

Building Research Collaborations to Understand Co-Occurring Conditions in Children and Adults with Down Syndrome

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Co-occurring Conditions in Down syndrome

<i>Hearing problems 75%</i>	<i>Vision problems 60–80%</i>	<i>Obstructive sleep apnea 50–79%</i>	<i>Otitis media with effusion 50–70%</i>	<i>Congenital heart disease 40–50%</i>	<i>Feeding difficulty 31–80%</i>
<i>Respiratory infection 20–36%</i>	<i>Dermatologic problems 56%</i>	<i>Hypodontia and delayed dental eruption 23%</i>	<i>Thyroid disease by adulthood 50%</i>	<i>Gastrointestinal conditions</i>	<i>Seizures 1–13%</i>
<i>Hematologic problems including malignancies</i>	<i>Autoimmune conditions</i>	<i>Symptomatic atlantoaxial instability 1–2%</i>	<i>Hirschsprung disease <1%</i>	<i>Moyamoya disease</i>	<i>Autism 7-19%</i>
<i>Alzheimer 90% lifetime prevalence</i>	<i>ADHD 31-44%</i>	<i>Orthopedic issues</i>	<i>Depression</i>	<i>Anxiety</i>	

Bull M et al, Health Supervision for Children and Adolescents With Down Syndrome. Pediatrics. 2022

Publication history

- Search term: Down Syndrome + Publication Year
 - 1970: 0
 - 1980: 47
 - 1990: 169
 - 2000: 162
 - 2010: 383
 - **2020: 610**
 - **2024: 1816**



NIH INCLUDE (INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE):

Conduct	Conduct targeted, high-risk, high-reward basic science studies on chromosome 21
Assemble	Assemble a large study population (cohort) of individuals with Down syndrome
Conduct	Conduct clinical trials inclusive of individuals with Down syndrome

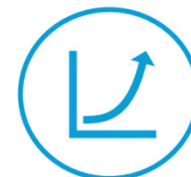
INCLUDE Project Goals

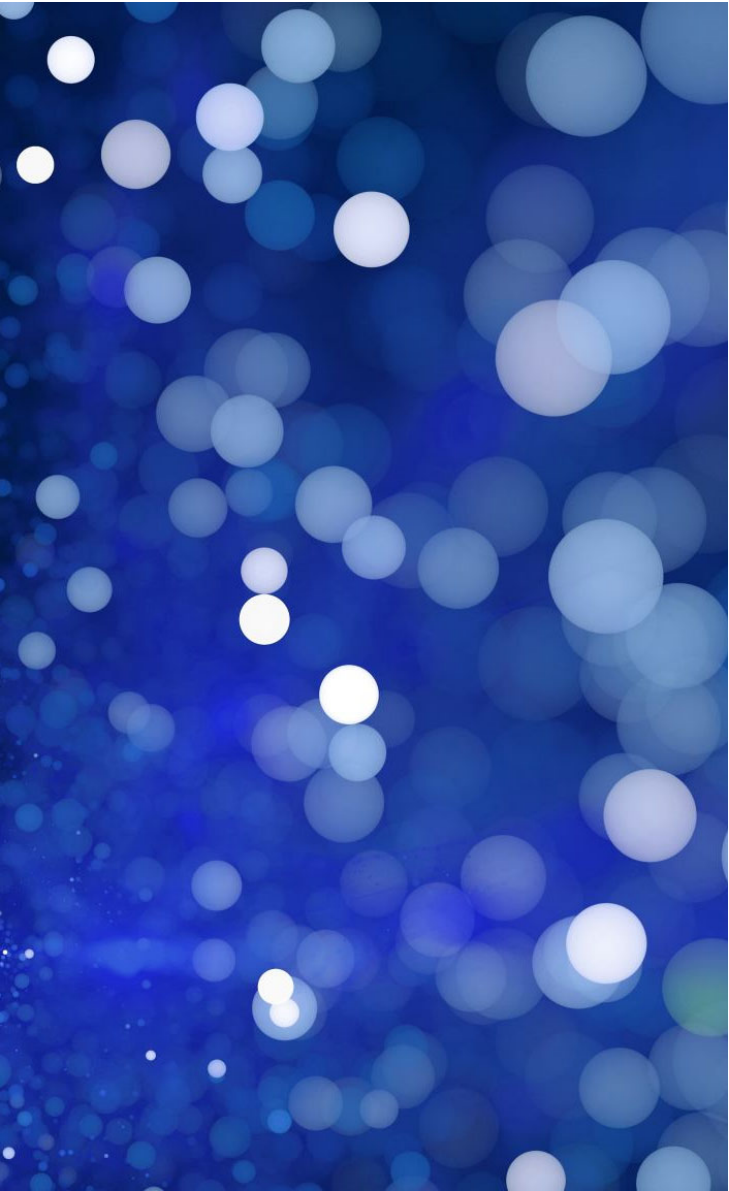


The INCLUDE Project launched in June 2018 to address a Congressional directive that called for a new **NIH-wide research initiative** on critical health and quality-of-life needs for individuals with Down syndrome.

The project will:

- **Investigate conditions** that affect individuals with DS and the general population, such as Alzheimer's disease, autism, cataracts, celiac disease, congenital heart disease, and diabetes.
- **Increase the number of investigators/trainees** studying DS.
- Engage with those with DS and their families from **diverse backgrounds**.





NIH INCLUDE Research Plan:

Goals and Objectives organized around 5 themes:

Basic Research

Cohort Development/Epidemiology

Clinical Research/Co-occurring Conditions

Living and Aging with DS/Services Research

Research Infrastructure and Tools

INCLUDE Project *at a glance*



389

Awards Funded



50

Funding Opportunities



450+

Publications



23

Community-Engagement and
Outreach Events attended by
INCLUDE Team



22

NIH IC Collaborators



15

Clinical trials



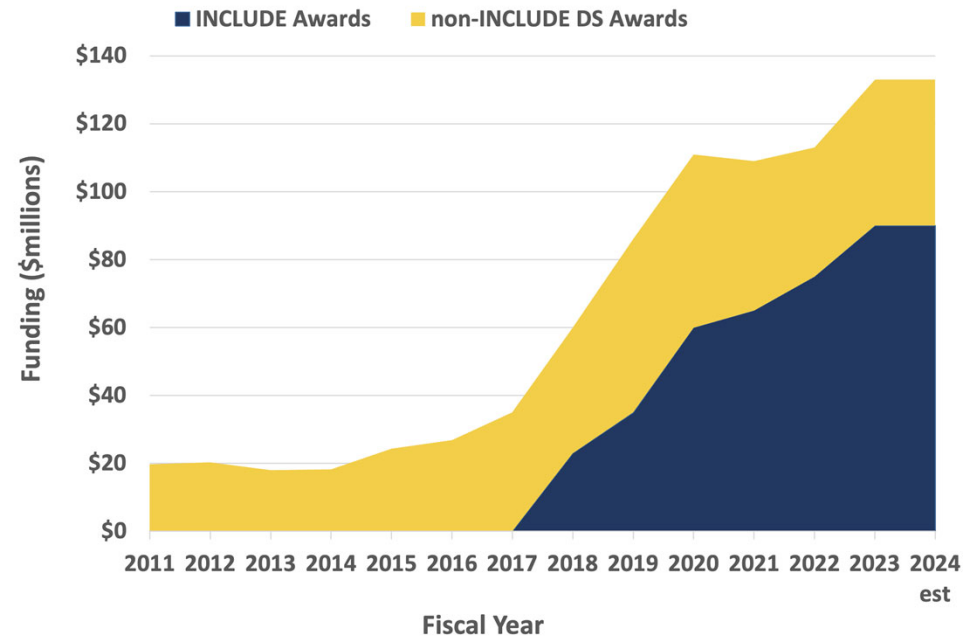
7,811

Individuals with DS
Represented in the
INCLUDE Data Hub

Down Syndrome Funding at NIH

FY	INCLUDE (\$M)	Non-INCLUDE DS (\$M)	Total DS (\$M)
2018	23	37	60
2019	35	51	86
2020	60	51	111
2021	65	44	109
2022	75	38	113
2023	90	43	133
2024	90	43	133 est
2025	90*	TBD	TBD

Down Syndrome Funding at NIH, FY 2011 - 2024



NIH has invested more than **\$438 million** over the past **7 years** on **389** awards issued through the **INCLUDE Project**

*Dependent on FY25 Congressional appropriations

INCLUDE Down
Syndrome
Cohort
Development
Program
(DS-CDP)

Working in partnership
with people with Down
Syndrome and their
families to learn about
DS and create future
opportunities for
research participation

INCLUDE DS-CDP Overview

Keeping the DS Community at the heart of our efforts to create an inclusive DS research program

Project Goals



- Improve our understanding of the natural history of Down syndrome
- Better determine the frequency and variability of co-occurring conditions
- Enhance our understanding of heterogeneity in Down syndrome, giving specific attention to neurocognitive, health-related, and functional outcomes in diverse populations
- Examine the impact of demographic, social, experiential, and environmental factors on outcomes
- Expand our understanding of currently used therapeutics across the lifespan and cultivate data critical to the initiation of drug trials

Identify genomic, biologic, and social determinants of risk and resilience, at levels spanning from individual to society



INCLUDE DS-CDP Overview

Keeping the DS Community at the heart of our efforts to create an inclusive DS research program

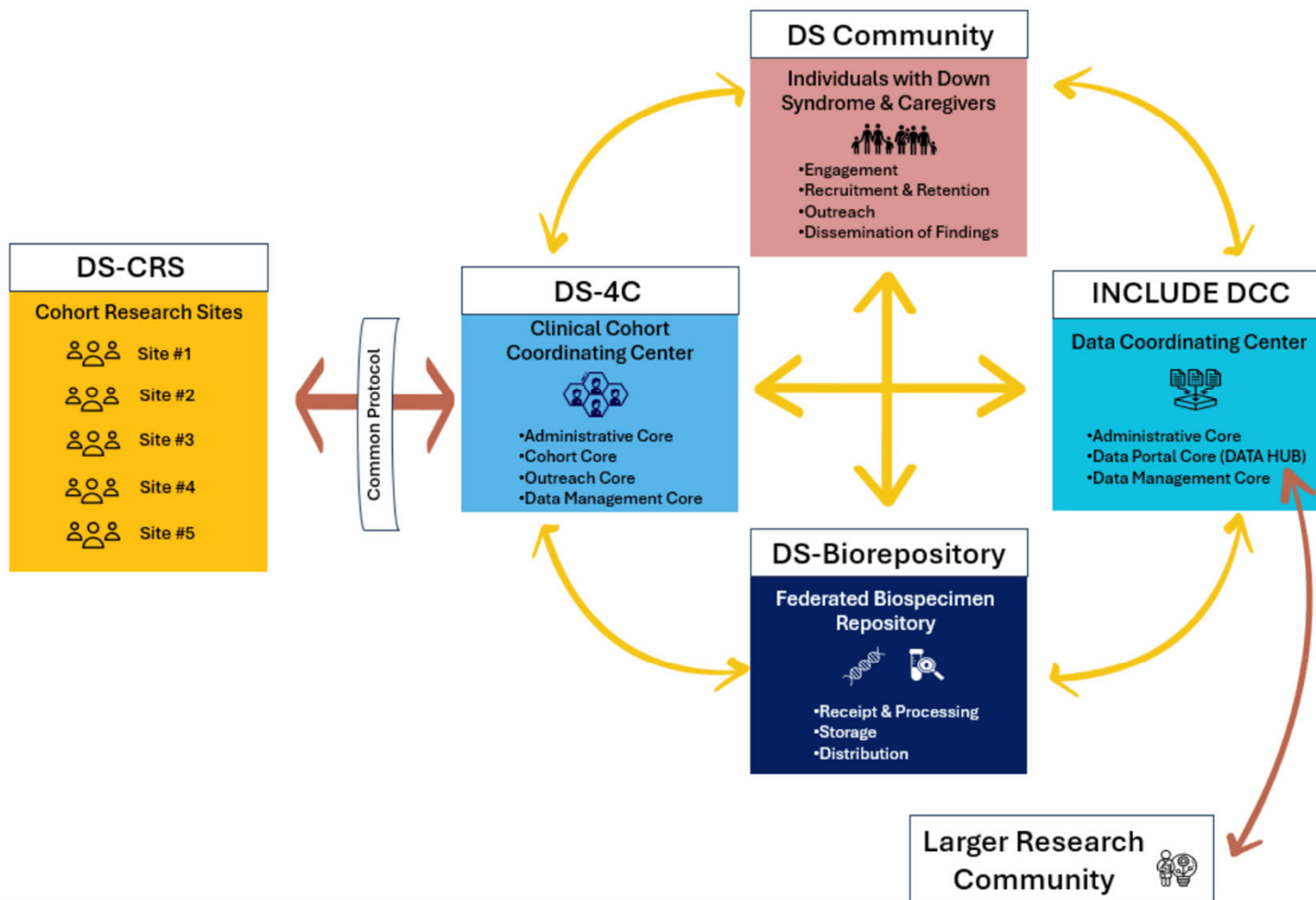
Project Activities



- Development of a comprehensive deep phenotyping and bio sample acquisition protocol ("**common protocol**")
- **Collection of demographic, clinical, laboratory, biospecimen, and imaging data** from people with DS to enable discovery and validation of new biologic targets
- **Outreach and recruitment** (RFI, focus groups, outreach protocol, etc.)

INCLUDE DS-CDP Overview

Program Structure



INCLUDE DS-CDP Overview

Cohort sites:

- **Metabolic, Health, Lifestyle and Risk of Co-Occurring Health Conditions in DS (Met-DS):** UW-Madison, Univ of Pittsburgh, Kansas Univ Med Center, Univ California-Irvine
- **Advancing the Lives & Health of Youth and young adults with DS (Ally-DS):** Children's Hosp of Philadelphia, Univ of Miami, Johns Hopkins Univ/KKI, Univ of Texas Health Science Ctr-San Antonio
- **Infant Down Syndrome Baby Brain Study (IBIS):** WU(?), Univ of North Carolina, Children's Hosp of Philadelphia, Seattle, Univ of Minnesota
- **Down syndrome Early Childhood Omics, Deep Phenotyping and Epidemiology In Texas (DECODE-IT):** Baylor College of Medicine/Texas Children's Hospital, Johns Hopkins
- **Human Trisome Project: Latin American Network:** US + Mexico, Columbia, Venezuela, Brazil, Argentina, Bolivia, Chile



MET-DS: UW site team:

- **Sigan Hartley, PhD (MPI):** Cognitive development and lifestyle assessment in DS
- **David Plante, MD, PhD:** Sleep Medicine
- **Maria Stanley, MD:** Developmental-Behavioral Pediatrics
- **Michelle Polfuss, PhD, RN, CPNP-AC, FAAN:** Obesity, Nutrition, Community Recruitment
- **Luis Columna, PhD:** Physical Activity and Community Recruitment
- **Qiang Chang, PhD:** Molecular processes and Genetics
- **Daifeng Wang, PhD:** Biostatistics
- **Community Advisory Board:** Self-advocates and family members

Strong commitment to Community Engagement

- Central and Local Community Advisory Boards (CABs) with self-advocate and family/caregiver participation
 - DS Community partnership throughout “Nothing about us without us”
 - Compensation for engagement of CAB members
- Team approach throughout
- Inclusive: functional ability, age, and geographic location
- Plan to give back to the Community:
 - Summary of findings in clear, understandable language

DS-CDP Cohort Research Site

Metabolic Health, Lifestyle, and Risk of Co-Occurring Health Conditions in Down Syndrome (MET-DS)

Approach: Deep-phenotyping of interplay between trisomy 21, metabolic dysregulation, obesity, lifestyle, and the development of co-occurring health conditions

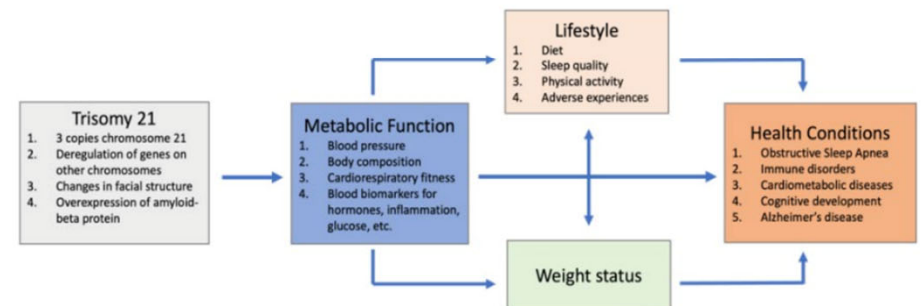
Planned enrollment: 200 individuals with DS; four sites - UW-Madison, KUMC, UPitt, and UC-Irvine (50 per site); follow annually across 3 data collection cycles

Population Specifics: aged 6-24 yrs; 25-30% from underrepresented racial/ethnic group

Primary phenotyping:

- **Blood:** clinical labs, genetics, protein, metabolism, immunophenotyping
- **Metabolic/Physiological:** resting BP, cardiovascular fitness, motor ability, hand grip strength
- **Anthropometry:** weight, waist & hip circumference
- **Lifestyle:** physical activity & sleep quality (actigraphy accelerometer), diet, ACEs & social determinants of health
- **Health conditions:** OSA, cardiometabolic disease, immune disorders, cognitive development, & early AD pathology

Unique considerations: ABC-DS investigators; measure/biomarker overlap with adult DS cohorts; inclusive of individuals with limited verbal skills





Waisman Center

Advancing knowledge of human development, developmental disabilities, and neurodegenerative diseases.

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Down Syndrome Hub

More than 400,000 individuals in the United States have Down syndrome, or trisomy 21—a chromosomal condition caused by an extra 21st chromosome. Down syndrome is the most commonly occurring chromosomal condition. Approximately one in every 733 babies is born with Down syndrome each year.

- [Waisman Down Syndrome Activities](#)
- [Studies Recruiting](#)
- [Events](#)
- [Researchers](#)
- [News](#)
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- [Additional Resources](#)



Down syndrome



Hypoglossal Nerve Stimulator Study (Stanley)

We are studying new ways to treat obstructive sleep apnea in children and young adults with Down syndrome who have persistent obstructive sleep apnea despite prior tonsillectomy.



Are you a young adult with Down syndrome looking to make brain waves for science? (Litovsky)

Our Goals: We hope you will be a part of the first study for young adults with Down syndrome to combine: Who can help? Young adults with Down syndrome who are: 18 to 24 years ...



Leveraging Technology to Identify Outcome Measures for Young Children with Down Syndrome (Sterling)

Our study aims to learn more about how language samples collected in the home can be used to measure the language development of children with Down syndrome.



Alzheimer's Biomarkers Consortium – Down Syndrome: ABC-DS (Christian & Hartley)

The National Institutes of Health-funded Alzheimer's Biomarkers Consortium – Down Syndrome (ABC-DS), a large multi-center research initiative to find biomarkers to track Alzheimer's disease in Down syndrome. The Waisman Center is part of this multi-site ...



Waisman BioLibrary: Down Syndrome Study (Chang)

Be included! Families of children with Down syndrome are invited to participate in our new study about genetics and health. The Waisman BioLibrary is recruiting youth with Down syndrome ages 0 – 17 years. Families ...

