Welcome to the

2025 South Carolina Rare Disease Symposium

Friday, February 28th
10:00 AM- 2:00 PM

A

SHOW YOUR STRIPES®

ON RARE DISEASE DAY®
FEBRUARY 28, 2025

NORD®
National Organization
for Rare Disorders

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FEBRUARY 28, 2025

South Carolina's Rare Disease State Report Card

Presented by Carolyn Sheridan, MPH, State Policy Manager, National Organization for Rare Disorders (NORD)

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FEBRUARY 28, 2025

Our Mission

Improving the health and well-being of people with rare diseases by driving advances in care, research, and policy.

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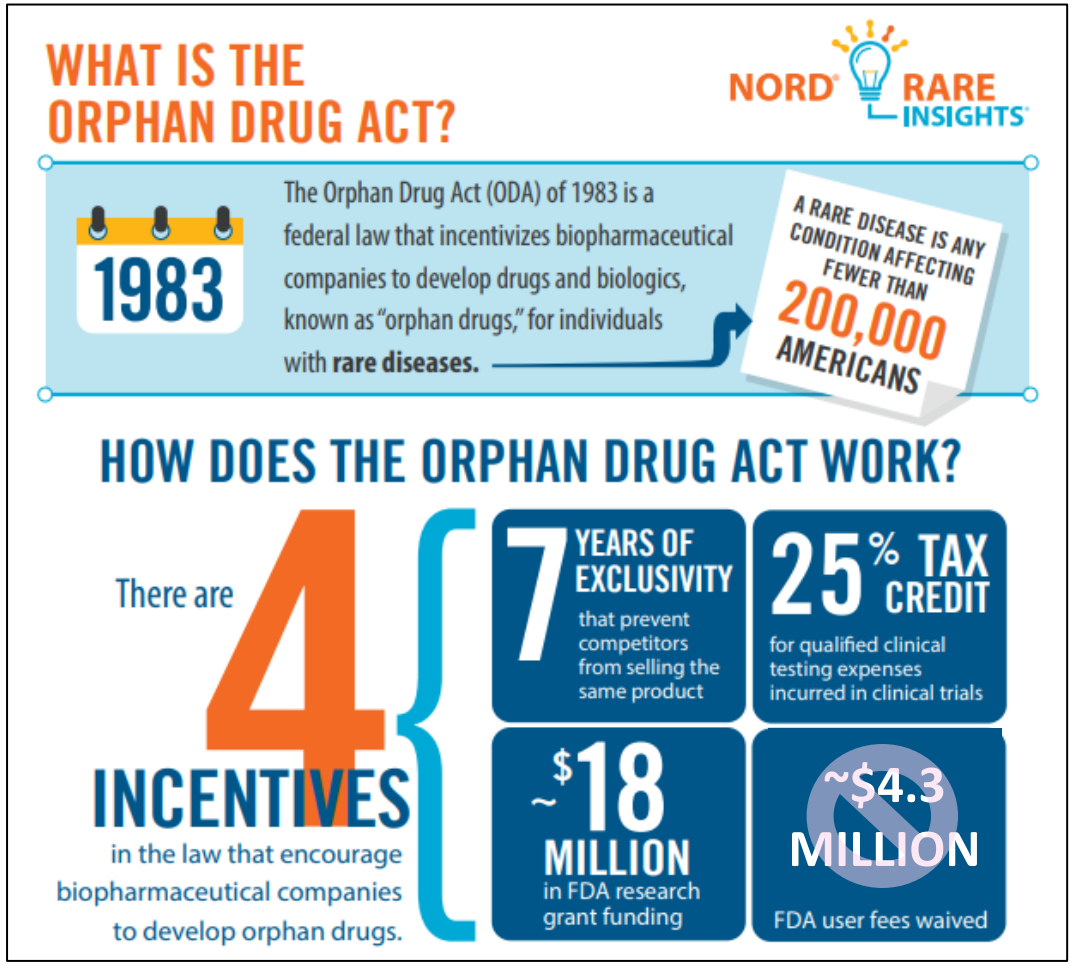
NORD, Rare Diseases and Disorders

Our Mission: Improving the health and well-being of people with rare diseases by driving advances in care, research and policy.

- NORD, is the only independent and nonpartisan U.S. organization working at the intersection of care, research, policy, and community for <u>all</u> rare diseases.



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What is the State Report Card?

- **Purpose:** It's not just a ranking – it's a **tool to push for policy change.**

- **How it works:** It benchmarks state policies on rare disease as of November 2024.

- Provides tangible **data** on:
  - ✓ Strengths
  - ✓Gaps
  - ✓Opportunities for Improvement

rarediseaseday.us | #ShowYourStripes

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As of November 2024:

- Since 2015, on an annual basis, NORD has evaluated how effectively states are serving people with rare diseases across nine issue areas:

Medicaid Financial Eligibility	D
Medical Nutrition	F
Newborn Screening	B
Prescription Drug Out-of-Pocket Costs	C
Protecting Patients in State Medicaid Programs	F
Protecting Patients in State Regulated Insurance	D
Rare Disease Advisory Council	YES!
Step Therapy (Fail First)	F
Telehealth	FAIL

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What are we seeking to understand across these nine categories?

Do **Medicaid income limits** provide all rare disease patients access to comprehensive coverage?	D
Does the state require insurance to cover **medical nutrition** products?	F
How strong is the state's **Newborn Screening p**rogram?	B
Are there state laws in place to help reduce **out-of-pocket costs** for patients?	C
Does the state use **§1115 Waivers** to tailor their Medicaid program? If yes, how?	F
Are **short-term limited duration health plans** regulated beyond federal requirements?	D
Does the state have a **Rare Disease Advisory Council** guiding policy?	YES!
Are patients protected from cumbersome **step therapy** requirements?	F
Is the state part of the **Interstate Medical Licensure Compact (IMLC)?**	FAIL

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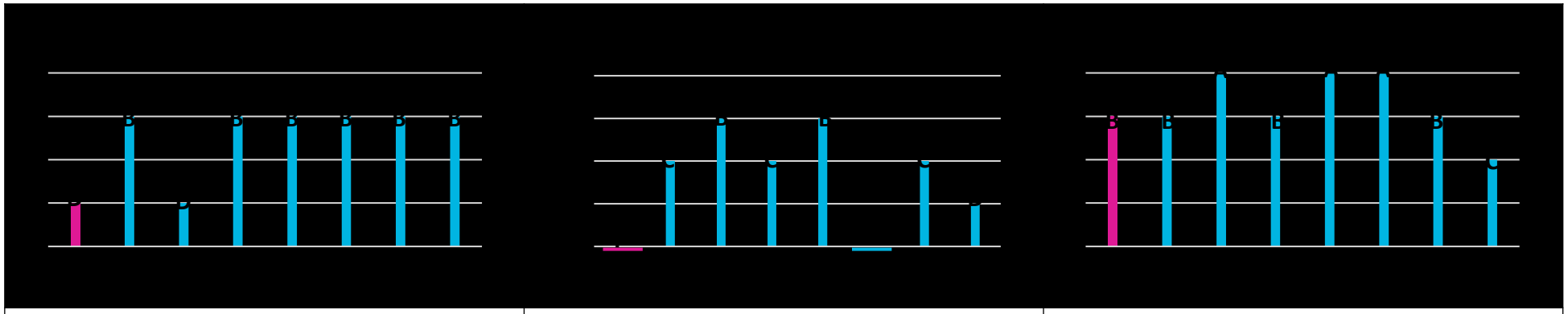
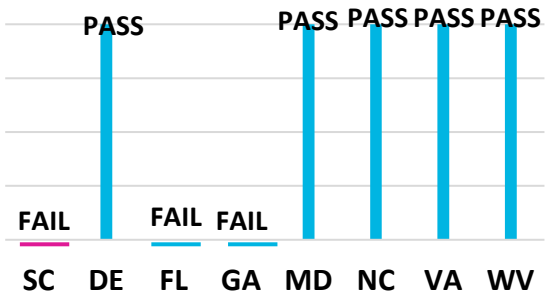
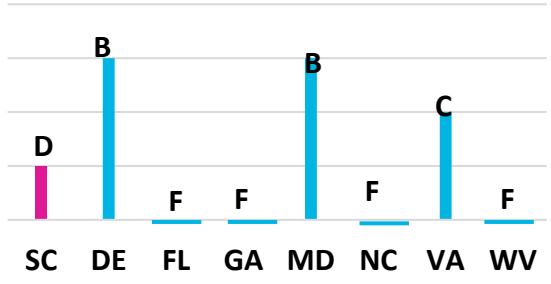
How Does South Carolina Compare?



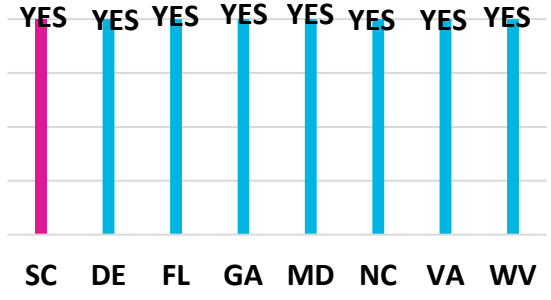
Medicaid Financial Eligibility



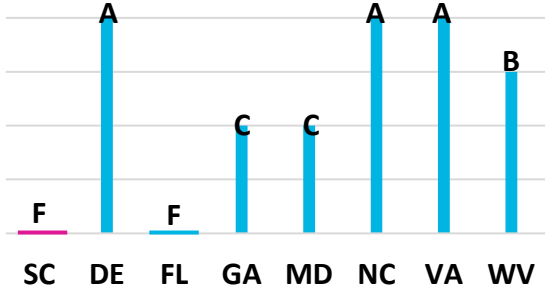
Medical Nutrition



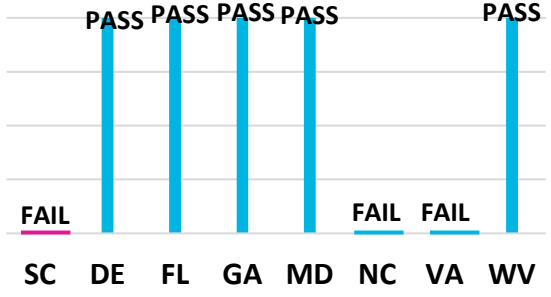
Newborn Screening



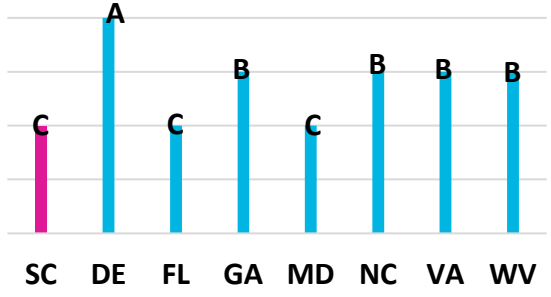
Protecting Patients - Medicaid



Protecting Patients – State Regulated



Rare Disease Advisory Councils



Step Therapy

Telehealth (IMLC)

Prescription Drug Out-of-Pocket Costs

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Opportunities for Positive Change in South Carolina

Prescription Drug Out-of-Pocket Costs (Grade: C)

Support recommendations to ban copay accumulator programs to reduce financial burdens

- *Active Bills: H.3934 (House) & S.330 (Senate)*

Medical Nutrition (Grade: F)

Recommend policies for insurance coverage of enteral formulas for home use.

Step Therapy Reform (Grade: F)

Advocate for reforms to limit delays in accessing effective treatments.

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Why This Symposium Matters

Raise Awareness

- Shine a light on rare disease challenges and opportunities in South Carolina.

Build Valuable Networks

- Foster collaboration between patients, advocates, policymakers, and healthcare providers.

Drive Meaningful Policy Change

- Share resources, strategies, and expertise to improve patient outcomes.

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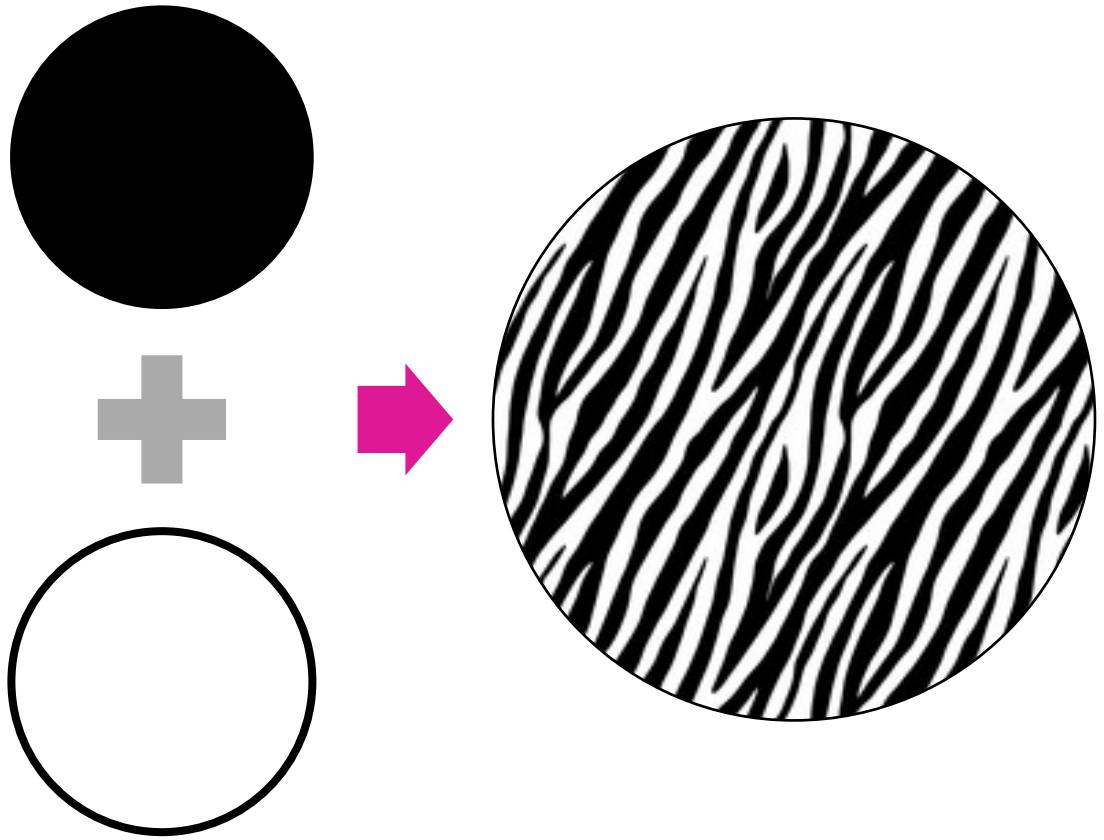
Alone We Are Rare, Together We Are Strong®

- When we come together, our uniqueness becomes our strength.
- A dazzle isn't just beautiful—it's powerful, creating change and protecting the whole community.



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THANK YOU

FOR PARTICIPATING IN RARE DISEASE DAY®

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National Organization for Rare Disorders

Successfully sharing your message – how to advocate with elected officials

- Emily Heatwole Keeney
- Government Affairs Advisor
- Adams and Reese LLP.

Keys to Advocacy

- Audience
- Messaging
- Connections
- Follow up
- Advocacy v Lobbying

126th General Assembly

House of Representatives

- 124 Representatives
  - 88 Republicans
  - 34 Democrats
  - 2 vacancies
  - 2024 – 17 new members elected

Senate

- 46 Senators
  - 34 Republicans
  - 12 Democrats
  - 2024 – 13 new members elected

Advocacy v. Lobbying

- The act of lobbying involves influencing or asking an elected official or other public official to take or not take an action
- Individuals may advocate individually
- Organizations, such as the RDAC, can provide information to public officials and elected officials without asking for an action.

History of the RDAC in South Carolina

2021 – H. 3956 filed by Leon Howard (D-Richland) then Chairman of the House 3M Committee

The bill passed the house by a vote of 63-45 with a minority report attached and a fiscal impact of $250,000 annually

June 2021 – the House Ways and Means Committee included Proviso 117.166 establishing the South Carolina Rare Disease Advisory Council to be housed at MUSC

2023 – language was added directing the Department of Health and Human Services to fund the RDAC

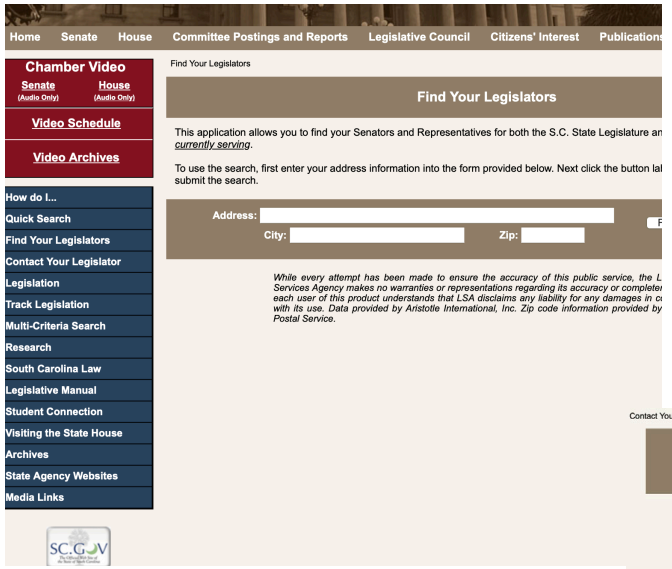
2024 – the Director of the Greenwood Genetic Center is added to the RDAC

Legislation/Law

- Title 44, Chapter 37 contains state requirements for neonatal and newborn testing (2019 last update)
- 2024
  - Act 26 – ensures the results of required neonatal testing may be shared with appropriate medical personnel to facilitate timely follow up visits
- 2023
  - S. 876 – Require whole genome sequencing

What can you do?

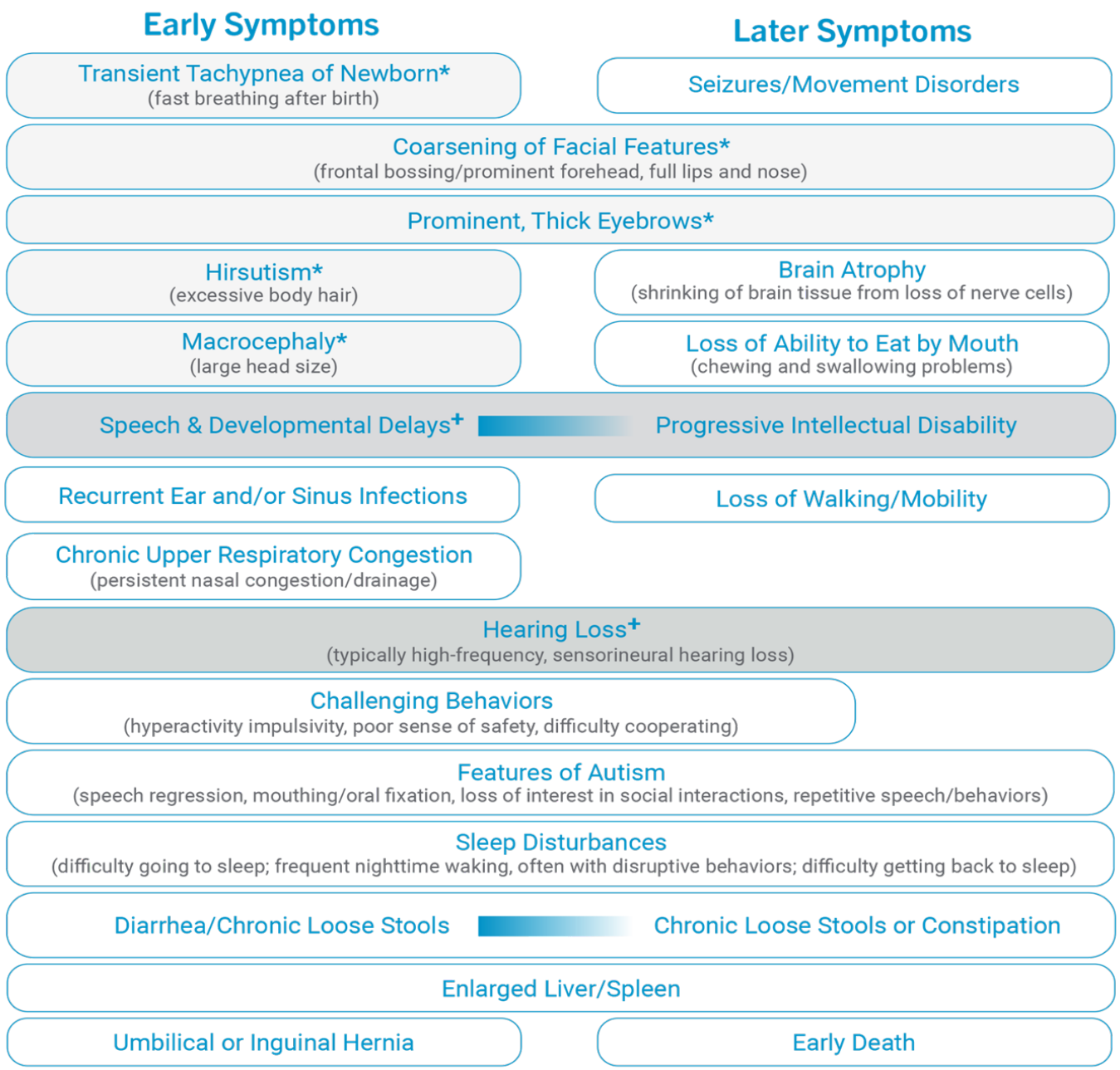
- How to contact your legislator
- When to contact your legislator
- Following up



Symptoms of Sanfilippo:

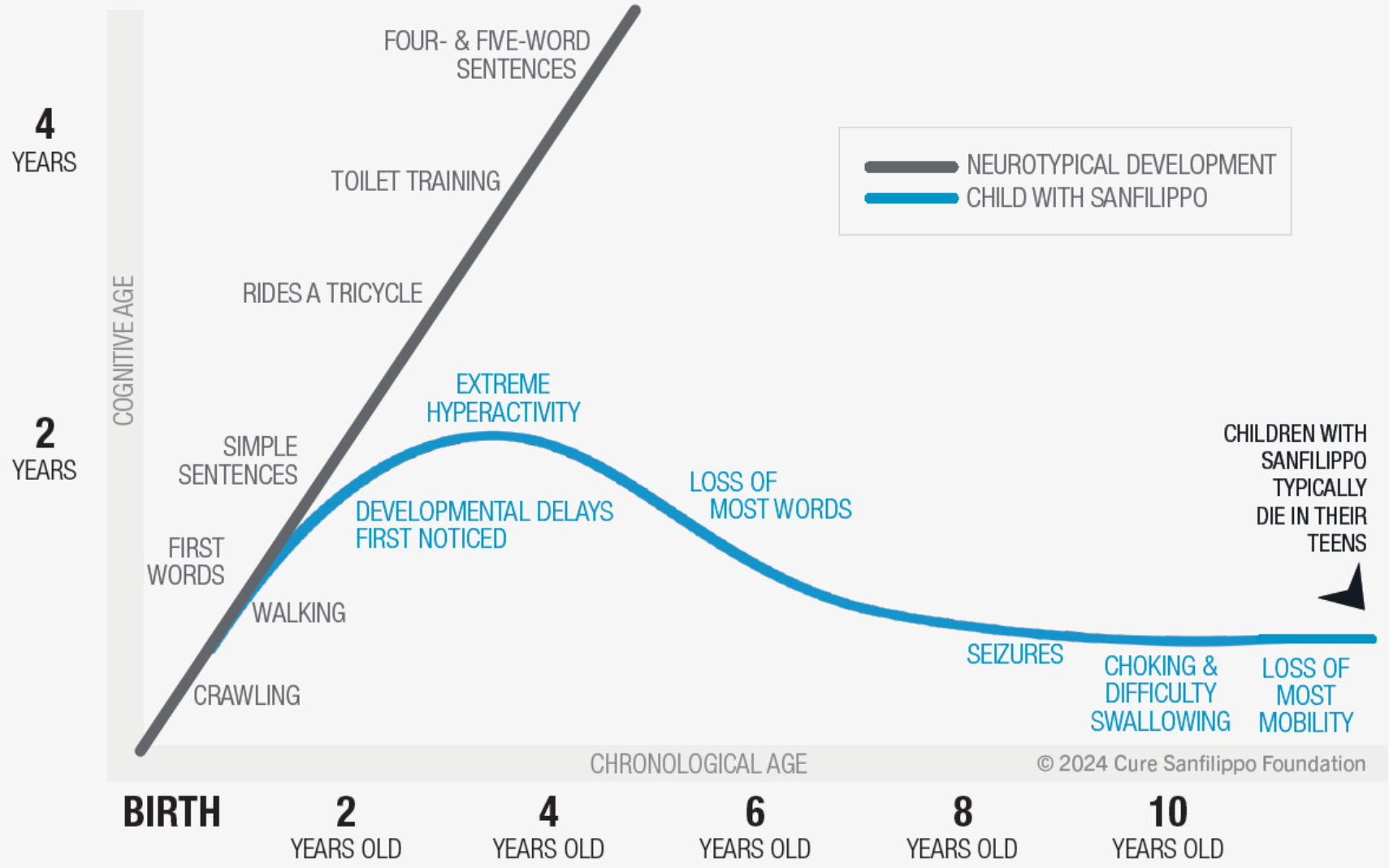
* Denote the most-specific indicators of Sanfilippo syndrome in infants.

+ Denote early neurological features of Sanfilippo.



Cure Sanfilippo Foundation – 501c3 nonprofit

IMPACT & PROGRESSION OF SANFILIPPO SYNDROME

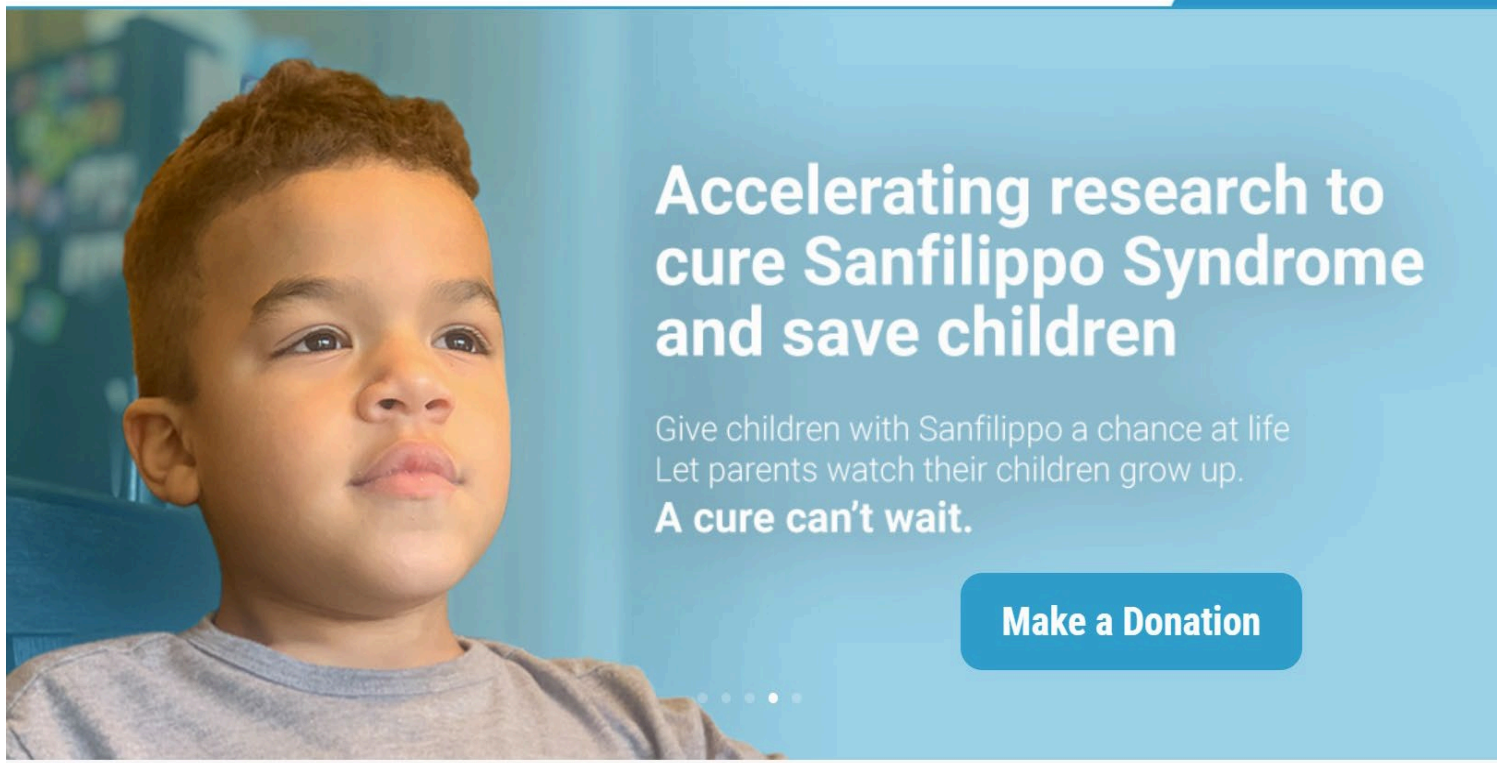


This figure is based on a natural history studies of disease progression in the classical, rapidly-progressing form of Sanfilippo Type A. While this illustrates the average course of disease progression, please note that individual children vary in the severity and specific timing of how the disease impacts their development.

CURE SANFILIPPO FOUNDATION

WHAT IS SANFILIPPO / MEET THE FAMILIES / WHAT WE DO / HOW TO HELP

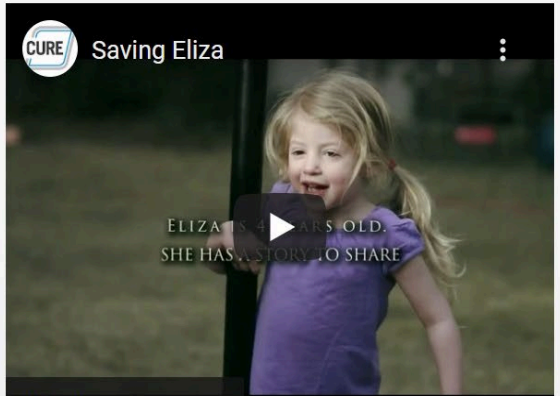
DONATE



Every parent dreams about their kid's future and watching it unfold.

Sanfilippo Syndrome takes all that away, replacing it with pain and suffering. The child experiences severe dementia and dies in their mid-teens. All before their parents eyes.

Cure Sanfilippo Foundation architects and funds



CURE SANFILIPPO FOUNDATION

a 501 (c)3 nonprofit
www.CureSFF.org

Natural History Study
2014 – 2015

Internet Rallies Around 4-Year-Old Eliza, Shatters Online Fundraising Record

Internet Rallies Around 4-Year-Old Eliza, Shatters Online Fundraising Record

By Robbie Couch

Jun 9, 2014, 03:38 PM EDT | **Updated** Dec 6, 2017

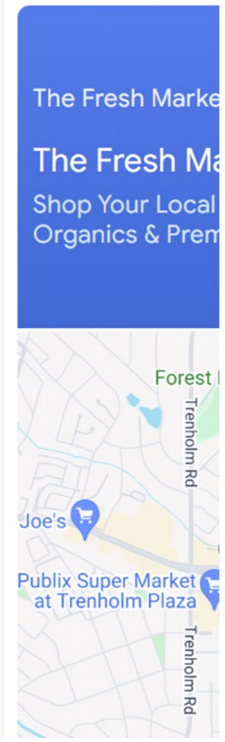
LEAVE A COMMENT

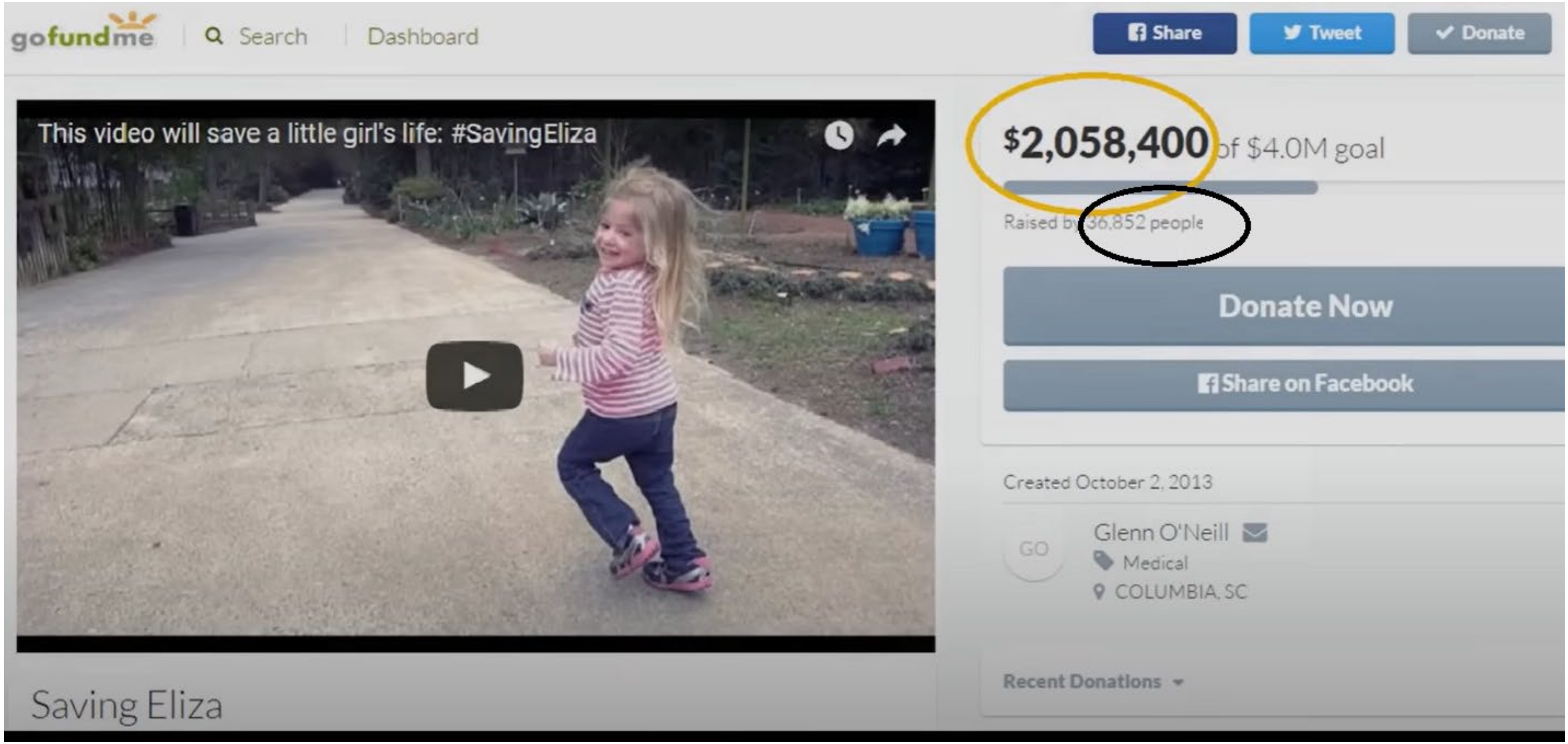
CURE SANFILIPPO FOUNDATION

Family breaks GoFundMe donation record with campaign to save daughter

By Emily Hales | Jun 12, 2014, 1:00am EST

SHARE




gofundme
Search
Dashboard
Share
Tweet
Donate
This video will save a little girl's life: #SavingEliza
$2,058,400 of $4.0M goal
Raised by 36,852 people
Donate Now
Share on Facebook
Created October 2, 2013
GO
Glenn O'Neill
Medical
COLUMBIA, SC
Recent Donations
Saving Eliza

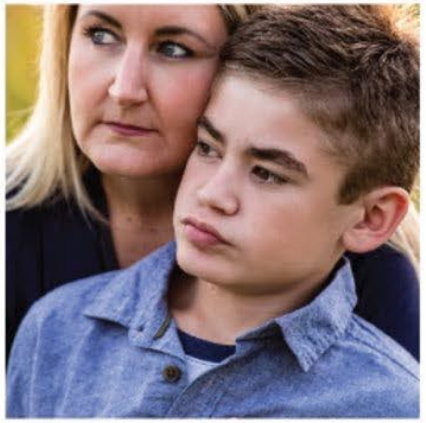

Saving
ELIZA
TODAY'S HEALTH
"SAVING ELIZA"
FAMILY LAUNCHES ONLINE CAMPAIGN TO HELP DAUGHTER
TODAY















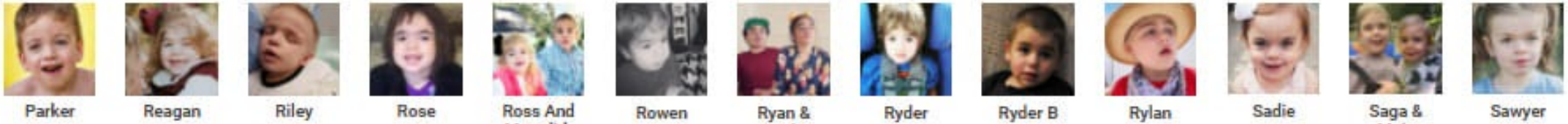

Abby Grace
Abby Wallis
Abigail
Aidan
Alex
Alexa & Lacey
Angelina
Artsemi
Autumn
Beckett
Belle
Blair
Caroline


Carson
Carter
Charlotte
Connor
Daniele
Danny
Declan
Elena
Eli
Eliza
Ellie
Emmy
Everett


Fiona
Francesco
Gabo
Gabriel
Garrett
Giorgio
Haidyn
Izzy
Jackson
Jacob
Jonah
Josiah
Karsyn


Keira
Kiernan
Landon & Blake
Landon
Leila
Levi
Liv
Logan
Logan
Loralei
Lucas
Luciana
Luke


Lulu
Maddie
Marco
Matteo
Matthew
Mia
Misha
Molly
Mya
Nola
Oliver
Oliver & Liam
Paisleigh


Parker
Reagan
Riley
Rose
Ross And Meredith
Rowen
Ryan & Laela
Ryder
Ryder B
Rylan
Sadie
Saga & Maia
Sawyer


Simon
Solomon
Spencer
Tosh
Trenton
Trinady
Tucker
Victoria
Waylon
Will
Zoe
Zoe
Frankie

First child treated with gene therapy at Nationwide May 10, 2016

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a 501 (c)3 nonprofit
www.CureSFF.org

Cure Sanfilippo progress (past 12 years)

- Have over 150 partner families around the country and the world
- Raised over $25M for research and clinical trials
- Funded over 50 grants around the world
- Helped fund 3 in-human clinical trials, which have treated 50+ children, with another trial to start in 2025 treating 30 children
- Created the first-ever Caregiver Preference Study for Sanfilippo
- Created the first-ever Global Clinical Guidelines for Sanfilippo
- ADVANCE Sanfilippo community conference

Springer Open | Journal of Patient-Reported Outcomes

J Patient Rep Outcomes. 2022 Dec; 6: 40. PMCID: PMC9038975
Published online 2022 Apr 25. doi: 10.1186/s41687-022-00447-w PMID: 35467223

Caregivers' assessment of meaningful and relevant clinical outcome assessments for Sanfilippo syndrome

Katherine Ackerman Porter,[1] Cara O'Neill,[2] Elise Drake,[2] Sara M. Andrews,[1] Kathleen Delaney,[3] Samantha Parker,[4] Maria L. Escolar,[5,6] Stacey Montgomery,[7] William Moon,[7] Carolyn Worrall,[7] and Holly L. Peay[✉1]

▸ Author information ▸ Article notes ▸ Copyright and License information PMC Disclaimer

Journal Article

Associated Data

▸ **Supplementary Materials**

▸ **Data Availability Statement**

Journal Article

Abstract

Go to: ▸

Objectives

Sanfilippo syndrome is a rare multisystem disease with no approved treatments. This study explores caregiver perspectives on the most impactful symptoms and patient-relevant clinical

Muschol et al.
Orphanet Journal of Rare Diseases (2022) 17:391
https://doi.org/10.1186/s13023-022-02484-6

Orphanet Journal of Rare Diseases

REVIEW Open Access

Sanfilippo syndrome: consensus guidelines for clinical care

Nicole Muschol[1], Roberto Giugliani[2], Simon A. Jones[3], Joseph Muenzer[4], Nicholas J. C. Smith[5], Chester B. Whitley[6], Megan Donnell[7], Elise Drake[8], Kristina Elvidge[7], Lisa Melton[7] and Cara O'Neill[8*] on behalf of MPS III Guideline Development Group

Abstract

Sanfilippo syndrome is a group of rare, complex, and progressive neurodegenerative lysosomal storage disorders that is characterized by childhood dementia. The clinical management of patients with progressive neurological decline and multisystem involvement requires a multidisciplinary team with experience in the management of neurodegenerative disorders. Best practice guidelines for the clinical management of patients with these types of rare disorders are critical to ensure prompt diagnosis and initiation of appropriate care. However, there are no published standard global clinical care guidelines for patients with Sanfilippo syndrome. To address this, a literature review was conducted to evaluate the current evidence base and to identify evidence gaps. The findings were reviewed by an international steering committee composed of clinical experts with extensive experience in managing patients with Sanfilippo syndrome. The goal was to create a consensus set of basic clinical guidelines that will be accessible to and informed by clinicians globally, as well as providing a practical resource for families to share with their local care team who may not have experience with this rare disease. This review distills 178 guideline statements into an easily digestible document that provides evidence-based, expert-led recommendations for how to approach common management challenges and appropriate monitoring schedules in the care of patients with Sanfilippo syndrome.

Keywords: Mucopolysaccharidosis type III, Sanfilippo syndrome, Diagnosis, Management, Recommendations

Background

Sanfilippo syndrome (mucopolysaccharidosis type III [MPS III]) is a group of inherited lysosomal storage disorders, manifesting progressive central nervous system (CNS) and systemic disease in childhood, with progressive neurocognitive deterioration and loss of functional abilities, and premature death [1]. There are four autosomal recessive subtypes (types A, B, C, and D) of Sanfilippo syndrome. Each subtype is caused by a deficiency of a different enzyme that degrades the ubiquitous glycosaminoglycan (GAG) heparan sulfate (Table 1), which leads to substrate accumulation and cellular dysfunction [2].

The combined estimated prevalence of Sanfilippo syndrome (types A, B, C, and D) is between 1:50,000 and 1:250,000 depending on the population studied [3]. Sanfilippo syndrome type A is the most common subtype globally; however, the prevalence of subtypes can vary depending on region, with Sanfilippo syndrome type A being more prevalent in Northern Europe and Eastern Europe than in Mediterranean countries [4–6]. In contrast, Sanfilippo syndrome type B is the most prevalent subtype in Southern Europe [4, 7]. Sanfilippo syndrome types C and D are much less common overall, with estimated global incidences of 1:1,500,000 and 1:1,000,000, respectively [1]. However, the total number of patients with Sanfilippo syndrome is most likely underestimated owing to delayed or missed diagnoses, particularly for the most slowly progressing phenotypes.

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Full list of author information is available at the end of the article

CURE SANFILIPPO FOUNDATION

profit
F.org

RESEARCH PROJECT DESCRIPTION

Scientific Research & Clinical Trials | Foundation-Initiated Projects

RESEARCH PROJECT DESCRIPTION	RESEARCH STAGE	YEAR GRANTED	SUBTYPE OF SANFILIPPO STUDIED	SUBTYPES TO WHICH FINDINGS COULD APPLY
Study of Cannabidiol in Sanfilippo Syndrome (contract pending)	Clinical Trial	2025	A B C D	A B C D
Establishing use of a novel nervous-system targeted gene therapy vector for Sanfilippo (contract pending)	Translational	2025	A	A B
In vitro evaluation of disease-modifying drugs for attenuated forms of Sanfilippo	Translational	2024	A	A
Combination of HSCP transplantation and cathepsin B inhibitors for treatment of Sanfilippo disease	Translational	2024	A B C	A B C
Peripheral neural stem cell models and drug discovery for Sanfilippo Syndrome	Translational	2024	A	A B C D
Fellowship Award | Multi-faceted treatment of Sanfilippo syndrome: Targeted therapies for inflammation, autophagy dysfunction, oxidative stress, and dopamine imbalance	Pre-Clinical & Clinical	2023 & 2024	A B C D	A B C D
Fellowship Award | Treating mucopolysaccharidosis Type IIIC with hematopoietic stem cell gene therapy	Pre-Clinical	2023 & 2024	C	A B C D
Evaluate intestinal motility absorption and look at the abnormalities of the intestinal tissue through histology, in the MPSIIIB mouse	Translational	2023	B	A B C D
Effects of TLR4 antagonism on brain and bone function in MPS IIIB	Translational	2023	B	A B C D
Pharmacological chaperone therapy and substrate reduction with N-substituted L-iminosugars for the treatment of Sanfilippo B disease	Pre-Clinical	2023	B	A B C D
Pre-clinical evaluation of an iPSC-based therapeutic modality to rescue MPS IIIA neuropathology, and characterization of MPS IIIC iPSC neural progenitor cells	Pre-Clinical	2023	A C	A C
Investigating neuroprotective peptides for treatment of Sanfilippo	Translational	2022	A B C D	A B C D
Identifying disease modifiers in drosophila models of MPS IIIA & IIIB	Basic Science	2022	A	A B C D
Discovery & validation of translational biomarkers for Sanfilippo childhood dementia	Translational	2022	A B	A B C D
Strengthening rationale for use of "molecular tweezers" CLR01 in Sanfilippo*	Translational	2021	A B C	A B C D
Exploring novel photobiomodulation parameters in Sanfilippo animal models	Translational	2021	A	A B C D
Investigating blood-based biomarkers for Sanfilippo progression and treatment	Translational	2021	A B C	A B C D
Support of ScreenPlus newborn screening pilot and its inclusion of Sanfilippo	Clinical Study	2021	A B	A B

- **Funding the most promising pathways to helping children as soon as possible**
- **A wholistic approach to ensure all children might have HOPE**

- First USA-based Sanfilippo community conference

- Parents, scientists/researchers, clinicians, therapists, educators, biotechs

- Available via replay at www.curesff.org/advance


CURE SANFILIPPO FOUNDATION


#iRun4Carson.com
Cure for Carson
INDY HALF MARATHON AT FORT WAYNE


FINISH


Saving Rylan
VOLS


Sanfilippo Superhero


When I can hang with this guy all day long instead?!
Get a job.
TikTok for a Cure
TikTok
@iammrsnesbitt
Things in our
Kitchen
That just make sense

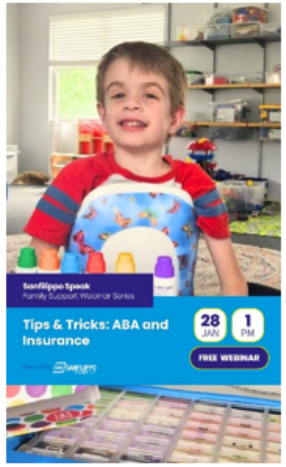
CURE SANFILIPPO FOUNDATION

Our Expanding Services for Families

Life with Sanfilippo syndrome can be extremely isolating for parents and siblings. Few understand the day-to-day challenges of caring for a person with Sanfilippo syndrome. One of the most important things Cure Sanfilippo Foundation can do is create opportunities that help families give their children a better quality of life and also assist them in navigating the myriad of daily decisions they face. The following are some of the ways we do so, and more are coming.

Sanfilippo Speak | Family Support Webinars

Sanfilippo Speak is a family support webinar series hosted by the Foundation to provide families, caregivers, therapists, educators, clinicians, and more with Sanfilippo-specific insights into and discussions around pivotal topics specific to navigating life with the disease. All Sanfilippo Speak webinars are free and open all. Topics so far have included assistive technology, durable medical equipment, ABA therapy, IEP and transition support, and more. On-demand archives of each session are available at CureSanfilippoFoundation.org/SanfilippoSpeak.



Community Engagement & Education

The Foundation keeps families abreast of important progress and milestones through regular emails, social media posts, and special-topic webinars. These channels are used to share breaking news, opportunities to engage with researchers, and more.

Additionally, the Foundation added a new position in 2024 to provide personalized, on-demand, and Sanfilippo-specific support and information to families. Families can reach out to Community Outreach and Education Coordinator Kassidie Reynolds at Kassidie@CureSanfilippoFoundation.org or 803-250-1985.

Sanfilippo Family Gatherings

It's comforting to spend time with others who understand life with Sanfilippo and can relate. These rare hours together provide families with an overwhelming feeling of togetherness and love. To make these important moments happen for families, the Foundation began hosting family gatherings around the country in 2023. They are free for families to attend. To learn more or find upcoming gatherings, go to: CureSanfilippoFoundation.org/Meet-the-Families/Partner-Family-Resources/Local-Family-Gatherings/

Clinical Trial Navigation

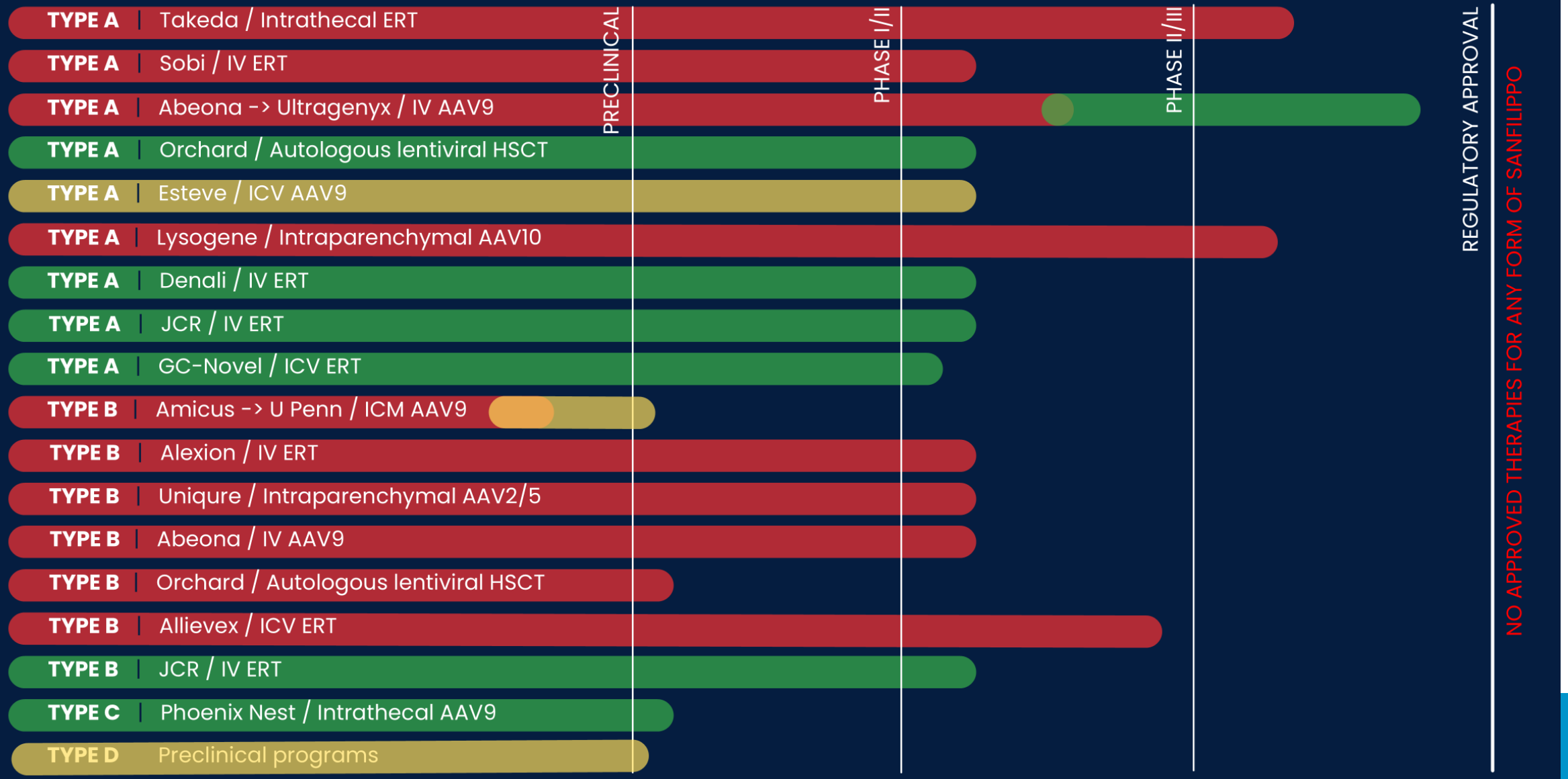
The Foundation serves as a navigator for families interested in participating in research studies and clinicians who would like to learn more about Sanfilippo clinical

- Expanding our services for families

- Hiring of our Community Engagement Coordinator

a 501 (c)3 nonprofit
www.CureSFF.org

SANFILIPPO SYNDROME (MPS III) THERAPEUTIC PIPELINE



Qualifying Biomarkers to Support Rare Disease Regulatory Pathways: Focus on Neuropathic MPS

February 29, 2024

Page content provided by: Cure Sanfilippo Foundation, National MPS Society, and The Ryan Foundation

For web accessibility options: Click/tap the floating blue icon on the right.

Speakers at the Feb. 21 "Qualifying Biomarkers to Support Rare Disease Regulatory Pathways" workshop hosted by Reagan Udall Foundation for FDA.

ultragenyx

Ultragenyx Submits Biologics License Application to the U.S. FDA for UX111 AAV Gene Therapy for the Treatment of Sanfilippo Syndrome Type A (MPS IIIA)

If approved, UX111 would be the first approved therapy in the U.S. for Sanfilippo Syndrome Type A

December 19, 2024 08:00 ET | Source: **Ultragenyx Pharmaceutical Inc.** Follow

Eliza & Our Family

2014

2023

7/17 - we found out the terrible news. For now I want to focus on her and her wonderful personality + life everyday. One of my goals is to keep her happy + smiling for as long as possible. I love her so much.

SUPER ELIZA 5K

benefitting CURE SANFILIPPO FOUNDATION

EVENT SPONSOR

HAWTHORNE PHARMACY & MEDICAL EQUIPMENT

March 29

EARLEWOOD PARK | 8 AM - 12 PM

www.SuperEliza5K.com

Thank You!

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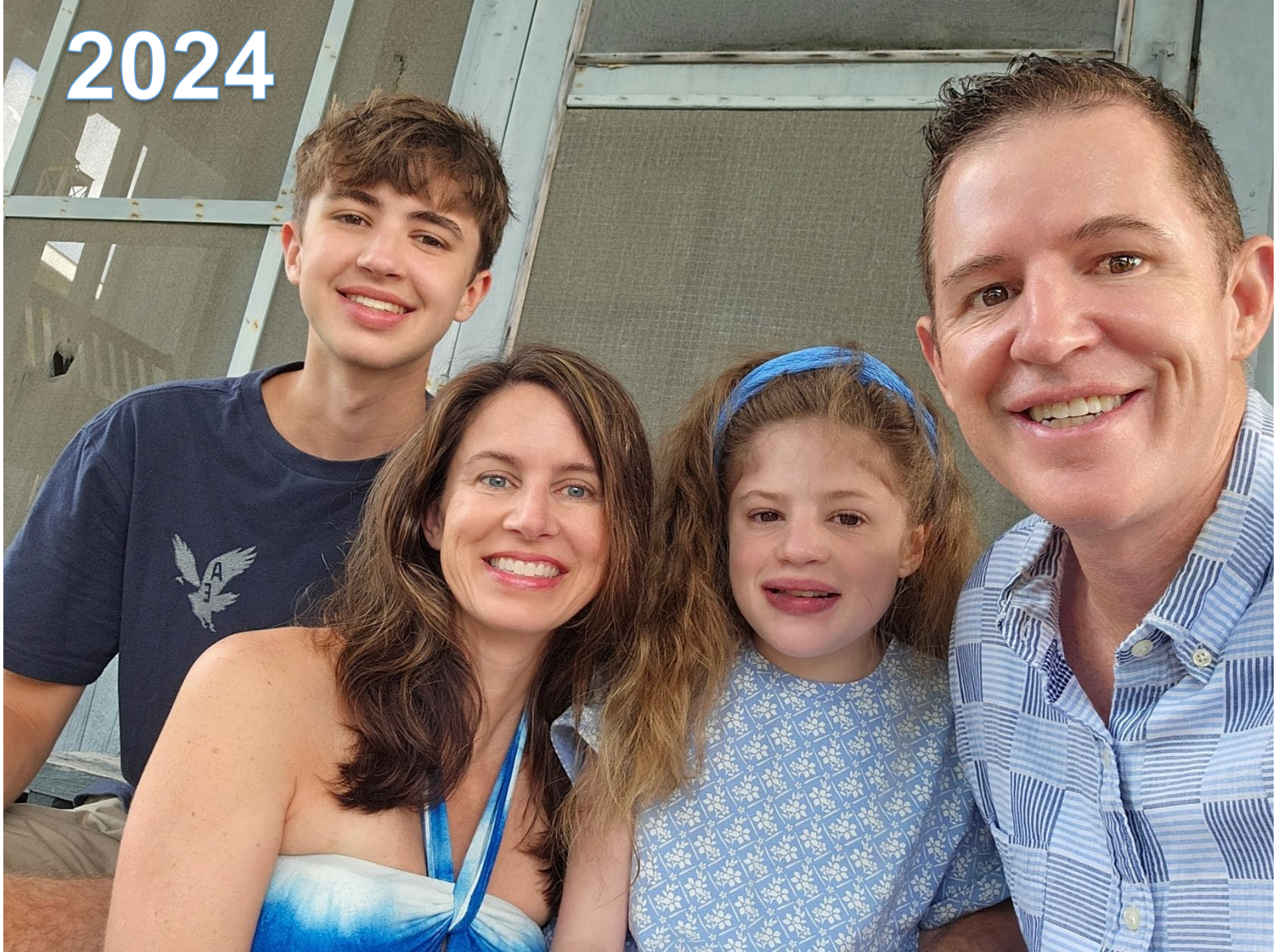

2024

CRITICAL PATH INSTITUTE 20 YEARS OF IMPACT

Off Label but On Target: Perspectives on and Examples of Drug Repurposing for Rare Diseases

Smith F. Heavner, PhD, RN, FCCM

“Smitty” Heavner

Sr. Scientific Director for Real-World Evidence
Data Collaboration Center, Critical Path Institute

Critical care nurse
Implementation scientist
Evaluator
Professor
Dog dad
Wine enthusiast

Disclosures

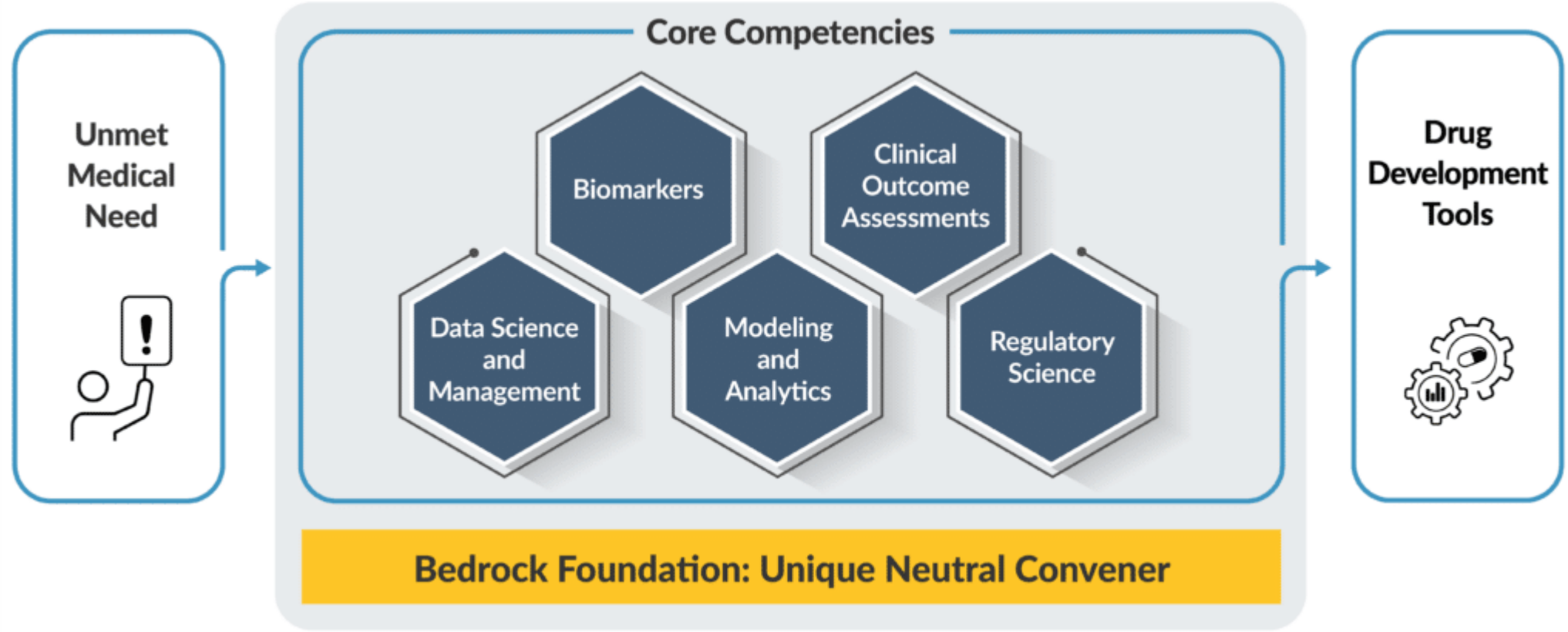
C-Path is a public-private partnership with US FDA.

Speaker receives funding from FDA, CDC, and NIH.

Content of this presentation is not intended to represent endorsement or approval from any organization or government entity.

C-Path

For 20 years, Critical Path Institute has been a trusted nonprofit that **generates solutions to facilitate scientific and regulatory pathways** that accelerate the development of therapies for people with unmet medical needs.



C-Path's Rare and Orphan Disease Program

Critical Path for Alpha-1 Antitrypsin Deficiency

Critical Path for Lysosomal Diseases Pre-Consortium

Critical Path for Rare Neurodegenerative Diseases

Critical Path to Therapeutics for the Ataxias

Duchenne Regulatory Science Consortium

Polycystic Kidney Disease Outcomes Consortium

Rare Disease Cures Accelerator-Data and Analytics Platform

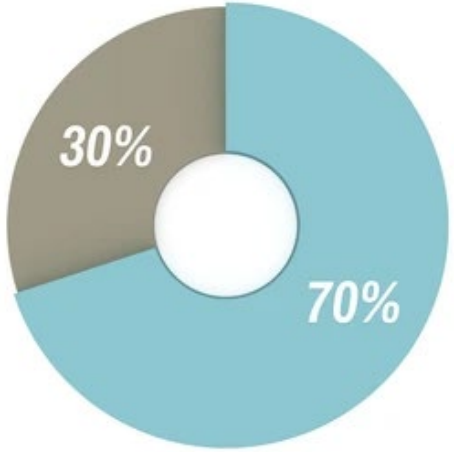
Rare Disease Clinical Outcome Assessment Consortium

Huntington's Disease Regulatory Science Consortium

The Challenge

- Close to 10,000 diseases and 2,500 FDA approved drugs
- Significant number of diseases with no approved treatment
- System in place that does not maximize the utility of existing
- Current regulatory system authorization sale of drugs is incentivized by financial market forces that are often not aligned with clinical or public health needs
- Once a drug is approved, based on knowledge and professional judgement, physicians may take the responsibility for prescribing drugs for a different indication

Diseases with FDA approved treatments

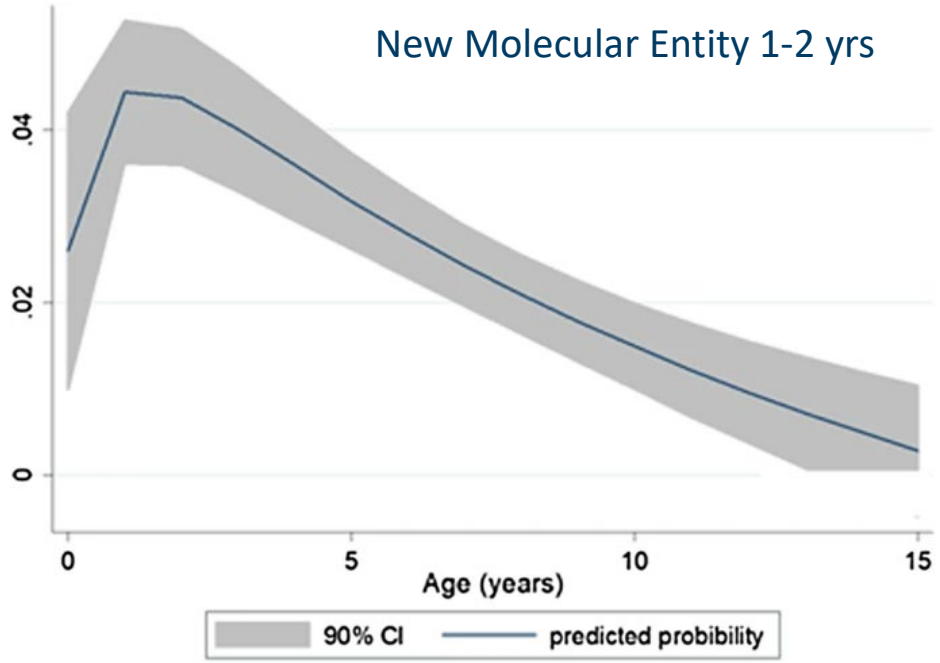


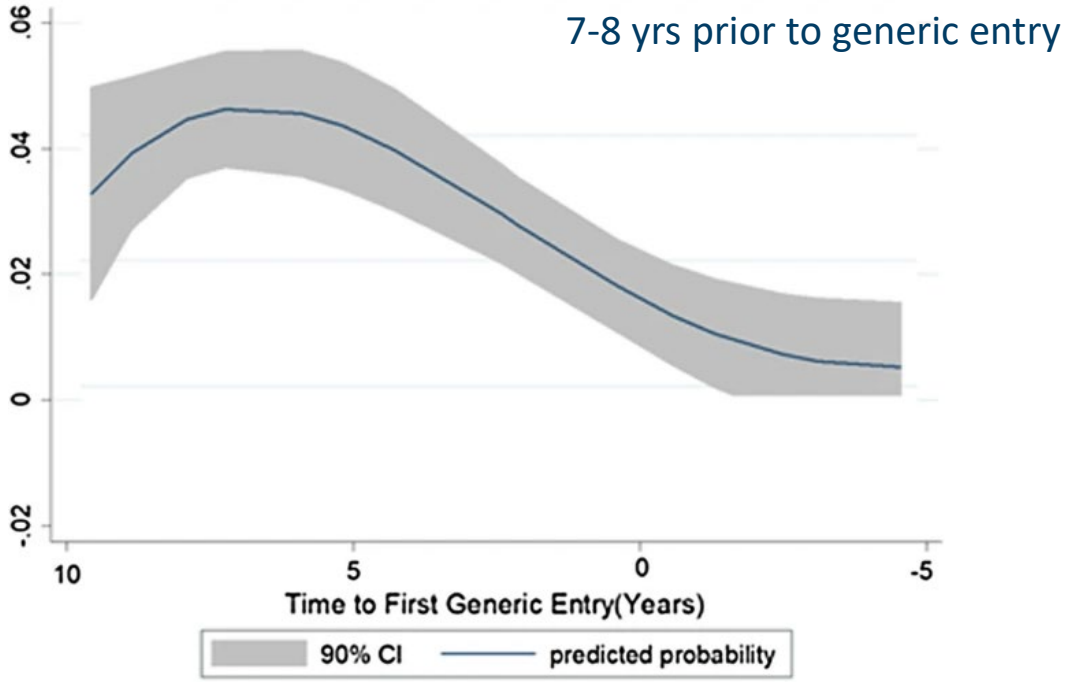
FDA labels

- Defines the indication for use that a sponsor sought, and FDA approved based on evidentiary standards
- Allows the sponsor (main benefactor) to market the drug for the approved indication
- Labels can only be updated by the New Drug Application (NDA) holder
  - Submit a new NDA 505 (b)(1)
  - Potential to explore the 505 (b)(2) pathway
  - Generic drugs 505 (j)
- Sponsor may be interested in label expansion from a financial perspective
  - But not always…

Repurposing drugs for new uses

- Probability of new indication exclusivity granted by FDA for drugs approved, 1997–2020.





- Of the 197 new drugs that subsequently experienced generic entry, only 64 (32%) had at least one new indication added
  - limited duration of exclusivity reduces the number of secondary indications significantly
  - much room for improvement for unlocking existing medicines' full therapeutic potential

Sahragardjoonegani et al. J of Pharm Policy and Pract 14, 3 (2021).

Do we need a label change?

- Without sponsor support, there is no mechanism under the current paradigm
  - Drug continues to be used off-label
  - Some potential mechanisms exist to obtain a label supplement
    - Orphan drug designation (incentives for sponsor)
    - Best Practice in Children's Act (BPCA) allows USG to submit data if sponsor refuses
- As a result
  - Safety and effectiveness remains a concern
  - Over time may be come standard of care
  - Loss of equipoise to assess in an RCT
- How can we address the loss of Equipoise?
  - Real-World Data
- Unintended consequences of adding a new indication to the label
  - Inexpensive generic drug without a label can suddenly become an expensive drug with a label for a new indication

Drug Repurposing

- The investigation of existing drugs for new therapeutic purposes
  - To maximize the effectiveness of our current arsenal of drugs
  - What can we learn from our colleagues globally?

- Drugs that target shared pathways
  - The biological target of the drug molecule is same, but the disease is different
  - Remdesivir (originally for the treatment of HCV, then Ebola as an RNA-dependent RNA polymerase, but failed in a phase II clinical trial) has been approved for COVID-19

- Drugs that may be effective through off-target pathways
  - Drugs act on new targets, out of the original scope, for new therapeutic indications.
  - Aspirin has been traditionally used as NSAID in the treatment of various pain and inflammatory disorders.
    - It also suppresses blood coagulation (clot formation) by inhibiting the normal functioning of platelets (antiplatelet drug).

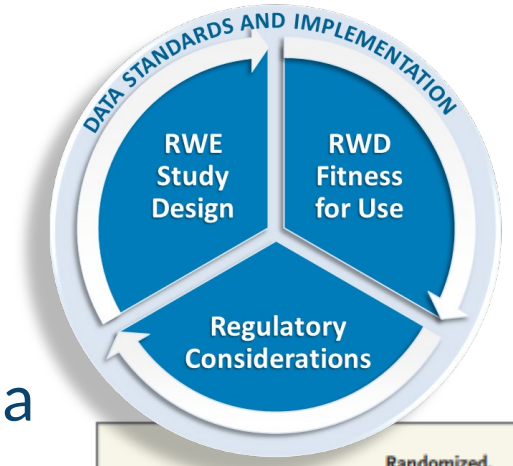
Major challenge to secure high-quality data due to lack of sponsors: Responsibilities (not exclusive)

- Financial
  - Protocol development
  - Trial insurance
  - Drug manufacture (QA/QC, safety, active pharmaceutical ingredient (API) management)
- Site selection and management
  - Site activation (clinical trial agreement, licences, approvals, site visits)
  - Quality management system including protocol specific SOPs, training documentation, analyte QA/QC
  - Data collection (IC, eligibility, missed visits, follow up, SAEs, study discontinuation…)
  - Financial agreements, training staff, records retention…
- Monitoring activities
  - Monitoring, Safety, and Risk management plans
- Regulatory Authority interaction (21 CFR 312 for IND submission, notification….)
  - RLD holder only authorized to engage FDA for pursuing supplemental labels
  - Intellectual property (IP) management at site level
  - Study Documents filing (Investigator Site File and Trial Master File)
  - Pharmacovigilance (PV) activities to comply with safety reporting obligations

Potential data sources for repurposed drugs

21st Century Cures Act

- FDA shall establish a program to evaluate the potential use of real-world evidence (RWE) to support:
  - Approval of new indication for a drug approved under section 505(c)
  - Approving a label expansion
  - Satisfy post-approval study requirements



Randomized, Interventional Study		Nonrandomized, Interventional Study	Nonrandomized, Noninterventional Study
Traditional randomized trial using RWD in planning	Trial in clinical practice settings, with pragmatic elements	Externally controlled trial	Observational study
RWD used to assess enrollment criteria and trial feasibility RWD used to support selection of trial sites	Selected outcomes identified using, e.g., health records data, claims data, or data from digital health technologies RCT conducted using, e.g., electronic case report forms for health records data or claims data	Single-group trial with external control group derived from RWD	Cohort study Case–control study Case–crossover study

Generation of RWE

Increasing reliance on RWD

Reliance on RWD in Representative Types of Study Design.

RCT denotes randomized, controlled trial; RWD real-world data; and RWE real-world evidence.

Concato J, Corrigan-Curay J. Real-World Evidence — Where Are We Now? N Engl J Med. 2022;386(18):1680-1682. doi:10.1056/NEJMp2200089

Generating RWE from Real-World Data

Real-World Data (RWD) sources include:

- Registries
- Electronic health records (EHR)
- Medical claims
- Natural history studies
- Certain types of clinical trials/observational studies

www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence

Selected Guidance

U.S. FOOD & DRUG ADMINISTRATION

- Framework for FDA's Real-World Evidence Program
- Use of Electronic Health Records in Clinical Investigations
- Real-World Data: Assessing Electronic Health Records and Medical Claims Data to Support Regulatory Decision-Making for Drug and Biological Products
- Data Standards for Drug and Biological Production Submissions Containing Real-World Data
- Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products
- Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products
- Submitting Documents Utilizing Real-World Data and Real-World Evidence to FDA for Drugs and Biologics
- Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products

Generating RWE from RWD

Imagine we instructed everyone in this meeting to collect the eye color, hair color, height, and coffee preferences of people at the grocery store.

- How would you store the data?
- What variable names would you use?
- How would you classify responses?
- Would you code responses? Free text?

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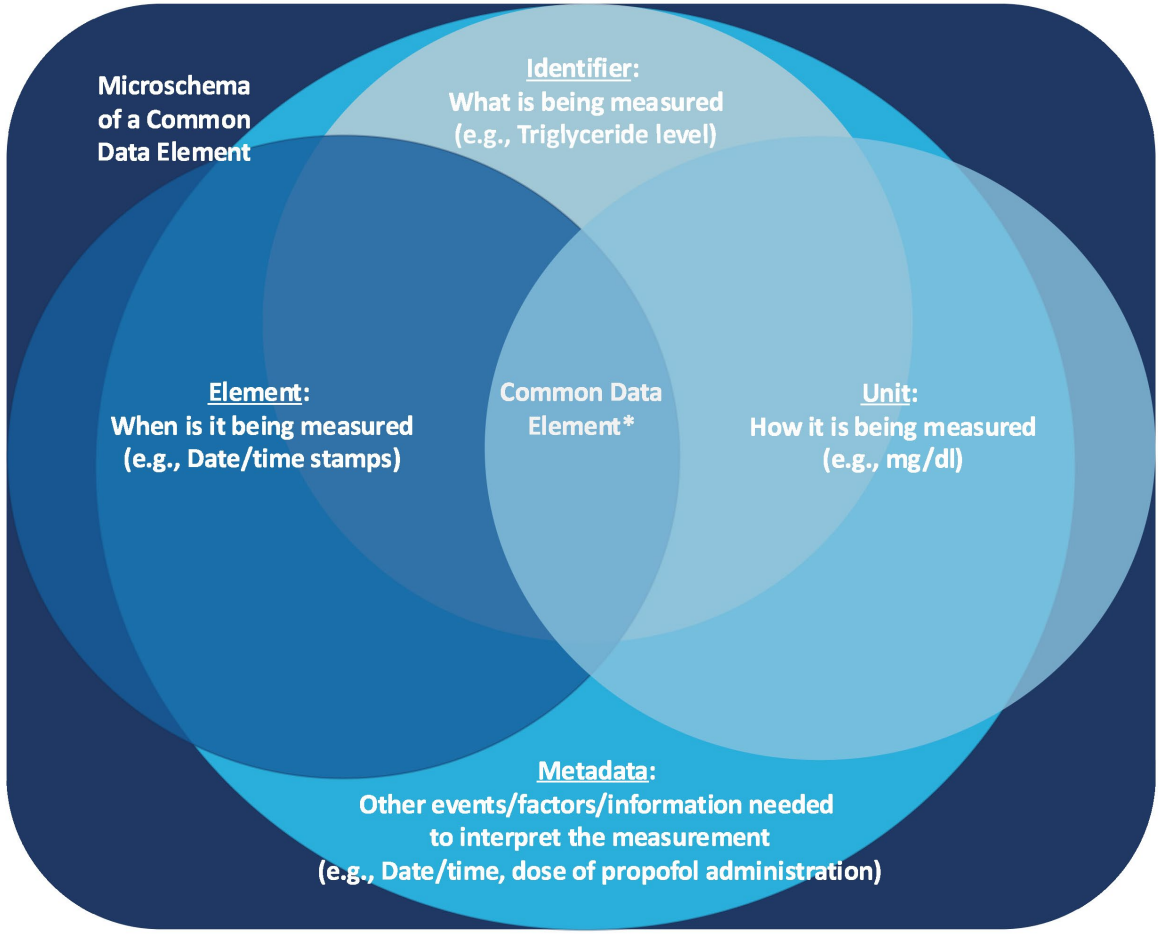
Eye_Color	Hair_Color	Height	Coff_Pref
Brown	Blonde	5ft6in	Black
Blue	Brown	5ft8in	Cream
Brown	Grey	4ft11in	Just sugar
Hazel	Brunette	6ft1in	Oat milk
Brown	Red	5ft11	Iced
Green	Dirty Blonde	5ft9in	Tea only

RWD: Data Harmonization

A common data element (CDE) helps capture all the information needed to harmonize variables.

Example: Triglyceride levels in metabolic syndrome:

- "Triglyceride as measured in mg/dL collected prior to the first administration of propofol."



Heavner SF, Kumar VK, Anderson W, et al. Critical Data for Critical Care: A Primer on Leveraging Electronic Health Record Data for Research From Society of Critical Care Medicine's Panel on Data Sharing and Harmonization. Crit Care Explor. 2024 Nov 15;6(11):e1179. doi: 10.1097/CCE.0000000000001179. PMID: 39559555; PMCID: PMC11573330.

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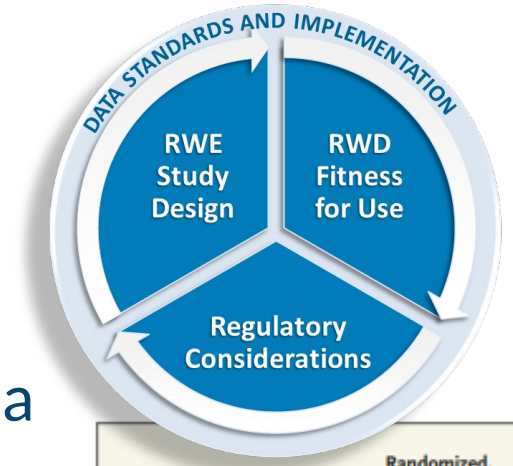

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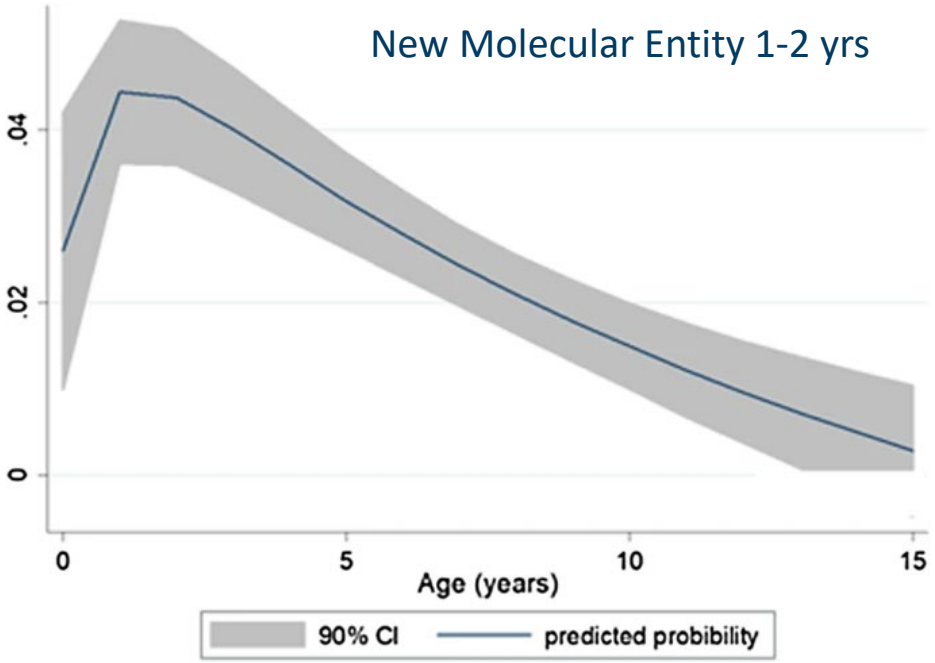
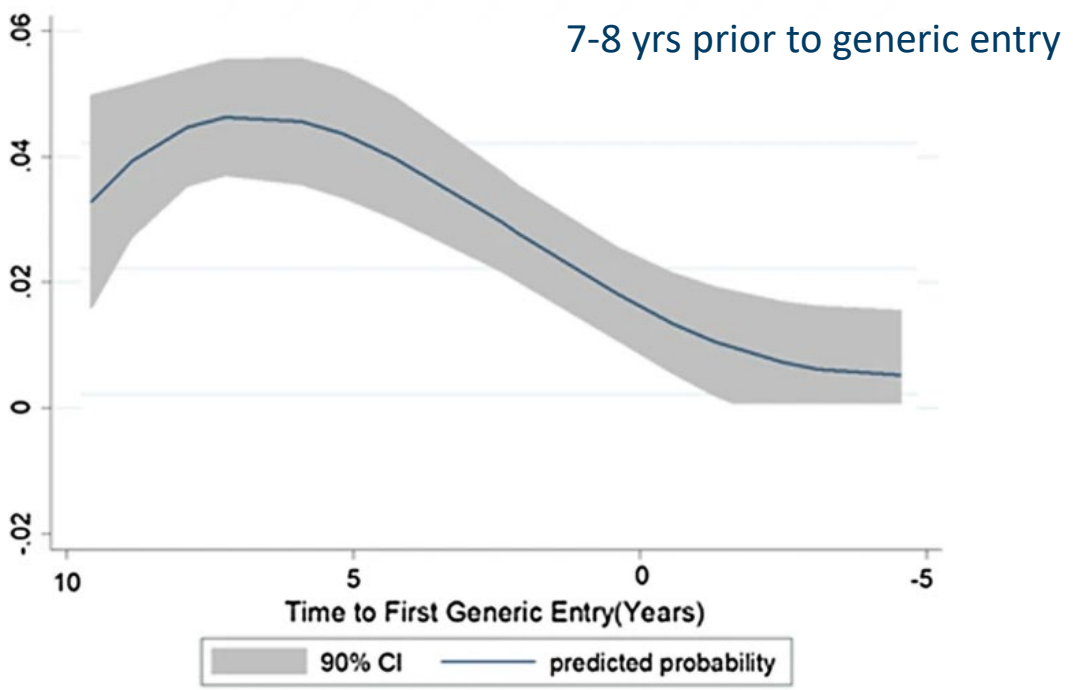
Let’s get back to drug repurposing

Repurposing drugs for new uses





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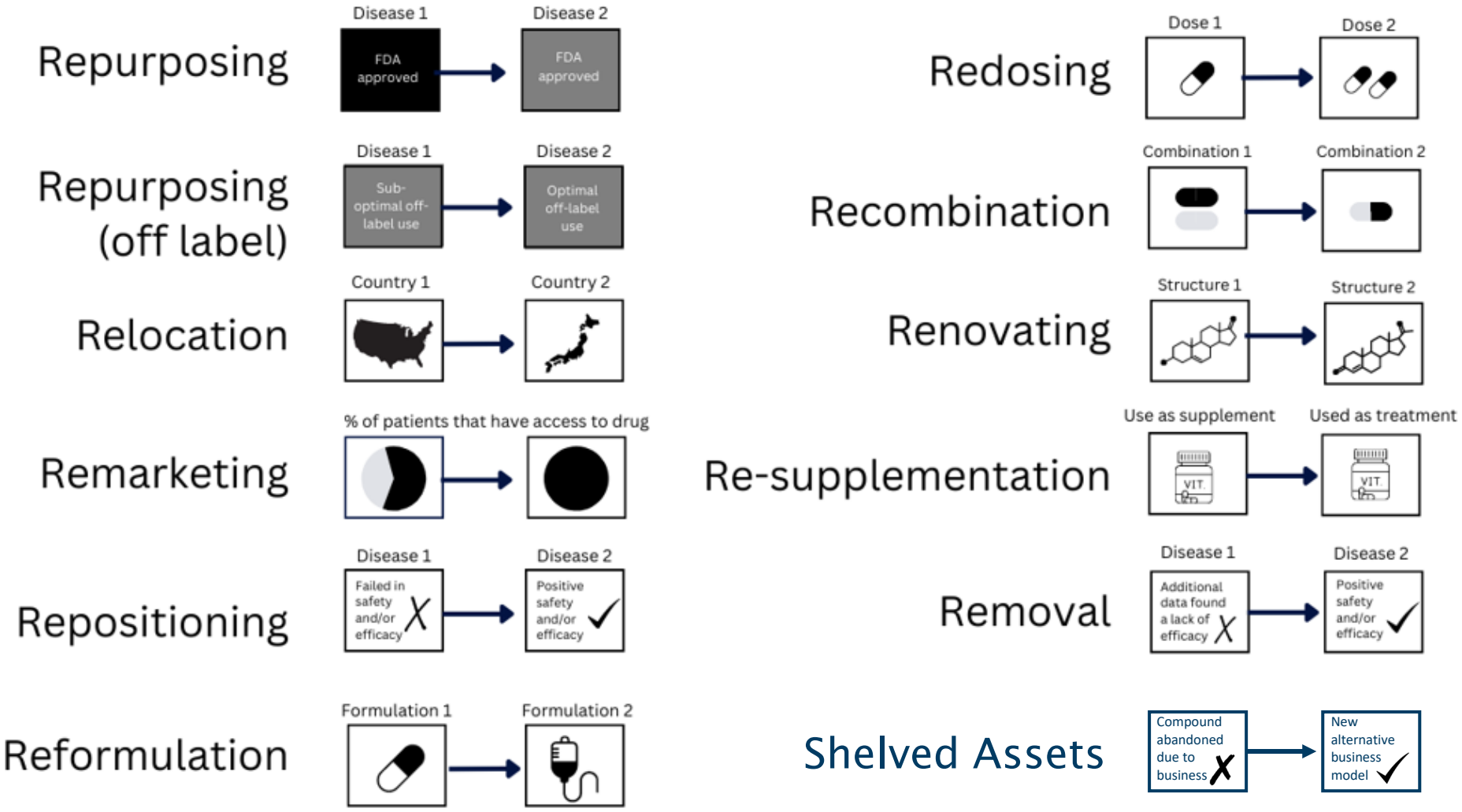
A Rose by Any Other Name



Drug Repurposing

Multiple approaches

beacon for rare diseases

ROADMAP

DNDi Drugs for Neglected Diseases *initiative*

DrugCentral Online drug Compendium

CDCN CASTLEMAN DISEASE COLLABORATIVE NETWORK

CuresWithinReach

NORD® National Organization for Rare Disorders

EVERY CURE

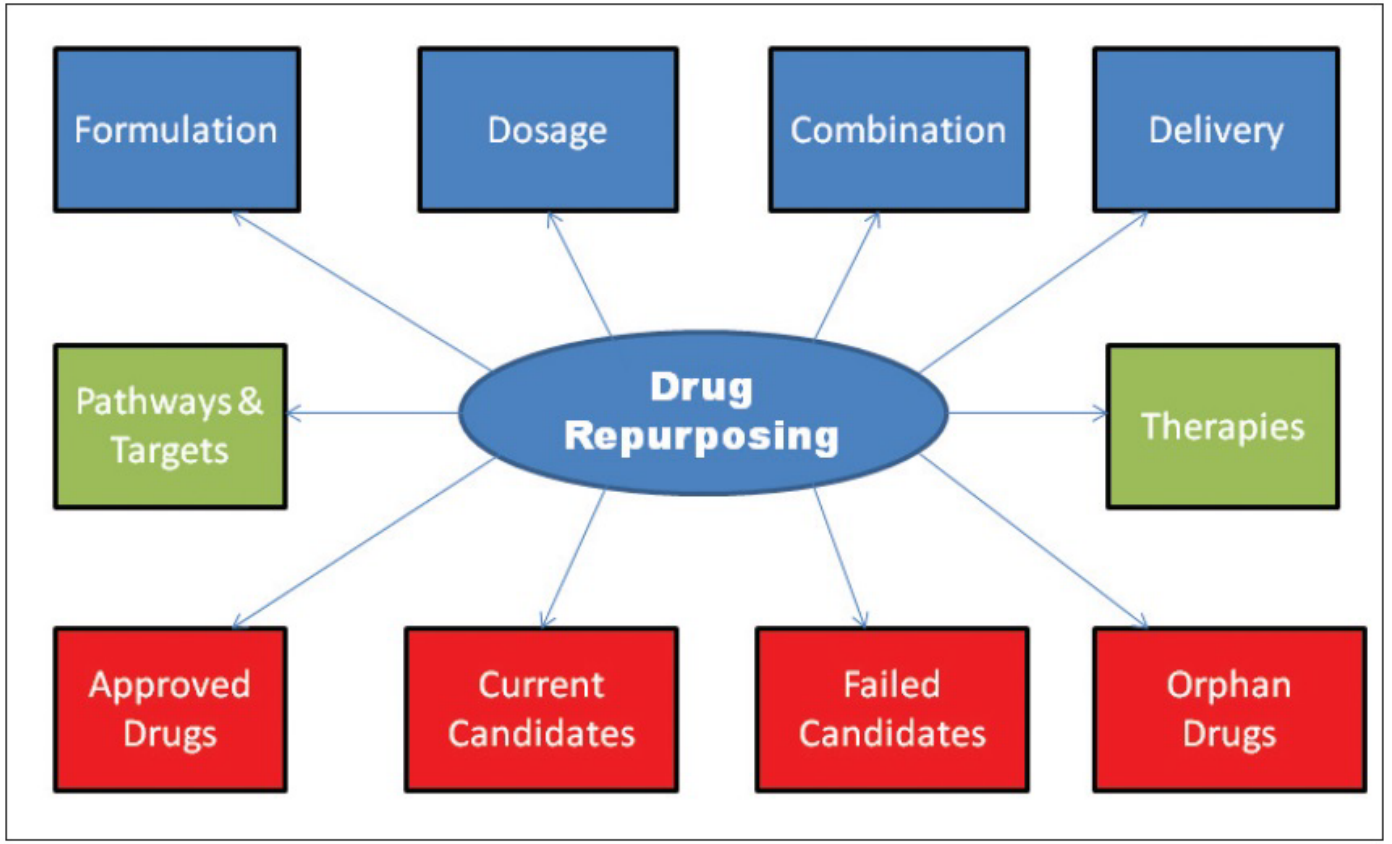


Figure I Potential drug repurposing strategies

https://www.ddw-online.com/therapeutic-drug-repurposing-repositioning-and-rescue-part-i-overview-1463-201412/

Special populations: pediatrics

Needs and Challenges	Rationale
Current needs of using off-label medication	Lack of studies in children often leads to off-label usage of drugs in children. There are delays in conducting clinical trials with children due to
	•Lack of financial incentives for sponsors to conduct drug trials with children
	•Many diseases are less common in children than in adults, so it requires more time to recruit child participants
	•Concerns regarding ethics, harm, and consent, making it difficult to obtain institutional review board approval to conduct clinical trials with children
	Unique challenges in conducting clinical trials in rare pediatric diseases:
	•Frequently underdiagnosed because of the heterogeneity in dis-ease presentation and limited clinical expertise outside of a few specialized centers
	•Natural histories are poorly characterized and phenotypic diversity within a disorder adds to the complexity
	•Study design is often restricted due to a small number of patients for each disorder
	•Clinical endpoints, *e.g.* biomarkers, are often not well-defined and there may be no regulatory precedence
Challenges of using off-label medication	There is substantial uncertainty for physicians to care for their patients with rare diseases using the off-label drug due to
	•Rare diseases are not often investigated within peer-reviewed journal articles
	•Results from failed clinical trials are rarely published
	•Lack of communication of benefits for off-label use and limited diffusion of off-label information
	•Even the information that is available generally is not specific to a particular rare disease

Table 1: Current needs and challenges of using off-label medication in rare pediatric diseases.

Fung et al. Off-label medication use in rare pediatric diseases in the United States. Intractable Rare Dis Res. 2021 Nov;10(4):238-245. doi: 10.5582/irdr.2021.01104. PMID: 34877235; PMCID: PMC8630459.

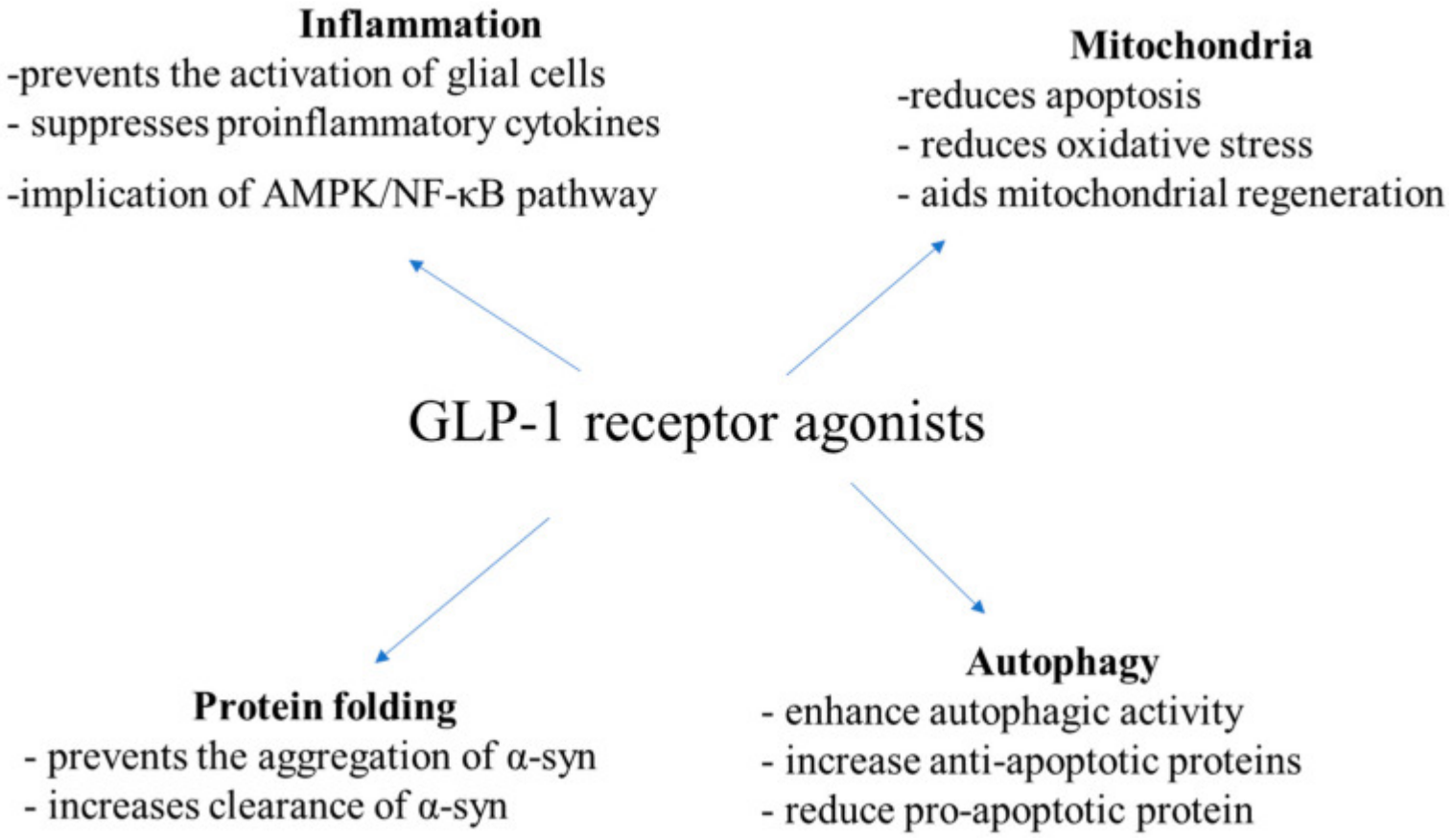
Example: GLP-1

Glucagon-Like Peptide-1

- Developed to treat diabetes

Repurposing:

- Obesity
- Obstructive sleep apnea
- Under review
  - Hepatic steatosis
- Studying
  - Parkinson's and other neuro-degenerative



Kalinderi K, Papaliagkas V, Fidani L. GLP-1 Receptor Agonists: A New Treatment in Parkinson's Disease. Int J Mol Sci. 2024 Mar 29;25(7):3812. doi: 10.3390/ijms25073812. PMID: 38612620; PMCID: PMC11011817.

Example : PEComa

Perivascular epithelioid cell tumors (PEComa)

- Standard of Care: sirolimus
  - mTOR (mammalian target of rapamycin) inhibitor
    - Loss of equipoise

Nab-sirolimus

- Sirolimus protein-bound particles
- FDA approved in 2021
  - Placebo controlled trial

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Improving Lives. Together.

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RARE DISEASE SYMPOSIUM

Q&A

MODERATED OPEN FORUM

Thank you for your participation!

Symposium Feedback Survey