Rare Bootcamp™

Intro to the world of the hyper-rare

Jill Wood

Phoenix Nest, CEO and Co-Founder

Jonah's Just Begun-Foundation to Cure Sanfilippo, former President and Co-Founder

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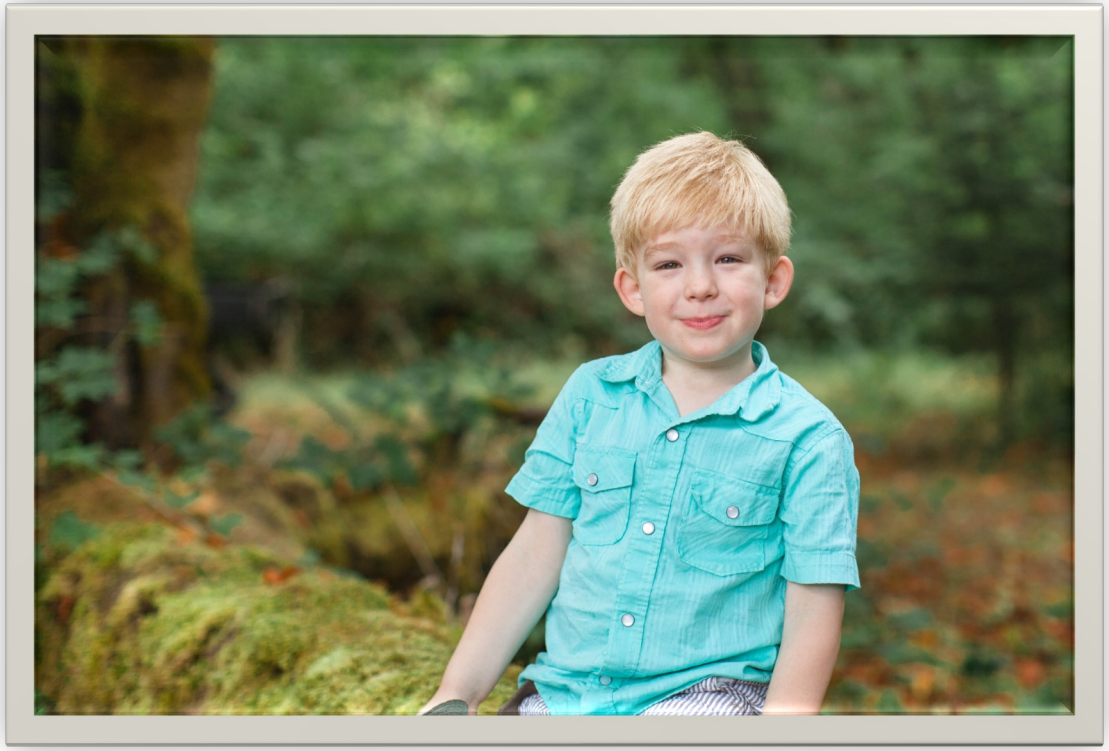
Jonah Wood Weishaar
DOB 7/30/2008

No Diagnostic Odyssey/No Blissful Ignorance

- Unsuspecting parents
  - Called out on his first year well visit
  - Head circumference ‘off the charts’
- From Brooklyn, surrounded by excellent hospitals
  - MRI Performed at NYU, Langone
  - Radiologists familiar with Jonah’s disorder



The silver lining

- Chance to fight Jonah’s fate
- Saved his hearing
- Received early intervention services
- Family planning

The Research
There is no Research

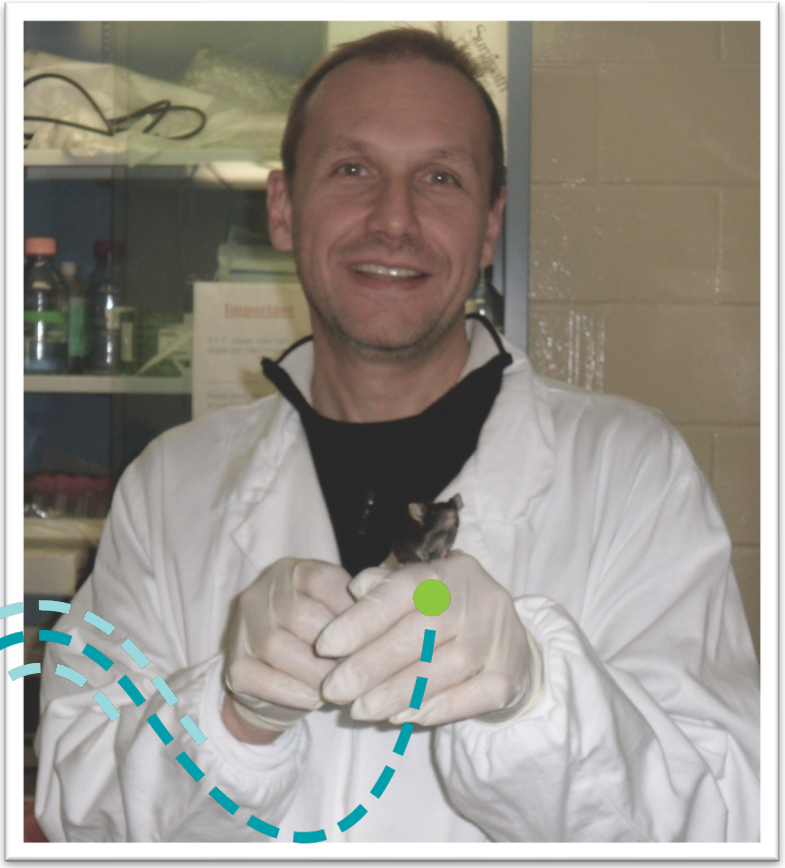
When I asked the geneticist if this was a death sentence?
She said: "***It doesn't have to be, there are treatments today never dreamed possible just 5 years ago.***"

Searched Pubmed

- Read everything we could on Sanfilippo syndrome
- Found researcher that discovered the gene Sanfilippo type C
  - Called Researcher
  - Initiated first knock out mouse model

What were others doing?

- Non-Profit-501c3
- Funding research
  - Created Jonah's Just Begun
  - **Met with rare disorder clinicians in NYC**



Alexey Pshezhetsky, PhD
CHU Sainte-Justine Research Center

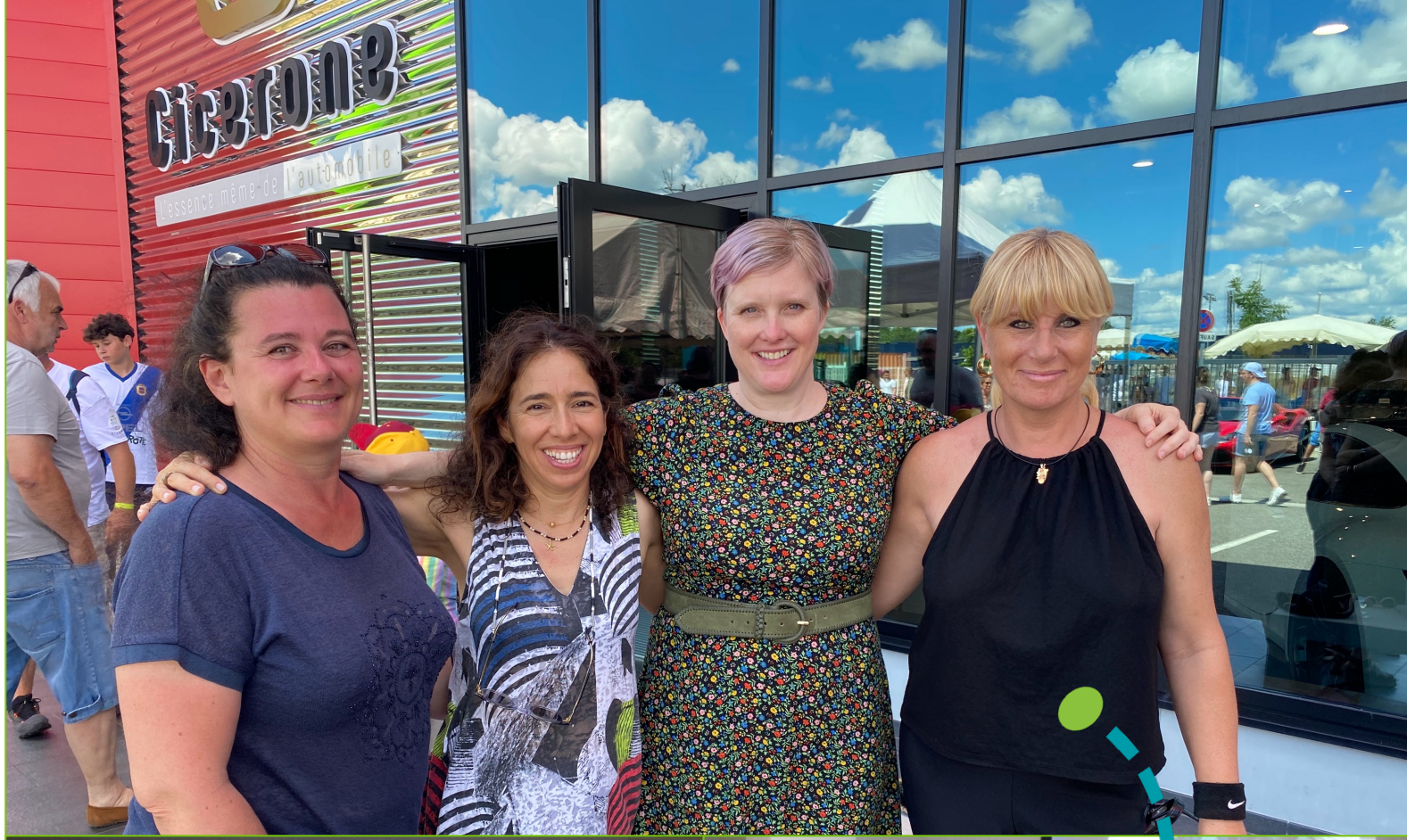
PATIENT PARENTS

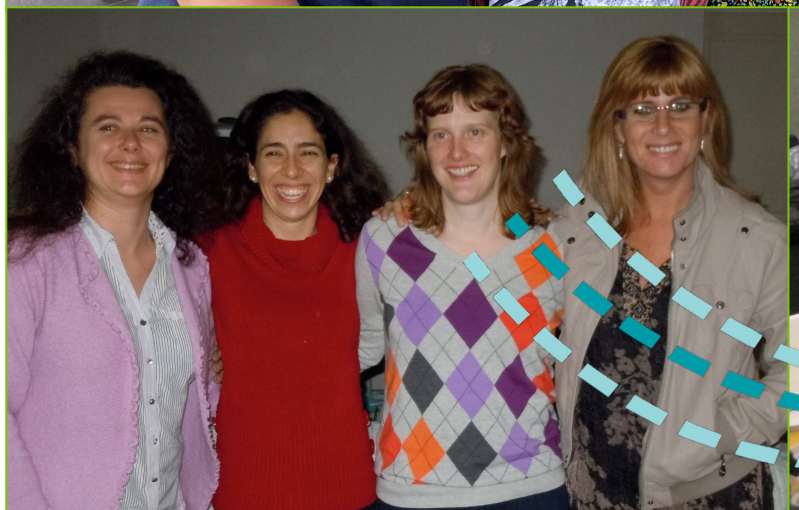
FIND YOUR TRIBE

- Inclusive
- Global
- Communicate
- Meet often
- Be transparent
- Work together
- Fundraise
- Network

ConnectMPS

Helping Advance Neurodegenerative Disease Science
JLK Sanfilippo Research Foundation
Sanfilippo Portugal
Jonah's Just Begun
Le combat de Haïtem contre Sanfilippo
Asociación Sanfilippo Barcelona
Sanfilippo Brasil
Sanfilippo Sud





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www.phoenixnestbiotech.com

Phoenix Nest INC

Rising up to meet the challenge

Phoenix Nest

Niche biotech focused on treatments for Sanfilippo

Est March 2012

NIH/NINDS SBIR Grants $ ~13m

Patient Foundation Funding $ ~1m

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Phoenix Nest

Pipeline

JLK-247: Gene Therapy for Sanfilippo type C

- 2011 Manchester w/Brian Bigger
  - ssAAV9
  - dual route of administration
  - 2021 FDA type C meeting
- 2022 take 2 Columbus Foundation/UTSW (Steve Gray)
  - scAAV9
  - IT-L injection
  - NIH/NINDS SBIR 2022 $3m

JLK-347: 2024 Natural History Study, France

ALL-127: Enzyme Replacement Therapy (ERT) Sanfilippo type D

- $10,750,320 NIH/NINDS SBIR
- 2014 Labiomed/Lundquist Institute w/ Patti Dickson and Tsui-Fen Chou
- Enzyme: master cell bank, scale-up manufacturing 2020-2025 ~3m

ALL-027: 2022 Natural History Study NCT 05648851

- 9 patients Columbia Presbyterian, NYC

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The less than 1%

US rare disease patient population of 200,000
Sanfilippo type C US patient population ~20
1 in 1.5 Million incident rate

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Play an Active Role

Pay Attention to Legislation

Reminder

- 7,000 Rare Diseases
- 10% have treatments
- Rare Disease 200,000
- Who would you create a treatment for?

Incentives for creating drugs for Rare Diseases

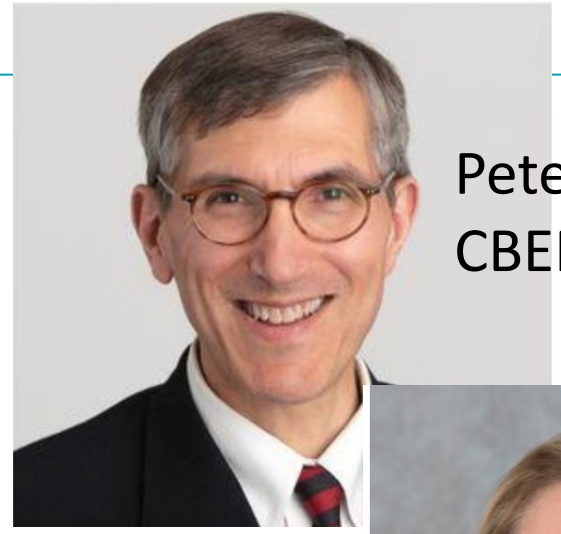
- 50% trial costs refunded
- 7 year market exclusivity
- Fast Track Designation
- Accelerated Approval
- Priority Review Vouchers

Educate yourself

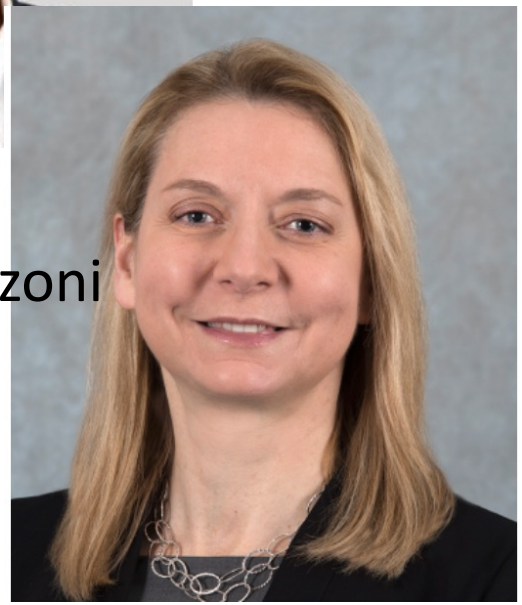
- What is happening in similar indications and drug approvals?
- What are the regulators saying about their endpoints?
- What can your community do to help?

Top FDA official overruled review team in approval of Sarepta's Duchenne gene therapy

In a memo made public Friday, Peter Marks, head of the agency office that oversees gene therapies, wrote that he disagreed with other reviewers and saw "compelling" evidence to clear Elevidys.



Peter Marks
CBER



Patrizia Cavazzoni
CDER

Sanfilippo Syndrome

Surrogate Endpoint Accelerated Approval

Sanfilippo syndrome

- Single gene defect, defect stops enzyme from producing
- Enzyme not there to do its job, substrate builds up (Heparan Sulfate)
- slowly progressing, neurodegenerative, lysosomal storage disorder

Example Sanfilippo syndrome

Biomarker: Heparan Sulfate

Surrogate endpoint: Reduction of Heparan Sulfate

Primary Endpoint: Undetermined. Patient has brain damage and cannot comply with COA

Secondary Endpoint: Hyperactivity, diarrhea, ear in, sleep quality, swallowing, gait, speech

Reasonably likely SEs **are reasonably likely to predict a clinical benefit.** They are supported by strong mechanistic and/or epidemiologic rationale, **but the amount of clinical data available is not sufficient to show that they are validated**. They can be used to support **accelerated approval,** but post-approval clinical trials are needed to show that these SEs can be relied upon to predict, or correlate with, clinical benefit**.**

What you didn't know about
Clinical Outcome Assessments

Clinical Outcome Assessments

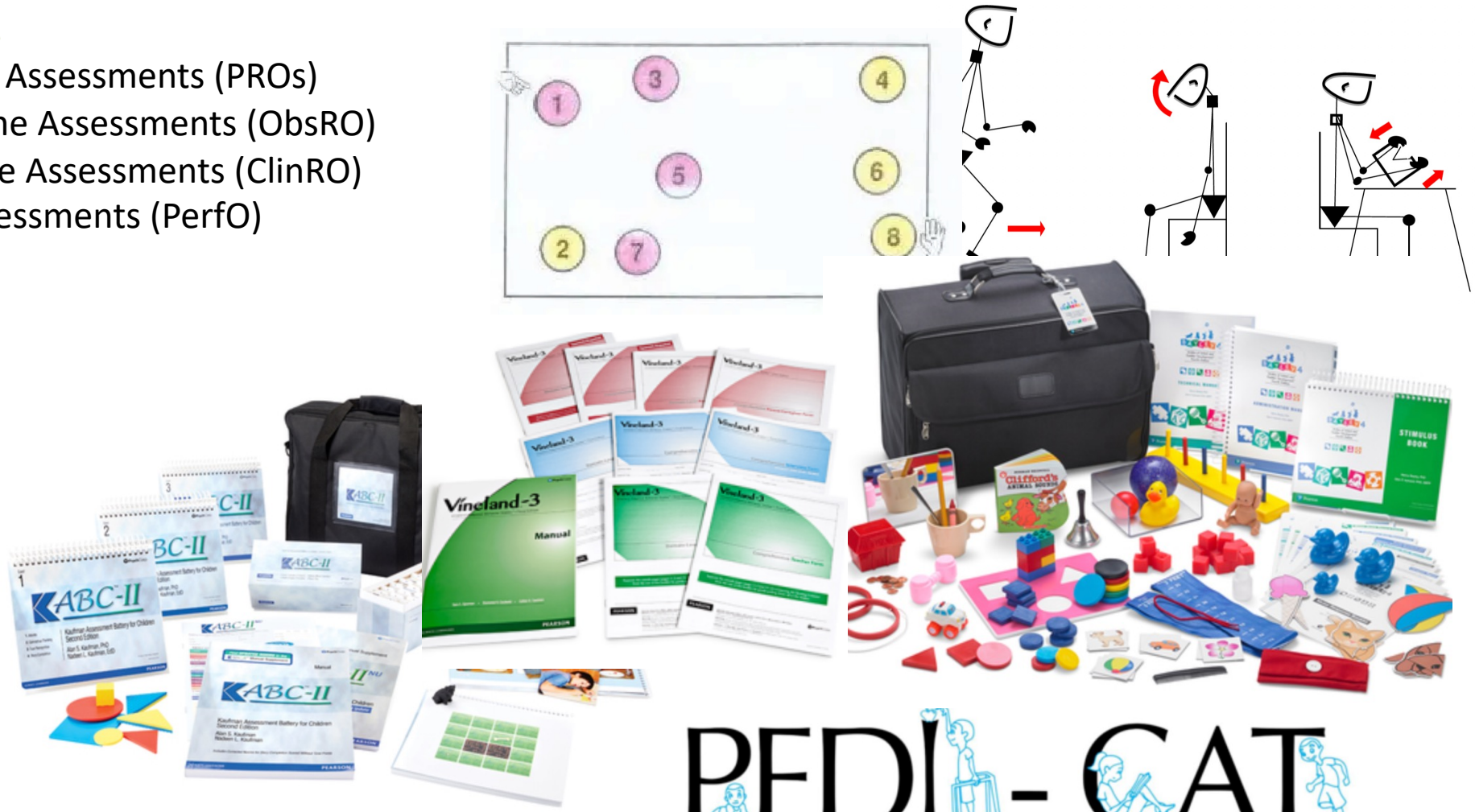
- Patient Reported Outcome Assessments (PROs)
- Observer Reported Outcome Assessments (ObsRO)
- Clinician Reported Outcome Assessments (ClinRO)
- Performance Outcome Assessments (PerfO)

Catch 22

- Validated
- Fit-for-Purpose
- Test learning
- Subjectivity
- Translations

PROPRIETARY

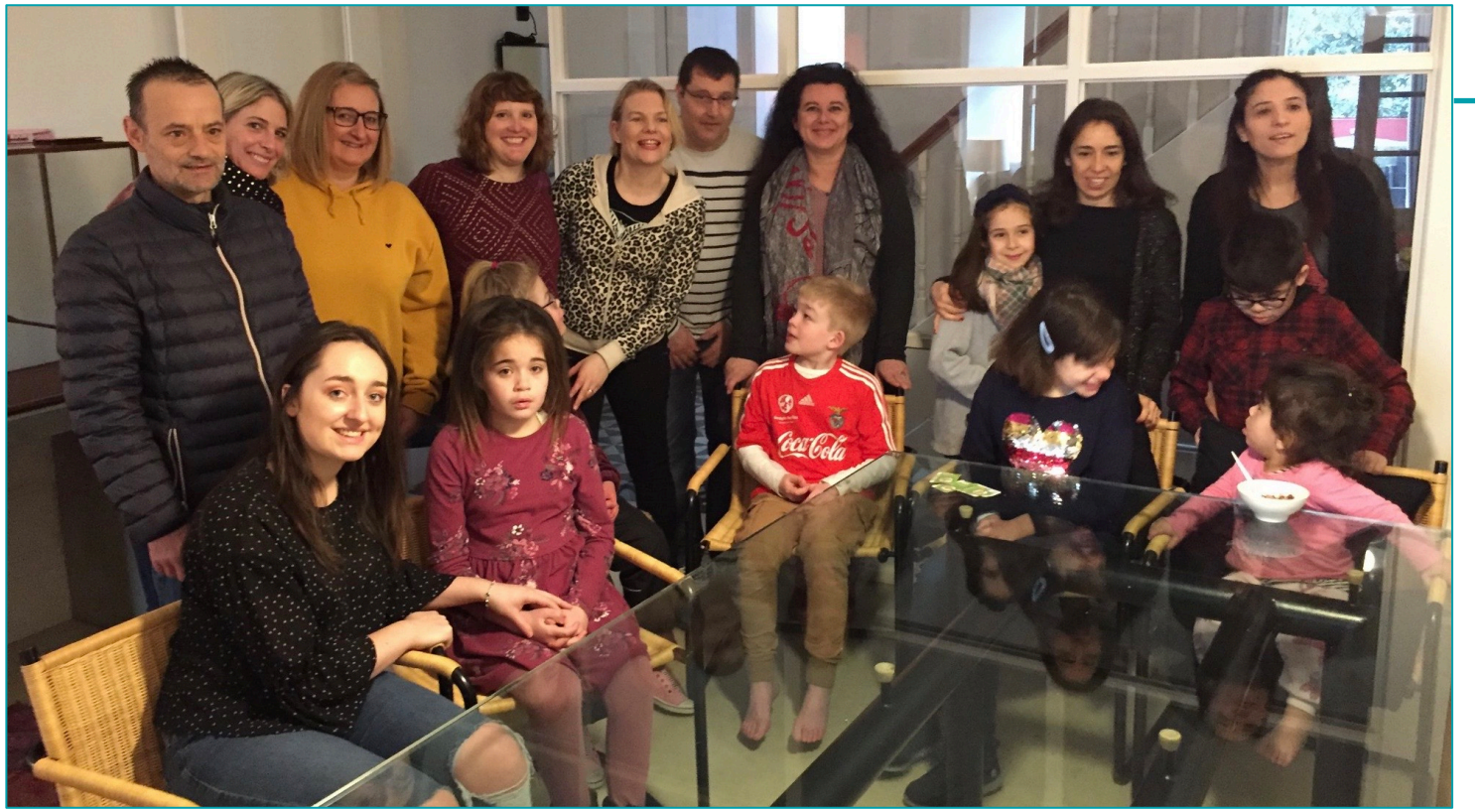
- ✓ Pearson
- ✓ PAR
- ✓ Stoelting



What you can do from home

Get Ready

- Create Questionnaires
- Record Video Assessments
- Gather Medical Records
- Build Patient Registry
- Write Papers
- Identify Endpoints
- Research COAs



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

Parent Experiences of Sanfilippo Syndrome Impact and Unmet Treatment Needs: A Qualitative Assessment

Katherine Ackerman Porter · Cara O'Neill · Elise Drake · Samantha Parker · Maria L. Escolar · Stacey Montgomery · William Moon · Carolyn Worrall · Holly L. Peay

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Thank You

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