DS-Connect®: Connecting families and those with Down syndrome to research that INCLUDEs them

Melissa Parisi, Sujata Bardhan, and Lisa Kaeser
October 25th, 2018
Outline

• Introduction to NIH research on Down syndrome

• DS-Connect®: The Down Syndrome Registry

• The INCLUDE Research Initiative
Down syndrome

- Most common genetic form of intellectual disability
- Incidence in U.S.: 1/700 newborns
- Most individuals: trisomy 21 (3 copies of chromosome 21)
- Co-occurring conditions:
  - Mild-moderate intellectual disability
  - Increased risk of Alzheimer’s Disease
  - Sleep apnea
  - Hearing loss
  - Autoimmune problems: celiac, hypothyroidism, diabetes
  - Congenital heart defects
The case for research in Down syndrome

• Each year, ~ 6000 infants with DS born in U.S.
• Lifespan for people with DS has doubled in 25 yrs
Research has led to improvements in care for children with DS and heart defects.

1970s: Cardiac surgery in infants becomes routine.


1994: AAP recommends cardiac screening for all infants with DS.


2015: Superior post-op outcomes in children with DS.

The National Institutes of Health (NIH) and biomedical research

• The U.S.’s national medical research agency
• The world’s largest funder of biomedical research
• Made up of 27 separate research institutes and centers
• Director since 2009: Dr. Francis Collins
• 85% of funds go to university research institutions based on peer review of grant applications
NIH leads the Down Syndrome Consortium

Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)
National Cancer Institute (NCI)
National Heart, Lung and Blood Institute (NHLBI)
National Institute of Mental Health (NIMH)
National Institute of Neurological Disorders and Stroke (NINDS)
National Institute on Aging (NIA)
National Institute on Minority Health and Health Disparities (NIMHD)
National Institute of Dental and Craniofacial Research (NIDCR)
National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
National Institute on Deafness and Other Communication Disorders (NIDCD)
National Human Genome Research Institute (NHGRI)
National Institute of Allergy and Infectious Diseases (NIAID)
National Center for Advancing Translational Sciences (NCATS)

Self-advocates
NIH Research Plan on Down Syndrome: Down Syndrome Directions

• Updated in 2014
• Available on NIH website
• 5 major Research areas:
  • Pathophysiology of Down Syndrome and Disease Progression
  • Screening, Diagnosis and Functional Measures
  • Treatment and Management
  • Research Infrastructure
  • Down Syndrome and Aging
• Goal: Develop research goals and objectives for NIH research
DS-Connect®: The Down Syndrome Registry

What it is:

A *secure, confidential*, online survey tool to collect basic information about people with Down syndrome from them and their families.

Features:

- Collects information from individuals with DS globally
- Provides a database and educational system for those with DS
- Enables researchers to use de-identified data to develop studies on the medical issues and treatments for DS

People with DS and their families can:

- Connect with researchers and health care providers
- Participate in surveys aimed at better understanding of the health of people with DS across their lifespans
- Participate in clinical studies on DS, including surveys, studies of new medications and other treatments
DS-Connect® is a powerful resource where people with Down syndrome and their families can:

- Connect with researchers and health care providers.
- Express interest in participating in certain clinical studies on Down Syndrome, including studies of new medications and other treatments.
- Take confidential health-related surveys. These surveys are aimed at better understanding of the health of people with Down Syndrome across their lifespans.

Launched Sept. 6, 2013
Multiple Survey Modules

Initial Health Survey with “Trigger Questions” that lead to other surveys:

- Initial Health Questionnaire
- Thyroid Questionnaire
- Heart Questionnaire
- Sleep Questionnaire
- Skeletal Questionnaire
- Gastrointestinal Questionnaire
- Diabetes Questionnaire
- Celiac Disease Questionnaire
- Leukemia Questionnaire
- Development Questionnaire
- Prenatal and Birth Questionnaire
- Adulthood Questionnaire
- Men’s Health Questionnaire
- Women’s Health Questionnaire
- Healthcare Transition Survey

Available to adults

New Survey for 12-30 yo
Transition to Adulthood Survey

• To understand whether adolescents/young adults are prepared to move to an adult-focused healthcare system

• Addresses transition readiness for:
  • Healthcare
  • Education and employment
  • Financial issues
  • Community/independent living
  • Legal issues

• Launched April 2018

www.GotTransition.org
A partnership with families…

- Access the health care provider list

Search the directory for your health care provider(s) by name, facility name, city or state (2 letter abbreviation). If your health care provider is not in the directory, use the Add a New Health Care Provider link to add them in the directory. Note that you will need to search for each physician individually before the Save button will be enabled.

Please note that this list of healthcare providers does not imply endorsement or recommendation of their services.

<table>
<thead>
<tr>
<th>Name/Institution</th>
<th>Specialty</th>
<th>Sees Adults or Youth?</th>
<th>Institution</th>
<th>City</th>
<th>State</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>John Avallone</td>
<td>Ophthalmology</td>
<td></td>
<td>Ophthalmology Associates</td>
<td>Arnold</td>
<td>MD</td>
<td>UNITED STATES</td>
</tr>
<tr>
<td>Mihee Bay</td>
<td>Developmental Pediatrics</td>
<td></td>
<td>Kennedy Krieger Institute</td>
<td>Baltimore</td>
<td>MD</td>
<td>UNITED STATES</td>
</tr>
</tbody>
</table>
A partnership with families…

- Print out the participant’s medical history

**Jane Smith**

DOB: 2011-01-01  
Gender: Female  
Registered By: Melissa Parisi  
Relationship: Biological Parent

**Initial Health Questionnaire**

**Diagnosis**

- What is the participant’s Down syndrome diagnosis?  
  Complete trisomy 21

- How was the diagnosis of Down syndrome made? (Select all that apply.)  
  Genetic testing in baby after birth (such as chromosome analysis, cytogenomic array, or fluorescence in situ hybridization (FISH))

- What was the participant’s age in years when the diagnosis of Down syndrome was made?  
  At birth
A partnership with families…

- Access the healthcare recommendations
- Personalized for the age of the person with DS

Health Care Guidelines For Individuals With Down Syndrome

Children with Down Syndrome: Health Care Information for Families (AAP)

Age-Specific Health Care Checklist (AAP) (144 KB PDF)

Aging and Down Syndrome: A Health & Well-Being Guidebook (NDSS) (8 MB PDF)

Links to AAP checklists

Links to NDSS guidebook
A partnership with families: Explore the data

Example: Sleep

Has the participant ever been diagnosed with any sleep problems? (1803 responses)

- 61.2% No
- 35% Yes
- Unsure

Which of the following sleep problems have been diagnosed? (Select all that apply.)

- None
- Sleep apnea
- Sleep-disordered breathing
- Snoring
- Narcolepsy
- Restless legs syndrome
- Excessive daytime sleepiness
- Insomnia (difficulty falling asleep)
- Unsure
- Other

1649 people provided 1993 response(s)
Portal for Professionals: Explore the data

• Professionals can apply to use DS-Connect to recruit for their studies
• If approved, they have no direct access to Registry participants
• Registry Coordinator will contact eligible families about the study or trial
• Participants can choose whether to contact investigators to join
What does it mean to be in a research study with DS-Connect®?

- Take a survey of their experiences
- Answer a questionnaire about health issues
- Record data from an activity tracker (e.g., Fitbit)
- Participate in a clinical study of a intervention
- Be in a clinical trial for a new drug or medication
- Participate in an “INCLUDE” study

✅ Any of the above! It’s your choice
Recruitment Supported by DS-Connect®

• About 30 studies supported so far. Some examples:
  • Studies of aging and risk of Alzheimer's disease in DS
  • Studies of sleep issues in children with DS
  • Studies of language development in children with DS

• Survey-based Studies:
  • Parental surveys of feeding their children with DS
  • Survey of opinions on medical research in DS
  • Attitudes about usage of green tea extract (EGCG) in those with DS
  • Gynecologic life course of women with DS
  • Social and communication skills of children and adolescents with DS
Recruitment Assistance from DS-Connect®

Dr. Amy Lewanda at Children’s National looking at Use of Nutritional Supplements in Children with DS

Goal: 500 participants
Had 140 participants before DS-Connect® notification

Patterns of Dietary Supplement Use in Children with Down Syndrome

**Conclusions**
Almost one-half of parents surveyed administer or have administered supplement(s) to their children with Down syndrome. Many of the supplements have concerning ingredient profiles and are given to children too young to articulate potential ill effects. Providers need to be aware of these products and question families about their use. (*J Pediatr* 2018;■■:■■■-■■■).
What Can You Do to Help?

• Encourage families to sign up!
• Spread the word
• Electronic Toolkit available:
  • Video Testimonial-YouTube
  • Facebook info-cards
  • Badges, Tweets, Flyers
• Help us reach our goal:
  • 6000 by Dec 31, 2018

• http://DSConnect.nih.gov
Distribute the DS-Connect® Flyer

DS-Connect®
The Down Syndrome Registry
A registry for people with Down syndrome

What is DS-Connect®?
DS-Connect®: The Down Syndrome Registry is a voluntary, confidential, online survey that collects basic health information about people with Down syndrome.

This resource was launched by the National Institutes of Health with help from the Down Syndrome Consortium, a group of national and international organizations that focus on and support the Down syndrome community (see below).

Why should I join DS-Connect®?
DS-Connect® participants can:
• Print out a summary of their health history
• Find health care providers in their area who care for people with Down syndrome
• Help health care providers improve care for people with Down syndrome
• Explore trends in the overall health of people with Down syndrome based on survey results
• Learn about new studies for people with Down syndrome
• Connect with scientists who study Down syndrome
• Help scientists develop new treatments for people with Down syndrome

How do I join DS-Connect®?
It’s easy, confidential, and secure:
1) Go to https://DSConnect.nih.gov.
2) Click the “Join the registry” link on the homepage.
3) Set up an account by creating a username and password.
4) Complete the consent/assent form.
5) Once you’ve created your profile, fill out the information about the person with Down syndrome, including the Initial Health Questionnaire and other related surveys.

Questions?
You can reach us at DSConnect@nih.gov or at https://DSConnect.nih.gov.

Available in Spanish also
Información en español
New U.S. Congressional Directive for DS

- Advocacy groups unhappy with NIH funding for DS
- In the FY 2018 budget legislation for NIH:
  - Develop a new trans-NIH initiative to study trisomy 21, with the aim of yielding scientific discoveries to improve the health and neurodevelopment of individuals with Down syndrome and typical individuals at risk for:
    - Alzheimer's disease
    - Leukemia
    - Heart defects
    - Immune system dysregulation
    - Autism
    - and other conditions

- NIH is spent $22.2 M in additional research money by Sept 30, 2018 on a new research initiative…

Protected from:
- Many cancers
- Heart disease and heart attacks
NIH Funding for Research on Down Syndrome
FY 2008 – FY 2018

Fiscal Year

Award Amount in U.S. Dollars (millions)


$16.9 $17.7 $21.5 $19.7 $20.3 $18.0 $18.3 $24.3 $26.9 $35.0 $59.0
INCLUDE (INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndrome)

3 components:

1. Conduct targeted, high-risk, high-reward basic science studies on chromosome 21.

2. Assemble a large cohort of individuals with Down syndrome for comprehensive analysis and biomarker evaluation.

3. Include individuals with Down syndrome in existing and future clinical trials while building a infrastructure for such trials.
FY2018 INCLUDE Funding

• $22.2 M supported 49 supplements
• Distributed among 13 ICs
• All 3 components addressed
• General areas
  • Leukemia and immune function development
  • Behavioral research on vocalization and language acquisition
  • Integrated screening for DS, ASD and Fragile X
  • Pulmonary function and sleep
  • Genomics
  • Aging and Dementia
Component 1: Targeted, high-risk, high-reward basic science studies

- Examine the roles of multiple genes on chromosome 21 simultaneously
- Explore chromosome silencing
- Evaluate epigenetic/ metabolomic/ transcriptomic profiling in model organisms/iPSCs/brain organoids in several model systems
- Develop novel model systems, including a molecular atlas for cardiac and other specimens

Emphasis on studies that can inform the other two components.
NIH Basic Science Research in DS: Mouse models

- Developed by The Jackson Laboratory
- Extra chromosome material derived from mouse chr 16 and 17
- Mice: DD/LD, hyperactive, poor growth, facial features, reduced fertility, develop amyloid plaques
Component 2: *Assemble a large cohort for pan-'omics and biomarker studies*

- Cofunded 2 KF X01 supplements: Genomic Analysis of CHD and ALL in Children with Down Syndrome; Myeloid malignancies
- **DS-Connect®**: The Down Syndrome Registry
  
Component 3: *Build a clinical trials network for inclusion in existing and future clinical trials*

- Extremely limited medication trials in DS have been underpowered and lacked efficacy
- Need to test how commonly used medications affect people with DS
- Need to develop clinical measures appropriate for DS
- Goal: full inclusion of people with DS in clinical trials
Alzheimer’s Disease in DS

- Many people with DS begin to show symptoms of Alzheimer’s disease (AD) in their 50s/60s
  - 3 copies of APP on trisomic chromosome 21
- Research in this area includes preparations for:
  - Clinical trials to test treatments for dementia in adults with DS
- Alzheimer’s Biomarkers Consortium of Down Syndrome (ABC-DS):
  - Funded by NIH (NIA and NICHD): ~$37 M over 5 years
  - > 500 volunteers who have Down syndrome, plus healthy siblings
  - Age >25 years
  - Studies of biomarkers that may help diagnose Alzheimer’s—even before symptoms appear: Cognitive tests, Brain imaging (amyloid, tau), Genetic studies, Blood/CSF biomarkers
- Leveraging ADNI: Alzheimer’s Disease Neuroimaging Initiative
THE INCLUDE PROJECT

2019 Funding and beyond:

- More funding opportunities
- Workshops:
  - Development of a cohort of individuals with DS across the lifespan
  - State of the science for clinical trials in DS
  - Planning clinical trials for Alzheimer’s disease in DS

URL: https://www.nih.gov/include-project
Q & A!

- DS-Connect:  http://DSConnect.nih.gov
- INCLUDE:  https://www.nih.gov/include-project

- Contact us!  DSConnect@nih.gov

Melissa Parisi
Lisa Kaeser
Sujata Bardhan