



# Your Voice in Science: Advancing Alzheimer's Disease in Down Syndrome Together

NDSS/MDSC Brighter Futures Conference  
March 27 - 28, 2026  
Worcester, MA



# Outline



1. Welcome and Introduction
2. Overview of the INCLUDE Project
3. Research and Resource Spotlight: Healthy Aging and Alzheimer's Disease
4. Lived Experience: Research Through a Family's Lens (Why participation matters)
5. Moving from Hugs to New Drugs
6. Looking Ahead: What's Next in DS Research
7. Q&A

# Acknowledgements

- The NIH-wide Down Syndrome INCLUDE Working Group
- Investigators and Trainees
- Children and adults with Down syndrome and their families



Karen Gaffney



David Egan



Mitchell Levitz

Self-advocates  
in the  
DS Consortium



Special Olympics

American Academy of Pediatrics  
DEDICATED TO THE HEALTH OF ALL CHILDREN®



# Meet Our Speakers



**Sujata Bardhan, PhD, MS**



**Annie Cohen, PhD**



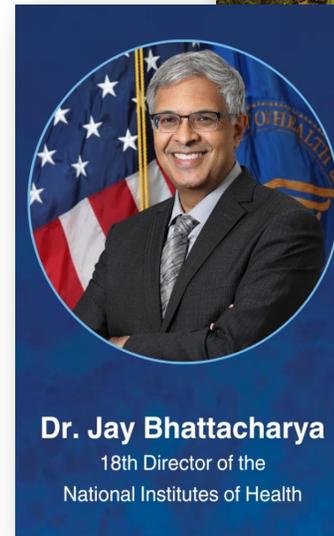
**David & Kathleen Egan, PhD**



**Beau Ances, MD**

# National Institutes of Health

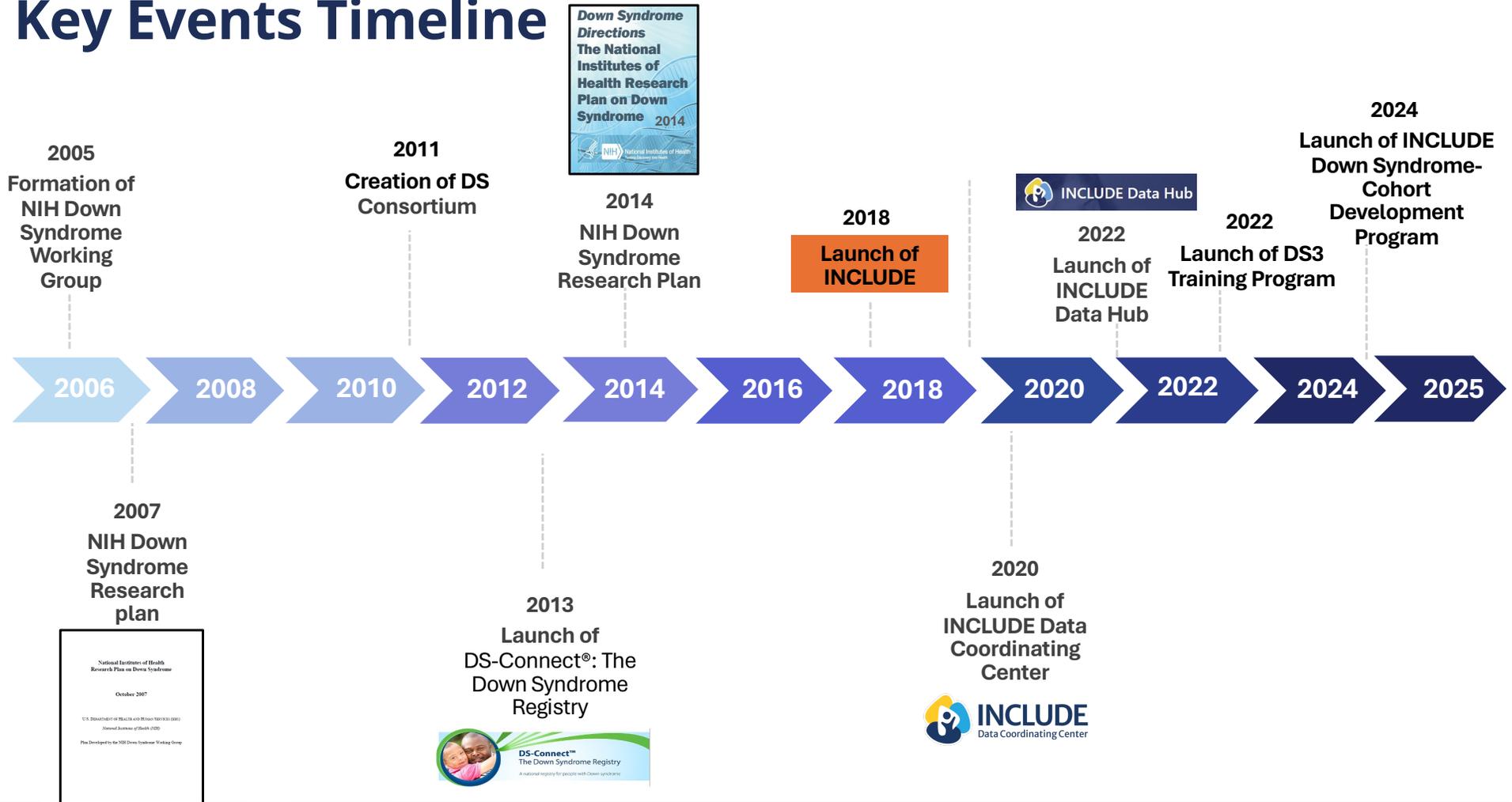
- The U.S.'s national medical research agency
- The world's largest funder of biomedical research
- 90% of funds go to university research institutions
- Dr. Jay Bhattacharya appointed 18th Director of NIH



**Dr. Jay Bhattacharya**  
18th Director of the  
National Institutes of Health



# Key Events Timeline



# INCLUDE Project: Established 2018



**Frank Stephens**  
Advocate, Actor, and Writer

“I am a man with Down syndrome,  
and my life is worth living.”

The INCLUDE Project launched in June 2018 to address a Congressional directive that called for a new **NIH-wide research initiative** on critical health and quality-of-life needs for individuals with DS.

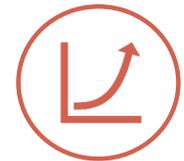
# INCLUDE Project: INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE

The INCLUDE Project launched in June 2018 to address a Congressional directive that called for a new **NIH-wide research initiative** on critical health and quality-of-life needs for individuals with Down syndrome (DS).



The INCLUDE Project:

- **Supports research that investigates conditions** that affect individuals with DS and the general population, such as Alzheimer's disease, autism, cataracts, celiac disease, congenital heart disease, and diabetes.
- **Aims to increase the number of investigators and trainees** studying DS.
- Works in partnership with the Down syndrome community to identify areas of need and **support work that benefits everyone.**



# INCLUDE Project *at a glance*



**400+**

Projects Funded



**450+**

Publications



**20+**

Community-Engagement and Outreach Events Hosted by INCLUDE Team Annually



**19**

ICO's Participating



**26**

Clinical trials



**15,800**

Individuals with DS Represented in the INCLUDE Data Hub

NIH has invested more than **\$528 million** over the past **8 years** on **412** unique awards issued through the **INCLUDE Project**

# Research and Resources: A Closer Look



# Alzheimer Biomarkers Consortium — Down Syndrome

- Most adults with DS develop **Alzheimer's disease (AD)** amyloid plaques by age 40, and most develop clinical symptoms of dementia by late 60s
- **ABC-DS was launched by NIA and NICHD in 2015**
- **Goal: Understand biological changes underlying AD in people with DS and develop clinical biomarkers**
  - Examines genetic factors and biomarkers with the potential to modify DS-AD risk
  - Develops precision medicine ready biomarkers for DS-AD clinical trials
  - Disseminates data and biospecimens to qualified researchers outside ABC-DS
- **Five-year longitudinal cohort enrolling up to 600 adults with Down syndrome (ages 25 and older)**



**ABC-DS**  
Alzheimer Biomarker Consortium-Down Syndrome

**454** Total Enrolled

**411** Individuals with DS

**43** Sibling Controls

**Advancing  
Research:  
26  
Clinical  
Trials  
Funded by  
INCLUDE**

### **Sleep & Apnea (OSA)**

- Medications for OSA to improve cognition in children with DS
- Effects of hypoglossal nerve stimulation on cognition and language in DS
- Positive airway pressure for OSA in children with DS
- Home Sleep Apnea Testing Compared to In-lab Polysomnography for the Evaluation of OSA in Children with DS
- Self-Supporting Nasopharyngeal Airway Treating Upper Airway Obstruction in Hypotonia
- A Personalized Surgical Approach for the Treatment of Children with Obstructive Sleep Apnea and Small Tonsils
- Randomized Controlled Trial of Oxygen Therapy in Children and Adolescents with DS and OSA

### **Alzheimer's Disease & Aging**

- Clinical trials to prevent Alzheimer's Disease in DS
- Addition of GM-CSF/sargramostim treatment to improve cognition in DS
- The Impact of Weight Loss on Alzheimer's Disease Risk in Adults with DS

### **Immune System Dysregulation**

- JAK inhibition for treatment of DS skin conditions

### **Neurodevelopment**

- Mechanistic investigation of therapies for Down Syndrome Regression Disorder
- Evaluating assessment and medication treatment of ADHD in children with DS

# DS-Connect<sup>®</sup>

The Down Syndrome Registry

## MAKE DISCOVERIES POSSIBLE

Easily share important information with researchers

## KNOW THE FACTS

Access expert-curated resources to guide healthcare decisions

## JOIN THE COMMUNITY

Be a member of an active community with a common cause

Join our nearly 6,000 registrants today!



[ds-connect.org](https://ds-connect.org)

Scan to Learn More  
and Register



en español: [ds-connect.org/es](https://ds-connect.org/es)



# NIH Establishes **\$20 million** program in 2024 to study Down syndrome from **birth** to **adulthood**



The **Down Syndrome Cohort Development Program (DS-CDP)** is a long-term study aimed at **improving health outcomes** for people with Down syndrome. This initiative represents a powerful collaboration, between the NIH, medical institutions, and community partners.

Research and clinical teams are developing the **Common Protocol**. Plan to **start enrolling families in early spring 2026**.

# DS-Connect<sup>®</sup>

The Down Syndrome Registry

Get DS-Connected!



English:  
[ds-connect.org](https://ds-connect.org)



Español:  
[ds-connect.org/es](https://ds-connect.org/es)



# INCLUDE

Collaboration for  
Down Syndrome Progress

Participate in Down syndrome research!



[includecdp.org](https://includecdp.org)

# ABC-DS

Alzheimer Biomarker Consortium-Down Syndrome

Learn more about ABC-DS



[abc-ds.org](https://abc-ds.org)



# INCLUDE

Data Coordinating Center

Sign up for our eNews!



[includedcc.org](https://includedcc.org)

# Thank You!



**Questions?**

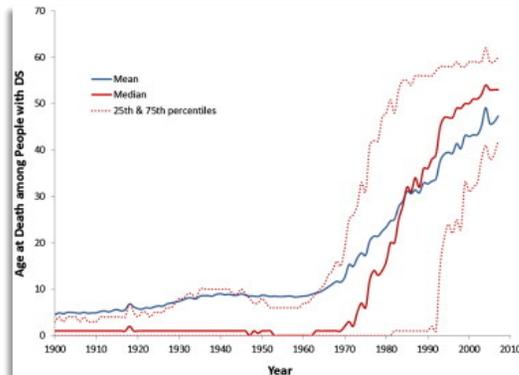
Sujata Bardhan  
[sujata.bardhan@nih.gov](mailto:sujata.bardhan@nih.gov)



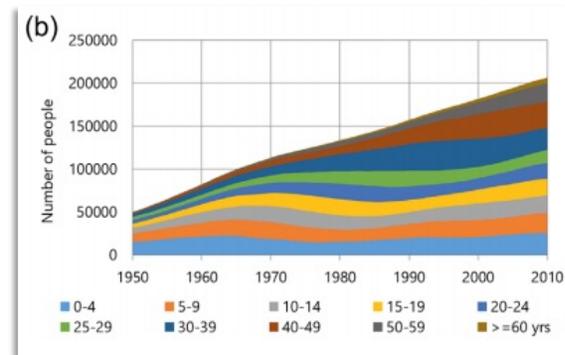
**Annie Cohen, PhD**  
Associate Professor of Psychiatry  
University of Pittsburgh School of Medicine

**UPMC ABC-DS**  
Alzheimer Biomarker Consortium-Down Syndrome

# People with Down Syndrome are Living Longer



A 3.75-fold increase in average life expectancy since 1970 (Presson et al., J Peds., 2013).



Fastest growing segment is 40-49 years of age (Hithersay et al., 2019)



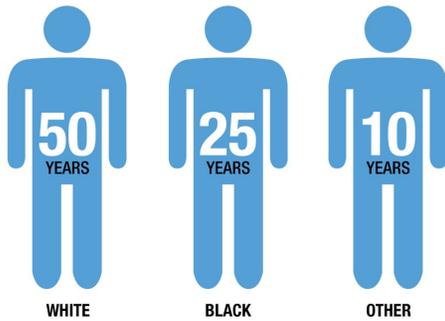
# Disparities

Pediatrics  
NATIONWIDE

12 years for other cases.

About

## MEDIAN AGE OF LIFE EXPECTANCY FOR PEOPLE WITH DOWN SYNDROME\*



\*Data from Yang Q, Rasmussen SA, Friedman JM. Mortality associated with Down's syndrome in the USA from 1983 to 1997: a population-based study. *Lancet*. 2002;359:1019-25.

ORIGINAL  
ARTICLES

www.jpeds.com • THE JOURNAL OF PEDIATRICS

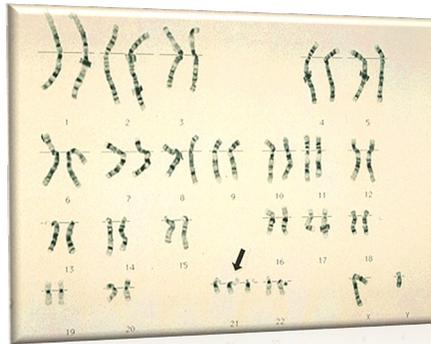


### Contributions to Racial Disparity in Mortality among Children with Down Syndrome

Stephanie L. Santoro, MD<sup>1</sup>, Anna J. Esbensen, PhD<sup>2</sup>, Robert J. Hopkin, MD<sup>3</sup>, Lesly Hendershot, PsyD<sup>4</sup>, Francis Hickey, MD<sup>5</sup>, and Bonnie Patterson, MD<sup>6</sup>

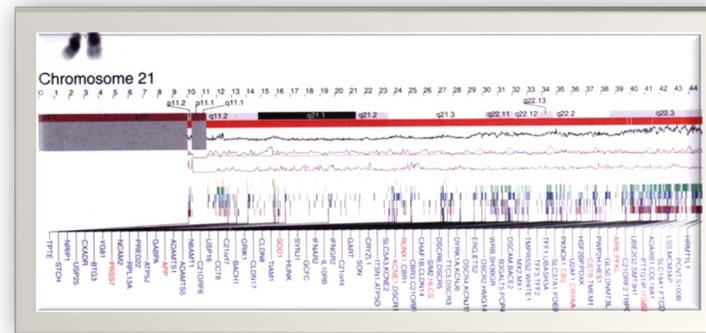


# Aging People with Down Syndrome are Vulnerable to Alzheimer Disease



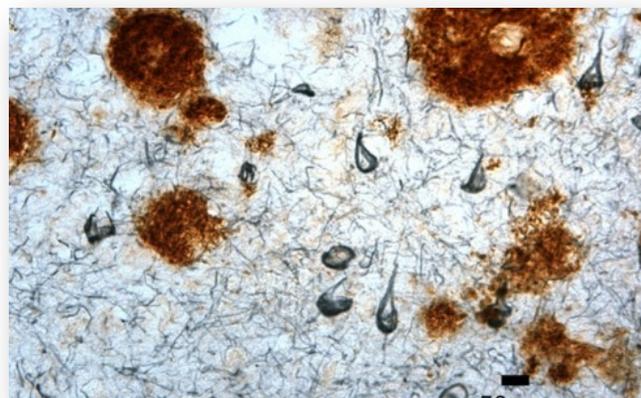
Amyloid precursor protein is present at 1.5 higher levels – overproduction of A $\beta$

People with Down syndrome are living longer and age is the biggest risk factor for Alzheimer disease

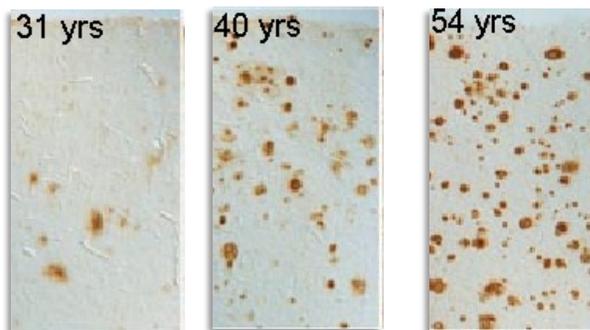


# What is Alzheimer Disease?

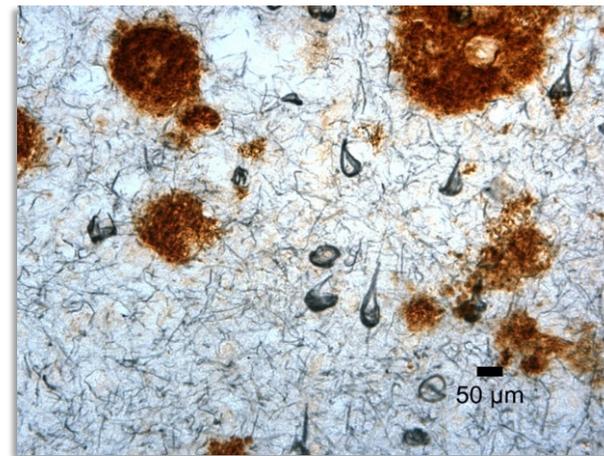
- Described by Alois Alzheimer in 1906
- The most common cause of dementia in the elderly
- Associated with a change in cognition and function that interferes with activities of daily living
- Diagnosed as possible or probable AD in the clinic
- Verified at autopsy – beta-amyloid plaques and neurofibrillary tangles



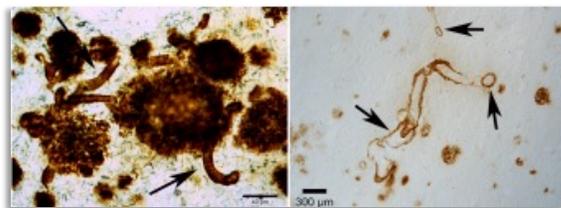
# People with DS are Vulnerable to AD with an Earlier Age of Onset



Head, Azizeh, Lott, Tenner, Cotman  
& Cribbs, 2001



Head & Lott, 2019

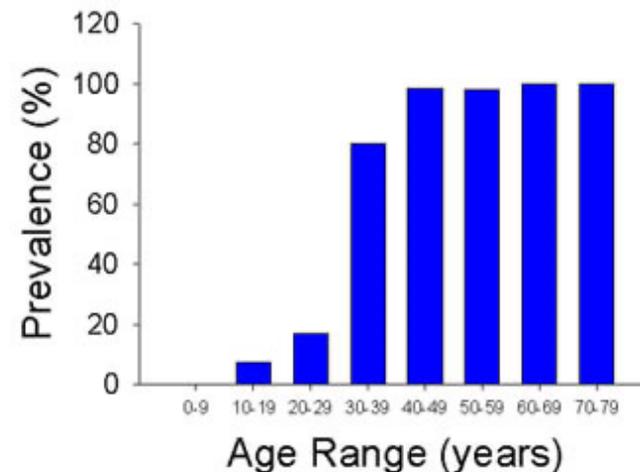


Thank you to our amazing brain  
donors for helping us understand  
how to find ways to prevent or treat  
AD!

# What is the Age of Onset of AD Neuropathology in Down Syndrome?

Virtually all adults with DS over the age of 40 years have sufficient neuropathology for AD (Struwe, 1929; Jarvis, 1948) – including plaques and tangles

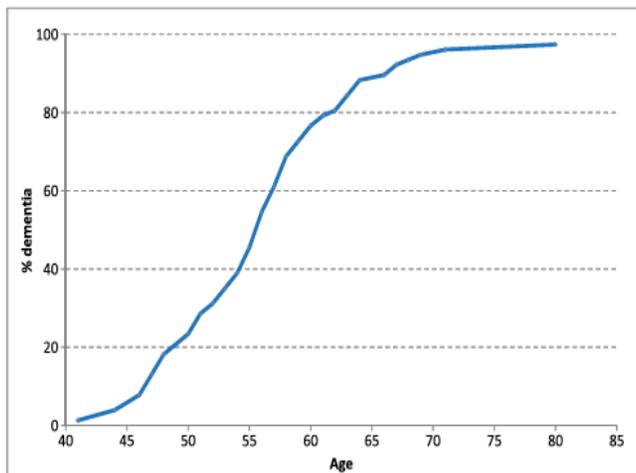
\*\*\*but wait there is more and its good news \*\*\*



Mann et al., 1993

# Alzheimer Disease in People with Down Syndrome – Some Sobering Facts

Near full penetrance of AD dementia



- AD limits the life expectancy for people with DS
- We need a treatment.

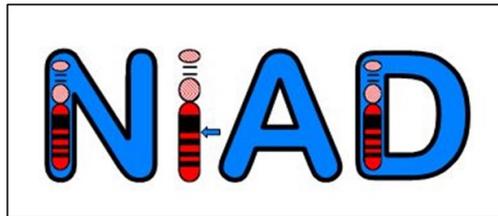
JAMA Network | **Open.**

Original Investigation | Neurology

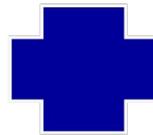
Association of Alzheimer Disease With Life Expectancy in People With Down Syndrome

María Florencia Iulita, PhD; Diana Garzón Chavez, RN; Maria Klitgaard Christensen, PhD; Natalia Valle Tamayo, MSc; Oleguer Plana-Ripoll, PhD; Sonja A. Rasmussen, MD; Marta Roqué Figuls, PhD; Daniel Alcolea, MD; Laura Videla, MSc; Isabel Barroeta, MD; Bessy Benejam, MSc; Miren Altuna, MD; Concepción Padilla, PhD; Jordi Pegueroles, MSc; Susana Fernandez, MD; Olivia Belbin, PhD; María Carmona-Iragui, MD; Rafael Blesa, MD; Alberto Lleó, MD; Alexandre Bejanin, PhD; Juan Fortea, MD

# Harmonized Project



Neurodegeneration in Aging  
Down Syndrome – PI Handen  
(UPitt)



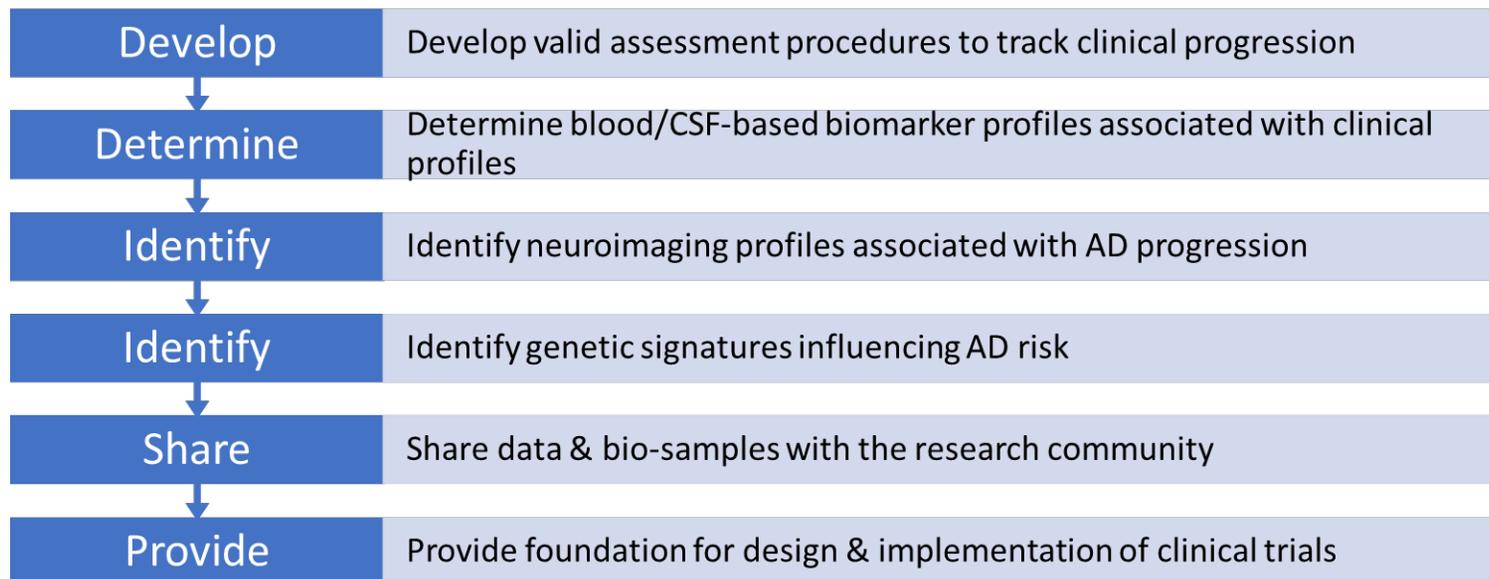
Alzheimer's Disease in Down  
Syndrome – PI Schupf (Columbia)



Alzheimer Biomarker Consortium –  
Down syndrome – MPI Handen (UPitt),  
Christian (UWisc Madison), Mapstone  
and Head (UCI)



# ABC-DS Study Aims



## ABC-DS Performance Sites (8)

Site	Location	PI
University of Pittsburgh*	Pittsburgh, PA	Handen
University of Wisconsin	Madison, WI	Christian
University of Cambridge	Cambridge, UK	Zaman
Washington University	St Louis, MO	Ances
University of Kentucky	Lexington, KY	Schmitt
Mass General /Harvard	Boston, MA	Rosas/Lai
UC Irvine	Irvine, CA	Lott/Head/Mapstone
Columbia University	New York, NY	Lee/Krinsky-Hale

\*Coordinating Site



# How Do We Become Good Partners?



## Ensure that community members with DS have a seat at the table

Seek feedback at every stage of research  
Advertising  
Informed consent  
Procedures  
Setting/ Location



## Acknowledge that traditional sources of DS recruitment have failed to engage diverse community members.

Care providers  
Support Groups  
Conferences



## Meet the community where they are

Identify how research can be of service to the community  
Community is acutely aware of "hit and run" approach



## Identify challenges and barriers to participation

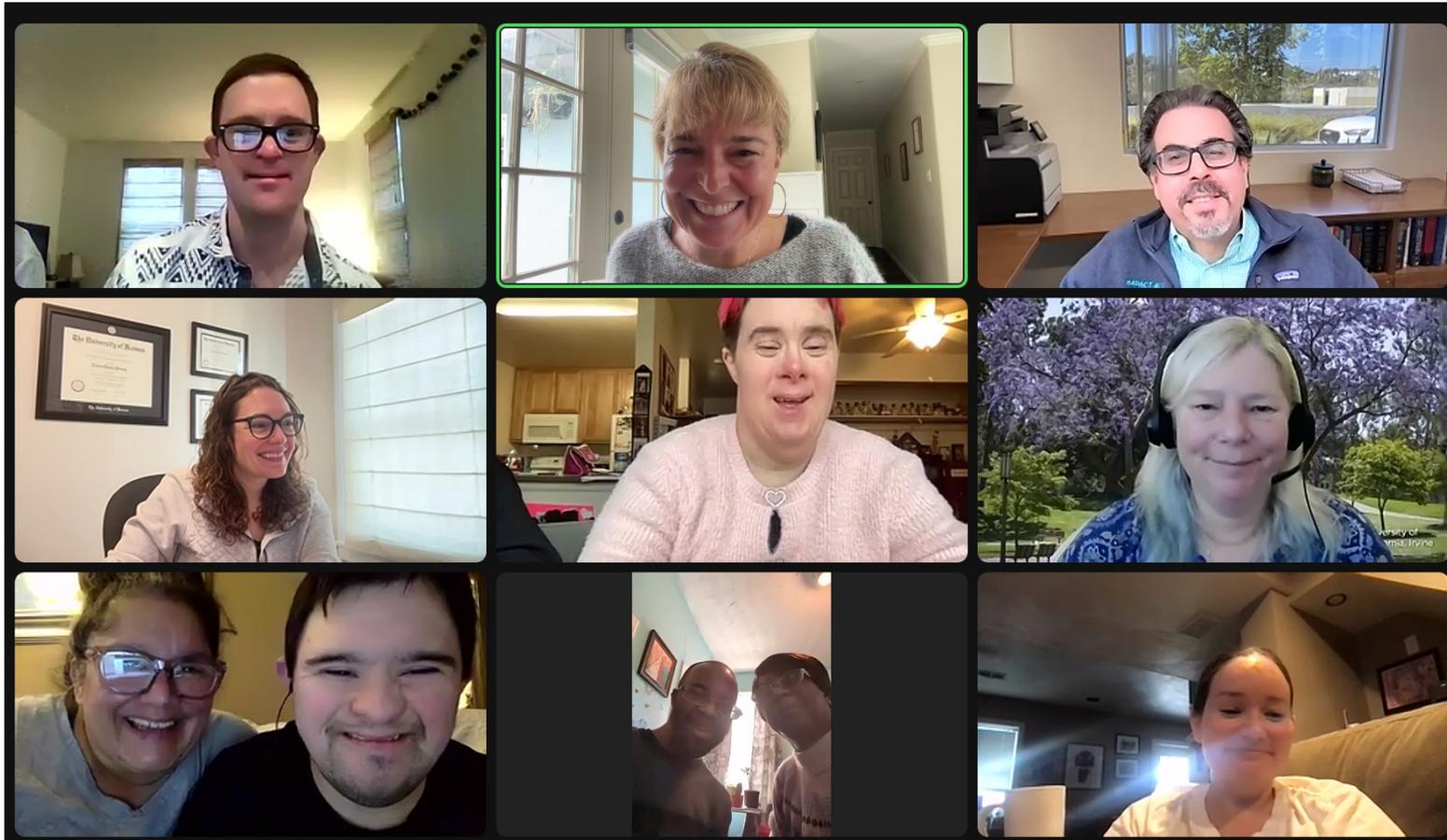
Costs both monetary and time  
Acknowledge that these factors may differ in diverse communities and attempt to design research studies that can be as inclusive as possible.

# Our Model



From: The Spectrum of Community Engagement to Ownership, Rosa González of Facilitating Power





# What Do We Hear From The Community?



- “We need to consider how adults with Down Syndrome communicate, my daughter would often describe neurological changes as ‘my head feels too full’, we really had to probe to understand what that means”
- “You have to meet people where they are. My son doesn’t do well with 2-3 step instructions or questions, that doesn’t mean he doesn’t understand it just means we have to take things slower and give him time to share his feelings about each step. He doesn’t have less value because it takes him longer to get there!”
- “We were among the first generation to get out and live independently and live in the community, she was that trailblazing cohort, they were the first to have full inclusions, there were so many things and possibilities.”



# How Do We Decide If Research Is Right For Us?

- Remember there are no “right” answers.
- ASK QUESTIONS!
  - Your health care team
  - The study team
  - Trusted family and friends



# What Kind of Questions do I Ask?

- What are the benefits of participating?
- What are the risks?
- What sorts of things will I be doing?
- Can I quit at any time
- How will participation affect my daily life?



# What Kind Of Questions Do I Ask?

- Always be sure that you understand what is being asked!
- If the explanations are unclear ask for them to be explained in a different way!
- Remember that your participation is voluntary and take as much time and gather as much information as you need to decide.



What You Need to Know Before Participating:

## PARTICIPANT BILL OF RIGHTS

Anyone who is thinking about giving consent to participate in clinical research or on behalf of someone else has the following rights:



- To be told the purpose of the clinical trial or study
- To be told all the potential risks, side effects, or discomforts
- To be told of any potential benefits
- To be told what will happen in the trial, including treatments they might get and what procedures might happen
- To be told if any procedures, treatments, or devices are different than those that are used as standard medical treatment
- To know how long a trial is expected to last
- To be told about all options available and how they may be better or worse than being in a clinical trial
- To ask any questions about the trial before giving consent and at any time during the trial
- To be told of any medical treatments available if medical problems occur during the trial
- To be told about any potential costs or payments
- To bring a trusted friend or family member to meetings with trial staff
- To receive materials in the language they prefer and to ask for an interpreter
- To receive a signed and dated copy of the informed consent form
- To refuse to participate, for any reason and at any time, before and after the trial starts
- To take their time deciding whether or not to participate

# Thank you!!

For more information about us:

- Go to [www.abc-ds.org](http://www.abc-ds.org) for more information and to join our mailing list
- OR SCAN to join



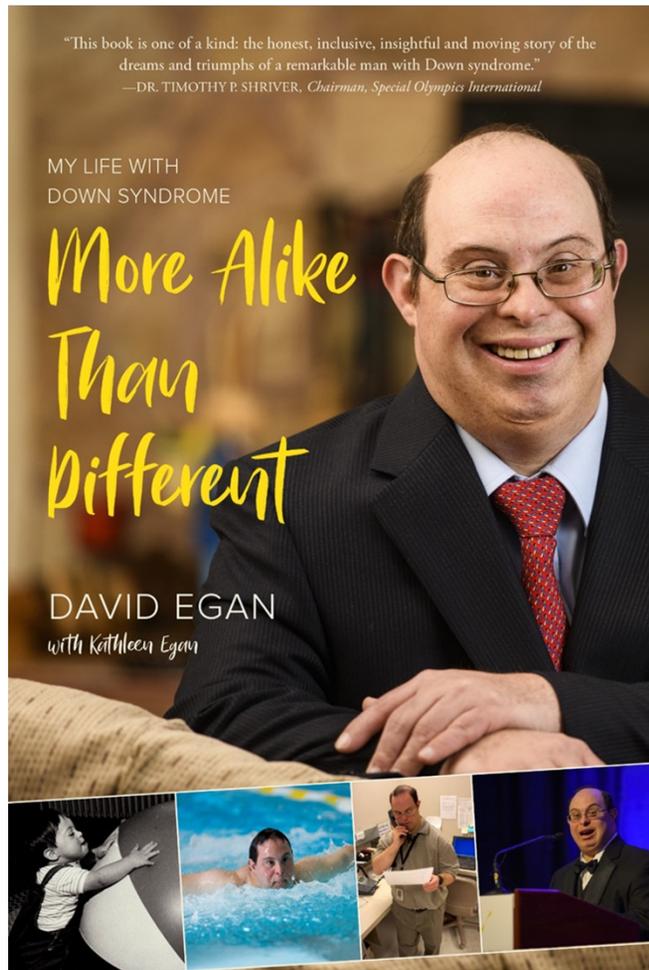


## David Egan

Self-Advocate, Author, Research Participant

## Kathleen, Egan, PhD

Proud Mother of David Egan  
Active Advocate for Individuals with  
Down syndrome and Other Disabilities



## David Egan

- I am a self-advocate and author of ***More Alike Than Different: My Life with Down Syndrome***.
- My book highlights how research, in part, has shaped my life.
- I encourage others to see shared humanity and possibility.
- I built a successful career with over 20 years of competitive employment.
- I was the first person with an intellectual disability selected as a **Joseph P. Kennedy Jr. Public Policy Fellow** on Capitol Hill.
- I am a member of the **NIH Down Syndrome Consortium** and actively involved in NIH-funded research efforts.
- Research has played an important role in my life, and I am grateful to NIH and the researchers advancing health outcomes.
- I am a **Special Olympics athlete, Sargent Shriver International Global Messenger**, and national advocate for self-advocates.

[davideganadvocacy.com](http://davideganadvocacy.com)



**Research has  
always been  
important to me  
and my family!**



**Madison WI  
1977**



**Scan to learn more**  
**[davideganadvocacy.com](http://davideganadvocacy.com)**



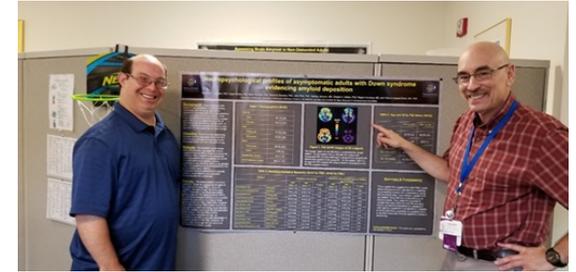
**With my brother**



**With Dr. Handen**



**With my dad at the Waisman Center**



**At ABC-DS in Pittsburgh**



- Research at the University of Wisconsin in Madison at a young age
- Waisman Center induced pluripotent stem cell research study with my dad
- NIH ABC-DS research at the University of Pittsburgh with my brother
- DS Connect & INCLUDE Data Coordinating Center

**I am DS-Connected, are you?**

**DS-Connect<sup>®</sup>**

The Down Syndrome Registry



**ds-connect.org**

Visit **abc-ds.org** to learn more and join their mailing list or simply scan the QR code to sign up



I created the **REACH-UP DS Campaign**

R

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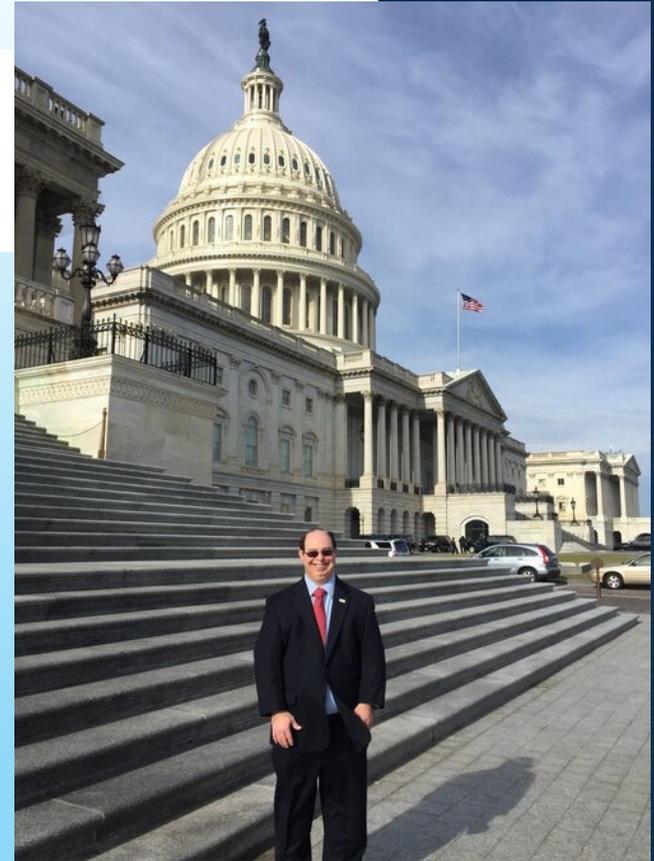
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# Alzheimer's Disease and Down Syndrome: Moving From Hugs to New Drugs

**Beau M. Ances, MD, PhD, MSc, FANA**

**Daniel J. Brennan Professor of Neurology**

**Vice Chair of Academic Affairs**

**Department of Neurology**



## Clinical Diagnosis of AD in DS Individuals Can Be Difficult

- Duration of the disorder from first symptoms to death is 8 years (range, 6-11 years), and the duration from diagnosis to death is 5 years (range, 5-12 years) (Raffi et al., 2020)
- The main clinical symptoms are memory loss, confusion, disorientation, and wandering.
  - Social withdrawal / apathy
  - Disorientation
  - Loss of daily living skills
  - Changes in personality
  - Loss of speech
  - Aggressive behaviors
  - Development of seizures
  - Changes in sleep patterns
  - Major weight change
  - Persistent forgetfulness



# Evaluation of Dementia in DS Individuals

## Differential Diagnosis

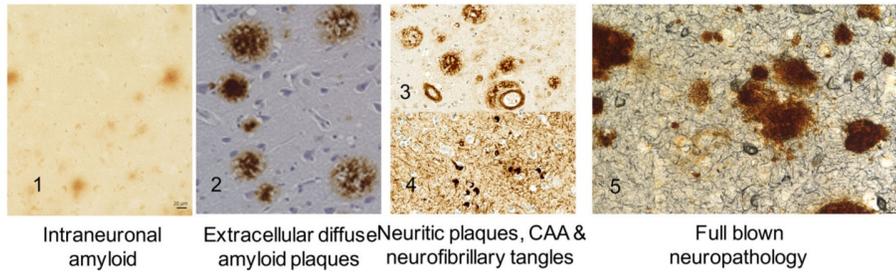
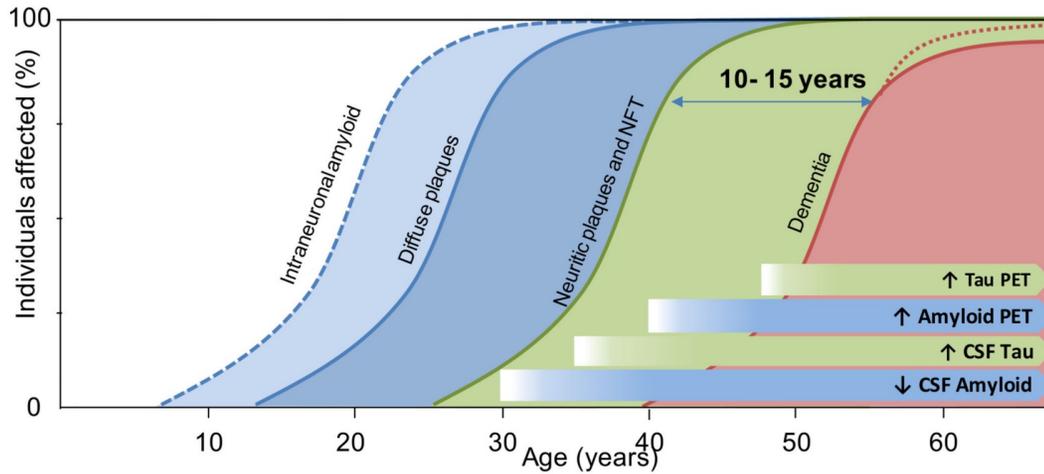
- *Depression, Anxiety, Psychosis*
- *Medical disorders* (e.g. hypothyroidism)
- *Sensory problems* (cataracts)
- *Medication*: Polypharmacy- potential role for deprescribing

## Evaluation

- Annual thyroid screening (TSH and T4)
- Ophthalmologic evaluation every two years (looking especially for cataracts)
- Fasting glucose, B12, and lipid panel
- Hashimoto's encephalopathy-anti-thyroglobulin, anti-thyroid peroxidase
- Cognitive testing- especially if change from premorbid functioning at 35 years old
- Brain imaging- can consider brain volumetrics to help track trajectories

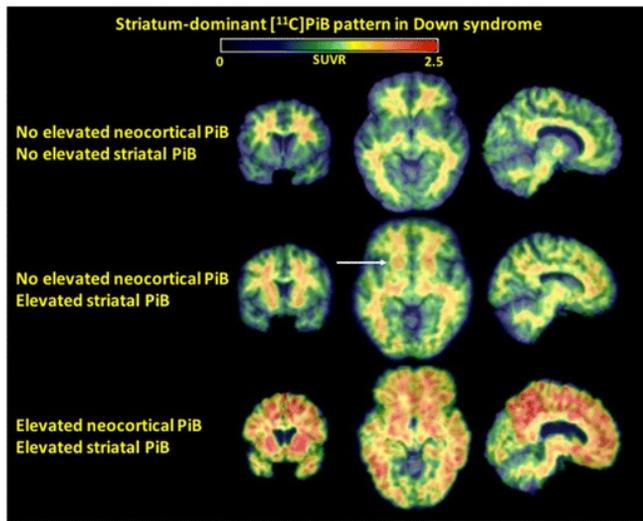


# Hypothesized Timeline of AD Changes in DS

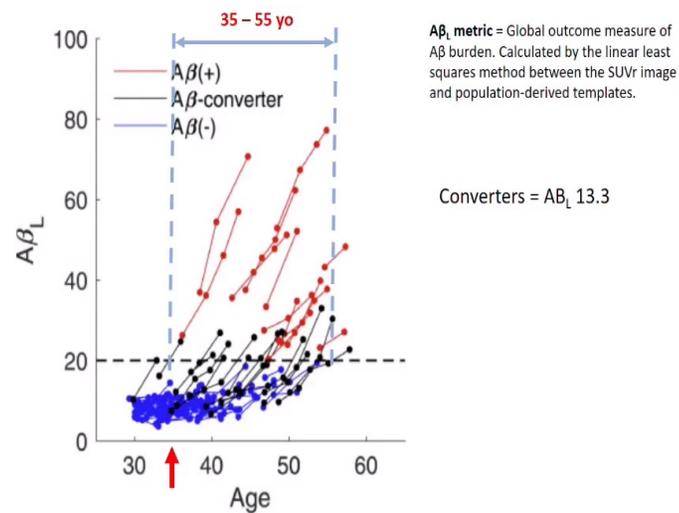


Forstea et al., *Lancet Neurol.*, 2021  
 Head and Ances, *Lancet*, 2020  
 Lott and Head, *Nat Rev Neurol*, 2019

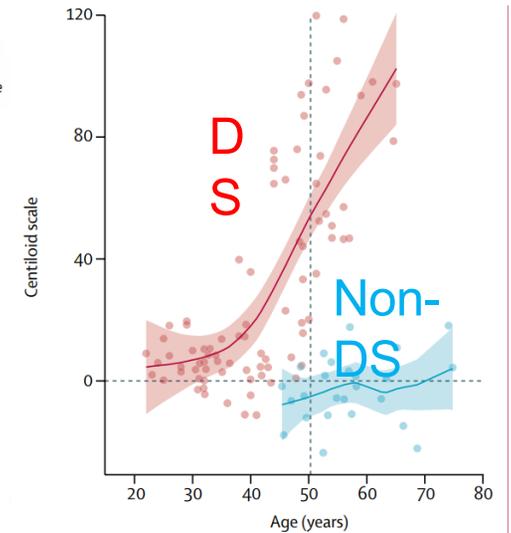
# Amyloid Deposits Quickly Accumulate in the Brain



Lao et al., *Brain Imaging and Behavior*, 2019



Zammit et al., *DADM*, 2020

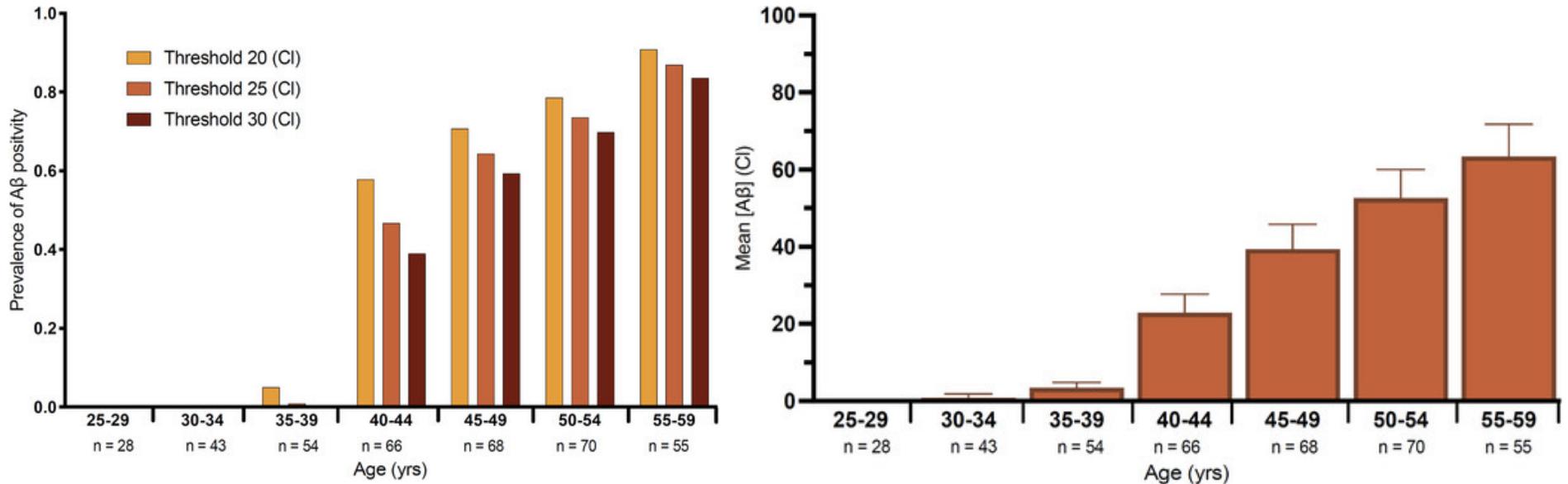


Fortea et al., *Lancet*, 2020

- Rates of amyloid accumulation is greater in DSAD compared to late onset AD



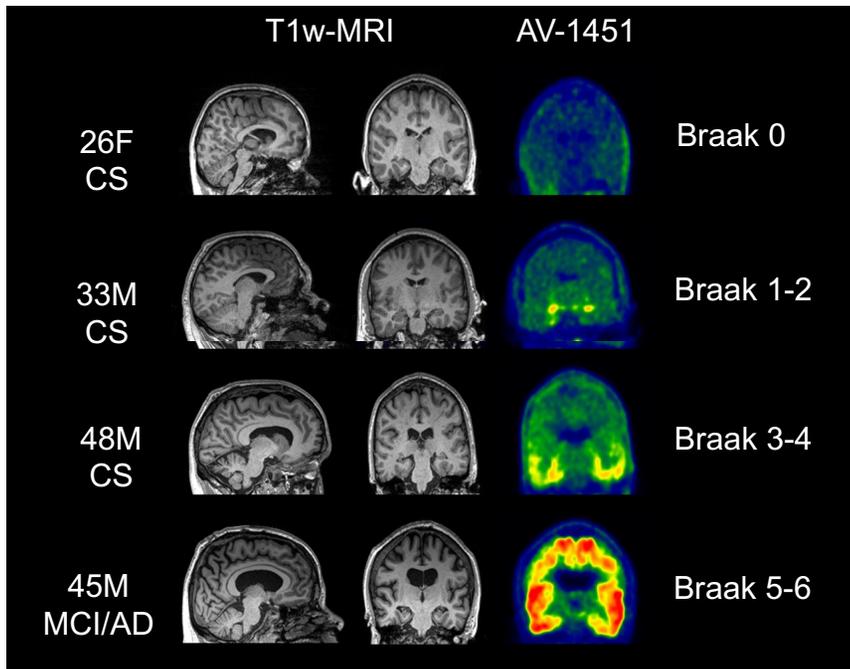
# Amyloid Increases with Age in DS



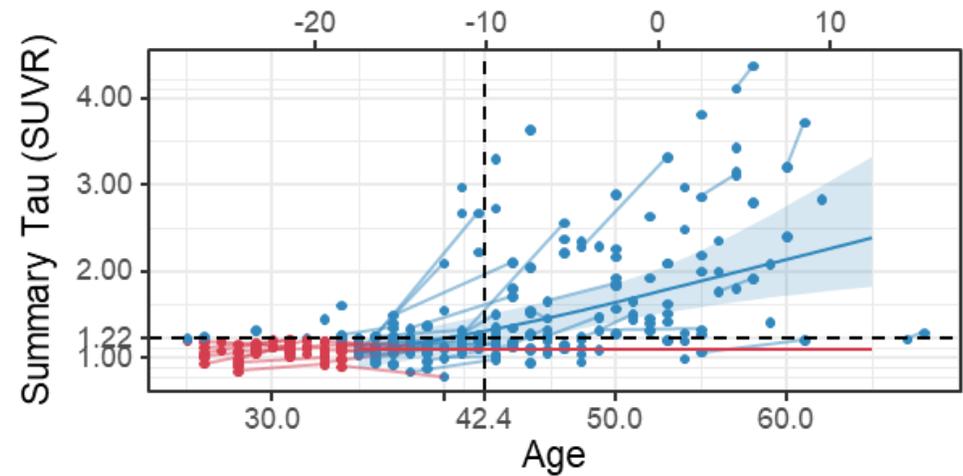
Krasny et al., *Alz Dem*, 2024



# Tau Changes Soon After Amyloid



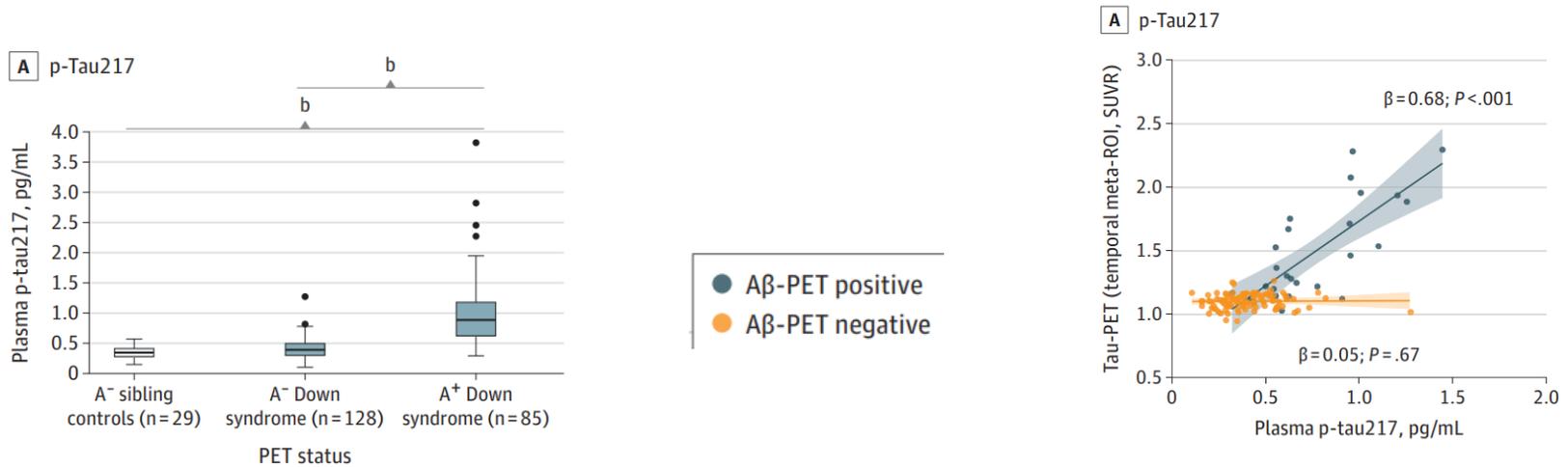
Rafii et al., 2017; Zammit et al., 2020



Wisch et al., *Brain*, 2025

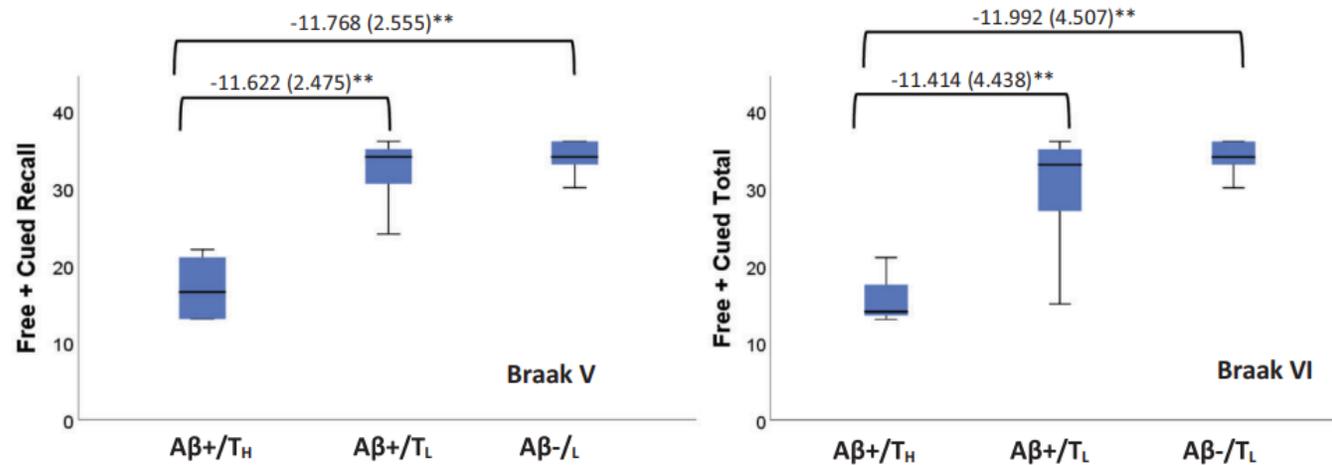
Tau is elevated in adults with DS adults who have amyloid

# Plasma P-Tau217 Detects Both Amyloid and Tau Pathology in DS



Janelidze et al., *JAMA Neurol.*, 2022

# Changes in Tau Are Associated With Worse Cognitive Performance

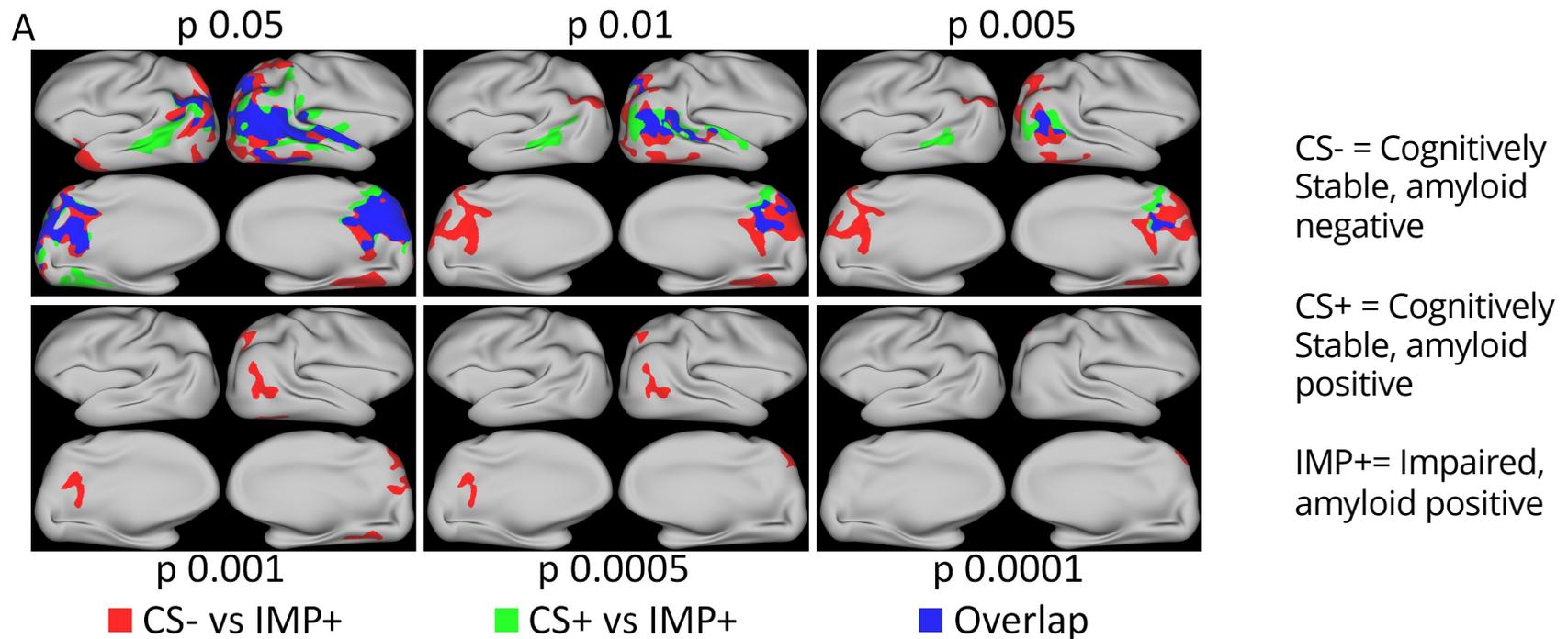


Hartley et al., *DADM*, 2021

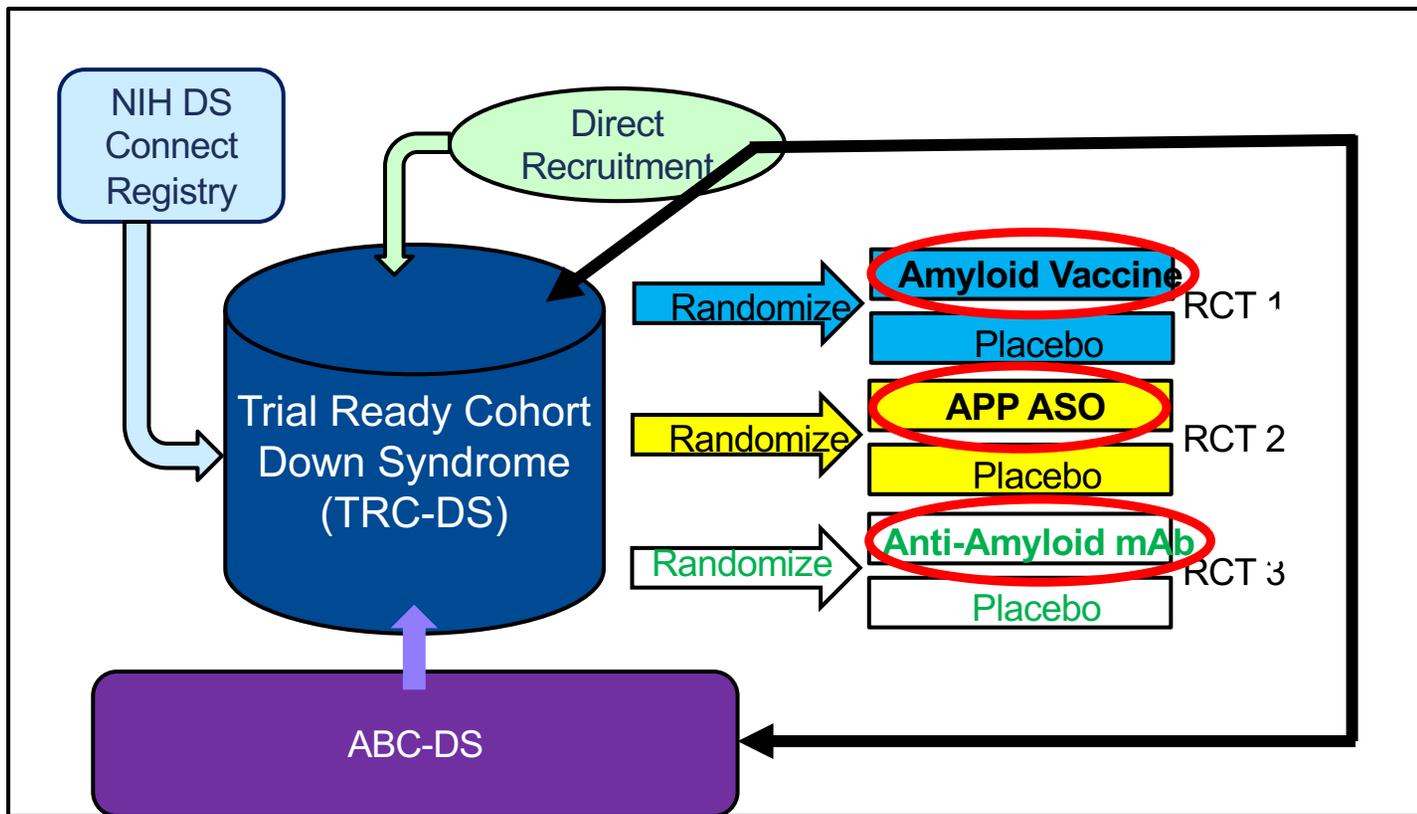
- Higher Amounts of Tau are Associated with worse cognitive performance



# Cortical Loss is in the Back of the Brain in DS



Kennedy et al. *Alz Dem*, 2025



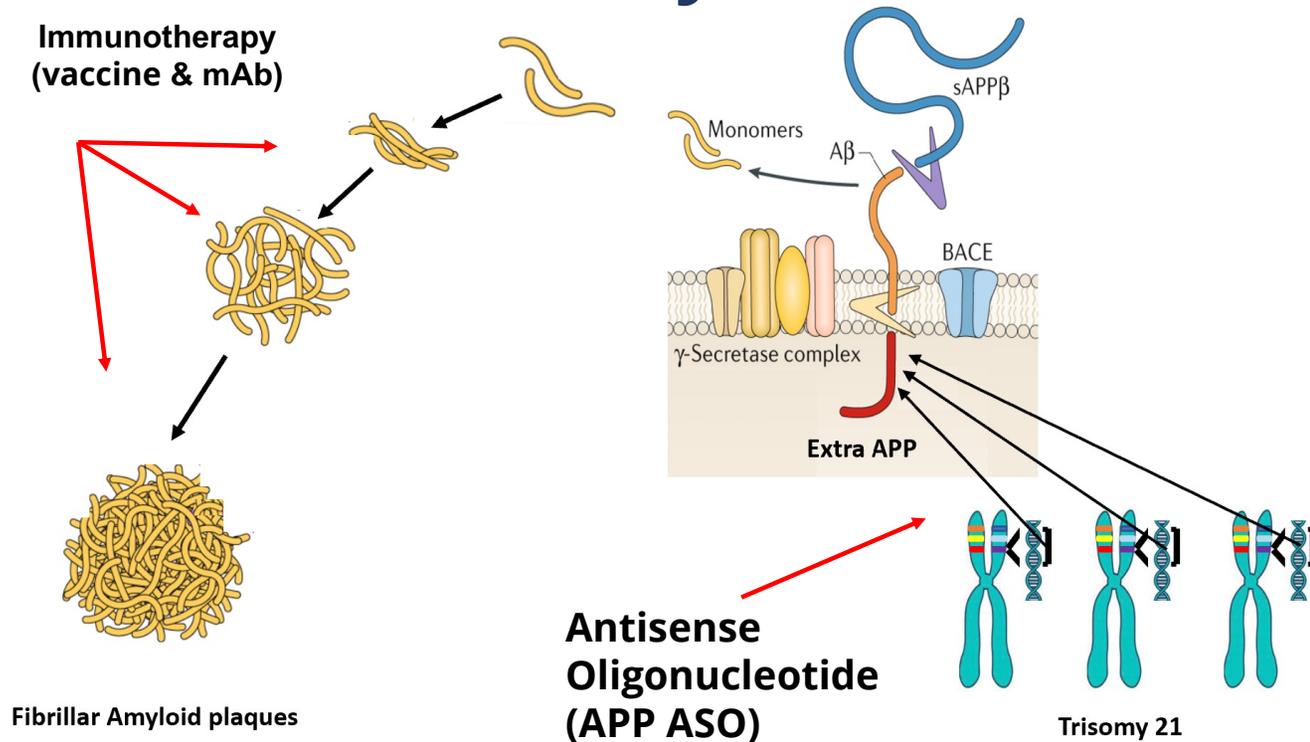
## Sites



Healthy DS adults between 25-55 years old



# New Therapeutic Targets for DSAD Include Beta-Amyloid and APP





# Vaccination for Amyloid Clinical Trial

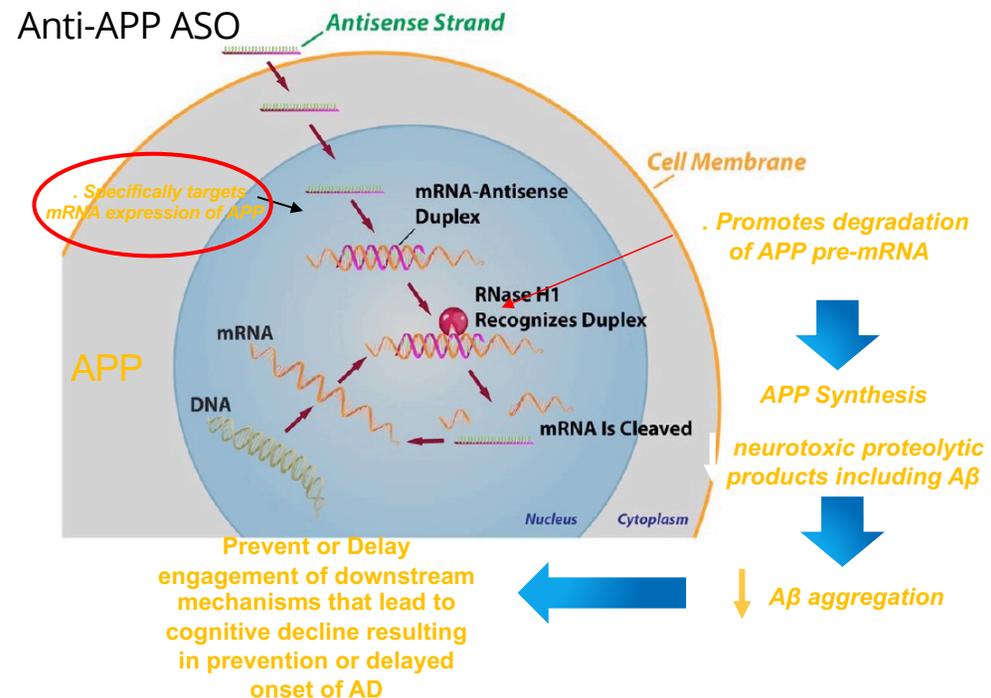
[www.abate-study.com](http://www.abate-study.com)

- A phase 1b/2, multicenter, double-blind, randomized, placebo-controlled study to assess the safety, tolerability, immunogenicity, and pharmacodynamic effects of ACI-24.060 in participants with prodromal Alzheimer's disease and in adults with Down syndrome (ABATE).
- A total of 35 participants worldwide will be enrolled-
- 35-50 years old persons with DS who are cognitively stable and have elevated brain amyloid
- Six intramuscular injections over 74 weeks with 26 weeks of observational follow-up.
- 14 sites (7 US and 7 Europe)
- Launched end of December 2023 - it will soon be completed



# Antisense Oligonucleotide (ASO) Targeting APP in DS

- Participants 35-55 years old with DS at risk for AD
- The study is specifically designed for people with DS before they have clinical symptoms of AD
- Main goals:
  - § To learn about the study treatment's safety
  - § To learn about how well the study treatment reduces levels of APP
- Study was stopped due to poor enrollment



# ALADDIN – Amyloid Lowering for Alzheimer’s in Down’s Donanemab INvestigation



- The study is specifically designed for people with DS and is testing the FDA-approved drug donanemab.
- We want to confirm its effect in people with DS so that it can be prescribed safely in this population.
- Recruitment expected to begin in Fall 2026.



# Take Home Messages

1. DSAD is a genetic form of AD with nearly full penetrance
2. Biomarkers of amyloid, tau, and neurodegeneration can help stage adults with DS
3. AD process is more compact in DS and may influence potential clinical trials
4. Multiple new AD therapies are now being investigated in DS.
5. Adults with DS are potential ideal population to understand the progression to AD. Results will not only help adults with DS but also the general population.



# Acknowledgements

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*In this lab,*  
**WE BELIEVE**



**SCIENCE**  
is real



**LOVE**  
is love



**BLACK LIVES**  
matter



**FEMINISM**  
is for everyone



**BRAINS**  
are cool



**IMMIGRANTS**  
are welcome

## ABC-DS Collaborators

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- NICHD
- Bright Focus
- Alzheimer Association

**Thanks to all of our amazing  
participants and families**



# Ances Bioimaging Laboratory Is Committed to Giving Back to the Community



**Vaccination Clinics**



**Step Up for DS**



**ADDORÉ Core**



**Bowling Night**



**Trivia Night**



**Artists Wall**



**Participant Breakfasts- we just had 6<sup>th</sup> Annual**



**Holiday Parties**



# How to Contact Us



 @anceslaboratory

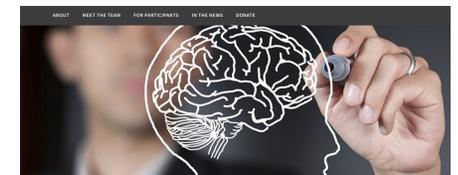
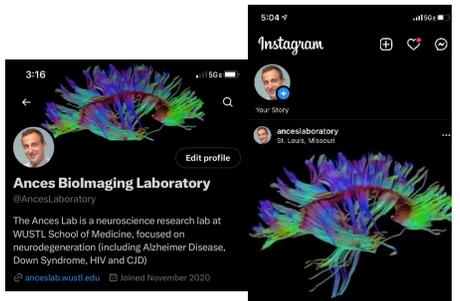
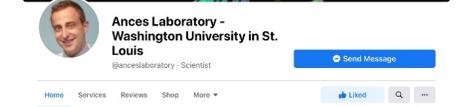
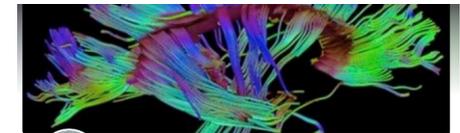
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 [anceslab.wustl.edu](http://anceslab.wustl.edu)

If you have questions or are interested in being seen  
for research or clinical evaluation

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**UUC ABC-DS**  
Alzheimer Biomarker Consortium-Down Syndrome



**Questions? Thank you!**