsy Program was developed and established by Peter Bladin in the Neurology Department. This was an important milestone for providing specialised care for people with epilepsy, as well as detailed data about the condition, paving a way for epilepsy research.

Epilepsy Research Centre (Melbourne Brain Centre)

The Epilepsy Research Centre is located within the Melbourne Brain Centre (Austin Health, Heidelberg) in Victoria. It is directed by Professor Samuel Berkovic and has several research programs in the areas of genetics (molecular, clinical and paediatric), outcomes (treatment and psychosocial), neurocognition, neuroimaging and clinical trials. The research centre is made up of clinical researchers and scientists from Austin Health, the Florey and Melbourne Neuroscience Institutes, and the Department of Medicine at the University of Melbourne. It also has collaborations with the Women's and Children's Hospital in Adelaide, the University of Adelaide, the Melbourne Brain Centre at the Royal Melbourne Hospital and the Royal Children's Hospital, Melbourne, and the University of Queensland.

Research projects undertaken at the centre have uncovered some major discoveries, including the identification of several epilepsy genes, genetic epilepsy syndromes (e.g. Autosomal Dominant Nocturnal Frontal Lobe Epilepsy (ADNFLE) and Generalised Epilepsy with Febrile Seizures Plus (GEFS+)), understanding the characteristics of memory disturbances, and the development of protocols for better post-operative outcomes.

http://www.epilepsyresearch.org.au/

Royal Melbourne Hospital

A Comprehensive Epilepsy Program has also been established at the Royal Melbourne Hospital directed by Professor Patrick Kwan. Within this service are research programs relating to genetics, treatment outcomes, neuropsychiatry, neuropsychology and dietary therapies. The Epilepsy and Neuropharmacology group, led by Professor Terence O'Brien, conducts both basic and clinical research (focusing on applied or translational research) to understand what determines treatment responses and outcomes and also what causes or contributes to neuropsychiatric co-morbidities in people with epilepsy. An international collaborative project exploring anti-epileptogenic therapy using bioinformatics is also being conducted.

Another significant project that is also undertaken by the program is the Australian Pregnancy Register for women on antiepileptic medication (www.apr.org.au). This voluntary, nationwide observational register (started in 1998) collects information about pregnant women with epilepsy, treated and untreated, to determine which medications are safest for their baby while protecting them from seizures. Currently, they have obtained outcomes for 2129 women, recording 89 live birth defects, 18 still births, 55 spontaneous abortions, 1 neonatal death and 36 sets of twins.

http://medicine.unimelb.edu.au/research-groups/medicine-and-radiology-research/royal-melbourne-hospital/epilepsy-and-neuropharmacology

Royal Children's Hospital

The Department of Neurology at the Royal's Children's hospital has an epilepsy and first seizure clinic. In its associated Murdoch Children's Research Institute paediatric epilepsy research is undertaken within the Neuroscience group, led by Associate Professor Richard Leventer. Basic and clinical research projects are conducted focusing on severe epilepsies of infancy (genetics), neuroimaging, clinical trials (antiepileptic medications), surgery and brain malformations such as focal cortical dysplasia and tuberous sclerosis.

https://www.mcri.edu.au/research/themes/clinical-sciences/neuroscience-research

St Vincent's Hospital

Within the neurology department at St Vincent's Private Hospital and the Bionics Institute, Professor Mark Cook and Associate Professor Chris Williams lead an epilepsy research program focusing on neuroimaging, surgical planning and experimental models of epilepsy and seizure prediction. Recent translational research has developed a new implant ('The Minder') to monitor seizures over long periods of time. Safety and effectiveness is currently being tested, but it is envisaged that this will be a useful technology to alert people with epilepsy when a seizure will occur.

http://www.bionicsinstitute.org/research/neurobionics/Pages/A-new-approach-to-epilepsy-diagnosis.aspx

Australian Epilepsy Research Register

To gather more data to inform improvements of services (and supports) and to a gain a better picture of the social impact on people living with epilepsy in Australia, a register was established in 2006 by social researchers for the Epilepsy Foundation (EF). Initially data was collected in the register from Victorians and then expanded to all Australian states in 2011 with the register being referred to as the Australian Epilepsy Research Register (AERR).

Participants on the register join voluntarily and can choose to leave at any time. When people join the register they are informed that their privacy will be respected and their details will not be shared

with anyone outside the EF research unit. The Register complies with Deakin University Human Research Ethics Committee.

A total of 750 people were recorded on the register in 2010. A survey (Wave 2) was distributed to participants on the register to explore their **needs, perceptions and experiences of living with epilepsy** in which 343 people participated – 72% people were living with epilepsy and 28% were family members or a representative. In 2013, there were a total of 883 people recorded on the register. Participants were surveyed on the **social impact of epilepsy** (Wave 3) - 324 people participated, 75% people were living with epilepsy. Collectively the results from both surveys showed that –

- Many respondents had **lower incomes** than the Australian average, and consequently faced out of pocket costs for their health care which they may not have been able to afford.
- A significant number had been **hospitalised for injuries** due to their seizures (62 – 64%), and many reported **taking multiple anti-epileptic drugs** at the one time (56 - 62%).
- Additionally, a **high proportion** reported having **anxiety** (46.9%) and **depression** (28.7%).

In 2017, there were a total of 1,328 eligible participants on the Australian Epilepsy Research Register. In all 393 of these completed the Wave 4 survey (response rate approximately 30%). Most were people with epilepsy (292) whilst 91 completed the survey on behalf of someone with epilepsy.

There were two distinct groups in the sample. The first had well controlled epilepsy or epilepsy in remission, and the second largely uncontrolled epilepsy with a greater need for support services.

The following were characteristics of the demographics and effects of epilepsy reflecting a level of need in these people.

- Employment and financial difficulty characterise a significant proportion despite high numbers with a university level education. Less than half were in paid employment
- Nearly one third were renting.
- Most received $250 - $499 per week in weekly individual income (see Figure 2) and more than one quarter could not pay their *electricity, gas or telephone bills* on time. Therefore there are unmet needs in the epilepsy community, especially for those with uncontrolled epilepsy.
- More than half had experienced *seizures* over the past year; with 14.8% having one or more per month; and 16% having one or more per week.
- 131(36.6%) had been *injured* as a result of a seizure in the past 3 years. 37% of these required hospital treatment
- 53(14.8%) had had *surgery* for epilepsy
- 44.5% said epilepsy affected their *ability to drive* a lot; for 35.5% it affected the *kind of paid work they could do* a lot, and for 33% it affected *their plans and ambitions for the future*
- The average *Quality of life* score in Wave 4 was 56.60 (on a scale of 0-100). This was slightly higher than that measured in Wave 2 (2010)
- The average *Overall health* score was 59.94 (on a scale of 0 – 100) which was lower than that reported in Wave 2 (2010)
- The most needed equipment was *emergency ID bracelets*, followed by *seizure alarms* and *seizure monitors*. Further 39 respondents needed but did not have an *anti - suffocation*

> *pillow*, slightly fewer required but did not have *other equipment such as lifting aids*, and fewer *emergency door hinges* (see below)

- The services needed most when initially diagnosed were *a neurologist, advice about treatment options and side effects, a GP* and *timely access to diagnostic investigations*
- *Psychological assistance* when first diagnosed*, family counselling* and *relationship counselling* were services not available but needed by many
- People felt they needed more support with *t*ransport (n=84); *attending/making appointments* (n=53); *social activities* (n=52); and *domestic duties* (n=49)
- Partner/spouse provide support for 42.4%; other family/friends for 32.9%; and 10.5% had no one to help

The WHO Resolution on the Global Burden of Epilepsy has set an agenda for member states and other partners to allocate resources to epilepsy research to promote action in the fight against epilepsy (Covanis et al, 2015). The Epilepsy Foundation recognises and supports this call to action.

The aim of the current report is to provide all the available evidence needed for the Epilepsy Foundation to develop a research framework and plan to establish a research program as part of one of its key strategic priorities.

The research program will include several components, one of which is a research funding scheme. This will be designed to support and develop high quality and outstanding epilepsy research.

2.0 – Priorities for Epilepsy Research

2.1 – Data collection and analysis

This report has utilised 3 different approaches to obtain data on priorities for epilepsy research to inform the development of a framework:

- A comprehensive review of all evidence from published studies in the literature (the last 10 years)
- Consultations conducted with key experts in epilepsy research
- A survey of the views of people in the epilepsy community and health professionals about different areas of epilepsy research

Comprehensive review of published studies from the literature

A systematic and comprehensive search for research publications and reports was performed in 4 electronic medical databases – MEDLINE (Ovid), EMBASE (Ovid), PsycINFO (Ovid) and CENTRAL (Cochrane Library) using the search terms epilepsy and seizures combined with research priorities and priority setting. An example of the search strategy for MEDLINE is shown below –

1. exp Epilepsy/
2. exp Seizures/
3. epileptic$.mp.
4. seizure$.mp.
5. or/1-4
6. research priorit$.mp.
7. priority setting.mp.
8. 6 or 7
9. 5 AND 8
10. Limit 9 to year [2006 – current] and English

A total of 79 citations were identified and after screening (using pre-determined inclusion/exclusion, see Appendix) 17 citations were reviewed in full text, of which 12 were included. A search of the grey literature was also performed in Google Scholar, the International League Against Epilepsy and International Bureau for Epilepsy websites and key journals in the field (Epilepsia, Epilepsy & Behavior and Seizure) using the words research priorities and epilepsy. The first 100 relevant citations were screened, 42 full text citations were identified and 5 were included. After de-duplication, 7 citations were included for data extraction and analysis.

The data extracted for each citation included the a) Perspective – e.g. biomedical, medical, community, etc.), b) Description (including aims, scope, methods), c) Results and d) Conclusion (see Appendix). The priorities from each citation were summarised in a table to provide an overview.

Consultations

Consultations were conducted with key individuals with experience in epilepsy research (12 people were invited from key research centres) to understand what their perspectives were on research and the role of the Epilepsy Foundation in developing a framework for a research program. The consultations were approximately 30 minutes and involved a semi-structured approach with the following questions:

- Briefly describe your experience in the field of epilepsy research
- From your perspective, what are the big challenges in epilepsy research today?
- What priorities do you think are important in epilepsy research in Australia?
- How do you think a research framework could best address these challenges?

Prompts were also used as follows:

- Can you tell me a bit more about that
- Earlier you mentioned…..what was that like for you?

Notes were recorded and a content analysis was performed to extract priorities and any key themes.

Survey of people in the epilepsy community and health professionals

A survey was developed to ask the community views of people with epilepsy, their family members/carers or friends, health professionals and researchers about what areas of epilepsy research are considered important to them. It was necessary to obtain the perspectives of all relevant stakeholders to guide the research framework to ensure that it is well-rounded and based on quality research methods.

The survey questions were informed by other surveys directly from the epilepsy field (ILAE Research Priorities Survey, 2016) and also from other similar neurological areas (MS Research Australia Community Consultation, 2016) following a search on the internet. Feedback was also sorted and provided by an independent researcher with experience in survey methods (CW). The final questions for the survey are available in the Appendix of this report.

People were invited to participate through the Epilepsy Foundation facebook page and the Research Newsletter using a link to Survey Monkey (https://www.surveymonkey.com/r/3L33CZH). Professionals were invited to participate through an email invitation by the Epilepsy Society of Australia using the same link to Survey Monkey.

2.2 – Results of the analysis

The results of each approach will now be discussed here, but it should be noted that there is some implicit bias due to the interests of the background of each group and type of stakeholder, e.g. people with epilepsy and their family members, neurologists, funding organisations, researchers, medical professional representative groups etc. which should be considered when interpreting the results.

Perspectives on research priorities gathered by a summary of research publications

Seven relevant publications were identified, 4 from the USA, 1 from Europe, 1 from Australia and 1 from the Asia-Oceania region. The perspectives of the publications included all areas – biomedical, medical, and community/social research (4 publications), public health (1 publication), biomedical (1 publication) and applied social/community research (1 publication). The publications are listed below with any related articles in order from the oldest to the most recent.

Included studies

1. Walker, C. Researching the personal impact of epilepsy. Victoria, Australia, Chronic Illness Alliance, 2007: 1 - 30.
2. IOM (Institute of Medicine). Epilepsy across the spectrum: Promoting health and understanding. Washington, DC: The National Academies Press. 2012.
    o England, M et al. Epilepsy across the spectrum: Promoting health and understanding. A summary of the Institute of Medicine report. Epilepsy & Behavior. 2012; 25: 266-276.
3. NINDS Benchmarks for Epilepsy Research, 2014, http://www.ninds.nih.gov/research/epilepsyweb/2014Benchmarks-Final_PDF.pdf
    o Kelley, M et al. The NINDS epilepsy research benchmarks. Epilepsia. 2009; 50(3): 579-582.
4. Baulac, M et al. Epilepsy priorities in Europe: a report of the ILAE-IBE Epilepsy Advocacy Europe Task Force. Epilepsia, 2015; 56 (11): 1687-1695.
    o Perucca, E et al. Epilepsy Research Priorities in Europe. 2013, Forum report
    o Baulac and Pitakenen, Research priorities in epilepsy for the next decade—A representative view of the European scientific community: Summary of the ILAE Epilepsy Research Workshop, Brussels, 17–18 January 2008. Epilepsia. 2009; 50(3):571–583.
5. Kwan, P., et al. Research priorities in epilepsy for the Asia-Oceanian region. Epilepsia. 2015; 56(5): 667-673.
6. Dumanis, S et al. Epilepsy: a giving smarter guide. Milken Institute, 2016. http://www.ilae.org/Visitors/Centre/documents/GivingSmarter-prioritizefundraising.pdf
    o Dumanis, S et al. Opportunities for epilepsy: Outcomes of the Milken Institute State of the Science Retreat. Epilepsy & Behavior. 2017; 68: 174 – 176.
7. Sahin, M., et al. Advances and future directions for tuberous sclerosis complex research: Recommendations from the 2015 strategic planning conference. Pediatric Neurology. 2016; 60: 1-1.

Other research efforts

The comprehensive search also identified an initiative currently in progress from the International League Against Epilepsy (ILAE). The ILAE has commissioned a task force to develop Global Research Priorities for epilepsy research. This task force have put together a survey containing a list of research priorities. This survey is currently open to the global community, however the results are not available at this time (https://www.surveymonkey.com/r/respriority).

Overview of the findings

From all the included studies identified, under the category of pre-clinical (biomedical) research (Table 1):

- 'Understanding the causes, risk factors and genetic basis' had the *highest* priority,
- 'Identifying new targets for innovative diagnostics and treatments' and 'Prevention and/or cure of epilepsy, e.g. biomarkers, new targets' were ranked with *moderate* priority, and
- 'Understanding epilepsy in the developing brain' with the *lowest* priority (1 publication only).

Under the category of clinical research (Table 1):

- 'Surveillance and population-based studies (data standards, screening and analytical tools, longitudinal studies on outcomes)', 'Improving health care and therapy (treatment options, reduce side-effects, access, utilisation, outcomes, decision-support tools)', 'Personalized medicine' and 'Limit or prevent adverse consequences of seizures and their treatment across the lifespan (PNES, SUDEP, quality of life, comorbidities, fetal/neonatal, intellectual disabilities)' were ranked with *moderate* priority, and
- 'Costs of Care (hospitalisations, emergency department use)', 'Collaborative service models', 'Identify interventions for comorbidities (mental health) and improvements in adverse outcomes', Risk factors for injuries, suicide, status epilepticus and SUDEP' and 'Population type issues (specific etiologies and comorbidities) - paediatric and aging populations, traumatic brain injury (TBI) and cognitive dysfunction' were all ranked with *low* priority

Under the category of social/community research (Table 1):

- 'Improving public knowledge, awareness and attitudes towards epilepsy (discrimination, disclosure)', 'Improving patient and family education, information, expectations and communication (information needs)', 'Employment (vocational rehabilitation programs) and access to education' and 'Quality of life issues (culture, resilience)' were ranked with *moderate* priority
- 'Mobility issues (inability to drive)', 'Sport (Social participation)', and 'Improving health professional education' were all ranked with *low* priority.

Under the category of research practice (Table 1):

- 'Translational studies and clinical trials' and 'Improve research infrastructure and capacity' were ranked with *moderate* priority
- 'Promote pre-clinical/clinical collaborations' and 'Models of funding for community service providers and collaborations' were ranked with *low* priority

Table 1 – Overview of all the research priorities identified by publication (not in any rank order)

Priority	Chronic Illness Alliance	Institute of Medicine	NINDS	ILAE-IBE Europe Task Force	ILAE Commission on Asia-Oceanian Affairs	Milken Institute	Tuberous Sclerosis Conference
Social/Community research							
Improving public knowledge, awareness and attitudes towards epilepsy (discrimination, disclosure)	✓	✓			✓		
Improving patient and family education, information, expectations and communication (information needs)	✓	✓				✓	
Mobility issues (ineligability to drive)	✓						
Employment (vocational rehabilitation programs) and access to education	✓	✓					
Quality of life issues (culture, resilience)	✓	✓			✓		
Sport (Social participation)	✓						
Improving health professional education		✓					
Clinical research							
Costs of Care (hospitalisations, emergency department use)	✓						
Surveillance and population-based studies (data standards, screening and analytical tools, longitudinal studies on outcomes)		✓			✓	✓	

Priority	Chronic Illness Alliance	Institute of Medicine	NINDS	ILAE-IBE Europe Task Force	ILAE Commission on Asia-Oceanian Affairs	Milken Institute	Tuberous Sclerosis Conference
Improving health care and therapy (treatment options, reduce side-effects, access, utilisation, outcomes, decision-support tools)		✓	✓		✓		
Collaborative service models		✓					
Identify interventions for comorbidities (mental health) and improvements in adverse outcomes		✓					
Risk factors for injuries, suicide, status epilepticus and SUDEP		✓					
Personalized medicine		✓				✓	
Population type issues (specific etiologies and comorbidities) - paediatric and aging populations, traumatic brain injury (TBI) and cognitive dysfunction				✓			
Limit or prevent adverse consequences of seizures and their treatment across the lifespan (PNES, SUDEP, quality of life, comorbidities, fetal/neonatal, intellectual disabilities)		✓	✓				
Research practice							
Translational studies and clinical trials				✓		✓	
Improve research infrastructure and capacity					✓	✓	

Developing a framework for epilepsy research - briefing report

Priority	Chronic Illness Alliance	Institute of Medicine	NINDS	ILAE-IBE Europe Task Force	ILAE Commission on Asia-Oceanian Affairs	Milken Institute	Tuberous Sclerosis Conference
Promote pre-clinical/clinical collaborations						✓	
Models of funding for community service providers and collaborations		✓					
Pre-clinical (biomedical) research							
Understanding epilepsy in the developing brain				✓			
Understanding the causes, risk factors and genetic basis		✓	✓		✓		✓
Identifying new targets for innovative diagnostics and treatments		✓	✓	✓			
Prevention and cure of epilepsy, e.g. biomarkers, new targets			✓	✓			✓

Developing a framework for epilepsy research – briefing report

Perspectives on research priorities gathered by consultation

A total of 8 people participated in consultations out of 12 people invited, reflecting a response rate of 67%. All experts who were interviewed revealed that although they had a specific interest in one area of epilepsy research, e.g. genetics or treatments, their interests were also broad, including most aspects of epilepsy due to its complex nature.

Experts were asked to reflect on what they perceived were the biggest challenges in epilepsy research. Several challenges were highlighted, the major ones being:

- ***'Finding the 'holy grail'* or developing precision treatment** - every patient wants to control or eliminate their seizures.
- **Understanding the causes of epilepsy -** focus has been mainly on treating seizures, not at what is causing them
- **Drug-resistant or refractory epilepsy** - the percentage of patients with this type of epilepsy has not shifted
- **An urgent need to change the approach to generating new drug treatments (e.g. disease-modifying or preventative treatments)** - in last 2 decades there have been approximately 25 drugs developed and made available, however most of them are from similar drug groups to the current ones.
- **Patient expectations and clinicians' expectations can be misaligned in clinical management** – it is difficult for patients to understand the treatment advice clinicians provide. Also, when patients want access to treatments which are not widely available or that do not have good evidence to show their effectiveness, this can be difficult for clinicians to explain to patients.
- **The difficulty in diagnosing and treating comorbidities** - the non-medical community doesn't like the association between mental health, e.g. anxiety, depression and cognitive issues, and epilepsy.
- **Patients who slip through the gaps** – ensuring that all patients have access to care and first seizure patients are followed up.
- **Engaging patients to take part in research**– to answer questions meaningfully there needs to be larger cohorts of patients to be representative for data collection. There is a lack of understanding by patients as to why research is important and how valuable their participation will be.
- **Lack of funding and community attitudes** - it is not one of the glamorous areas to research and it is not recognised as a priority by the government so attracting funding can be difficult.
- **Ensuring there is a next generation of leaders** to continue research and improve care for patients - encouraging young clinicians and early career researchers to engage and to stay in this area of research.
- **Breaking down the divide between the community service organisations and the epilepsy research community** - building partnerships and working together as a whole unit to improve information and education.

Experts were also asked what priorities they thought were important in epilepsy research in Australia. The *highest priority* identified was to improve health care, including access to health services and access to new treatments, understanding the experience of patients undergoing genetic testing, as well as translating the progress made in research into treatments into clinical practice for

better outcomes for patients. Precision medicine and identifying new targets for treatments, in particular for drug-resistant or refractory epilepsy were the next two priorities ranked as *high*.

Modifying and/or preventing epilepsy and other support were ranked as *moderate* priorities. These were followed by comorbidities (diagnosis and treatment of mental health, speech, gait issues, autism, SUDEP), Patient management and outcomes, and Community attitudes (stigma) which were *low to moderate* priorities.

The following aspects were identified by one or two experts only as priorities (not in any order) – Improving public knowledge and awareness, Improving health professional education (specialist training), Understanding the causes of epilepsy, Improving patient and family education, information and expectations, Promoting collaboration (pre-clinical and clinical), Engagement and patient participation, Qualitative research to inform management, Medicinal cannabis, Improving research capacity (interest in the area, sustainability, and partnerships), and Data collection.

Experts commented that the priorities should not be considered solely in terms of the focus on impact in Australia, rather considering them in the context of their importance for global impact to improve epilepsy worldwide.

The importance of a research framework was agreed by all experts to facilitate funding opportunities, provide avenues for research to build upon, better define different types of epilepsy to find more appropriate treatments, exploring behaviours underlying the stigma of the condition (similar to conditions such as HIV or hepatitis) and gaps in care. It was seen to be opportunistic for the Epilepsy Foundation to develop the framework and set the research agenda due to their knowledge of people's needs and real life experiences and being able to provide the consumer input.

The framework needs to consider several aspects, in particular setting up a research fund or grant scheme and raising money for funding research aligned to the framework. The amount of funding available and whether small or large projects are feasible is the next consideration. The framework needs to provide funding for research training fellowships (local and international candidates) that are offered in partnership with a research facility such as the Melbourne Brain Centre to attract high quality researchers. It also needs to include clear outcomes and short, medium and long-term goals/milestones. A scientific advisory committee should be established to oversee and approve proposals that include some members who are external to the research. Researchers who are successfully funded should provide the outcomes to the public in a way that they can understand it.

The framework should also provide specialist training to up skill professionals with the necessary information and education.

Survey of the community

Overall, the survey had a total of 76 responses received from the community. There were 20 professionals, most of which described their role as a neurologist (both general and epileptologists) and 56 consumers of which most were people with epilepsy (70%).

Most aspects of applied social/community research were rated as high or moderate to low priority by consumers. Professionals only rated a couple of aspects as high, with most being ranked with

moderate priority. There were two aspects ranked with high priority by both professionals and consumers – Improving public knowledge, awareness and attitudes towards epilepsy and mobility issues, e.g. inability to drive. Consumers ranked improving education for patients and family, and for health professionals as high but this was not shared by professionals who ranked it with moderate priority. The lowest priorities were person-centred communication and patient engagement and participation in clinical trials.

There were 4 aspects of clinical research ranked with the highest priority by both professionals and consumers –

- Improving health care and therapy (treatment options, reduce side-effects, access, utilisation, outcomes, decision-support tools),
- Identify interventions for comorbidities (mental health) and improvements in adverse outcomes,
- Risk factors for injuries, suicide, status epilepticus and SUDEP, and
- Limit or prevent adverse consequences of seizures and their treatment across the lifespan (Psychogenic Non-Epileptic Seizures, SUDEP, quality of life, comorbidities, fetal/neonatal, intellectual disabilities)

Personalised medicine was ranked as moderate by both professionals and consumers. Professionals ranked Costs of Care (hospitalisations, emergency department use) as low priority, whereas the level of priority could not be determined by consumers. There were 3 aspects ranked with low priority by consumers - Surveillance and population-based studies (data standards, screening and analytical tools, longitudinal studies on outcomes), Population type issues - paediatric and aging populations, traumatic brain injury (TBI) and cognitive dysfunction and Collaborative service models. However, these were ranked with moderate to low priority by professionals.

The aspect of pre-clinical research which was ranked as high by both professionals and consumers was the Prevention and/or cure of epilepsy, e.g. biomarkers, new targets, and Understanding the causes, risk factors and genetic basis. Low priority was rated for Identifying new targets for innovative diagnostics and treatments by both professionals and consumers.

All the aspects of research practice were ranked similarly by professionals and consumers. The aspects were ranked as follows –

- Translational (bench) to bedside studies and clinical trials – *High priority*
- Improve research infrastructure – *High priority*
- Promote pre-clinical (lab)/clinical collaborations – *Moderate priority*
- Models of funding for community service providers and collaborations – *Low priority*

People were asked to rank the priorities of other chronic conditions that epilepsy can affect. Professionals and consumers both rated 3 types the same – people who have had an acquired brain injury, e.g. a stroke or traumatic brain injury (High), people who have autism (moderate) and people who have dementia (low). Consumers ranked people with psychogenic non-epileptic seizures (PNES) and people with intellectual disabilities as high. However, professionals ranked people with intellectual disabilities as moderate priority and people with psychogenic non-epileptic seizures (PNES) as low.

3.0 – Conclusion

In summary, the major challenges reported by key experts in epilepsy research included understanding the causes of epilepsy, recognising the urgent need to change the approach in generating new drugs, the difficulty in diagnosing and treating comorbidities, the lack of funding and community attitudes, ensuring there is a next generation of leaders, engaging patients to take part in research, and breaking down the divide between community service organisations and the epilepsy research community.

Overall, there were 10 aspects across 4 different types of epilepsy research areas identified with high priority (in no particular order) –

Pre-clinical research

1. Understanding the causes, risk factors and genetic basis of epilepsy
2. Prevention and/or cure of epilepsy

Applied/Translational research

3. Translating progress made in research into treatments in clinical practice, and improving research infrastructure to facilitate translation

Clinical research

4. To improve health care, including access to health services and treatments
5. Risk factors for injuries, status epilepticus, SUDEP and suicide
6. Understanding the experience of patients undergoing genetic testing
7. Limit or prevent adverse consequences of seizures and their treatment across the lifespan (e.g. SUDEP, comorbidities)

Social/community

8. Improving public knowledge, awareness, and attitudes towards epilepsy
9. Improving education for patients and family and for health professionals (social/community research)
10. Mobility issues, e.g. inability to drive

There was agreement by professionals and consumers that 3 groups of people with other established conditions and epilepsy should be considered with high priority –

- People who have had an acquired brain injury, e.g. a stroke or traumatic brain injury
- People with autism
- People with intellectual disabilities.

Interestingly, consumers ranked people with psychogenic non-epileptic seizures (PNES) as high priority, but professionals ranked them as low priority.

Experts reported that developing a framework is necessary to facilitate funding opportunities, provide avenues for research to build upon, better define different types of epilepsy to find more

appropriate treatments, exploring behaviours underlying the stigma of the condition (similar to conditions such as HIV or hepatitis) and gaps in care.

The findings reflect the importance of developing a research framework to align the interests of experts in the local epilepsy research field with the necessary priorities considered by all stakeholders. The framework will also be beneficial in providing a strategy for solving the challenges identified by experts in epilepsy research.

3.1 – Next steps

- Reflection on the evidence reported to identify 5 key priorities for epilepsy research in Australia.
- Consider what factors may be barriers or factors that could enable the framework to be successful.
- Establish a plan for implementation - document the resources available for the framework and appropriate timelines for achieving the framework.
- Evaluate the impact of the framework and consider extending it nationally to progress research in the field of epilepsy.

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4.0 - References

Australian Institute of Health and Welfare 2016. Australian Burden of Disease Study: Impact and causes of illness and death in Australia 2011. Australian Burden of Disease Study series no. 3. BOD 4. Canberra: AIHW.

Australian Institute of Health and Welfare 2016. Australian Burden of Disease Study: Impact and causes of illness and death in Aboriginal and Torres Strait Islander people 2011. Australian Burden of Disease Study series no. 6. Cat. no. BOD 7. Canberra: AIHW.

Baulac, M et al. Epilepsy priorities in Europe: a report of the ILAE-IBE Epilepsy Advocacy Europe Task Force. Epilepsia, 2015; 56 (11): 1687-1695

Bell, Neligan and Sander. An unknown quantity--the worldwide prevalence of epilepsy. Epilepsia. 2014; 55(7):958-62. doi: 10.1111/epi.12605.

Bladin, P. Reflections on a life in epilepsy. Evolution of epileptology in Australia: Early days. Epilepsy & Behavior. 2017; 71: 108 – 115.

Covanis, et al. From global campaign to global commitment: The World Health Assembly's Resolution on epilepsy. Epilepsia. 2015; 56(11):1651–1657, doi: 10.1111/epi.13192.

Brown, K. Indicators of the social consequences of epilepsy in Society behaviour and epilepsy'. Pinicinhara, J and Walker, C editors, Nova Biomedical, New York, 2011, pp.17-28.

Dumanis, S et al. Epilepsy: a giving smarter guide. Milken Institute, 2016. http://www.ilae.org/Visitors/Centre/documents/GivingSmarter-prioritizefundraising.pdf

England, M et al. Epilepsy across the spectrum: Promoting health and understanding. A summary of the Institute of Medicine report. Epilepsy & Behavior. 2012; 25: 266-276

Epilepsy Research Centre Melbourne, Australia, Research Programs. Available at - http://www.epilepsyresearch.org.au/, Last modified 1 February 2012. Accessed on 17 July 2017.

Fisher R, Acevedo C, Arzimanoglou A et al, A practical clinical definition of epilepsy. Epilepsia 2014 55(4): 475-482.

IOM (Institute of Medicine). Epilepsy across the spectrum: Promoting health and understanding. Washington, DC: The National Academies Press. 2012.

International League Against Epilepsy Global Research Priorities and Advocacy Task Force. ILAE Research Priorities survey, 2017. Available at - https://www.surveymonkey.com/r/respriority

Kwan, P, et al. Research priorities in epilepsy for the Asia-Oceanian region. Epilepsia. 2015; 56(5): 667-673.

MS Research Australia. MS Community Consultation on Priorities for MS Research: Detailed report. 2017. Accessed 12 April 2017. Available at - https://msra.org.au/news/priorities-research-listening-ms-community-2/

Ngugi et al, Incidence of epilepsy: a systematic review and meta-analysis. Neurology. 2011; 77(10):1005-12. doi: 10.1212/WNL.0b013e31822cfc90.

NINDS Benchmarks for Epilepsy Research, 2014, http://www.ninds.nih.gov/research/epilepsyweb/2014Benchmarks-Final_PDF.pdf

Peterson CL, Walker C, Shears G. The social context of anxiety and depression: exploring the role of anxiety and depression in the lives of Australian adults with epilepsy. Epilepsy & Behavior. 2014; 34: 29 – 33. http://dx.doi.org/10.1016/j.yebeh.2014.03.005

Sahin, M., et al. Advances and future directions for tuberous sclerosis complex research: Recommendations from the 2015 strategic planning conference. Pediatric Neurology. 2016; 60: 1-1

Walker, C. Researching the personal impact of epilepsy. Victoria, Australia, Chronic Illness Alliance, 2007: 1 - 30.

Walker and Peterson. Australian Epilepsy Longitudinal Study, Wave 3: The Social Impact of Epilepsy. Epilepsy Foundation. December 2014. Available at - http://epilepsyfoundation.org.au/australian-epilepsy-research-register/

5.0 – Appendix

5.1 - Inclusion/Exclusion criteria for the comprehensive literature search

Inclusion criteria

- **Population:** People with epilepsy (any age, any type), experts in epilepsy research
- **Intervention:** research strategy, agenda, priority setting, applied research
- **Study type:** Systematic Reviews, primary studies, reports
- **Date range:** 2007 - current (last 10 years)
- **Language:** English

Exclusion criteria

- Primary studies or reviews in which there is *no direct engagement* with the population of interest
- Studies examining research priorities within biomedical research only
- Case reports, invited commentary, editorials, abstracts or proceedings

5.2 – Data extraction of included studies from the literature

1. **Walker, C. Researching the personal impact of epilepsy. Victoria, Australia, Chronic Illness Alliance, 2007: 1 – 30**

Perspective - Applied social research (community)

Description (including aims, scope, methods)

The Chronic Illness Alliance received a grant in 2007 to undertake a project exploring the personal impact (social and emotional issues) of epilepsy.[1] The aims of the project included (page 7) -

1. To contribute information on the needs of people with epilepsy to an applied research agenda
2. To improve the services currently offered to clients by the Epilepsy Foundation
3. To develop a better community understanding of the needs and capacities of people with epilepsy

The rationale for this project was to inform an applied research strategic plan for the Epilepsy Foundation.

Data was collected from approximately 100 people in total. There were 5 workshops held involving 73 people, a group interview with 4 people, individual interviews with 2 people and several telephone interviews (number not reported). The researchers noted that contact with people from indigenous, culturally and linguistically diverse (CALD) and prison/justice backgrounds were attempted but were not successful. Discussions focused on social and emotions impacts of epilepsy, in particular around social exclusion.

Themes were drawn from data collected into broad categories and analysed in greater detail.

Results

The main themes identified in order of priority under the umbrella term of 'social exclusion' were –

1. Community awareness
2. Mobility issues
3. Employment and education
4. Disclosure
5. Quality of life issues
6. Sport
7. Costs of care
8. Information about treatments, complementary therapies, support services

Conclusion

"Further applied research be undertaken in those areas identified by the workshop participants where they experience exclusion, such as sport, education, employment. Applied research projects should address the social exclusion people experience." (page 3)

2. **IOM (Institute of Medicine). Epilepsy across the spectrum: Promoting health and understanding. Washington, DC: The National Academies Press. 2012.**

Related publications –

- England, M et al. Epilepsy across the spectrum: Promoting health and understanding. A summary of the Institute of Medicine report. Epilepsy & Behavior. 2012; 25: 266-276
- Hesdorffer, D et al. Research implications of the Institute of Medicine Report. Epilepsia. 2013; 54 (2): 207-216

Perspective – Public Health (community)

Description (including aims, scope, methods)

'In 2010, the Institute of Medicine (IOM) was asked to examine the public health dimensions of the epilepsies with a focus on four areas:

- public health surveillance and data collection and integration;
- population and public health research;
- health policy, health care, and human services; and
- education for providers, people with epilepsy and their families, and the public.

The committee was asked not to examine biomedical research priorities because the Epilepsy Research Benchmarks, developed in 2000, continue to be updated by the National Institute of Neurological Disorders and Stroke and collaborating agencies and organizations. To accomplish its task, the IOM convened the Committee on the Public Health Dimensions of the Epilepsies, which comprised 17 members with expertise in epilepsy care, health services research, epidemiology,

public health surveillance, mental health services, health care services and delivery, health literacy, public health, education, and communications. (page 2 and 3)' [2]

Results

Surveillance and prevention (Box 1, page 268)

- Studies to identify effective interventions for epilepsy accompanied by mental health comorbidities
- Studies that test whether treatment of comorbid mental health conditions ameliorates adverse outcomes
- Case–control studies of risk factors for injuries, suicide, status epilepticus, and sudden unexpected death in epilepsy (SUDEP)
- Population-based studies using existing data resources that have included epilepsy, such as the National Survey of Children's Health
- Studies to examine the capacity of data systems to link seizure medication use and birth outcomes
- Continued research on the risk factors for epilepsy of unknown, genetic, or presumed genetic cause
- Studies on the directionality of the relationship between epilepsy and its comorbidities, risk factors for developing an epilepsy comorbidity, and prognosis of epilepsy in people with comorbidities present before the onset of epilepsy
- A longitudinal study that examines epilepsy's outcomes (for example, a study of cognition in people with different syndromes, seizure types, and seizure frequencies that includes a sufficient number of older adults to enable studies of risk factors for cognitive deterioration)
- Long-term prospective studies that examine the effects of epilepsy surgery on cognitive function and that include appropriate control groups
- Studies or analyses that inform new approaches to randomized controlled trials in epilepsy, in order to minimize the time spent on placebo or on a study drug that is ineffective and thus minimize the risk for SUDEP
- Studies that develop and evaluate educational programs to improve the knowledge of coroners and medical examiners about SUDEP and other epilepsy-related deaths
- Evaluation of behavioral interventions on health outcomes and quality of life for people with epilepsy
- Development of screening methods and criteria to identify children with epilepsy and cognitive comorbidities through the use of educational records

Improving health care (Box 2, page 270)

- Development of methods for early identification of and new treatment approaches for refractory epilepsy
- Development of screening tools (useful in clinic settings) for the early identification of people with epilepsy who have potential cognitive impairments

- Development of decision-support tools for electronic health records for use by primary care and emergency room providers regarding care of persons with epilepsy, the use of screening tests, and referral steps for further evaluation and care
- Comparisons of the efficacy of brand and generic formulations of seizure medications
- Comparative effectiveness studies of epilepsy therapies and of treatments used to manage epilepsy (including reducing medication side effects) and comorbidities, with initial attention to setting priorities for this research
- Health services research on the provision and effectiveness of epilepsy care by primary care providers, neurologists, and epileptologists, including referrals to epilepsy centers and to specialists for care of comorbidities
- Assessment of differences in the utilization of epilepsy health care services, particularly for underserved populations
- Studies of the capacity of the workforce that cares for people with epilepsy
- Studies that examine value measures for epilepsy care as well as potential reductions in health care costs through changes in access to specialized care and improved coordination with providers caring for comorbid health conditions
- Analysis of cost savings by reducing emergency department use and hospitalizations
- Assessment of incentive strategies for the participation of clinical staff in collaborative service models and co-management of complex cases, including strategies to promote timely referral to surgery, mental health services, and higher levels of care

Health professional education (Box 3, page 271)

- Identification of knowledge gaps across health professions that relate to areas such as seizure recognition and classification; new treatment options; sudden unexpected death in epilepsy (SUDEP); and appropriate treatment modalities for specific subpopulations, including infants and children, women, individuals with severe epilepsy syndromes, people with complex comorbidities, and older adults
- Development and testing of educational interventions and incentives that will expand the reach of education and training opportunities about epilepsy and its associated comorbidities for health professionals outside of the epilepsy field (e.g., primary care, psychiatry, psychology, nursing)
- Assessment of current attitudes and beliefs of U.S. health professionals about epilepsy and the impact of these beliefs and attitudes on stigma and on access to and quality of care
- Evaluation of curricula and content of advanced training programs for physicians, nurses, and physician assistants for epilepsy-specific content and identification of specific opportunities and strategies for improving these types of programs
- Evaluation of innovative teaching strategies, such as online epilepsy education and simulation programs, to determine their suitability as models for a range of health professionals and others who interact with people with epilepsy, including teachers, daycare workers, coaches, and social workers
- Assessment of the format and frequency of educational and training opportunities existing within epilepsy centers in order to establish best practices for engaging clinicians in continuous, interdisciplinary learning

- Development and assessment of educational interventions and resources focused on communication skills and strategies for discussing sensitive topics (e.g., SUDEP, suicide, risks associated with medication nonadherence, and treatment preferences)

Improving quality of life and community resources (Box 4, page 271)

- Development of interventions to identify academic problems and improve academic achievement in students with epilepsy
- Identification of factors that increase the resiliency of the individual and family and of behaviors that improve quality of life
- Evaluations of community programs that go beyond process measures and assess outcomes for people with epilepsy and their families
- Evaluations of the effectiveness of vocational rehabilitation programs
- Identification of creative and innovative models of funding community service providers and collaborations
- Development of performance indicators for vocational and other community services and independent living programs

Improving patient and family education (Box 5, page 272)

- Assessment of the information needs of specific subpopulations, including women, men, older adults, children and adolescents, youths transitioning to adulthood, racial/ethnic minorities, people with low socioeconomic status, individuals with more severe forms of epilepsy or comorbidities and their families, individuals with cognitive limitations, and individuals with seizure-like events with a psychological basis
- Assessment of information needs associated with epilepsy related risks such as injuries, suicide, status epilepticus, and sudden unexpected death in epilepsy
- Identification of best practices, effective strategies and preferred formats, and innovative mechanisms for educating patients and families, especially individuals in underserved populations
- Development of a knowledge base to support comprehensive educational programs that feature content for epilepsy specific self-management as well as relevant aspects of the chronic care management models
- Testing of methods for developing educational programs and resources that appropriately reflect health literacy, cultural diversity, developmental stage, cognitive ability, and gender
- Examination of the role that educational materials and programs, support groups, and counseling resources may play in helping individuals and their families successfully cope with stigma and related concerns, such as the fear of having a seizure in public.

Improving public knowledge and awareness (Box 6, page 273)

- Surveys (e.g., General Social Survey, HealthStyles Survey) that capture trends in knowledge and awareness, and attitudes and beliefs about epilepsy over time and in specific subpopulations
- Evaluations of websites seeking to promote accurate knowledge about epilepsy (e.g., Talk About It) to determine effective strategies for educating the public through online resources

- Evaluation of public awareness campaigns that include documentation and analysis of pre- and post-campaign data to assess changes in public understanding of and beliefs about epilepsy and to establish best practices in developing public awareness efforts

Conclusion

"Given the current gaps in epilepsy knowledge, care, and education, there is an urgent need to take action—across multiple dimensions—to improve the lives of people with epilepsy and their families. The realistic, feasible, and action-oriented recommendations in this report can help enable short- and long-term improvements for people with epilepsy." (page 266)

3. **National Institute of Neurological Disorders and Stroke (NINDS) Epilepsy Research Benchmarks, 2014. Available at -** **http://www.ninds.nih.gov/research/epilepsyweb/2014Benchmarks-Final_PDF.pdf**

Related publications –

Kelley, M et al. The NINDS epilepsy research benchmarks. Epilepsia. 2009; 50(3): 579-582.

Perspective – Biomedical (scientific community)

Description (including aims, scope, methods)

'On April 17-19, 2013, NINDS hosted Curing the Epilepsies 2013: Pathways Forward, the third in a series of Curing the Epilepsies conferences held in partnership with epilepsy advocacy and professional organizations to assess progress in epilepsy research and help set an agenda for future years. As an important outcome, these conferences have led to the development of Benchmarks for Epilepsy Research, which reflect priorities for research toward clinically meaningful advances in understanding and treating the epilepsies. Following this tradition, and with input received during and prior to the April 2013 conference, NINDS has developed 2014 Benchmarks for Epilepsy Research as a framework for focusing research and benchmarking progress over the next five to ten years.' [3]

Results

'Understand the causes of the epilepsies and epilepsy-related neurologic, psychiatric, and somatic conditions.

A. Identify new genes and pathways associated with the epilepsies and epilepsy-related conditions.

B. Identify new infectious, immune, age-related, environmental, or other causes and risk factors associated with the epilepsies and epilepsy-related conditions.

C. Determine whether factors related to age, gender, race/ethnicity, socioeconomic status, and other features of specific populations affect risk and mechanisms of epilepsy and epilepsy-related conditions.

D. Determine whether the bi-directional relationships that exist between the epilepsies and several co-occurring conditions (e.g., neuropsychiatric or neurodevelopmental disorders) result from the same underlying causal mechanisms, interacting mechanisms, or are a consequence of the first presenting condition.

Prevent epilepsy and its progression.

A. Understand epileptogenic processes involved in epilepsies with neurodevelopmental origins, including those due to genetic or presumed genetic causes.

B. Understand epileptogenic processes involved in the development of epilepsy following traumatic brain injury, stroke, brain tumor, infections, neurodegeneration, or other insults to the brain.

C. Identify biomarkers that will aid in identifying, predicting, and monitoring epileptogenesis and disease progression, including markers early after injury/insult that identify those people at risk for epilepsy.

D. Develop or refine models aligned with the etiologies of human epilepsies to enable improved understanding of epileptogenesis and rigorous preclinical therapy development for epilepsy prevention or disease modification.

E. Identify new targets and develop interventions to prevent or modify epileptogenesis and the progression of epilepsy and epilepsy-related conditions.

Improve treatment options for controlling seizures and epilepsy-related conditions without side effects.

A. Understand the initiation, propagation, and termination of seizures at the network level in different forms of epilepsy.

B. Identify biomarkers for assessing or predicting treatment response, including markers that may identify specific populations that are likely to have good outcomes or develop adverse responses.

C. Develop or refine models that are aligned with etiologies and clinical features of human epilepsies, especially treatment resistant forms, to enable improved understanding of ictogenesis and preclinical development to improve seizure control with fewer side effects. Establish the sensitivity and specificity of these models with regard to current therapies.

D. Identify, develop, and improve interventions to detect, predict, prevent, or terminate seizures, including approaches suitable for use in the home and other non-medical settings.

E. Identify, develop, and improve anti-seizure therapies that target (either alone, or in combination) novel or multiple seizure mechanisms.

F. Develop, improve, and implement interventions for effective self-management, including treatment adherence.

G. Develop and validate objective patient-centered outcome metrics for clinical studies.

Limit or prevent adverse consequences of seizures and their treatment across the lifespan.

A. Understand and limit adverse impacts of seizures on quality of life, including effects on neurodevelopment, mental health, intellectual abilities, and other neurological and non-neurological functions.

B. Understand and limit adverse impacts of anti-seizure treatments (medical, surgical, or other interventions) on quality of life, including effects on neurodevelopment, mental health, intellectual abilities, and other neurological and non-neurological functions.

C. Understand risk factors and mechanisms involved in non-epileptic seizures (NES). Develop effective approaches for earlier and accurate diagnosis and treatment.

D. Identify causes, risk factors, and potential preventive strategies for sudden unexpected death in epilepsy (SUDEP) and other epilepsy-related mortality (for example, suicide) in people with epilepsy.

E. Identify the impact of pharmacological treatment of the epilepsies on fetal and neonatal development. Develop strategies to control seizures in pregnancy without causing harm to either the mother or child.

Conclusion

'As a final note, while the scope of the Benchmarks broadly encompasses many areas of biomedical research on the epilepsies, NINDS recognizes that important advances may also come from areas not explicitly highlighted. Moreover, focusing on the Benchmarks and biomedical research alone will not be sufficient to ensure better outcomes and improved quality of life for people with epilepsy. A report from the Institute of Medicine recently established recommendations and priorities that address public health aspects of the epilepsies beyond biomedical research, including issues related to surveillance and population research, measures for and access to high-quality care, patient and health care provider education, and public awareness. Together, the Benchmarks and the IOM report serve as complementary guides for the efforts of diverse stakeholders.' (page 2) [3]

4. **Baulac, M et al. Epilepsy priorities in Europe: a report of the ILAE-IBE Epilepsy Advocacy Europe Task Force. Epilepsia, 2015; 56 (11): 1687-1695**

Related Articles –

- Perucca, E et al. Epilepsy Research Priorities in Europe. 2013, Forum report
- Baulac and Pitkanen. Research priorities in epilepsy for the next decade—A representative view of the European scientific community: Summary of the ILAE Epilepsy Research Workshop, Brussels, 17–18 January 2008. Epilepsia, 2009; 50(3):571–583

Perspective – All (biomedical, medical and community)

Description (including aims, scope, methods)

'The European Forum on Epilepsy Research (ERF2013), which took place in Dublin, Ireland, on May 26–29, 2013, was designed to appraise epilepsy research priorities in Europe through consultation with clinical and basic scientists as well as representatives of lay organizations and health care providers. (page 1687) ' [4]

Results

"Priorities should include –

(1) development of innovative biomarkers and therapeutic targets and strategies, from gene and cell-based therapies to technologically advanced surgical treatment;

(2) addressing issues raised by pediatric and aging populations, as well as by specific etiologies and comorbidities such as traumatic brain injury (TBI) and cognitive dysfunction, toward more personalized medicine and prevention; and

(3) translational studies and clinical trials built upon well-established European consortia." (page 1693) [4]

Conclusion

'This report provides a summary of recommendations that emerged at ERF2013 about how to (1) strengthen epilepsy research, (2) reduce the treatment gap, and (3) reduce the burden and stigma associated with epilepsy.' (page 1687)

….

'Major research priority areas discussed at the Forum (Table 2) include (1) understanding epilepsy in the developing brain; (2) identifying new targets for innovative diagnostics and treatments; (3) prevention and cure of epilepsy; and (4) understanding epilepsy comorbidities with special focus on aging and mental health.' (page 1693)

5. **Kwan, P et al. Research priorities in epilepsy for the Asia-Oceanian region. Epilepsia. 2015; 56(5): 667-673.**

Perspective – All (biomedical, medical and community)

Description (including aims, scope, methods)

Developing a framework for epilepsy research - briefing report

To help promote research in the region, the Commission on Asian and Oceanian Affairs (CAOA) of the International League Against Epilepsy (ILAE) appointed the Research Task Force (RTF) to facilitate the development of research priorities for the region. Each Chapter in the region was asked to nominate a representative to join the discussion group based on their expertise. The group held a series of face-to-face meetings, teleconferences, and email communications between 2008 and 2012 in consultation with the CAOA and individual Chapters. Relevant literature was reviewed and a draft of the report was prepared by the 2009–2013 term of the RTF. The draft was finalized in May 2014 and formally approved by the CAOA in July 2014.' (page 667-8) [5]

Results

Priority Dimension I— Recognizing the Burden

Goal: To improve the access to epilepsy care and reduce the treatment gap (high priority)

Priority Dimension II - Understanding the Causes

Goal 1: To understand the etiologic or modifying factors for the development of epilepsy (high priority)

Goal 2: To identify the pathologic basis of epilepsy

Goal 3: To understand the lifestyle risk factors of epilepsy

Goal 4: To understand the genetic basis of epilepsy (high priority)

Priority Dimension III—Lessening the Consequences

Goal 1: To reduce the stigma and discrimination against people with epilepsy (high priority)

Goal 2: To improve the quality of life of persons with epilepsy in the region

Goal 3: To determine the impact of culture/social perception on epilepsy care and outcomes

Priority Dimension IV—Better Therapy

Goal 1: To close the epilepsy treatment gap (high priority)

Goal 2: To improve treatment delivery to people with epilepsy

Goal 3: To improve therapeutic outcomes

Goal 4: To enhance the utilization of epilepsy surgery

Goal 5: To evaluate the effectiveness of complementary and alternative medicine

Priority Dimension V—Improving Research Infrastructure

Goal: To improve the infrastructure and capacity in epilepsy research (high priority)

Conclusion

'We propose research "dimensions" as priorities within the Asia-Oceanian region. These are studies (1) that would lead to fuller appreciation of the health burden of epilepsy, particularly the treatment gap; (2) that would lead to better understanding of the causes of epilepsy; (3) that would alleviate the psychosocial consequences of epilepsy; (4) that would develop better therapies and improved therapeutic outcomes; and (5) that would improve the research infrastructure.' (page 667) [5]

6. **Dumanis, S et al. Epilepsy: a giving smarter guide. Milken Institute, 2016.**
   http://www.ilae.org/Visitors/Centre/documents/GivingSmarter-prioritizefundraising.pdf

Related articles –

- Dumanis, S et al. Opportunities for epilepsy: Outcomes of the Milken Institute State of the Science Retreat. Epilepsy & Behavior. 2017; 68: 174 - 176

Perspective – All (biomedical, medical and community)

Description (including aims, scope, methods)

'In 2016, the Milken Institute Center for Strategic Philanthropy launched an Epilepsy Giving Smarter Program, to inform philanthropists on the state of the science, as well as identify the challenges and investment opportunities that would impact the trajectory of the field. As part of the process, our Center convened epilepsy experts to discuss research roadblocks toward improved therapeutics and care for epilepsy. (page 174 of related articles)'

Results

Priority Areas for investment to accelerate epilepsy research (in order of priority) –

Data Standards/Analytical Tools

Build an epilepsy clinical data commons platform

Young Investigator Support

Invest in Human Capital

Developing a framework for epilepsy research - briefing report

Support Extension of Staff at epilepsy centers

Pre-clinical/Clinical collaboration

Promote cross-sector collaborations especially between basic scientists,

preclinical researchers, clinicians, and patients

Seizure Detection/Prediction Tools

Improve Precision Diagnostic Tools

Precision Medicine Infrastructure

Create large-scale infrastructure to support biomarker discovery using Patient Samples

Improving high throughput screens

Improve Current drug-screening assays

Proof of concept clinical trials

Create A Coordinated PreClinical Trial infrastructure

Communication initiatives

Promote epilepsy health literacy among the patient and medical community

Conclusion

"The Milken Institute Center for Strategic Philanthropy has developed this Epilepsy Giving Smarter Guide with the express purpose of empowering patients, supporters, and stakeholders to make informed, strategic decisions when directing their philanthropic investments and energy into research and development efforts." (page 8) [6]

7. **Sahin, M., et al. Advances and future directions for tuberous sclerosis complex research: Recommendations from the 2015 strategic planning conference. Pediatric Neurology. 2016; 60: 1-1**

Perspective – All (biomedical, medical and community)

Description (including aims, scope, methods)

'On March 10 to March 12, 2015, the National Institute of Neurological Disorders and Stroke and the Tuberous Sclerosis Alliance sponsored a workshop in Bethesda, Maryland, to assess progress and new opportunities for research in tuberous sclerosis complex with the goal of updating the 2003 Research Plan for Tuberous Sclerosis.

…

The conference brought together 82 participants including investigators and clinicians with diverse expertise, industry representatives, patient advocates and TSC family members, and representatives from seven NIH Institutes and Centers, the DOD TSCRP, and the TS Alliance.' (page 1-2) [7]

Results

- Priority Area I: Understanding phenotypic heterogeneity in TSC
- Priority Area II: Gaining a deeper knowledge of TSC signaling pathways and the cellular consequences of TSC deficiency
- Priority Area III: Improving TSC disease models
- Priority Area IV: Developing clinical biomarkers for TSC
- Priority Area V: Facilitating therapeutics and clinical trials research

Conclusion

'Here we summarize the outcomes from the extensive premeeting deliberations and final workshop recommendations, including (1) progress in the field since publication of the initial 2003 research plan for tuberous sclerosis complex, (2) the key gaps, needs, and challenges that hinder progress in tuberous sclerosis complex research, and (3) a new set of research priorities along with specific recommendations for addressing the major challenges in each priority area. The new research plan is organized around both short-term and long-term goals with the expectation that progress toward specific objectives can be achieved within a five to ten year time frame.' (page 1-2) [7]

5.3 - Survey

The Epilepsy Foundation is seeking your feedback on our future research program. We would like to understand which areas of epilepsy research are considered important by people living with epilepsy in the community and their family or friends, health professionals and researchers.

If you could spare just a few minutes and answer a couple of questions we would greatly appreciate your participation. The survey is anonymous, your name will not be collected. All personal details collected at the end of the survey will be used only for the purpose of analysing the survey results.

Section 1 -

1. **Applied Social/Community research**

Please rank EACH of the following research topics in the order of what you feel is the highest priority (1) to the low priority (9) using the drop down arrows

a) Improving public knowledge, awareness and attitudes towards epilepsy (discrimination, disclosure)
b) Improving patient and family education, information, and expectations (information needs)
c) Person-centred communication
d) Mobility issues (e.g. inability to drive)
e) Employment (e.g. vocational rehabilitation programs and access to education)
f) Quality of life issues (e.g. culture, resilience)
g) Social participation (e.g. sport)
h) Improving health professional education
i) Patient engagement and participation in trials

2. **Clinical research**

Please rank EACH of the following research topics in the order of what you feel is the highest priority (1) to the lowest priority (10) using the drop down arrows

a) Costs of Care (hospitalisations, emergency department use)
b) Surveillance and population-based studies (data standards, screening and analytical tools, longitudinal
studies on outcomes)
c) Improving health care and therapy (treatment options, reduce side-effects, access, utilisation, outcomes,
decision-support tools)
d) Qualitative research on the experience of epilepsy care (e.g. genetic testing, participating in trials)
e) Collaborative service models
f) Identify interventions for comorbidities (mental health) and improvements in adverse outcomes
g) Risk factors for injuries, suicide, status epilepticus and SUDEP
h) Personalised medicine
i) Population type issues (specific etiologies and comorbidities) - paediatric and aging populations, traumatic
brain injury (TBI) and cognitive dysfunction
j) Limit or prevent adverse consequences of seizures and their treatment across the lifespan (Psychogenic Non-
Epileptic Seizures, SUDEP, quality of life, comorbidities, fetal/neonatal, intellectual disabilities)

Developing a framework for epilepsy research - briefing report

3. **Research Practice**
Please rank EACH of the following research topics in the order of what you feel is the highest priority (1) to the lowest priority (4) using the drop down arrows

a) Translational (bench to bedside) studies and clinical trials
b) Improve research infrastructure and capacity
c) Promote pre-clinical (laboratory) / clinical collaborations
d) Models of funding for community service providers and collaborations

4. **Pre-clinical (biomedical/laboratory) research**
Please rank EACH of the following research topics in the order of what you feel is the highest priority (1) to the lowest priority (4) using the drop down arrows

a) Understanding epilepsy in the developing brain
b) Understanding the causes, risk factors and genetic basis
c) Identifying new targets for innovative diagnostics and treatments
d) Prevention and cure of epilepsy, e.g. biomarkers, new targets

Section 2 –

5. Epilepsy can affect anyone at any age. Epilepsy can also affect people with other established chronic conditions.

Please rank EACH of the following in the order of what you feel is the highest priority (1) to the lowest priority (5) using the drop down arrows

a) People with Psychogenic Non-Epileptic Seizures (PNES)
b) People with intellectual disabilities
c) People who have had an acquired brain injury, e.g. a stroke or traumatic brain injury
d) People who have dementia
e) People who have autism

6. Please tell us if you feel there is a crucial research question that should be prioritised that has not been covered in the previous questions

7. For professionals or researchers - Please tell us what your connection to epilepsy is, e.g. what is your professional role? (please select all that apply)

- Researcher
- Nurse
- Neurologist - specialist epileptologist
- Neurologist - general
- Clinical neuropsychologist
- Allied Health professional (please specify below)
- Technician
- Social worker
- Health service manager
- Staff member at a community support organisation
- Not applicable
- Other (please specify)

8. **For people in the epilepsy community -**
Do you have epilepsy?
- Yes
- No
- Not applicable

9. **For people in the epilepsy community -**
Do you have a family member or friend with epilepsy?
- Yes
- No
- Not applicable