Your Research Toolbox: How to talk with ease about Down Syndrome Research

February 19, 2022

Hampus Hillerstrom
Chief Executive Officer

Dr. Jim Hendrix
Chief Scientific Officer

Michelle Slape
Director of Family Programs
Introduction & Overview
Small group activity: How to talk about research

PART 1: Understanding the Basics of Down Syndrome research,
Down syndrome research advancements, and current challenges
  •  Alzheimer’s disease
  •  Sleep apnea & cognition
  •  Independence

PART 2: Why these conversations and your leadership are critical to future of research

PART 3: Examining the Down Syndrome Research Toolkit
  •  Materials, tools specifically for Affiliate Leaders
  •  Materials and resources for your community

Q&A
Who We Are

We envision a world where every person with Down syndrome thrives with improved health, independence, and opportunities to reach their fullest potential.

• To realize our vision, we...

  • accelerate research to increase availability of therapeutic, diagnostic, and medical care options

  • provide resources and support to a vibrant online community of individuals with Down syndrome and their caregivers

  • connect the Down syndrome and research communities with an agile team of 16 people
Our History

• 2004: Earliest incarnation, Down Syndrome Research and Treatment Foundation (DSRTF), is founded by two families seeking better futures for their children after the decoding of the human genome opened the door to biomedical research for people with Down syndrome.

• 2015: DSRTF merges with the Research Down Syndrome (RDS) Foundation, becoming LuMind RDS Foundation.

• 2019: LuMind RDS merges with the International Down Syndrome Community (IDSC), creating our current organization, LuMind IDSC Foundation.
Working with Partners to Accelerate Community Impact
Please break into small groups of 3-4 people, complete your worksheet and share your answers...
Three key elements for speaking effectively about research:

You don’t have to be a subject matter expert in order to be a research advocate and amplifier!

• Rely on or adapt existing resources – you aren’t expected to be an expert on everything.
• Use metaphors and simple language. Don’t over-complicate the message.
• Identify meaningful calls to action and ways to get involved.
Part 1: Understanding the basics

- Overview of Advances & Momentum in DS research
- Alzheimer’s Disease
- Sleep Apnea
- Independence
Why Accelerate Research Now?

Life expectancy for people with Down syndrome has increased dramatically.

1960s

Life expectancy was 10 years.

1980s

Life expectancy was 25 years.

2020s

Life expectancy is 65+ years.
Why We Accelerate Research

95% risk of Down syndrome-associated Alzheimer’s disease at age 65. It is the leading cause of death for adults with Down syndrome.

100% of adults experience obstructive sleep apnea. 60% of children experience abnormal sleep by age 4.

97% of families report lack of independence as a critical concern for their loved one.

99% almost all children and adults with Down syndrome have speech and cognitive delays.
How We Accelerate Research

We invest in translational research

We build awareness of Down syndrome research & the importance of participating in it

We remove barriers to clinical trials
Growing Down Syndrome Research Momentum

- NIH Include Project ~$77M
- NIH DS Connect Registry > 4,500
- NIH ABC-DS Biomarker > 450
- NIH ACTC-DS Emerging network

- LonDowns cohort <452>
- Horizon21 network 11 sites
- DABNI cohort <485>

- Human Trisome Project <700>
- DS-CTN network with 15 sites
- DS Cognition Project cohort ~300
- LIFE-DSR cohort <270>

In 2019, 429 Researchers from 36 countries attended Trisomy21 Research Society Meeting in Barcelona, Spain.
What Are Clinical Trials?

- **Clinical research** that is performed on humans.

- **Double-blind placebo-controlled trials** are the gold standard for determining the safety and efficacy of a new treatment. **Be skeptical of results from other types of trials!**

- The **drug development process** is long, expensive and risky but still the best way to find new treatments.

- Typically **3 phases in clinical trials** in the drug development process.
Best Practices for Clinical Trials

- Independent oversight of trials ensures high ethical standards.
- Informed consent is used to protect the rights of people participating in clinical trials.
- Clinical trial results should be published in a timely manner.
What Do We Know About Alzheimer’s and Down Syndrome?
Prevalence of Alzheimer’s disease

95% of people with Down syndrome develop Alzheimer’s disease by age 65+

12% of the general population of people age 65+ have AD


History of Alzheimer’s Disease

tangles

plaques
Down Syndrome & Alzheimer’s Genetics

The amyloid precursor protein gene (APP) is located on chromosome 21.

Toxic Amyloid Plaques

Amyloid Protein

APP gene
Alzheimer’s vs. Dementia

Alzheimer’s is a specific brain disease that accounts for 60-80% of dementia cases.

Dementia is a general term for symptoms like decline in memory, reasoning or other thinking skills.

Source: Alzheimer’s Association
Progression Over Time

- Alzheimer’s is a disease of progressive decline
  - Rate of decline varies from person-to-person and over time
  - Plateaus, sudden drops, etc.
- Possible causes of sudden changes
  - Stroke
  - Infection
  - Depression
  - New onset or change in metabolic condition (e.g., diabetes)
Alzheimer’s or Regression?

What is similar?
• Both involve decline in skills
• Both are (probably) neurological conditions that often have psychological symptoms
• Both are challenging for the individual and families
• Both need more research, including ways to support the individual and family

What is different?
• Alzheimer’s disease
  • Age of onset = > 40
  • Not reversible
• Regression syndrome
  • Age of onset = teens, early 20s
  • Sometimes reversible
• Not all decline in skills in those age ranges is either Alzheimer’s disease or regression
Alzheimer’s Treatments

**FDA Approved Drugs**
- Cholinesterase inhibitors (e.g., donepezil / Aricept)
- NMDA receptor antagonist (memantine / Namenda)
- Anti-Amyloid Monoclonal Antibody: Aduhelm (aducanumab)

**Non-Drug Strategies**
- Create schedules and routines
- Promote lifestyle changes:
  - Sleep
  - Healthy eating
  - Physical activity
  - Encourage safe social interactions
Aducanumab (Aduhelm)

Early AD

PET(+) Brain Imaging

Apr 2019 Futility Analysis

↓ beta-amyloid (PET)  
↑ cognition (CDRsb & MMSE)

Oct 2019 Data Shows Efficacy

FDA Review

FDA granted accelerated approval in June

Not one participant with Down syndrome. Will treatments work in people with Down syndrome if they are not part of trials?
Aducanumab and Down Syndrome?

**Efficacy**
- Aducanumab is a human monoclonal antibody reduces amyloid in the brain.
- If Aducanumab slows progression of sporadic AD, it may also slow AD in Down syndrome.

**Safety**
- ARIA (Amyloid Related Imaging Abnormalities) is a known side effect. ARIA-E is edema (brain swelling) and ARIA-H is microhemorrhage (bleeding in the brain).
- The incidence of ARIA is high.
- 25% of participants in the 6 mg/kg dose group and 33% of those receiving 10 mg/kg developed ARIA-E, compared with 10% in the placebo group.
- 17% of people on drug developed ARIA-H microhemorrhages, compared with 6% in the placebo group.
- Microhemorrhages are more common in older adults with Down syndrome than the general population. **Will aducanumab increase this risk?**
Research on Down syndrome-associated Alzheimer’s disease
Vision to Tackle Alzheimer’s

Advance effective treatments for people with DS
• Infrastructure to support trials
• Natural history study (LIFE-DSR)
• Develop assessment scales

Significantly and tangibly improve the care of those with DS
• Support families in studies and trials
• Connect to best medical health resources

Attract more public and pharmaceutical industry sponsors to clinical trials for DS
• Collaborate with NIH
• Engage with pharmaceutical industry
Down syndrome Clinical Trial Network

DS-CTN is built to conduct large-scale, multi-site trials under the supervision of experienced clinicians who are experts at providing medical care for individuals with Down syndrome.
Our Research Initiatives: LIFE-DSR

What is LIFE-DSR?

• A multi-year, coordinated natural history study by medical and academic professionals
• Will track and analyze medical & physical data of 270 adults with Down syndrome; no drug or therapy trials
• Participants complete 3+ visits to their DS-CTN site over two years

Why is LIFE-DSR important?

• Will help researchers understand link between DS and Alzheimer’s
• Understanding physiology of people with DS may help solve other health/ Quality of Life challenges
• Increased understanding of biomarkers (reliable predictors and indicators of disease) in DS-AD can be used as bridge to AD biomarkers in general population to better understand disease progression and drug effects
What Do We Know About Sleep Apnea?
Sleep and Cognition in Down Syndrome

Sleep correlates with:

- **Behavior and attention in development**, particularly in symptoms of ADHD and executive control
- **Brain structure and Alzheimer’s disease pathology in DS**
- **Memory consolidation**: studies in young infants and typical children show that they retain more over longer time if they nap after learning.
How do we measure sleep?

1. **Polysomnography**
   - In clinic, overnight sleep lab
   - Gold standard – Wealth of information
   - Challenging in people with sensory difficulties
   - Testing availability (long wait times, poor availability in rural areas)

2. **Actigraphy**
   - Measures movement, not necessarily sleep

3. **Caregiver report / diary**
Types of Sleep Apnea

Obstructive Sleep Apnea
- Snoring, choking, gasping
- Associated with adverse cognitive, quality of life and cardiovascular effects
- Only ~2-5% of children overall

Central Sleep Apnea
- Silent pauses
- Uncommon in children
  - Typically associated with neurologic or neuromuscular conditions
  - May be seen in infants
- Not clear how common this is in Down syndrome
Prevalence of OSA in Down Syndrome

31% of infants with Down syndrome experience OSA

>50% of children with Down syndrome experience OSA
among those children, 50% of cases are severe

>82% of adults with Down syndrome experience OSA
Complications of diagnosing OSA among children with Down syndrome

• Many parents of children with DS don’t report symptoms of OSA such as snoring

• Screening of all children with DS recommended by age 4

• One study showed only 25% of children with DS had Polysomnography by age 4
### OSA Treatment in Down Syndrome

#### Standard/Traditional Approaches
- Adenotonsillectomy
- Continuous Positive Airway Pressure therapy (CPAP)

#### Alternative/Emerging Approaches
- Weight loss (easier said than done)
- Dental approaches
  - Palate expansion
  - Mandibular advancement device
- Myofunctional therapy (speech therapy)
- Anti-inflammatory medications
- Small improvements seen with Singulair® or intranasal steroid treatments
- Hypoglossal Nerve stimulation
Standard OSA Treatments in DS

Adenotonsillectomy

- 1st Line approach for most children
- Unlikely to resolve OSA in children with DS
  - 65-73% have some OSA after adenotonsillectomy

CPAP

- Pressurized air delivered through a mask and hose
- Very efficacious, but...
- Limited adherence
  - 46% adherence in children with DS (Trucco, et.al. 2018)
  - 2 hours per night in one trial (Konstantinopoulou, et.al. 2016)
LuMind Caregiver Survey: Sleep Apnea Diagnosis and Treatment

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 yrs</td>
<td>Median age of person with Down syndrome (Age range 0-67 yrs)</td>
</tr>
<tr>
<td>84%</td>
<td>Diagnosed with sleep apnea (half were asymptomatic)</td>
</tr>
<tr>
<td>59%</td>
<td>Caregivers who were aware of the AAP guidelines</td>
</tr>
<tr>
<td>82%</td>
<td>Prescribed adenotonsillectomy</td>
</tr>
<tr>
<td>62%</td>
<td>Prescribed CPAP</td>
</tr>
<tr>
<td>16%</td>
<td>Aware of hypoglossal stimulation</td>
</tr>
<tr>
<td>16%</td>
<td>Repeated the sleep study to monitor OSA with aging</td>
</tr>
<tr>
<td>30%</td>
<td>Waited more than 4 years between sleep studies</td>
</tr>
</tbody>
</table>
Research & Clinical Trials in Sleep Apnea and Cognition
Hypoglossal Stimulation for Sleep Apnea in DS

- Implant a device to stimulate the tongue to open airway at night
- **FDA approved for adults 18 years and above**
- Ongoing 50 participant trial at sites across the US

Exciting interim results (data on 21 patients):
- 84% reduction in sleep apnea index
- 7.9 hour/night compliance (compared to ~3 hours for CPAP alternative)

LuMind IDSC working with principal investigator Dr. Chris Hartnick (Mass Eye & Ear) to accelerate availability of this approach for children.
- Data collection
- NIH application
- Interaction with study sponsor
- Recruitment
Anecdotal reports of improvement of speech/cognition with Hypoglossal stimulation

• “The smoothness of conversation has gained since the surgery but the most gain has been with articulation. Everything has improved!”

• “He will be a senior in high school next year, he never ever would have made it without hypoglossal stimulation and sleep, his speech has improved enough he can be understood in school.”

• “The IEP showed increase fluency in speech, more organized in thoughts and organization. He showed an ability to self monitor speech and to regulate his speech. He was able to pay attention and focus in class. He showed an increase from previous evaluation.”

LuMind IDSC funds the collection of speech/cognition data in 6 or more participants in ongoing clinical trial
Hypoglossal stimulation recruitment

Researchers are looking for children with DS, ages 10-21, who have had an adenoidectomy and tonsillectomy but who still have severe sleep apnea and who cannot tolerate CPAP therapy.

Current Research Site Locations

- Massachusetts Eye and Ear (Boston, MA)
- Henrietta Egleston Hospital for Children (Atlanta, GA)
- Cincinnati Children’s Hospital (Cincinnati, OH)
- Children’s Hospital of the King’s Daughters (Norfolk, VA)
- University of Texas Southwestern Medical Center (Dallas, TX)
- Children’s Hospital of Philadelphia (Philadelphia, PA)

Questions about the study should be sent to Dr. Chris Hartnick of Massachusetts Eye and Ear
(Christopher_Hartnick@meei.harvard.edu)
Research on Medications for OSA Treatment

Testing a combination of two drugs, atomoxetine and oxybutynin
- Appears effective in adults without DS with a 76% improvement in apnea-hypopnea index (AHI)
- Increases airway muscle tone during sleep

Dr. Daniel Combs and Dr. Jamie Edgin, U. of Arizona, have a NIH grant to study this treatment in 27 children with DS (ages 6-17).
- LuMind IDSC funded a small grant to add speech and cognition testing to the study.
- The study started recruiting this year but has been paused by COVID-19.
Practice Healthy Sleep Habits

Regular Sleep Schedule: Maintain a consistent sleep pattern, getting up at the same time every day.

Relaxing Bedtime Routine: Spend time before bed relaxing: read a book, have a shower or bath.

Avoid Stimulants: Don’t drink caffeine, sugary or energy drinks in the evening.

Good Sleep Environment: Keep your bedroom aired, cool and comfortable with a quality mattress and bedding.

Block Out Noise and Light: Make sure the bedroom is dark and quiet or use white noise, a fan or music to mask external noise.

Only Sleep and Intimacy: Avoid watching TV or using other devices, such as cell phones, in bed.

Exercise and Daylight: Try to do regular exercise, but not too intense before bedtime. Spend time outside in the daytime. Even a short walk during the day can improve sleep.

Eat Well: Try to eat a balanced, healthy diet. Avoid heavy, fatty, fried, or spicy food late in the evening if you get indigestion. Bananas, yogurt or healthy cereal are good bedtime snacks.
Understanding & Prioritizing Independence for people with Down Syndrome
Independence for People with Down Syndrome

Survey respondents: 400 caregivers from across the U.S.

- 80% of caregivers were 35-64 years;
- 92% of the persons with DS were 0 – 35 years (36% 13-22 years)

96% of caregivers surveyed said Independence was important to their family

- >89% of respondents indicated they want their loved one with Down syndrome to be “As independent as possible”
- 9% indicated they wanted to see “some independence”

### Top Ten “Independence” Goals Identified by Caregivers

<table>
<thead>
<tr>
<th>ACHIEVED</th>
<th>MIXED LEVELS OF ACHIEVEMENT</th>
<th>NOT YET ACHIEVED</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Able to be left with babysitter</td>
<td>• Traffic Safety</td>
<td>• Stranger Danger</td>
</tr>
<tr>
<td>• Bolting/Eloping</td>
<td>• Home alone for 2+ hours,</td>
<td>• Kitchen Safety</td>
</tr>
<tr>
<td>• Water Safety</td>
<td>• Verbal Abuse/Bullying</td>
<td>• Sexual Abuse</td>
</tr>
</tbody>
</table>

80% of caregivers were 35-64 years; 92% of the persons with DS were 0 – 35 years (36% 13-22 years)
Survey respondents’ top five “First Choice” priorities for Independence

**Daily Living**
- Carry out domestic activities, (make bed, pick up around the house, light housecleaning, etc.)
- Eat meals independently
- Use money
- Weight management
- Living independently / semi-independently

**Self-Care**
- Wash himself/herself (shower or bath)
- Healthy understanding of sexuality
- Self-reporting feelings and health
- Use toilet independently
- Healthy eating / portion control

**Safety**
- Safely crossing a street / parking lot
- Social media safety
- Bolting / Elopement
- Stranger danger
- Sexual abuse
Survey respondents’ top five “First Choice” priorities for Independence

**Communication**
- Expresses emotions appropriately
- Understand what he/she reads
- Use verbal communication
- Be understood by others, even with limited language
- Communicating wants and needs

**Vocational/Employment**
- Navigating public transportation alone
- Time management
- Appropriate behavior
- Ability to ask for help when needed
- Reading and writing

**Social/Leisure**
- Participate in hobbies (painting, gardening, writing, dancing, etc.)
- Hanging out with friends
- Able to manage disruptions to routines or schedules
- Engages in leisure time appropriately
Additional diagnoses that could impact Independence

<table>
<thead>
<tr>
<th>Percent of individuals with an additional diagnosis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep Apnea</td>
<td>32%</td>
</tr>
<tr>
<td>Obesity</td>
<td>12%</td>
</tr>
<tr>
<td>ADHD</td>
<td>9%</td>
</tr>
<tr>
<td>Other (i.e., Apraxia/Speech, hearing loss, Hypothyroidism, heart issues)</td>
<td>36%</td>
</tr>
</tbody>
</table>
Part 2: Preparing for Research Readiness

- The importance of conversations
- The transition from Research awareness to participation is a big leap we’re taking together as a community
Big Picture: Why Talk About Research?

What do we hear from the community?

- Why isn’t there a drug for AD?
- Why don’t they invent something?
Big Picture: Why Talk About Research?

_They can't do anything without research and trial participation, without **YOU**, without the greater **US**._
Big Picture: Why Talk About Research?

Without participation in clinical trials ➔

- No drug is approved.
- No new treatments get to market.
- IF new treatments do get to market in DS, most get to market *without ever having been tested in DS.*
92% of families surveyed by LuMind IDSC indicated they wanted clinical trials to focus on the health care needs of people with Down syndrome.

Fewer than 15% of families said they had ever participated in a clinical trial or an observational study.
Research Participation Needed

The number of clinical trials and observational studies in adults with Down syndrome grew from one trial in 2016 to four in 2021.

5-10 studies are expected by 2024.
Your mission, should you choose to accept it...

- In order to meet the growing need for Down syndrome research, our community must prepare for more studies and clinical trials
- Raising awareness among families is a big job, but one we can accomplish together
Down Syndrome Research Toolbox

Part 3: Using all the tools in the toolbox

• Resources for you as a leader
• Resources and materials for your community
• Ongoing support, information
Resources for you: Affiliates Page

A portal focused on the needs of busy community leaders who need reliable materials that are:

• Curated and vetted from reputable sources
• Easy to use, share, send
• Multi-tied materials that can be aligned for different audiences, from caregivers to self-advocates to clinical support staff and volunteers

www.LuMindIDSC.org/affiliates
Resources for you: Awareness Page

• One central hub for community-facing turnkey materials, infographics, videos, social posts
• All available for co-branding
• Designed to build awareness and comfort around research.

myDSmoment
They Did. I Can. We Will.

www.LuMindIDSC.org/myDSmoment
A Resource for Your Community

myDSC

A free, online library of 700+ trusted resources and useful materials that can be personalized to each member’s interests.

myDSC is a useful tool for: people with Down syndrome, their families, and the wider community that supports them. Free for all at: myDSC.org
Resources for the Community

Registering is easy – and free!
myDSC.org

1. Visit myDSC.org and click "Join"
2. Fill out the Account Request form
3. Log in, and start browsing
Resources for Your Community

DS-AD specific resources on LuMindIDSC.org

Guides, explainers, webinars, and more – in English and en Español

www.lumindidsc.org/alzheimersdisease
Resources for Your Community

Sleep Apnea in myDSC, and at:
www.LuMindIDSC.org/sleep
Clinical Trial Finder Online

LuMindIDSC.org/ClinicalTrialFinder

List of clinical trials that can be filtered by type, gender, age, category and recruitment status
LuMind IDSC
COVID-19 Family Resources

1. COVID-19 Resources on our website
2. COVID-19 Q&A
   • Co-led and disseminated with 7 DS organizations
3. T21RS/Emory survey on DS COVID-19 cases & vax
   • Co-funded and disseminated by 8 DS organizations

All resources are available on LuMind IDSC’s website in the COVID-19 Resources section
(www.lumindidsc.org/covid19)
Please keep in touch!

facebook.com/LuMindIDSC
twitter.com/LuMindIDSC
instagram.com/LuMindIDSC
linkedin.com/company/LuMindIDSC
youtube.com/c/LuMindIDSC
LuMindIDSC.org/news