

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

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Agenda



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.



Down Syndrome Research Toolbox



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.



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





Growing Down Syndrome Research Momentum



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

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

Human Trisome Project <700>

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

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 <u>Alzheimer's</u> 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







Down Syndrome & Alzheimer's Genetics



Alzheimer's vs. Dementia





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)





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?

- 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

EFFICACY

- 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 syndromeassociated Alzheimer's disease

Vision to Tackle Alzheimer's





Down Syndrome Clinical Trial Network





Longitudinal Investigation for Enhanced Down Syndrome Research (LIFE-DSR) 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.

MGI





GENERAL HOSPITAL



Down Syndrome Clinic and Research Center at Kennedy Krieger Institute



RUSH







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





"OK, Mrs. Tully. We want you to relax, get a good night's sleep, and we'll evaluate any sleep issues that you have."

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







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





Before Surgery

After Surgery



- 1st Line approach for most children
- Unlikely to resolve OSA in children with DS
 - 65-73% have some OSA after adenotonsillectomy (Shete, et.al. 2010, Thottam, et.al. 2013, da Rocha, et.al. 2017)

<u>CPAP</u>

- 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



[724] | 96% Parents

12 yrs	Median age of person with Down syndrome (Age range 0-67 yrs)
84%	Diagnosed with sleep apnea (half were asymptomatic)
59%	Caregivers who were aware of the AAP guidelines
82%	Prescribed adenotonsillectomy
62%	Prescribed CPAP
16%	Aware of hypoglossal stimulation
16%	Repeated the sleep study to monitor OSA with aging
30%	Waited more than 4 years between sleep studies



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 (<u>Christopher_Hartnick@meei.harvard.edu</u>)



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



Sexual Abuse

Survey respondents: 400 caregivers	80% of caregivers were 35-64 years;						
from across the U.S.	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							
ACHIEVED Able to be left with babysitter Bolting/Eloping 	 MIXED LEVELS OF ACHIEVEMENT Traffic Safety Home alone for 2+ hours, 	NOT YET ACHIEVED Stranger Danger Kitchen Safety 					

Verbal Abuse/Bullying

ullet

• Water Safety

Survey respondents' top five "First Choice" priorities for Independence



35%

	Eat meals independently						
	(make bed, pick up around the house, light housecleaning, etc.)						
Daily Living	Use money	,					
	Weight management						
	Living independently / semi-independently	,					
	Wash himself/herself (shower or bath						
Solf Caro	Healthy understanding of sexuality						
	Self-reporting feelings and health						
	Use toilet independently						
	Healthy eating / portion contro						
	Safely crossing a street / parking lo						
	Social media safety	+					
<u>Safety</u>	Bolting / Elopement						
	Stranger dange						
	Sexual abuse						
		0%	5%	5% 10%	5% 10% 15%	5% 10% 15% 20%	5% 10% 15% 20% 25%

Survey respondents' top five "First Choice" priorities for Independence



15%

20%

25%

30%

35%

10%

	Expresses emotions appropriately
	Understand what he / she reads
Communication	Use verbal communication
	Be understood by others, even with limited language
	Communicating wants and needs
	Navigating public transportation alone
Vecetional	Time management
vocational	Appropriate behavior
<u>Employment</u>	Ability to ask for help when needed
	Reading and writing
	Sports activities
	Participate in hobbies (painting, gardening, writing, dancing, etc.)
Social/Leisure	Hanging out with friends
	Able to manage disruptions to routines or schedules
	Engages in leisure time appropriately

0%

5%



Age of individual with Down syndrome (years)

Achievement of skills by category, %

Additional diagnoses that could impact Independence





Percent of individuals with an additional diagnosis				
Sleep Apnea	32%			
Obesity	12%			
ADHD	9%			
Other (i.e., Apraxia/Speech, hearing loss, Hypothyroidism, heart issues)	36%			

Down Syndrome Research Toolbox



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?



Big Picture: Why Talk About Research?



They can't do anything without research and trial participation, without <u>YOU</u>, without the greater <u>US</u>.



Big Picture: Why Talk About Research?



Without participation in clinical trials \rightarrow

No drug is approved.

No new treatments get to market.

IF new treatments do get to market in DS,

⁹ most get to market *without ever having been tested in DS*.







Research Participation Disparity



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



5-10 studies are expected by

2024

2024

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



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

Skin Conditions and Down Syndrome February 22, 2022 **Skin Conditions and Down Syndrome Down Syndrome** Down Syndrome Adoption and COVID-19: What You Need to Know Date: November 4, 2021 Time Speakers: Dr. Brian Skotko and **CONEXIÓN EN ESPAÑOL** Dra. Ana Claudia Brandão Moderator: Claudia Moreira Free Access HOME > NEWS > CONEXIÓN EN ESPAÑO https://www.youtube.com/watch? v=0qtwz-BLtag Conoce Más Acerca Mi Familia Es Mi Señales de que su de la Enfermedad ser auerido con Orgullo de Alzheimer y Su síndrome de Down Roberto Ojeda es un atleta y Conexión Con el debería de visitar a un padre dedicado que irradia un especialista de Síndrome de Down amor y orgullo por su familia. la enfermedad de Su hija, Mariana, tiene Hoy en día, los individuos con síndrome de Down, lo cual -por Alzheimer sindrome de Down logran vivir motivo de la falta de educación hasta sus sesenta años, v de recursos - aún es visto La enfermedad de Alzheimer gozando de una esperanza de como un diagnóstico tiene gran prevalencia en la vida más larga de lo que había vergonzoso en países como población con síndrome de sido históricamente. México, donde Roberto y su Down. Es por eso por lo que los

padres y cuidadores debemos

de prestar atención a cam

familia viven. A pesar de eso, se

han mantenido optimistas v

Desafortunadamente, existe un

nuevo reto que las personas

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.

*my***DSmoment**



www.LuMindIDSC.org/myDSmoment





#myDSmoment Testimonial #1 Featured in Video: Michelle Sullivan YouTube Link: <u>https://youtu.be/8XENJvN_yLo</u>

#myDSmoment Testimonial #2 Featured in Video: The Cronin Family YouTube Link: <u>https://youtu.be/D8hLKtBZLRk</u>



#myDSmoment Testimonial #3 Featured in Video: The Nothnagles YouTube Link: <u>https://youtu.be/CH1E-8BajXY</u>



#myDSmoment Testimonial #4 Featured in Video: Alex & Kari Jones YouTube Link: <u>https://youtu.be/Ez4APpZMnCQ</u>



#myDSmoment Testimonial #5 Featured in Video: David Egan YouTube Link: <u>https://youtu.be/IShCHd58LsQ</u>



#myDSmoment Testimonial #6 Featured in Video: Jo Ann Simons YouTube Link: https://youtu.be/71ohkd7UarQ

A Resource for Your Community



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







Resources for Your Community



Sleep Apnea in myDSC, and at: www.LuMindIDSC.org/sleep





FI SEVIER



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!



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