2014 NINDS Benchmarks for Epilepsy Research

History and evolution

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Epilepsy Research Benchmarks Stewards 2000-2014
Disclosure

Name of Commercial Interest: NONE

Type of Financial Relationship: NONE
Learning Objectives

• Review the origins of the epilepsy benchmarks concept and how it has evolved to the present

• Have an introduction to the latest iteration of the benchmarks
Overview

• History and origins of the Benchmarks
• Highlights of research progress
• New 2014 Benchmarks
• AES/NINDS Epilepsy Research Benchmarks Stewards
History of the Benchmarks

Curing Epilepsy 2000: Focus on the Future

- White House-initiated conference
- Developed the first Epilepsy Research Benchmarks
- “No seizures, no side effects, and the prevention of epilepsy”

Curing Epilepsy 2007: Translating Discoveries into Therapies

- Developed 2007 Benchmarks
- New emphasis on comorbidities and SUDEP
The Benchmarks make a difference

Raise awareness of priorities across community
- Comorbidities of epilepsy and SUDEP
  - Growth in research since addition to the Benchmarks

Inform priority-setting for NINDS investments
- Epilepsy Centers without Walls program
  - Genetic causes, epileptogenesis, SUDEP

Provide a shared framework for tracking progress
- How far have we come?
- What needs and challenges remain?
- Have new opportunities emerged?
Novel causes of epilepsy
• Advances in genetics (next generation sequencing and role of de novo mutations)
• Autoimmune mechanisms
• Congenital HPV infection as a potential cause of cortical dysplasia

Preventing epileptogenesis
• Strong evidence base for roles of REST, mTOR, BDNF, and inflammatory pathways
• Studies in animal models show promise for antiepileptogenic interventions

New and improved animal models
• Infantile spasms, TSC/cortical dysplasia, viral encephalitis, comorbid conditions, zebrafish

Understanding network activity
• Advancing tools for measuring and analyzing seizure-related activity
• Potential biomarkers of epileptogenicity
• Development of devices for seizure prediction and control

Comorbidities
• Evidence for shared pathogenicity and impact of chronic seizures and their treatment
• Potential mechanisms and therapeutic targets beginning to emerge

SUDEP
• Identification of risk factors
• New surveillance efforts will enable further research
• Developed 2014 Benchmarks
• Broader topics capture more opportunities for progress
• Reorganized representation of “comorbidities”
  – Encourages integration of research on epilepsy-related conditions and consequences beyond seizures into epilepsy research as a whole
  – Begins to clarify complex relationships these conditions have with epilepsy and seizures, underlying disease mechanisms, and effects of epilepsy treatment
2014 NINDS Benchmarks for Epilepsy Research

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 shared across the epilepsy community for research toward clinically meaningful advances in understanding and treating the epilepsies. Since their initial development in 2000, the Benchmarks have brought attention to goals such as preventing epileptogenesis, addressing aspects of epilepsy beyond seizures, and confronting the challenge of sudden unexpected death in epilepsy (SUDEP).

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. The final 2014 Benchmarks incorporate revisions in response to public comments on a draft posted in October 2013.

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**2014 NINDS Benchmarks for Epilepsy Research**

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

II. Prevent epilepsy and its progression.

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

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

View **2014 Benchmarks with introductory preamble**: [PDF, 320 kB]

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Learn More:

- [2000 and 2007 Epilepsy Research Benchmarks and progress reports](#)
- [Curing the Epilepsies 2013: Pathways Forward](#)

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2014 NINDS Benchmarks for Epilepsy Research

I. 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.
2014 NINDS Benchmarks for Epilepsy Research

II. 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.
2014 NINDS Benchmarks for Epilepsy Research

III. 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 likely to have good outcomes or develop adverse responses.

C. Develop or refine models 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.

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 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.
2014 NINDS Benchmarks for Epilepsy Research

IV. 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.


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.
Epilepsy Research Benchmarks Stewards

- **Began** as a group of researchers who volunteered after the first Curing Epilepsy conference to promote and track progress in areas highlighted by the Benchmarks
  - Reported research advances and opportunities to NINDS
  - Raised awareness of the Benchmarks among researchers, including junior investigators entering the field
  - Forged partnership with AES to integrate the Benchmarks into Annual Meeting programs and materials

- **Now** an AES committee, working in partnership with NINDS
  - Enhanced visibility of Stewards’ activities
  - Increased opportunities for AES members to participate
  - Achieves further integration of the Benchmarks as shared framework for guiding and tracking research progress
Past Stewards

Matthew Anderson, MD, PhD
Jocelyn Bautista, MD
Anne Berg, PhD*
Edward Bertram, MD
Amy Brooks-Kayal, MD*
Marc Dichter, MD, PhD
Jerome Engel, MD, PhD*
Tracy Glauser, MD
Bruce Hermann, PhD
Molly Huntsman, PhD
Ruben Kuzniecky, MD
John Langfitt, PhD
Brian Litt, MD*
Solomon Moshé, MD
Patricia Shafer, RN, MN
Alexander Rotenberg, MD, PhD
Elsun So, MD
Susan Spencer, MD*
John Swann, PhD
Carl Stafstrom, MD
H. Steve White, PhD
Karen Wilcox, PhD

* Benchmarks Area Co-Chairs
I. Understand the causes of the epilepsies and epilepsy-related neurologic, psychiatric, and somatic conditions.

Co-Chairs: Heather Mefford, Rochelle Caplan, Madison Berl, Bernard Chang, Jack Lin, Annapurna Poduri, Andrey Mazarati

II. Prevent epilepsy and its progression.

Co-Chairs: Aristeia Galanopoulou, Michael Wong, Devin Binder, Adam Hartman, Elizabeth Powell, Avtar Roopra, Richard Staba

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

Co-Chairs: Dennis Dlugos, Gregory Worrell, Chad Carlson, Kathryn Davis, Jacqueline French, Patrice Jackson-Ayotunde, Andres Kanner, Tobias Loddenkemper, Michael Rogawski, William Stacey, Sridhar Sunderam, Jerzy Szaflarski

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

Co-Chairs: W. Curt LaFrance, Jr., Alica Goldman, Miya Asato, Timothy Benke, Robert Doss, Daniel Drane, Samden Lhatoo, Alison Pack, Tanvir Syed
감사합니다

Danke Եւխարիստիէς  Dalu Κόσζονोμ
Grazie სპასიბო  Dank  Gracias
Thank You  Tack  Seé
谢谢  Dank  Seé
Merci ありがとう