

Curing The Epilepsies: Patient Advocates Assess Progress

In March 2000, the White House gathered prominent epilepsy research scientists, health care providers, and leaders of epilepsy organizations for a seminal conference to discuss what it would take to reach a cure for epilepsy.¹ Twenty years later, patient advocates are taking stock on the progress that has been made.

PATIENT ADVOCATE AND RESEARCHER COLLABORATION HAS EXPANDED THE SCOPE OF EPILEPSY RESEARCH

Since 2000, the Curing the Epilepsies conference has repeated every seven years.² Participation of the patient advocates has increased each meeting from the early days when the meeting was exclusively researchers to patient advocates attending as participants, to later testifying as presenters, to ultimately serving in 2020 as Co-Chairs with the Stewards and as members of a Work Group engaged in the strategic planning, creation of manuscripts, agenda development, speaker solicitations, and more. The influence of the advocates has not only broadened the stakeholder voices represented during each consecutive conference but has impacted the scope of the Benchmarks' substance as well. The Benchmarks have evolved from focusing narrowly on research for treating seizures to include research initiatives toward understanding causes of epilepsy, as well as understanding comorbidities of epilepsy, and improving management of both and finding cures. At the urging of the advocates, the Benchmarks have expanded to include other critical topics like Sudden Unexpected Death in Epilepsy (SUDEP) and quality of life as well.

The Benchmarks have been used to guide research priorities at NIH, as well as at nonprofit organizations that support epilepsy research.³ Researchers use the benchmarks as justification in their grant applications. The American Epilepsy Society (AES) Epilepsy Research Benchmark Stewards Committee use them to measure progress on priority research areas. The Interagency Collaborative to Advance Research in Epilepsy (ICARE) uses them to code the funding for grant awards across all funding agencies (federal government and patient advocacy groups and AES). They are used as well by patient advocates and professional societies to inform their strategic planning and research grant programs. They are cited in research articles and reviews. Over the past two decades, patient advocates and researchers have come to appreciate the shared responsibility for the realization of the Benchmark objectives.

OUTCOMES FOR EPILEPSY PATIENTS REMAIN LARGELY UNCHANGED

While the Curing the Epilepsies conference and processes have become more inclusive and epilepsy research has yielded exciting advances⁴ across many areas of the Benchmarks, unfortunately the outcomes for patients and their families with epilepsy have not significantly changed in 20 years. Moreover, even comparing statistics from 2000 to 2020 is a challenge given the overall lack of regular, consistent, in-depth data collection and tracking.

¹ National Institute of Neurological Disorders and Stroke. 2000 Epilepsy Research Benchmarks: A Guide for the General Public. Accessed on October 7, 2020 at <https://www.ninds.nih.gov/About-NINDS/Strategic-Plans-Evaluations/Strategic-Plans/2000-Epilepsy-Research-Benchmarks-Guide>.

² [Curing Epilepsy: Focus on the Future \(March 2000\)](#), [Curing Epilepsy 2007: Translating Discoveries into Therapies \(March 29-30, 2007\)](#); [Curing the Epilepsies 2013: Pathways Forward \(April 17-19, 2013\)](#)

³ <https://journals.sagepub.com/doi/full/10.1177/1535759719888646>

⁴ National Institute of Neurological Disorders and Stroke. Curing the Epilepsies: The Promise of Research webpage. Accessed on October 7, 2020 at <https://www.ninds.nih.gov/Current-Research/Focus-Research/Focus-Epilepsy/Curing-Epilepsies-Promise-Research>

	2000	2010	2020	Percent Change
People living in the US				
Adults		2.3M ⁵	2.9M ⁷	26% ¹⁰
Children		438,000 ⁶	470,000 ⁸	9%
Total		2.7M	3.4M ⁹	26% ¹¹
Epilepsy Control				
Clinical samples		25% refractory	30-40% refractory ¹²	
Community-based sample		n/a	56% uncontrolled ¹³	
Mortality				
Overall (expected)		n/a	25,000/yr ¹⁴	
SUDEP (percentage of deaths)		7-17%	10% ¹⁵	
Causes of Epilepsy			50% unknown ¹⁶	
Anti-seizure medications on the Market¹⁷	~16		~32	

⁵ Based on 2010 National Health Interview Survey data (source:

https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6145a2.htm?s_cid=mm6145a2_e

⁶ Based on a pediatric epilepsy prevalence estimate of 0.6% from Russ et al. 2012 (that used 2007 National Survey of Children's Health data) extrapolated to the 2010 U.S. Census estimate for children ≤ 17 years of age.

⁷ Based on 2015 National Health Interview Survey and 2015 National Survey of Children's Health. These are the latest published estimates available.

⁸ Based on a pediatric epilepsy prevalence estimate of 0.6% from Russ et al. 2012 (that used 2007 National Survey of Children's Health data) extrapolated to the 2010 U.S. Census estimate for children ≤ 17 years of age.

⁹ Based on 2015 National Health Interview Survey and 2015 National Survey of Children's Health. These are the latest published estimates available.

¹⁰ This increase is likely due to population growth from 2010 to 2015 and the aging of the population over this time.

¹¹ This increase is likely due to population growth from 2010 to 2015 and the aging of the population over this time.

¹² Dalic L, Cook MJ. Managing drug-resistant epilepsy: challenges and solutions. *Neuropsychiatr Dis Treat.* 2016;12:2605-2616. Published 2016 Oct 12. doi:10.2147/NDT.S84852

¹³ At least one self-reported seizure in the past 12 months –

source: https://www.cdc.gov/mmwr/volumes/67/wr/mm6715a1.htm?s_cid=mm6715a1_e

¹⁴ CDC, unpublished estimate. Age-adjusted epilepsy mortality rates (as any-listed cause of death) per 100,000 significantly increased from 0.58 in 2005 to 0.85 in 2014 (47% increase). This is likely an underestimate because of the underreporting of epilepsy on death certificates. Source : Greenlund SF, et al. *Epilepsy Behav.* 2017;69:28-30.

¹⁵ Thurman DJ, et al. Sudden unexpected death in epilepsy: Assessing the public health burden. *Epilepsia.* 2014;55(10):1479-85

¹⁶ https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Hope-Through-Research/Epilepsies-and-Seizures-Hope-Through#3109_4

¹⁷ Email exchange with David G. Vossler, M.D., [A Summary of Antiseizure Medications Available in the United States: 2020 Update](#)

Cost of Epilepsy	\$12.5B ¹⁸		\$20B ¹⁹	
Federal Investment in Epilepsy	\$76M		\$152M ²⁰	

Table 1. Comparison of statistics from 2000 to 2020

Statistics are more difficult to procure for 2000; however, in 2010, there were 2.3 million people living with epilepsy in the US.²¹ Today, there are 3.4 million people believed to have epilepsy and 470,000 are children.²² That represents a 26% increase for adults²³ and a 9% increase for children.²⁴ In addition to children, epilepsy is increasing among older adults as well.²⁵

Statistics for epilepsy control have not changed either in 20 years - approximately 30-40% of the epilepsy population remain refractory or uncontrolled.²⁶ This despite the exponential growth of epilepsy drug development over the last twenty years.²⁷ Although a large body of research shows that epilepsy surgery should not be considered a last resort, surgery remains underutilized in both pediatric and adult populations.^{28, 29} Approximately 4,000 epilepsy surgeries are performed annually in the United States, even though 100,000 - 200,000 patients are likely surgical candidates.³⁰ Despite explosive advances in genomics and imaging, the cause remains unknown in at least 50%.³¹

¹⁸ Epilepsy Foundation of America. Epilepsy: a Report to the Nation. Page 10. Landover MD: January 1999. Cost figures estimate direct costs (eg healthcare spending) and omit indirect costs (e.g., caregiving costs; loss of earnings/productivity and therefore underestimate the overall costs.

¹⁹ Epilepsy Foundation. Fiscal Year 2021 Labor, HHS, and Education Appropriations Bill position statement. Accessed on October 7, 2020 at https://cqcengage.com/efa/file/4lff3VMaRS0/CDC_final.pdf

²⁰ National Institute of Neurological Disorders and Stroke. Focus on Epilepsy Research webpage. Accessed on October 7, 2020 at <https://www.ninds.nih.gov/Current-Research/Focus-Disorders/Epilepsy>.

²¹ Based on 2010 National Health Interview Survey data (source: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6145a2.htm?s_cid=mm6145a2_e

²² CDC MMWR for the 3.4 million estimate from the 2015 National Health Interview Survey data and National Survey of Children's Health: <https://www.cdc.gov/mmwr/volumes/66/wr/mm6631a1.htm>

²³ 2.3 million estimated adults in 2010 data increased to 2.9 million estimated adults from 2015 data. This increase may be due to population growth from 2010 to 2015 and the aging of the population over this time period.

²⁴ A 1995 study estimated there are 6/1000 children with epilepsy. <https://onlinelibrary.wiley.com/doi/10.1111/j.1528-1157.1995.tb01629.x> Applied to the 2000 U.S. census estimate of children yields an estimated 429,600 children with epilepsy in 2000—compared to 470,000 children in 2015. So the increase from 2010 to 2015 for children is 9%. This could be attributed to population growth over the time period—because (fortunately) the prevalence estimate did not change—still 6 children with epilepsy per 1,000 children.

²⁵ Institute of Medicine Committee on the Public Health Dimensions of the Epilepsies. 2012. [Epilepsy across the spectrum](#), pp. 24-25. National Academies, Washington, DC.

²⁶ Dalic L, Cook MJ. Managing drug-resistant epilepsy: challenges and solutions. *Neuropsychiatr Dis Treat*. 2016;12:2605-2616. Published 2016 Oct 12. doi:10.2147/NDT.S84852

²⁷ A. Golyala, P. Kwan. Drug development for refractory epilepsy: the past 25 years and beyond. *Seizure*, 44 (2017), pp. 147-156.

²⁸ Englot DJ. The persistent under-utilization of epilepsy surgery. *Epilepsy Res*. 2015;118:68-69;

²⁹ Pestana Knight EM, Schiltz NK, Bakaki PM, Koroukian SM, Lhatoo SD, Kaiboriboon K. Increasing utilization of pediatric epilepsy surgery in the United States between 1997 and 2009. *Epilepsia*. 2015;56(3):375-381;

³⁰ England MJ, Liverman CT, Schultz AM, Strawbridge LM. Epilepsy across the spectrum: promoting health and understanding: report to the institute of medicine's committee on the public health dimensions of the epilepsies. Washington, DC: National Academies Press (US); 2012.

³¹ https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Hope-Through-Research/Epilepsies-and-Seizures-Hope-Through#3109_4

The cost has grown as well from \$12.5 billion in 2000³² to nearly \$20 billion in 2020.³³ And while our federal investment in epilepsy research has increased from \$76 million in 2000 to \$152 million in 2019³⁴ it has not kept pace with the prevalence of the disease, the complexity of the disease, the growing medical costs, or the population burden across the lifespan of patients from birth through death. Notwithstanding, federal and private funding increases for other diseases including Alzheimer's, Multiple Sclerosis, and Parkinson's have outpaced investment in the epilepsies despite higher prevalence.³⁵

Most important of all is we have seen little quality of life improvement for our patients and their families over the last 20 years. Epilepsy affects newborns through the elderly with a lifetime burden experienced by the patient and extended family. Epilepsy is a spectrum disease comprised of many diagnoses and experiences. No two are alike. Nevertheless, common among both patients whose seizures are well controlled to those for whom they are not are disruptions to mental activities like thinking, concentrating, and memory. People with epilepsy still experience disproportionate challenges in daily activities like school, employment, driving, relationships, and social interactions. Academic underachievement is frequent in children with epilepsy, placing them at high risk of unemployment as adults.³⁶ People with epilepsy are frequently impacted by comorbidities including psychiatric disorders, cognitive disorders, migraine and sleep disorders.³⁷ Other conditions often reported in people with epilepsy include cardiovascular, respiratory, inflammatory and other disorders.³⁸ In addition to seizure side effects, many patients experience severe medication-related physical and mental side effects. And for the patients diagnosed with the most severe and intractable epilepsies (the developmental epileptic encephalopathy or DEEs) many are living day by day fighting for survival. Many of these patients require round the clock care, life-saving equipment, frequent hospital visits, and extensive support and services.

Not only are people with epilepsy impacted, but caregivers of epilepsy patients are also under extraordinary stress in their physical and emotional health, social relationships, employment, and finances.³⁹ They are also at increased risk for post, or more appropriately, ongoing traumatic stress, anxiety, and depression.

The financial toll for families across the epilepsy spectrum can be extraordinary in both direct costs including access to care, treatment, and management⁴⁰, as well as indirect costs including work productivity, employment status and caregiver burden.⁴¹ In 2016, epilepsy ranked 69th among 154 common health

³² Epilepsy Foundation of America. Epilepsy: a Report to the Nation. Page 6. Landover MD: January 1999.

³³ Epilepsy Foundation. Fiscal Year 2021 Labor, HHS, and Education Appropriations Bill position statement. Accessed on October 7, 2020 at https://cqrceengage.com/efa/file/4lff3VMaRS0/CDC_final.pdf.

³⁴ National Institute of Neurological Disorders and Stroke. Focus on Epilepsy Research webpage. Accessed on October 7, 2020 at <https://www.ninds.nih.gov/Current-Research/Focus-Disorders/Epilepsy>.

³⁵ Meador, K., French, J., Loring, D., and Pennell, P. Disparities in NIH funding for epilepsy research. *Neurology* 2011;677:1305-1307. Accessed at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3265048/pdf/zn1305.pdf>

³⁶ Lah, S., Castles, A., Smith, ML. Reading in children with temporal lobe epilepsy: A systematic review. *Epilepsy and Behavior*. 68 (2017) 84-89.

³⁷ *Future Neurol*. 2009 Sep 1; 4(5): 663–668. doi: [10.2217/fnl.09.32](https://doi.org/10.2217/fnl.09.32)

³⁸ <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6243a2.htm>

³⁹ Puka K, Tavares TP, Anderson KK, Ferro MA, Speechley KN. A systematic review of quality of life in parents of children with epilepsy. *Epilepsy Behav*. 2018 May;82:38-45. doi: 10.1016/j.yebeh.2018.03.008. Epub 2018 Mar 23. PMID: 29579553.

⁴⁰ Begley CE, Durgin TL. The direct cost of epilepsy in the United States: A systematic review of estimates. *Epilepsia*. 2015 Sep;56(9):1376-87. doi: 10.1111/epi.13084. Epub 2015 Jul 27. PMID: 26216617. <https://pubmed.ncbi.nlm.nih.gov/26216617/>

⁴¹ Clinical Brief: Examining the Economic Impact and Implications of Epilepsy. *American Journal of Managed Care*. February 13, 2020. Accessed at <https://www.ajmc.com/view/examining-the-economic-impact-and-implications-of-epilepsy>

conditions, with an estimated \$8.6 billion in health care spending attributed to public insurance, private insurance, and out of pocket payments.⁴²

Finally, while statistics were unavailable for death by SUDEP in 2000, it is believed to be responsible for 10% of all epilepsy deaths in 2020.⁴³ The risk of death increases for people with epilepsy with an estimated 10 years of life lost for people whose epilepsy has a known cause, and 2 years lost for people with epilepsy from an unknown cause.⁴⁴ Risk of death is not decreasing despite improved treatments. The European Academy of Neurology (EAN) Virtual Congress shows the burden of potentially avoidable epilepsy-related deaths in young adults remains large, with those aged between 16 and 24 having a six-fold increased risk of epilepsy-related death.⁴⁵ Age-adjusted epilepsy mortality rates (as any-listed cause of death) per 100,000 significantly increased from 0.58 in 2005 to 0.85 in 2014 (47% increase).⁴⁶ It is likely underestimated because of the underreporting of epilepsy on death certificates.

WE NEED TRANSFORMATIVE CHANGE AND WE NEED IT NOW!

We commend the NINDS and Benchmark Stewards for using the conference delay caused by the COVID19 pandemic to go beyond merely refining the Benchmarks by also issuing a call for ideas for transformative change. This is imperative because there remain significant gaps in the current epilepsy research and healthcare ecosystem that prevent research progress from translating to meaningful change for patients.

To catalyze a new era of research in the epilepsies, we recommend the creation of a NIH supported national network of specialty centers across the United States actively engaged in clinical trials and other research studies to expedite the diagnosis and treatment of all epilepsies in children and adults, including those that are rare and complex. This is not a new idea – the landmark Epilepsy Across the Spectrum report published by the Institute of Medicine (now the National Academies of Science Engineering and Medicine) in 2012 called for accredited epilepsy centers “to form an Epilepsy Care Network that includes data sharing, clinical trial and other research networking, professional education, and other collaborative activities” – and while progress has been made in achieving this goal in a number of areas, it is clear that there is more work to be done. Through the years, dedicated epilepsy leaders have driven the development of many valued epilepsy provider and research networks including National Association of Epilepsy Centers (NAEC) established in 1987, the Veterans Affairs Epilepsy Centers of Excellence established in 2008, the Pediatric Epilepsy Research Consortium (PERC) established in 2010, and more recently the Epilepsy Health Learning System (EHLS) and Pediatric Epilepsy Health Learning System (PEHLS). While different in their inception, each network is dedicated to improving the standard and quality of care to improve outcomes for people with epilepsy. However, what is missing is the financial support and stimulus to seed and sustain clinical research and promote the transfer of research findings into state-of-the-art care.

⁴² Dieleman et al. US Health Care Spending by Payer and Health Condition, 1996-2016. *JAMA* 2020; 323(9):863-884.

⁴³ Thurman DJ, et al. Sudden unexpected death in epilepsy: Assessing the public health burden. *Epilepsia*. 2014;55(10):1479-85 reported about 2,750 SUDEP deaths in the United States. This probably represents about 10% of *all* deaths among U.S. persons with epilepsy (at least 25,000 deaths of people with epilepsy per year). It is estimated that at least 2,750 SUDEP deaths occur per year in the U.S.

⁴⁴ Institute of Medicine Committee on the Public Health Dimensions of the Epilepsies. 2012. *Epilepsy across the spectrum*, p. 137. National Academies, Washington, DC.

⁴⁵ European Academy of Neurology. Epilepsy-related deaths common in young adults and are not reducing, new research shows. *Medical Express* May 25, 2020. Accessed October 7, 2020 at <https://medicalxpress.com/news/2020-05-epilepsy-related-deaths-common-young-adults.html>

⁴⁶ Greenlund SF, et al. Epilepsy by the Numbers: Epilepsy deaths by age, race/ethnicity, and gender in the United States significantly increased from 2005 to 2014. *Epilepsy Behav*. 2017;69:28-30.

For inspiration, we look to the NIH's Children's Oncology Group,⁴⁷ a National Cancer Institute supported clinical trials group, as well as the European Reference Network for Epilepsy, supported by the European Union.⁴⁸ The reimagined NIH funded network would expedite clinical evaluation and diagnosis, hasten the development and dissemination of treatment protocols, accelerate the monitoring of standardized outcomes, address deficits and disparities in care, and strengthen registry participation and collaborative research. The network would have as a primary focus improving tangible outcomes for patients and their caregivers including both seizure cessation and control as well as the quality of life for a broad range of individuals struggling with epilepsy comorbidities, and treatment effects regardless of the cause or functional status. We urge the Benchmark Stewards to focus the Curing the Epilepsies conference on engaging with thought leaders to evaluate how existing and new assets in the epilepsy space could be leveraged to achieve this transformative idea.

These are aggressive goals that will require proportionate, substantial, and coordinated funding commitments from federal and private sources. This will include providing new mechanisms to support public-private partnerships of all stakeholders. Only this will foster the broad institutional changes needed to support the breadth of collaborative efforts required to better align the allocation of resources with strategies that hold promise to dramatically improve the outcomes for all those living with epilepsies. Transforming epilepsy research will transform the lives of people with epilepsy and their families.

Now is the time to accelerate improvements in what we know and do about the epilepsies. Now is the time for collaboration. Now is the time for information sharing. Now is the time to improve outcomes for people with epilepsy.

Prepared by the Epilepsy Leadership Council Patient Advocacy Research Benchmarks Work Group to The Curing the Epilepsies Conference (2020/2021). Members: Mary Anne Meskis, Dravet Syndrome Foundation; JayEtta Hecker, Wishes for Elliott; Heidi Grabenstatter, PhD, International Foundation for CDKL5 Research; Brandy Fureman, PhD, Epilepsy Foundation; Steve Roberds, PhD, Tuberous Sclerosis Alliance; Vanessa Vogel-Farley, Dup15q Alliance; Brandy Parker-McFadden, My Epilepsy Story; Amber Freed, SLC6A1Connect; Monika Jones, JD, The Brain Recovery Project: Childhood Epilepsy Surgery Foundation; and Alison Kukla, Epilepsy Foundation/Epilepsy Learning Health System and Co-Chairs Laura Lubbers, PhD, CURE Citizens United for Research in Epilepsy & Ilene Penn Miller, JD, LLM, Rare Epilepsy Network (REN). With gratitude to Anne Gramiack of American Epilepsy Society as well.

Endorsed by:

1. Child Neurology Foundation
2. CURE Epilepsy
3. Danny Did
4. Dravet Syndrome Foundation
5. Dup15q Alliance
6. Epilepsy Foundation
7. FamilieSCN2A Foundation

⁴⁷Children's Oncology Group Website. Accessed October 7, 2020 at <https://www.childrensoncologygroup.org/index.php/aboutus>

⁴⁸EpiCARE: a European Reference Network for rare and complex epilepsies website. Accessed on October 7, 2020 at <https://epi-care.eu/>

8. Hope for Hypothalamic Hamartomas
9. Hope for ULD™
10. International Foundation for CDKL5 Research
11. LGS Foundation (Lennox-Gastaut Syndrome)
12. Milestones for Maxwell & SLC6A1 Connect
13. National Association of Epilepsy Centers (NAEC)
14. Phelan-McDermid Syndrome Foundation
15. Ring14 USA
16. TESS Research Foundation
17. The Brain Recovery Project: Childhood Epilepsy Surgery Foundation
18. Tuberous Sclerosis Alliance
19. Wishes for Elliott