NIH StrokeNet

PREVENTION | TREATMENT | RECOVERY

NINDS UPDATE

Scott Janis, PhD, MA

NINDS Perspective: What we have learned from the past to help us guide our future

MUSC Medical University of South Carolina

NIH

UNIVERSITY OF Cincinnati

NINDS StrokeNet TEAM

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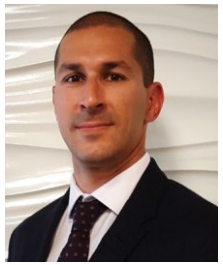

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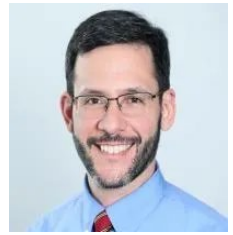

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Sandra Hewett, PhD
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Division of Neuroscience

Jim Koenig, PhD
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Division of Neuroscience

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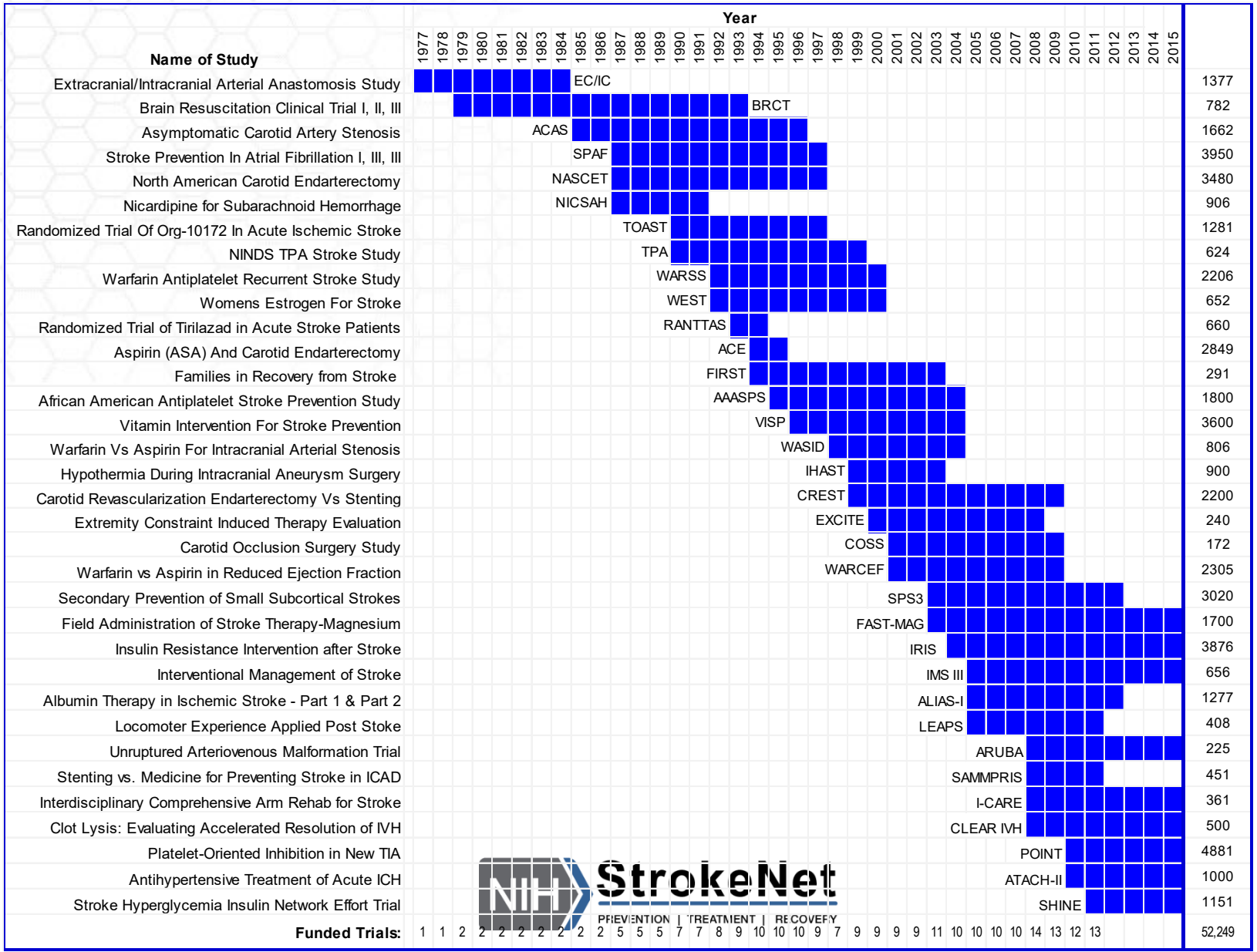
Major Clinical Trials in Stroke 1977-2011

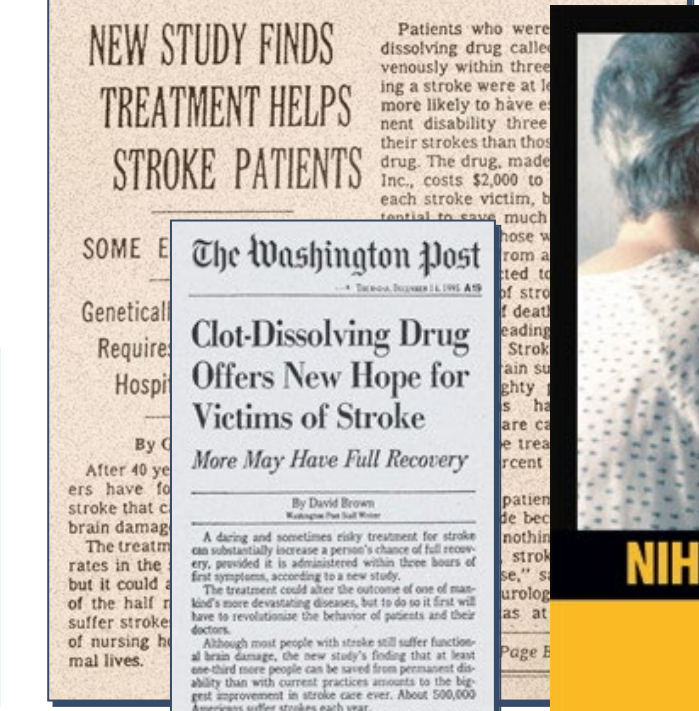


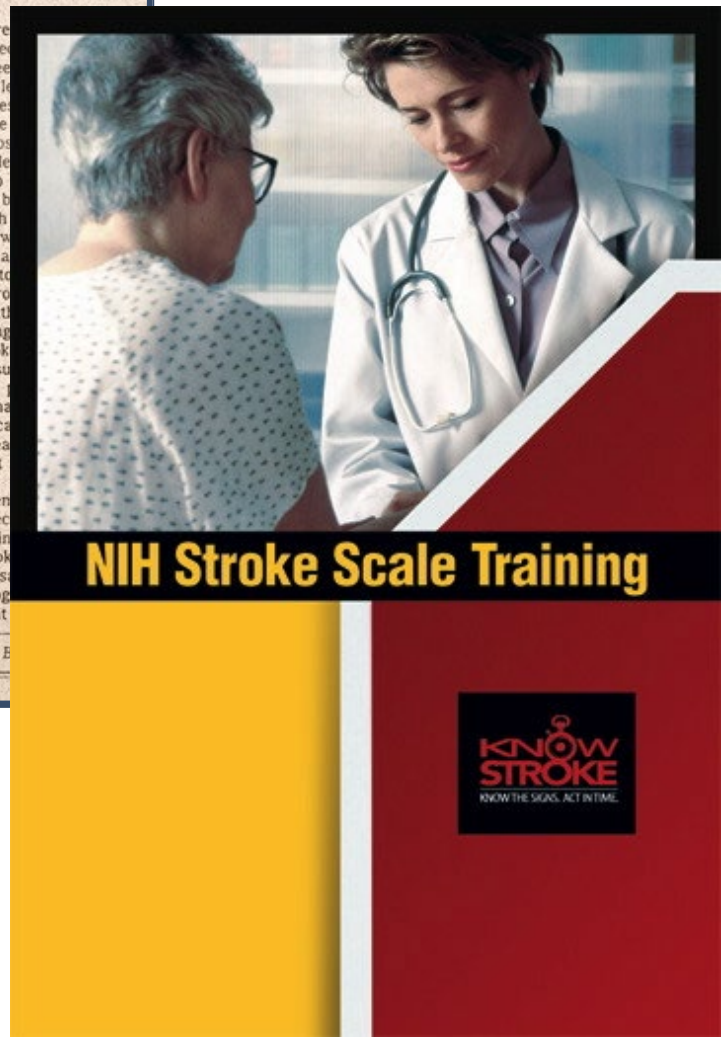
Getting NINDS Trials Started

- The Extracranial - Intracranial Bypass Trial
  - Started 1977
  - Ended 1984
  - Pivotal event in history of stroke clinical trials
  - Established that the stroke community could tackle very difficult questions and get answers that would be accepted and applied in practice
  - Set high standards of performance
- Brain Resuscitation Clinical Trial
  - Emergency consent

The Stroke Master Agreement

- Pilot studies
- Led to three trials
  - TOAST
  - NICSAH
  - NINDS TPA Study
- NIH Stroke Scale
- 50 center network





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Report of the Stroke Progress Review Group - April 2002

Stroke Priorities for the 21st Century

National Institute of Neurological Disorders and Stroke

During the Presidentially designated Decade of the Brain—1990 to 2000—scie progress in improving our unde also called "brain attack." Str cause of death in the United St long-term disability, and a sign health worldwide.

scientists are improving our understanding of differences various popula- earn how ffect these

- Develop regional stroke center networks that will improve information-sharing and collaboration among health care providers, both regionally and nationally.

Research on stroke is among National Institute of Neurological component of the Federal govern

SPOTRIAS. **In May 2001, NINDS initiated the SPOTRIAS, to facilitate translation of basic research findings into clinical practice in settings where patients with acute ischemic and hemorrhagic stroke are evaluated and treated very rapidly after onset of their symptoms. Broader goals of this program include career development opportunities for new investigators, sharing of human tissue resources, and encouragement of collaborations among investigators across institutions.**

SPOTRIAS

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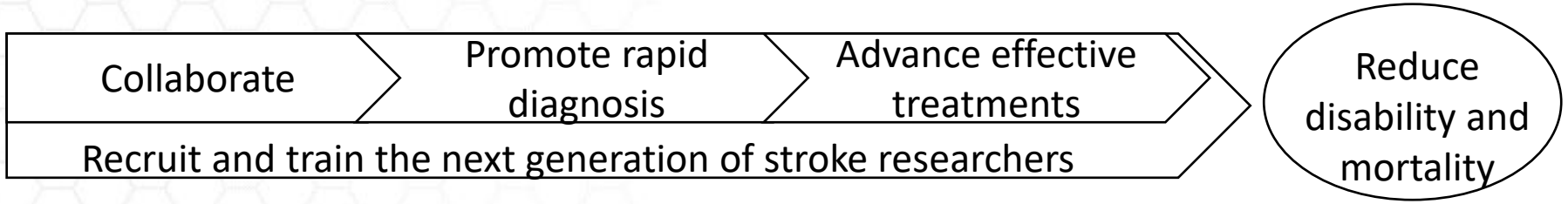
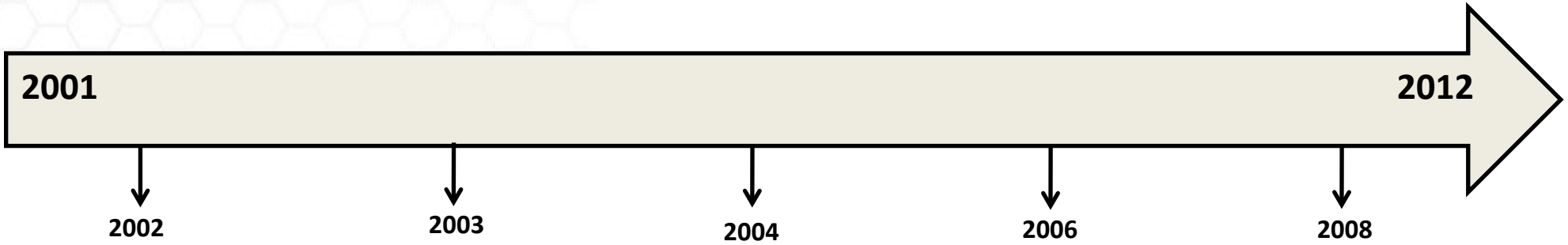
SPOTRIAS aimed to promote new therapeutic approaches for acute stroke

Conceptual model for SPOTRIAS





Centers:

UC Health

UCLA Health System

Columbia University Medical Center

Partners HealthCare

Washington University in St. Louis

UTHealth

UC San Diego Health System

National Institute of Neurological Disorders and Stroke

SPOTRIAS

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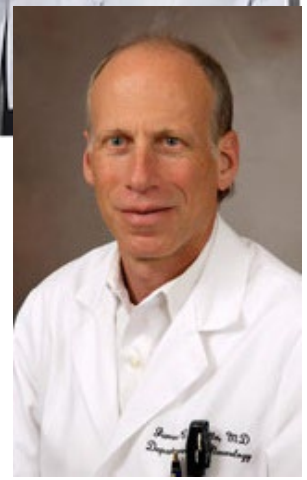
Building a team

2008 Greater Cincinnati/Northern Kentucky Stroke Team

Front Row: Aigang Lu; Pooja Khatri; Jeanne Sester; Jenny Osborne; Dan Woo; Dawn Kleind
Joe Broderick; Matt Flaherty; Joe Clark; Brett Kissela; Ed Jauch; Kathy Franklin
Back Row: Diana Oberschmidt; Alisha Hodge; Mary Haverbusch; Kathy Alwell; Charlie Moo
Janice Carrozzella; Angela Merritt; Irene Ewing; Pam Schmit; Liz Venn; Jane Eile
Julie Brock; Bonnie Combs; Elaine Miller; Judy Spilker

UNIVERSITY OF Cincinnati College

University of Texas-Houston Stroke Center



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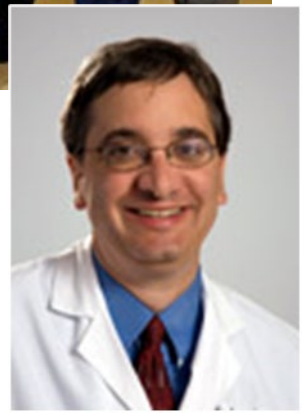
Building a team

UCSD Stroke Center

UCLA Stroke Center



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MR Rescue

Building a team

NINDS Intramural

Columbia University Medical Center

Partners Stroke Team

Washington University stroke center

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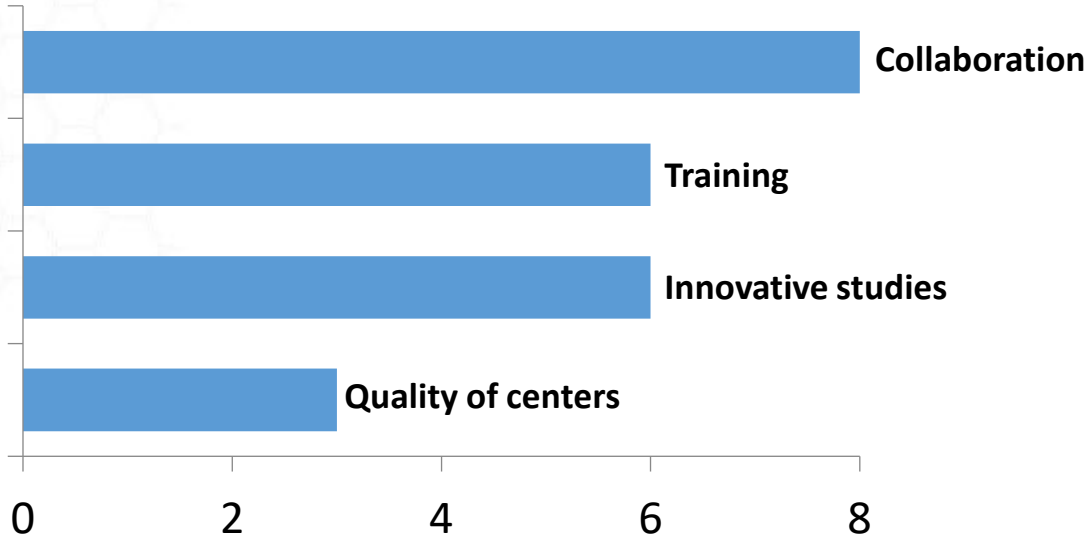
Collaboration was a clear strength of the SPOTRIAS program

Top listed strengths of SPOTRIAS

Methodology

- Asked interviewees to list the top three strengths of SPOTRIAS
- Answers that were stated two or more times were included in analysis

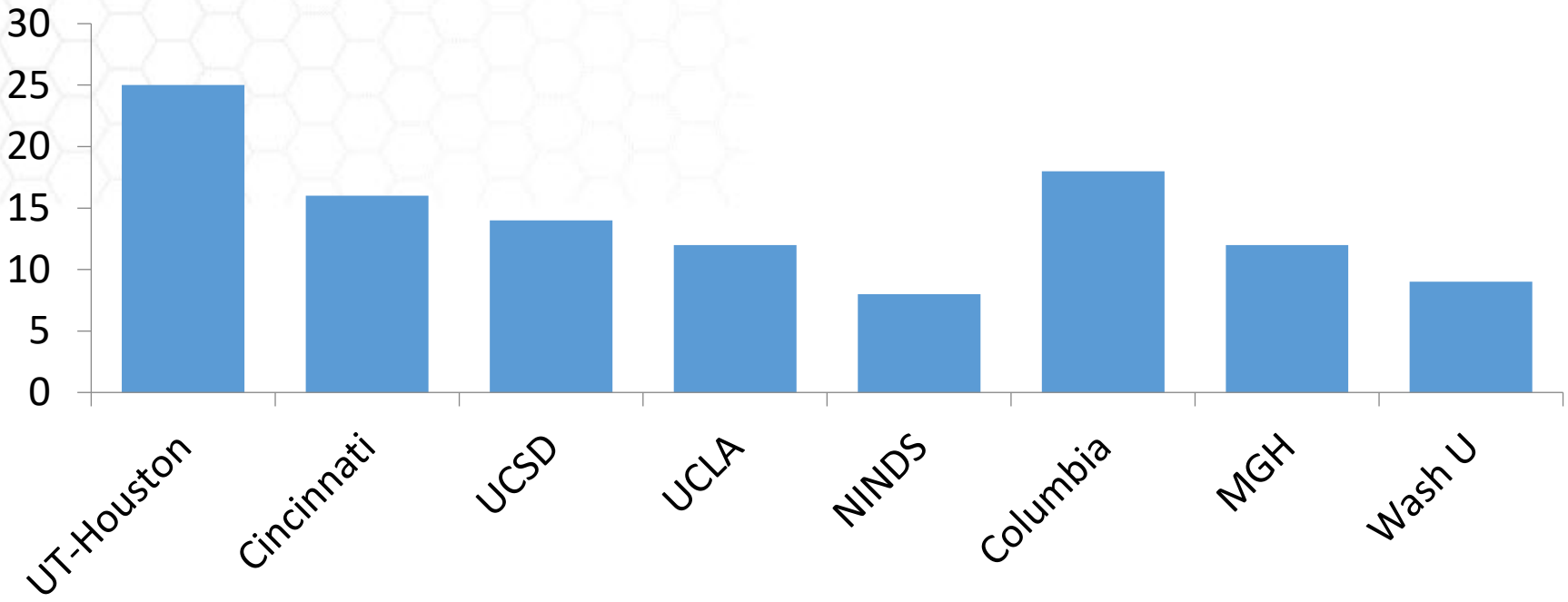


The SPOTRIAS collaboration requirement "changed the culture" of research across departments and institutions

Source: Interviews

SPOTRIAS centers have trained the next generation of stroke researchers

Number of total fellowship trained researchers from each SPOTRIAS center*



*Centers listed by date of entry into the SPOTRIAS program

Source: http://www.spotrias.org/training/,accessed July 17, 2012

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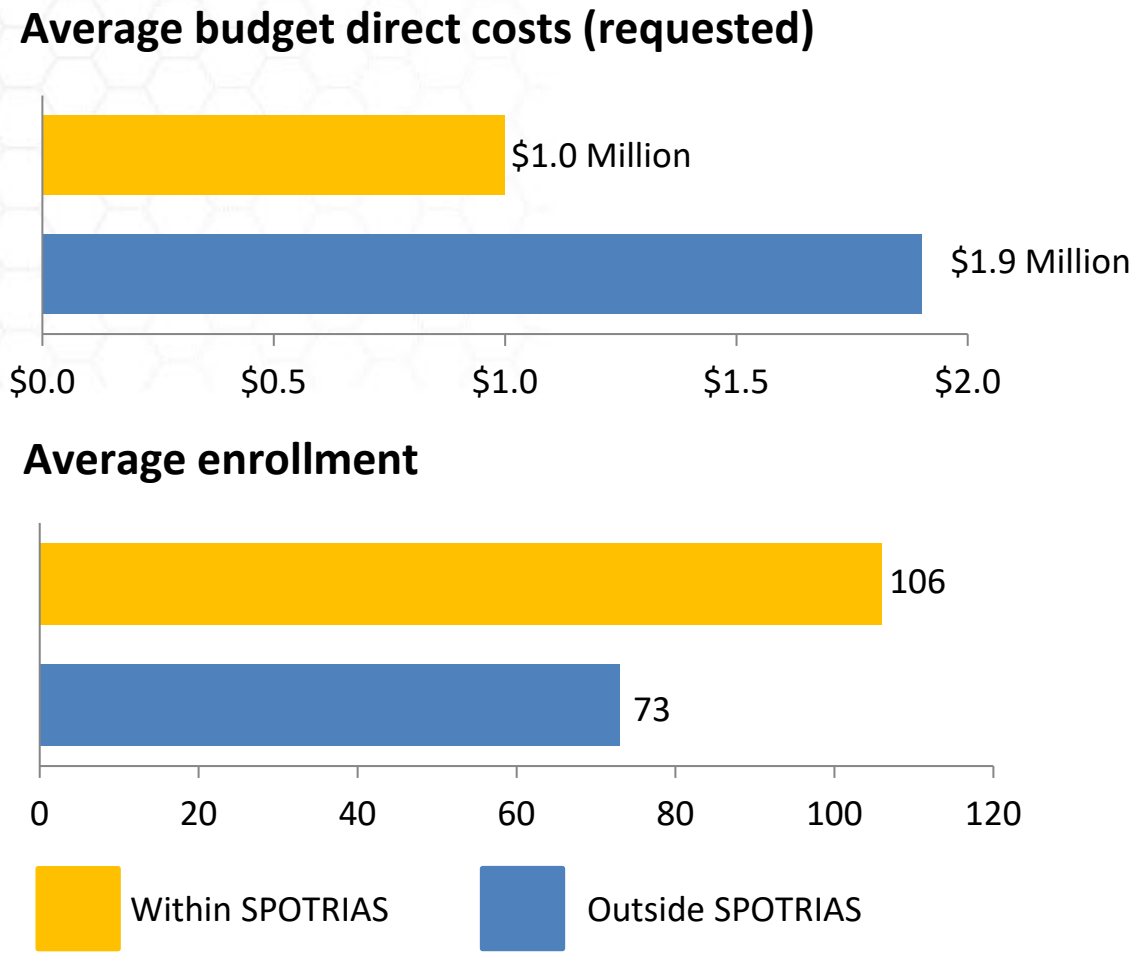
Funded SPOTRIAS clinical trials tended to have smaller requested budgets than NINDS trials outside SPOTRIAS



Source: www.clinicaltrials.gov; SPOTRIAS grants; NINDS

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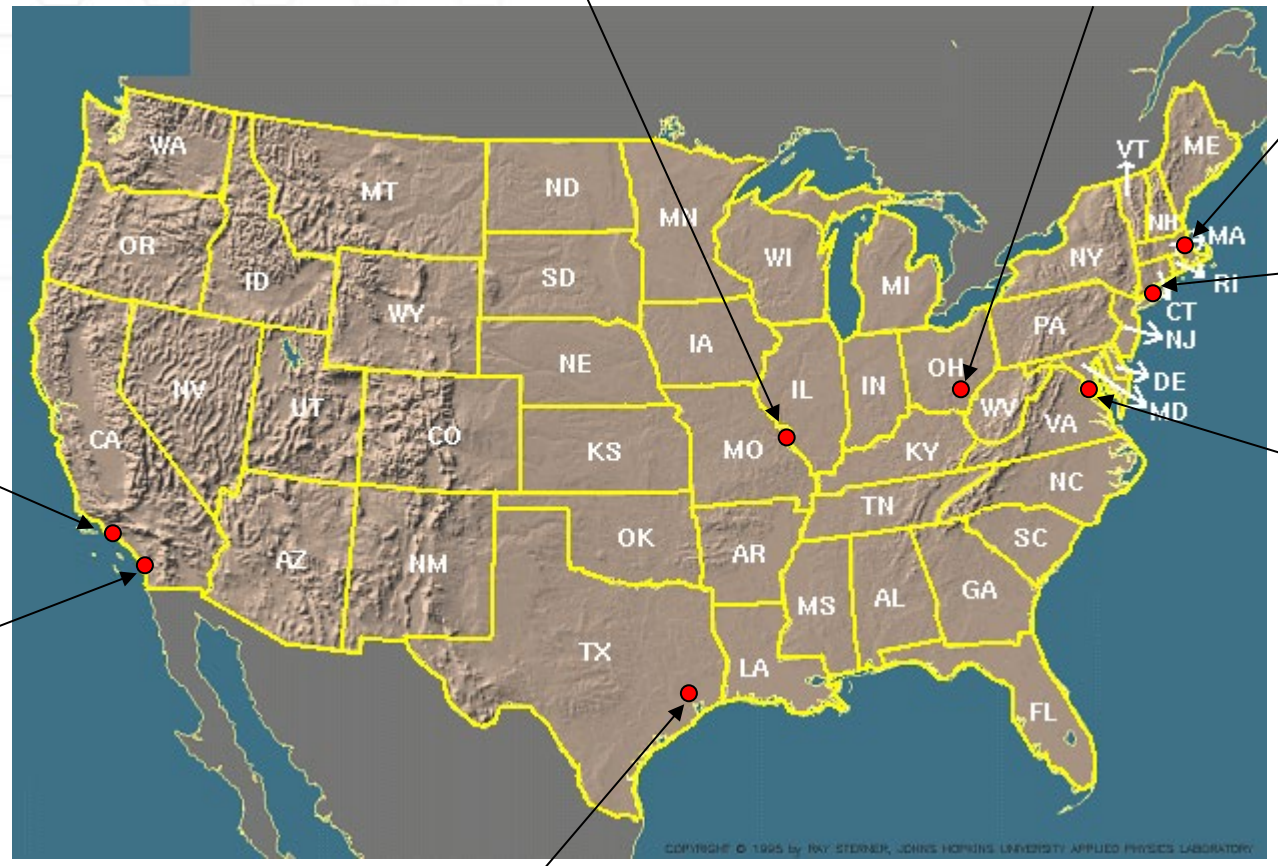
Beginning of a Stroke Network



Washington University in St. Louis

UC Health

Partners HealthCare

Columbia University Medical Center

UCLA Health System

National Institute of Neurological Disorders and Stroke

UC San Diego Health System

UTHealth

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Stroke Research Priorities Meeting 2012

Research Priority Setting

A Summary of the 2012 NINDS Stroke Planning Meeting Report

Barbara G. Vickrey, MD, MPH; Thomas G. Brott, MD; on behalf of the Stroke Research Priorities Meeting Steering Committee and the National Advisory Neurological Disorders and Stroke Council; Walter J. Koroshetz, MD; on behalf of the National Institute of Neurological Disorders and Stroke

Prevention

1) Prevention of Vascular Cognitive Impairment (VCI)
2) Imaging Biomarkers in Stroke Prevention: From Bench to Bedside
3) Expediting High Priority Comparative Effectiveness Research (CER) Trials in Stroke Prevention

Treatment

1) Preclinical and Clinical Studies to Improve Early Reperfusion Therapy and Establish Limitations of Late Reperfusion Therapy
2) Preclinical and Clinical Studies to Achieve Robust Brain Protection
3) Expand and Integrate Existing Stroke Trial Networks to Accelerate Translation

Recovery

1) Translational Research Using Neural Interface Devices for Stroke and Other Neurologic Disorders
2) Program for Translational Research Targeting Early Recovery after Stroke in Humans

Cross-cutting

Accelerate the Translation of Stroke Research in Preclinical Animal Models into Clinical Studies of Highly Promising Treatments

The NINDS Stroke Clinical Trial Network (NIH StrokeNet)

Infrastructure established in 2013; renewed in 2018 and 2023

Goals:

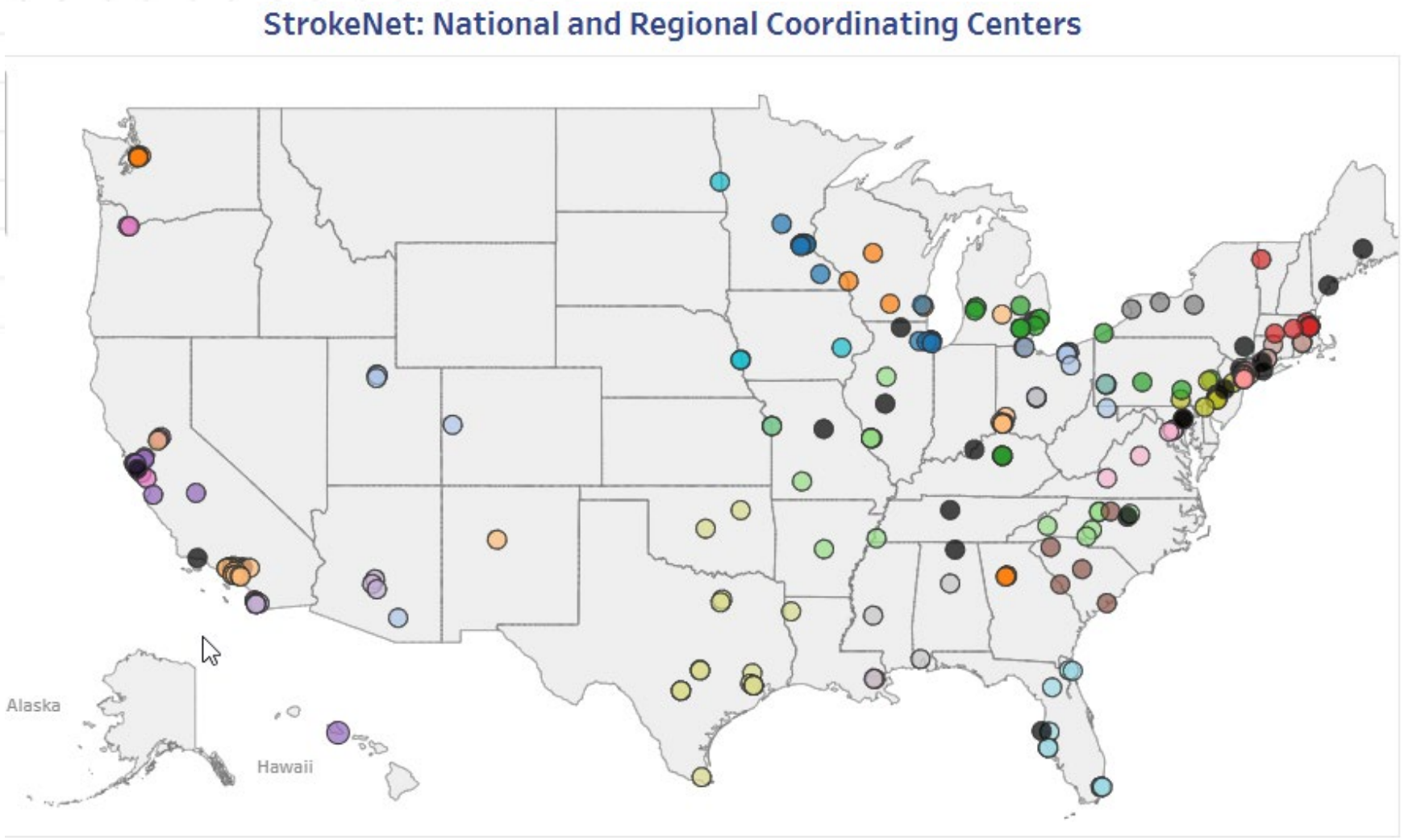
- Maximize efficiencies to develop and conduct a balanced portfolio of high-quality, multi-site phase 1, 2 and 3 clinical trials in stroke prevention, treatment, and recovery
  - Includes biomarker validation and ancillary studies to StrokeNet trials
- Educate future stroke researchers

Infrastructure:

- National Coordinating Center (NCC)
- National Data Management and Statistical Center (NDMC)
- 27 Regional Coordinating Centers (RCCs) with clinical performance and satellite sites representing over 700 stroke hospitals (including Canada, Europe, and Japan)
- Central Institutional Review Board; central research pharmacy, imaging core, and a training and education core
- Each RCC has annual support for portion of a trainee's effort

Clinical trials and studies funded separately from the infrastructure, through peer-reviewed funding mechanisms open to investigators from academia, foundations, or industry

NIH StrokeNet Sites



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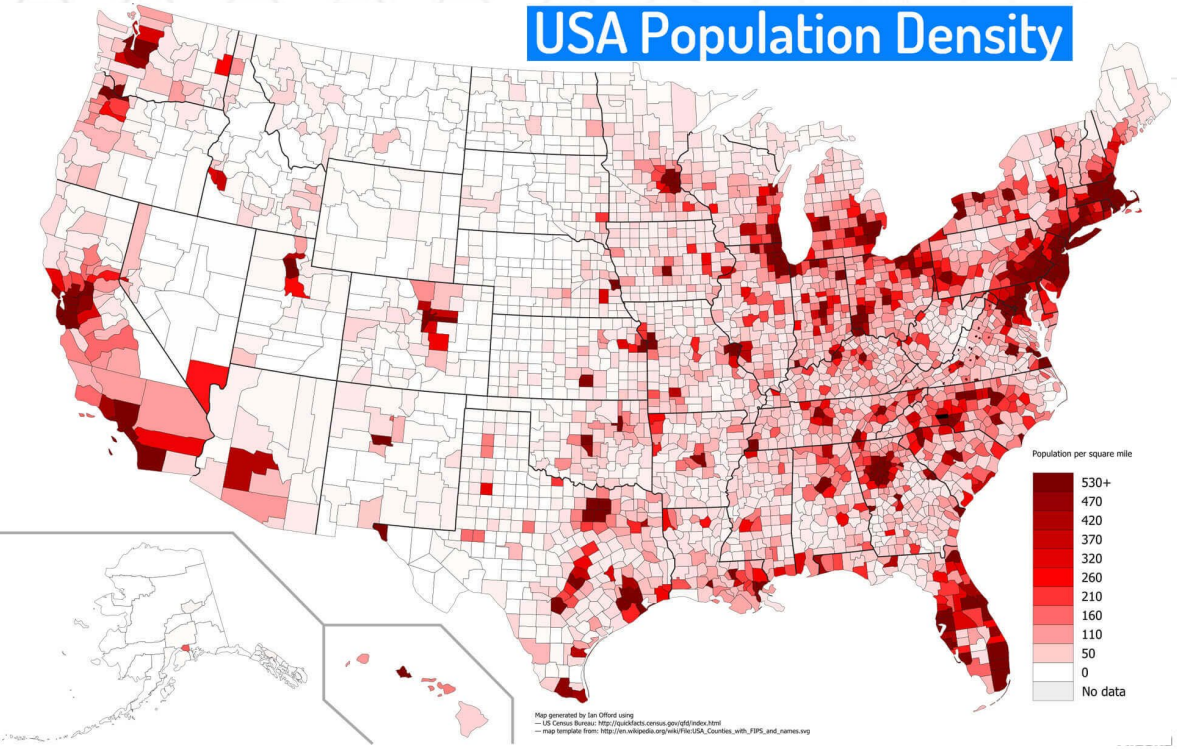
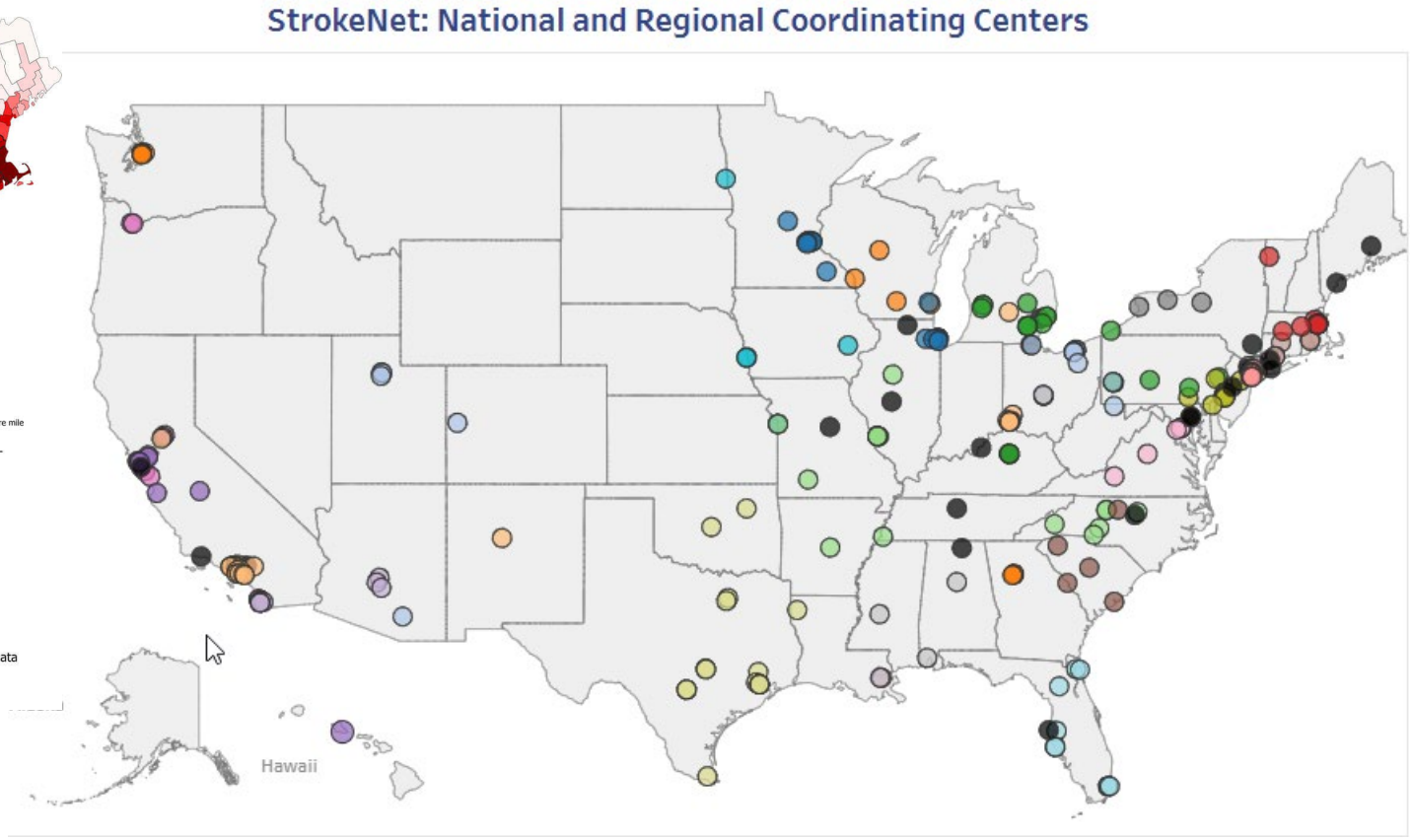
Coverage of U.S. Population





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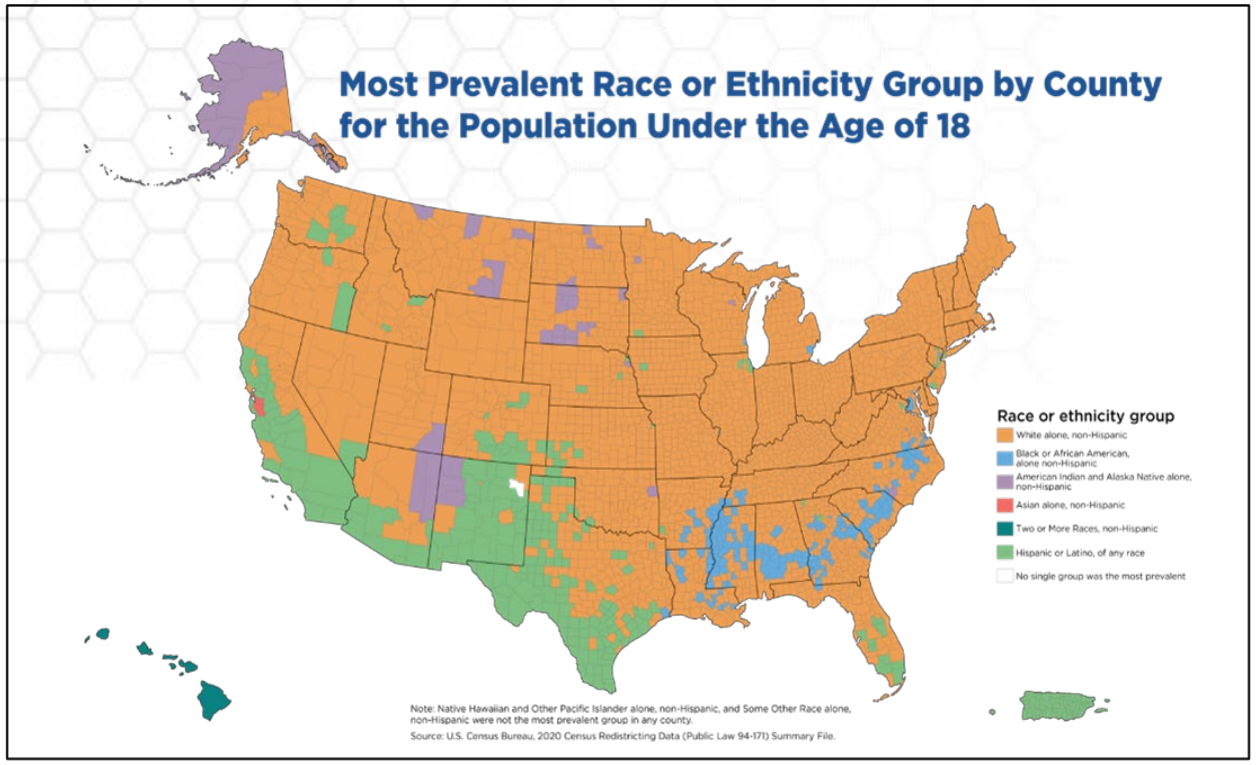
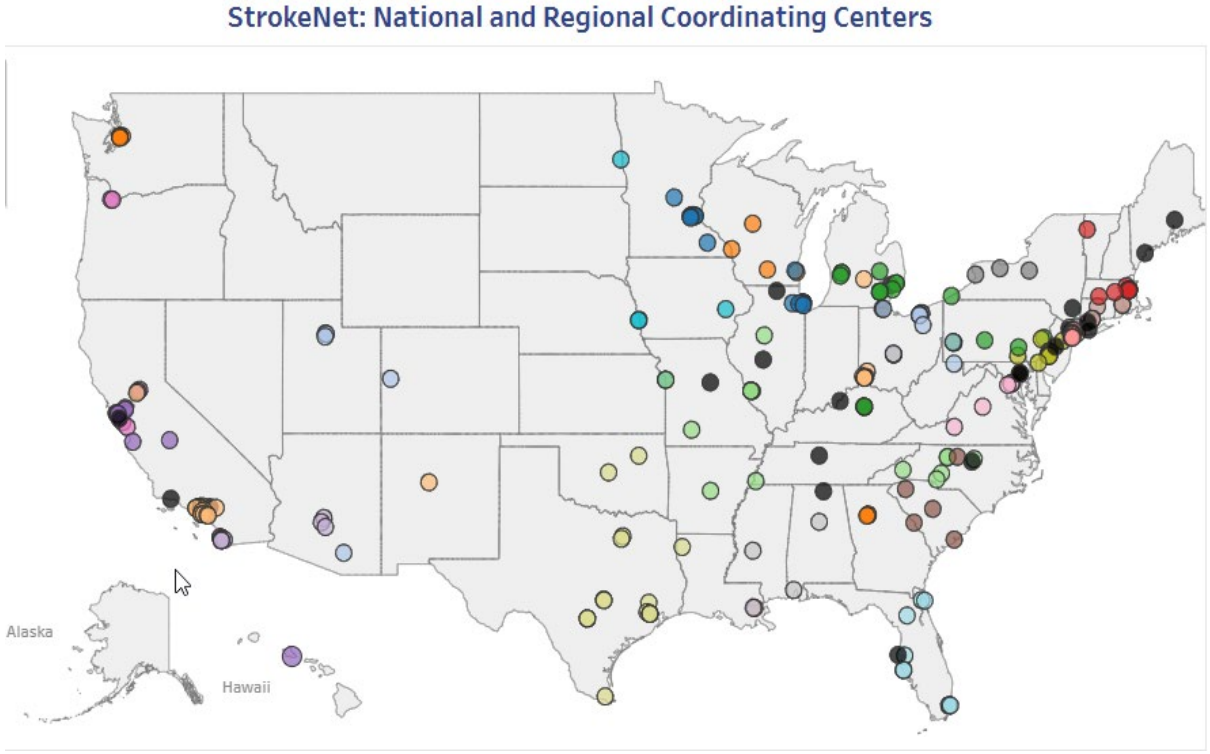
U.S. Race and Ethnic Population





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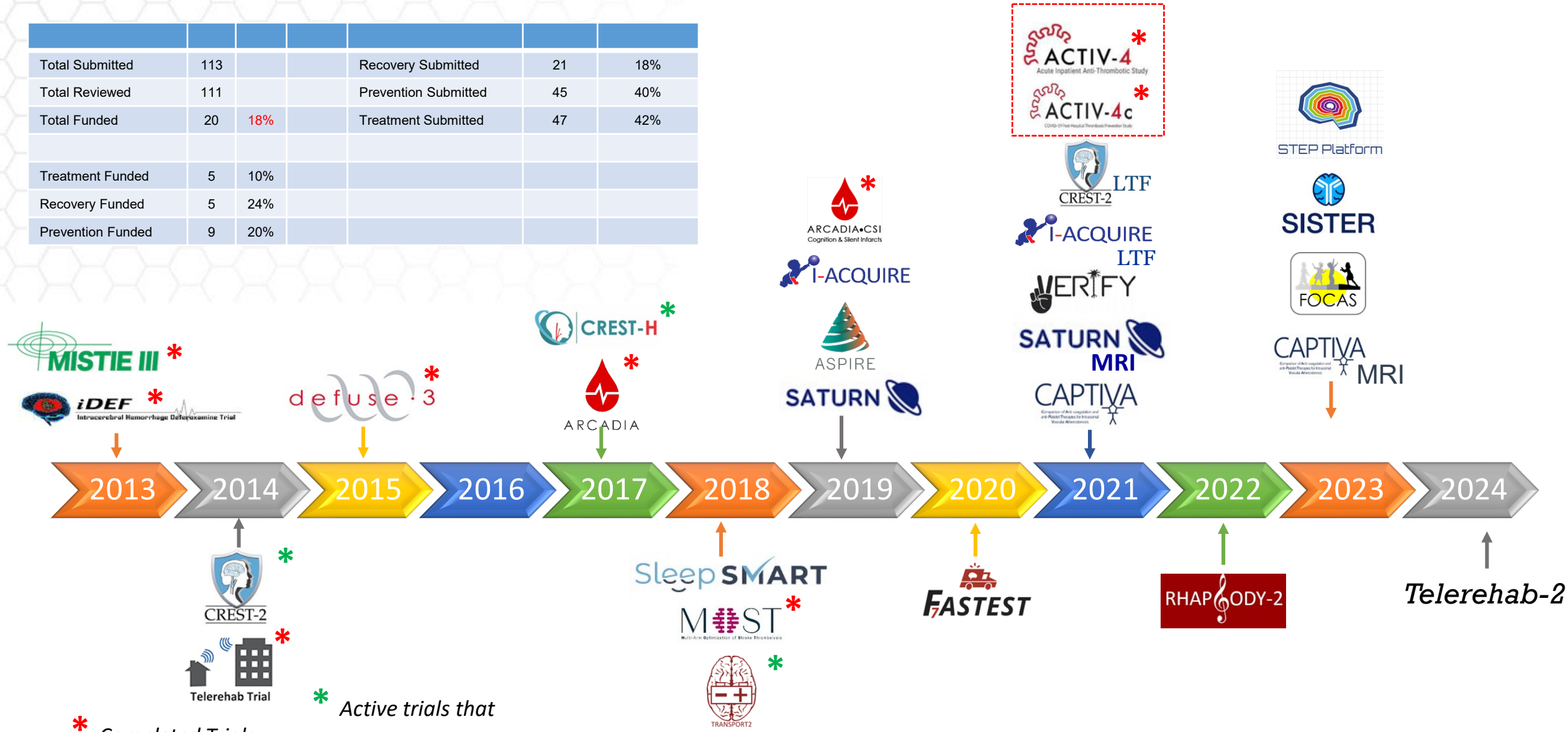
NIH StrokeNet by the Years

*As of 8/31/24, the network has consented and enrolled **13,823** and randomized **7492** participants in a StrokeNet study*

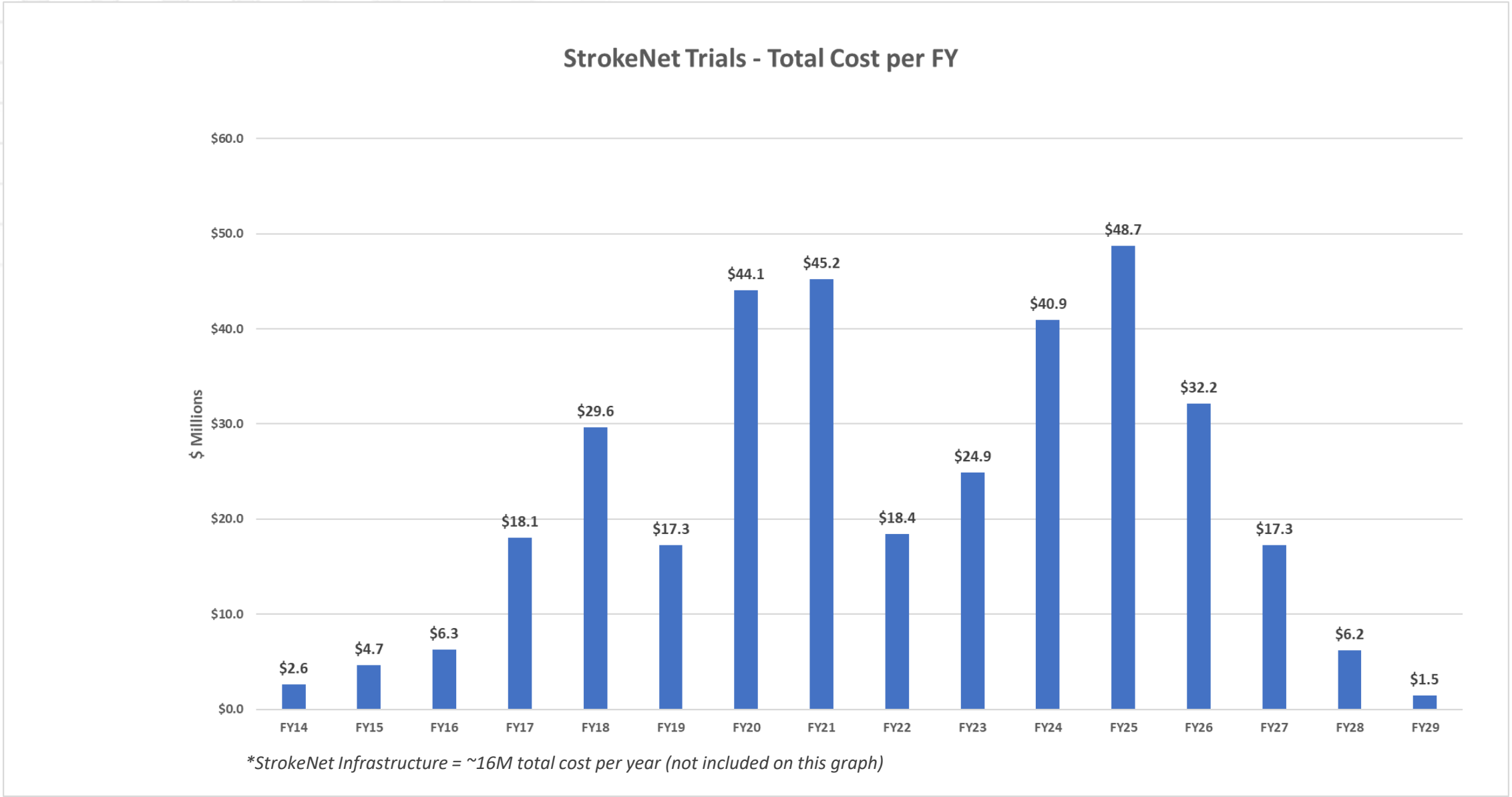
Total Submitted	113			Recovery Submitted	21	18%
Total Reviewed	111			Prevention Submitted	45	40%
Total Funded	20	18%		Treatment Submitted	47	42%
Treatment Funded	5	10%				
Recovery Funded	5	24%				
Prevention Funded	9	20%				



* *Completed Trials*

* *Active trials that completed enrollment*

StrokeNet Projects (funded cooperative agreements)



StrokeNet Infrastructure = ~16M total cost per year (not included on this graph)

Time from Submission to First patient enrolled

Application to Funding Approval (Days)	Application to Award Start (Days)	Funding Approval to Award Start (Days)	Application to First Patient Enrolled (days)	Award Start to Study Start (Days)	Award Start to First Patient Enrolled (Days)	
523	758	233	1093	295	319	Mean Days
260	297	106	372	113	122	Std Dev
486	712	223	1084.5	270	304.5	Median Days
16.2	23.7	7.4	36.2	9.0	10.2	Months
198	392	19	528	127	100	Min Days
1223	1427	465	1838	570	642	Max Days

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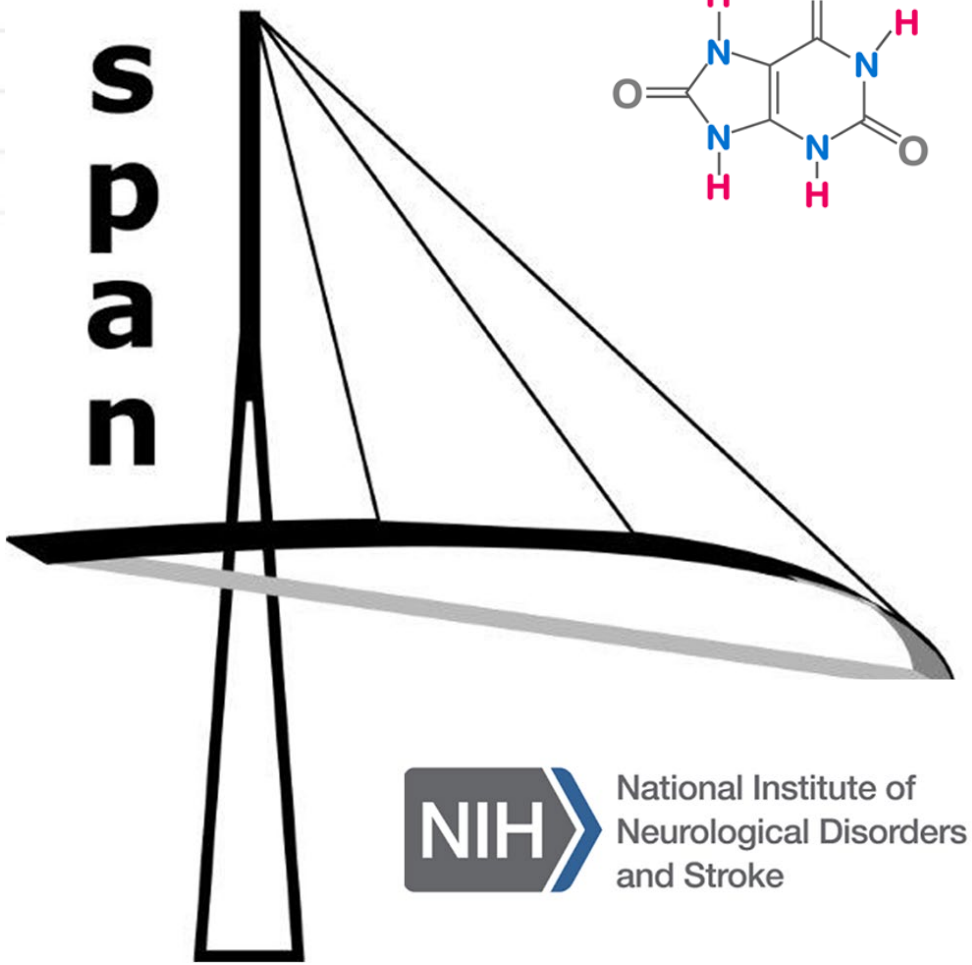
Stroke Preclinical Assessment Network (SPAN)



The Stroke Pre-Clinical Assessment Network (SPAN) seeks to conduct late-stage preclinical studies of putative neuroprotectants combined with reperfusion.

NIH National Institute of Neurological Disorders and Stroke

JOHNS HOPKINS MEDICINE

UNIVERSITY OF CALIFORNIA SAN DIEGO

UNIVERSITY OF IOWA HEALTH CARE

MCG REMOTE ISCHEMIC CONDITIONING

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MGH 1811

NEURO VASCULAR RESEARCH

Clinical Networks Evaluation Working Group

of the National Advisory Neurological Disorders and Stroke (NANDS) Council

- Presentation to the NANDS Council
- February 2, 2022

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Top-line Recommendations

Top 2 Recommendations

Proactively identify priorities

Monumentally improve pre-award/review efficiency

Strengthen internal and external community engagement

Set explicit goals to address equity, diversity, and inclusion and resource achieving them

Enhance clinical workforce development, readiness, and retention

Strengthen regular network evaluation and timely improvement

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Workable solutions based on the NINDS Clinical Networks Evaluation Working Group

Proactively identify priorities

- Work with community (through workshops/conferences, strategic planning) to identify areas of high unmet need and scientific priority
- Strengthen generation of research ideas through existing network structures, (e.g. disease area interest groups)
- Require appropriate representation of diverse populations

Monumentally improve pre-award/review efficiency

- Innovate and accelerate Network award and review processes
- Streamline NINDS extramural pre-review processes
- Consider Administrative Core for non-academic coordination functions

Strengthen regular network evaluation and timely improvement

- Develop 5-year network evaluation plan
- Conduct Listening Sessions with investigators and community partners 2x/year for input on performance

Strengthen internal and external community engagement

Set explicit goals to address equity, diversity, and inclusion and resources for achieving them

Enhance clinical workforce development, readiness, and retention

StrokeNet Thrombectomy Platform (STEP)

Objective: To determine the optimal strategy for treatment of patients with Arterial Ischemic Stroke (AIS) due to Large Vessel Occlusions (LVOs) or Medium Vessel Occlusions (MVOs)

Population: Patients with AIS due to proximal large or distal medium vessel occlusion who are potentially amenable to endovascular therapy

1995 - 2018

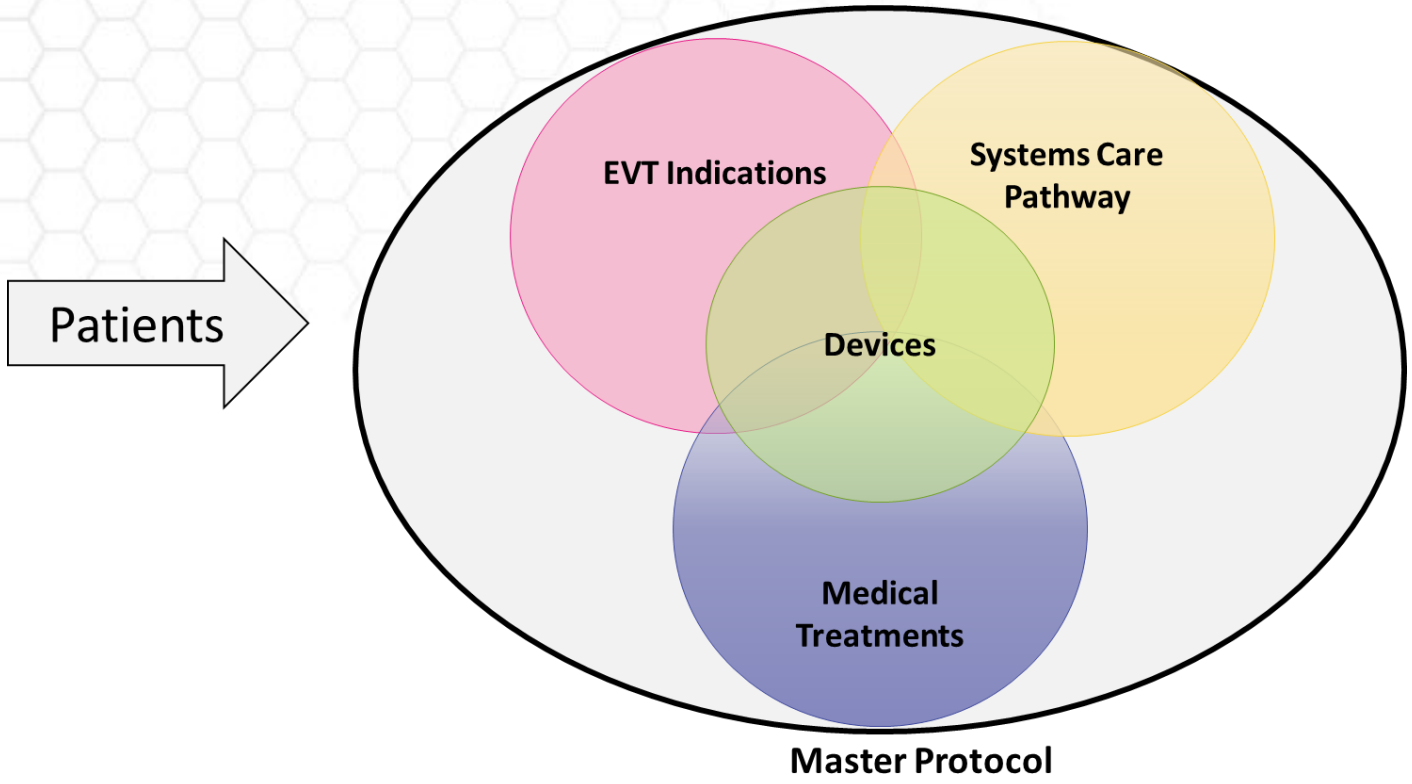
- 1999 - EMS Bridging Trial
- 2004 - IMS I
- 2007 - IMS II
- 2012 - DEFUSE 2
- 2012 - IMS III
- 2012 - MR RESCUE
- 2018 - DEFUSE 3

2018 - 2023

	STAMPEDE	GBM AGILE	Healey Center for ALS	HEAL	ACTIV
Platform	STAMPEDE	GBM AGILE	Healey ALS	EPPIC NET (HEAL)	ACTIV
Condition	Prostate CA	Glioblastoma	ALS	DPN	COVID-19
Year started	2005	2019	2020	2020	2020
Agents/pops tested	10	4	5	>4	27
Centers	>120	>23	>54	>24	>620
Patients	>10,000	>550	>1000	>1000	>20,000

Building of previous and growing experience, the NINDS pursued a clinical trial platform to answer the many questions that we have been receiving in the EVT space

What types of questions for STEP



Clinical trials that will address:

- Indication expansion of current endovascular therapy (EVT) criteria
  - *e.g., EVT for low NIHSS, children, etc.*
- Concomitant medical therapies added to EVT
  - *e.g., BP control, avoiding tPA, general anesthesia or sedation, novel neuroprotective agents, etc.*
- Systems of care for EVT
  - *e.g., prehospital identification for EVT routing, etc.*
- Novel EVT devices

How to Apply – Research Opportunity Announcement

Participating Organization(s)	National Institutes of Health (NIH)
Components of Participating Organizations	National Institute of Neurological Disorders and Stroke (NINDS)
Research Opportunity Title	**StrokeNet Thrombectomy Platform (STEP) – Domain Clinical trials to be conducted in STEP: Stage 1 Preliminary Application (OT2)**
Activity Code	OT2: Application for an Other Transaction Agreement
Research Opportunity Number	OTA-24-009
Related Notices	
Key Dates:	Posted Date: February 8, 2024
	Open Date (Earliest Submission Date): March 1, 2024
	Application Due Date(s): Rolling Submission

13 Proposals already submitted

- Biospecimen Core funded for baseline blood collection
  - 24hr blood draw
  - Isolation of DNA that can be used for genetics and epigenetics and RNA for transcriptomics
  - Isolation of plasma for proteomic analyses
  - ***Future opportunities*** for R01 applications

https://www.ninds.nih.gov/funding/find-funding-opportunities/research-opportunity-announcements

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Enhance clinical workforce development, readiness, and retention

Setting our priorities

- Again, NINDS is engaged in a planning our next set of stroke priorities. But this time we are looking to leverage the scientific powerhouse we have in the network to work with our broader stroke community.
- Goal is not to use our time to pitch the trials we are working on.
- Identify scientific gaps and the opportunities that we can use our stroke network to advance.
- Starting with the network as a think tank. Then will move to include the boarder stroke community.
- The format will be a Princeton like conference that we will support through a conference grant.
- Objective is to help us (NINDS) prioritize funding and look for opportunities to streamline our research mechanisms (i.e., STEP and SPAN).
- ALL voices are important! We are here and we are listening…