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Evidence Based Education in Rare Disease

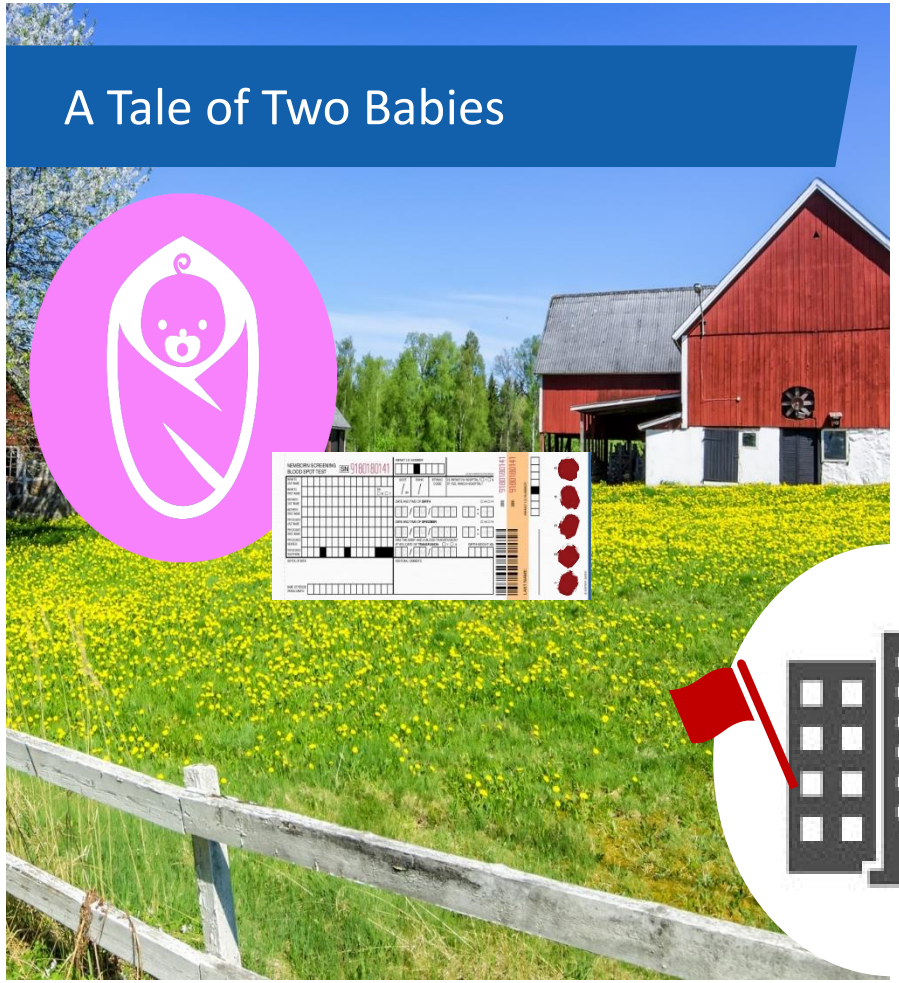
Debra S. Regier, MD PhD
Chief, Genetics and Metabolism.
Interim Director, Children's National Rare Disease Institute, Washington DC

December 1, 2023

Disclosures

Educational grants from Takeda and Travere Pharmaceuticals.
Educational grants from NICHD (NIH) and CZI

A Tale of Two Babies



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Newborn Screening Detects Dozens of Disease.

Metabolic Disorders (5.5)

Endocrine Disorders (16)

Hemoglobin Disorders (2.75)

Immune Disorders

Lysosomal Storage Disorders

Critical Congenital Heart Disease

Hearing Loss

Other Disorders (CF 5)

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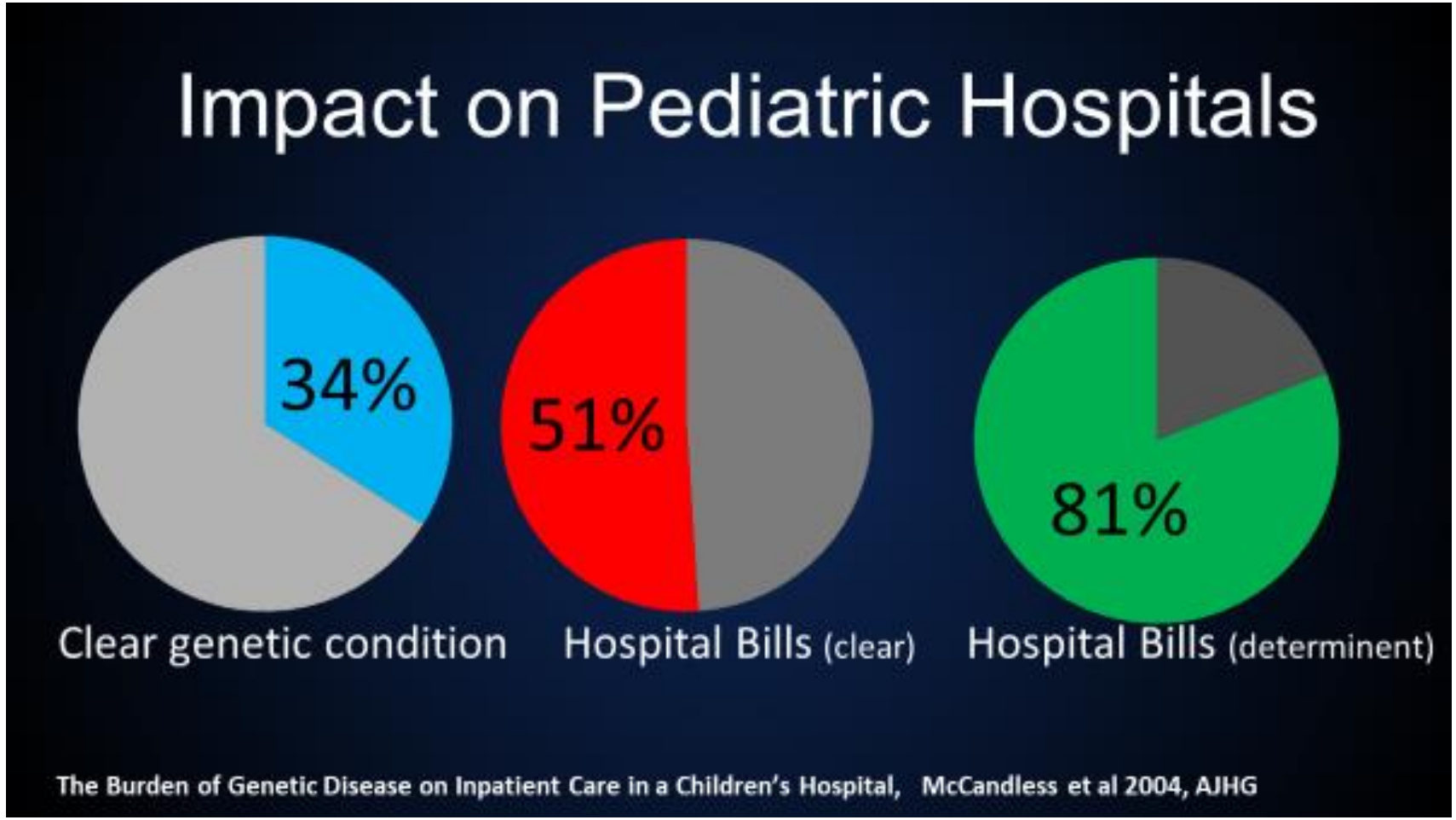
https://www.maine.gov/dhhs/mecdc/population-health/mch/cshn/bloodspot-screening/documents/Bloodspot%20Screening%20Databrief%202021.pdf

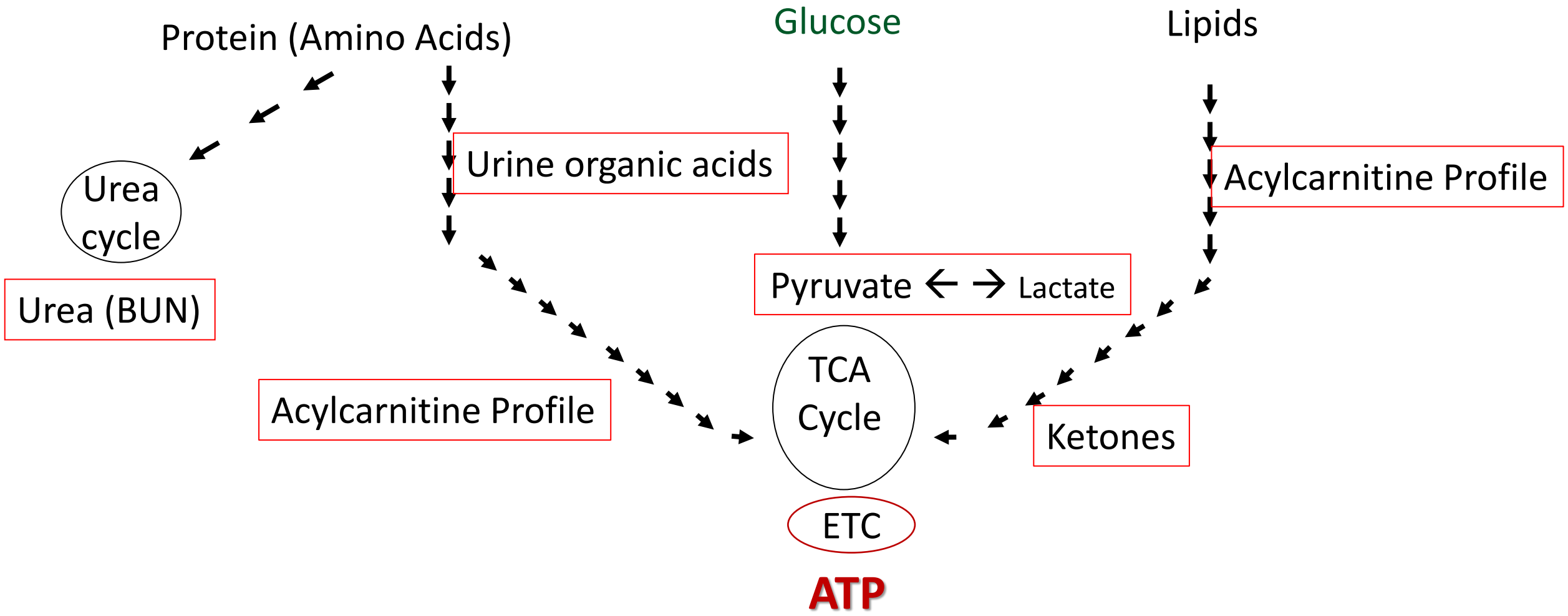
A Tale of Two Boys….

We KNOW We Are Missing Genetic Patients!



But How Can We Find the Other Patients??

- Increase Publications (well read by other geneticists!)
- Teach more people pathways so they can find patients
- Increase the number of rare disease doctors (we'll help patients in 20 years!)



https://www.youtube.com/watch?v=NX-R1qDxvgA
>23K views as of 07/17/2023!

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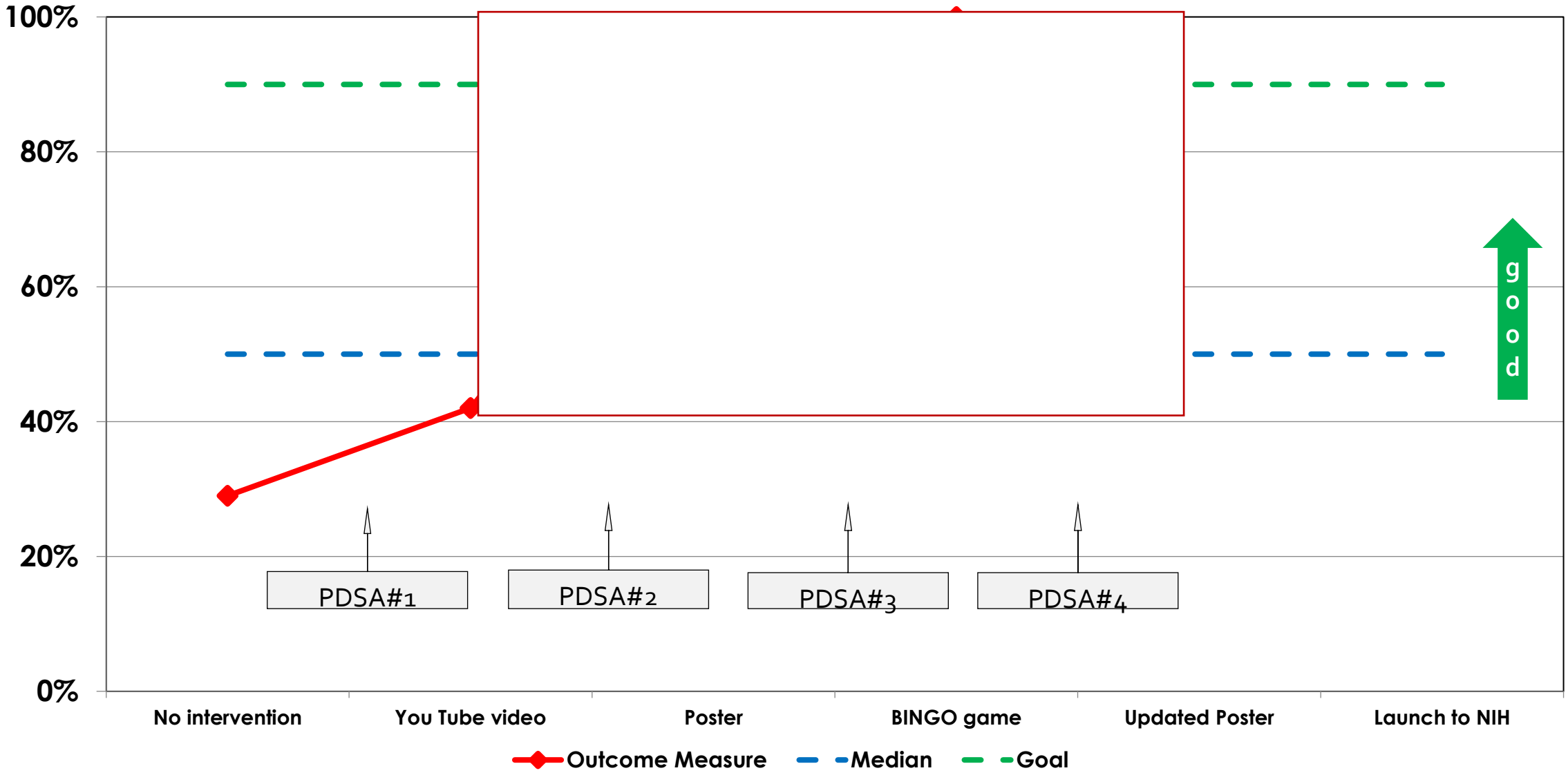
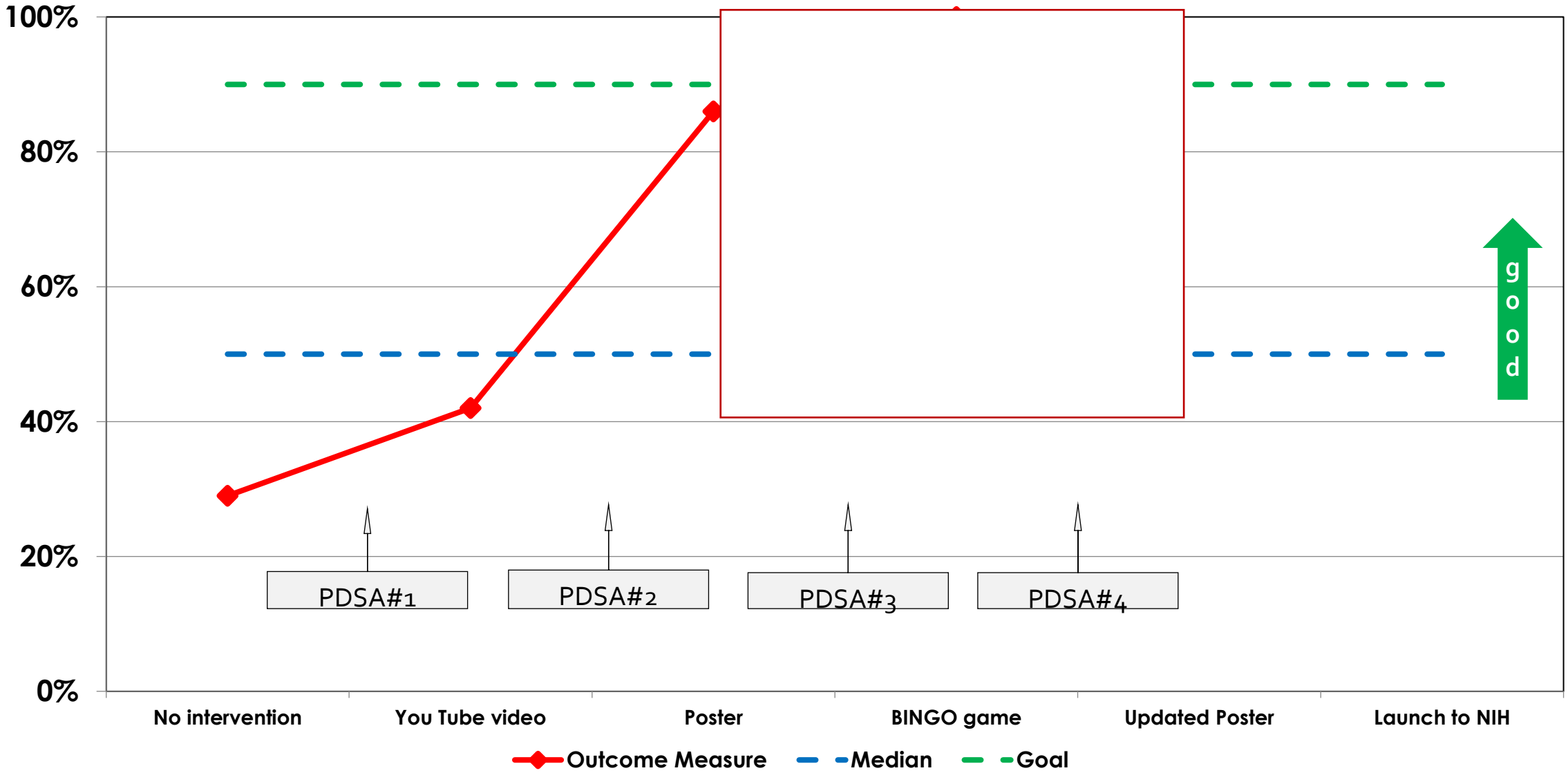

100%
80%
60%
40%
20%
0%
good
PDSA#1
PDSA#2
PDSA#3
PDSA#4
No intervention
You Tube video
Poster
BINGO game
Updated Poster
Launch to NIH
Outcome Measure
Median
Goal

…and then we realized not everyone loves a pathway!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Top 5 Reasons for Metabolic Admissions…

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Metabolism Situational Awareness:
(Example Sick Metabolic Kid Phrases for IPASS signout)

Not Sure??? On-call Genetics and Metabolism at pager 50010

Brain Edema

"Patient at risk for brain edema (ICP, herniation) If vitals are altered or mental status changes, contact genetics ASAP. Do NOT stop fluids."

For Ammonia Disorders, add:

"Send STAT free-flowing ammonia level after calling genetics"

Leucine Disorder:
- Maple Syrup Urine disease

Ammonia Disorders:

Urea cycle disorders
- OTC deficiency
- CPS deficiency
- Citrullinemia
- Arginase deficiency
- AS Lyase deficiency

Organic Acidemias
- MMA (also kidney failure)
- PA (also cardiac risk)
- IVA (in severe cases)
- 3-MCC deficiency

Strokes/Thrombosis

"Patient at risk for thrombosis and/or strokes. Contact genetics immediately for any bleeding, clotting, or thrombosis concerns or mental status changes."

Homocystinuria
Severe MTHFR disease
Cobalamin deficiencies
- eg Cobalamin C

Glutaric Aciduria Type 1
Isovaleric Aciduria
Methylmalonic Acidemia
Propionic academia
MELAS
Some other mitochondrial conditions (ask us!)

Hypoglycemia

"Patient at risk for hypoglycemia. Do NOT stop fluids. If any concerns, call Genetics ASAP and check glucose."

Fatty acid oxidation defects
- VLCAD (also cardiac risk)
- LCHAD (also cardiac risk)
- MCAD
- Trifunctional Protein Deficiency
- CPT1 or 2

Glycogen Storage Disorders
- GSD 1a, 1b
- GSD 0
- Other GSDs

(in patients who are are sick or young

Mitochondrial Disorders
(ask us if unsure!)

Rhabdomyolysis

"This patient is at risk for rhabdomyolysis, If any concerns, STAT Creatine Kinase, do NOT stop fluids"

Glycogen storage
- GSD-V (aka McArdle disease)

Fatty acid oxidation defects
- VLCAD
- LCHAD
- MCAD
- Trifunctional Protein Deficiency
- CPT1 or 2

Lipin defects
- LPIN1 deficiency

Cardiac Events

"This patient is at risk for cardiomyopathy or arrhythmias, contact genetics if any concerns, or if acute concern consult cardiology. Do not stop fluids without consulting genetics"

Propionic Acidemia [1 SEP]

Fatty acid oxidation defects
- LCHAD
- VLCAD
- CPT deficiency [1 SEP]
- Trifunctional Protein Deficiency

Storage disorders
- Pompe disease
- Fabry disease [1 SEP]

Mitochondrial disorders
- Barth syndrome
- Kearns-Sayre
- CPEO
- MELAS
- MERRF

Something You've Never Heard Of (or NOT Listed on This Poster):

"This patient followed by genetics and metabolism. Call for any questions or concerns you or their family have about their care."
Check Genetics out-patient note or consult note, and give us a call if you're not sure what to expect! Page to 50010

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#1 Admission Reason: Brain Edema

Leucine Elevation

- Maple Syrup Urine Disease

Ammonia Elevation

- Urea Cycle Disorders
  - OTC
  - CPS1
  - Citrullinemia
  - Arginase
  - AS Lyase
- Organic Acidemias
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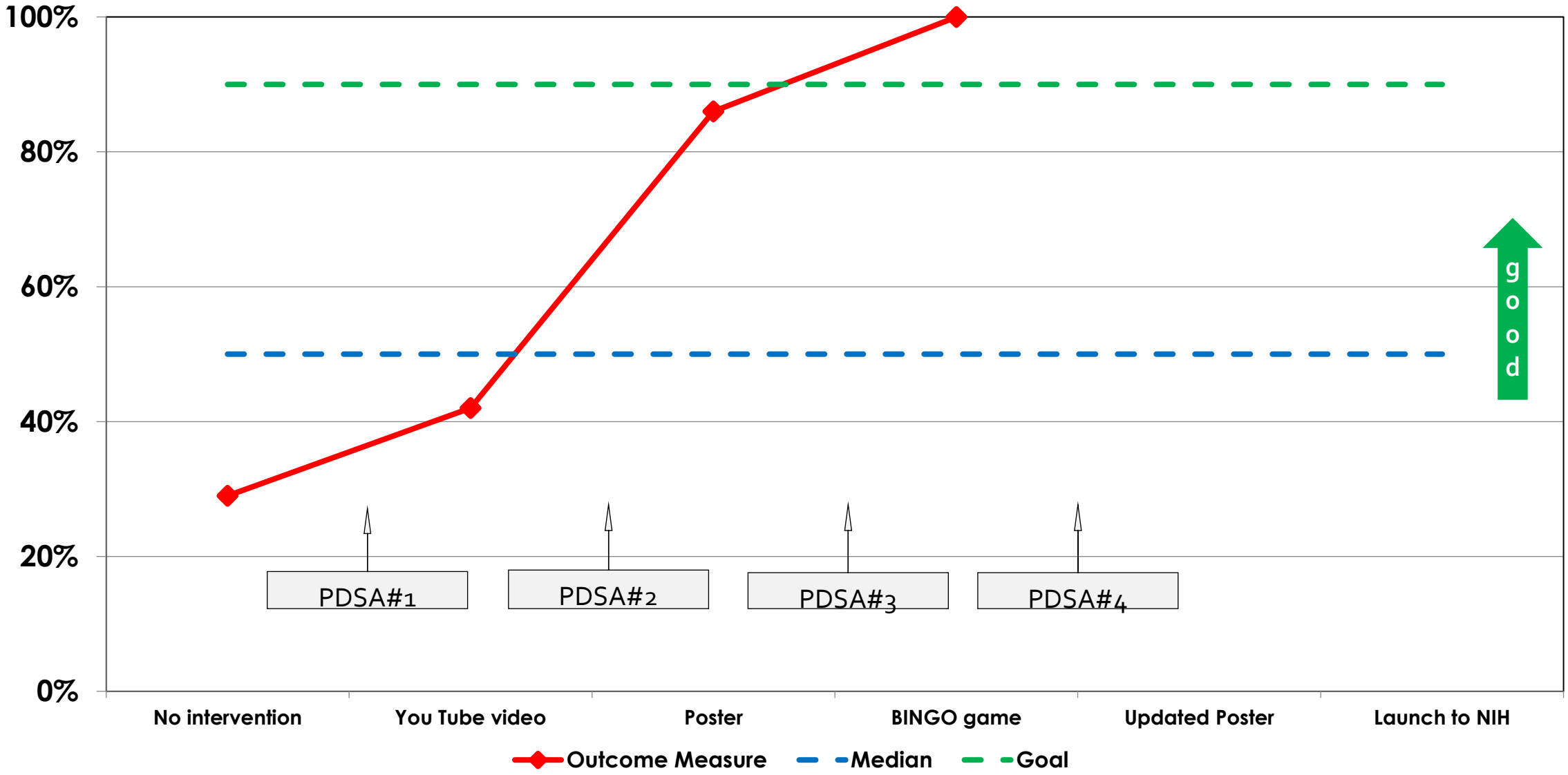
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Genetics Bingo of Treatments (Each Team During COVID)

M	E	T	A	B
D10 Normal	Confirm the Newborn Screen ASAP	Give MCT oil (medium chain triglyceride)	Get a STAT Ammonia	More Protein
Essential Amino Acids	Start Cornstarch	Send Urine Organic Acids	Send Urine AMINO ACIDS (NOT!!!)	D10 ½ Normal Saline
Find out how they are making formula	Give a low protein diet	**CALL A METABOLIST: FREE!!!**	Intralipid	GIR (fill in the blank)
Send Acylcarnitine Profile	No Protein	Start an ammonia scavenger	Give a lowfat diet	Check Plasma Amino Acids
Cerebral Edema Risk	Start valine and isoleucine (even with MSUD!)	Give the 40 year old his formula ASAP	Call the metabolic dietitian	Never Stop the Fluids

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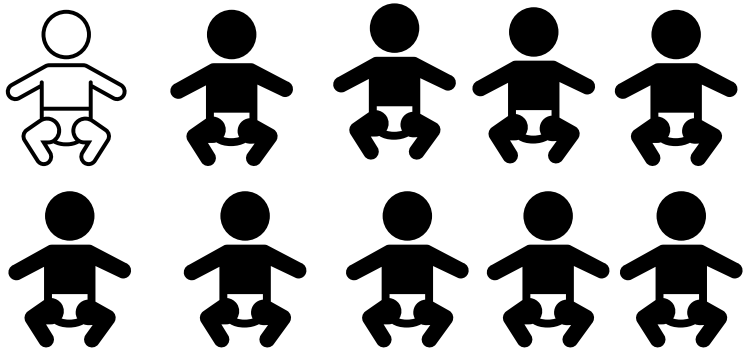
Even My Best Wasn't Enough

~9,000 visits per year
12 physicians
10 genetic counselors
2 advanced practice providers
Enough clinic space
40% telemedicine for access

……

Still a 9 month wait!



RARE DISEASE FACTS

NORD® National Organization for Rare Disorders

Learn more at: **rarediseases.org**

RARE DISEASE:
Any disease, disorder, illness or condition affecting fewer than **200,000** people in the United States is considered rare.[1]

There are approximately **7,000** **RARE DISEASES.**[2]

More than **90%** of rare diseases are **WITHOUT** an FDA-approved treatment.[9]

It's estimated that **25-30** **MILLION AMERICANS** (almost 1 in 10) have rare diseases.[7]

Most rare diseases are **genetic** or have a genetic component.[3]

For many rare diseases, signs may be observed at birth or in childhood.[5]

ALL PEDIATRIC CANCERS are rare.[8]

There are more than **500** types of **rare cancers.**[6]

Many rare diseases result in premature deaths of infants and young children, or are fatal in early childhood.[4]

https://rarediseases.org

Special Announcement: Letter from NORD's CEO, Peter L. Saltonstall

For Patients & Caregivers | For Clinicians & Researchers | For Patient Organizations | NORD en Español | Contact NORD

NORD® RARE. STRONG. TOGETHER. 40 YEARS

Rare Disease News | Resource Library | About Us | Events | Donate

Understanding Rare Disease | Living with a Rare Disease | Community Support | Advancing Research | Driving Policy | Get Involved

We have a Beautiful & RARE Chance

NORD advances practical, meaningful, and enduring change so people with rare diseases can live their fullest and best lives. Every day, we elevate care, advance research, and drive policy in a purposeful and holistic manner to lift up the rare disease community.

National Organization for Rare Disorders

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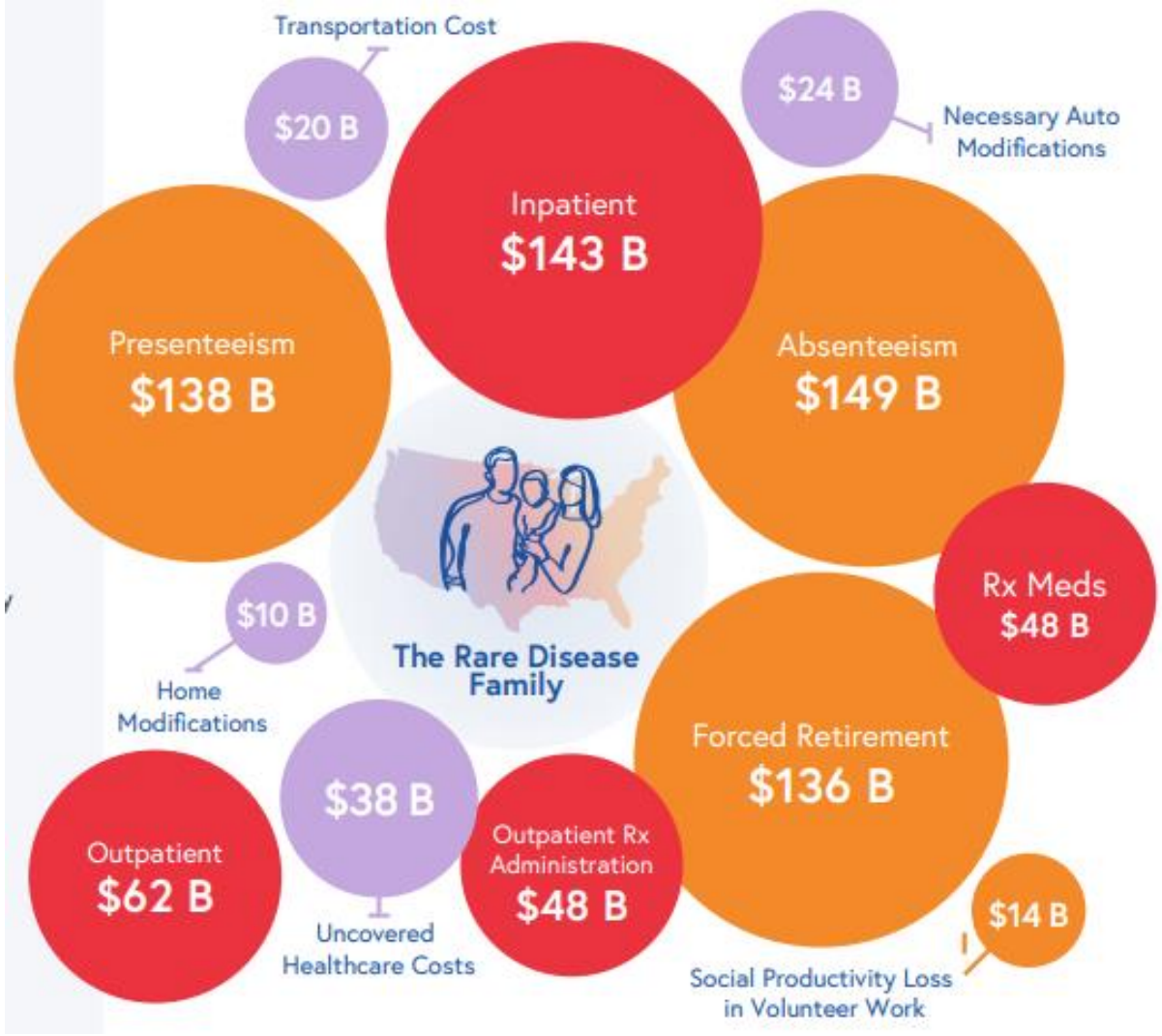
Economic Burden of Rare Disease: Almost 1 Trillion/Year



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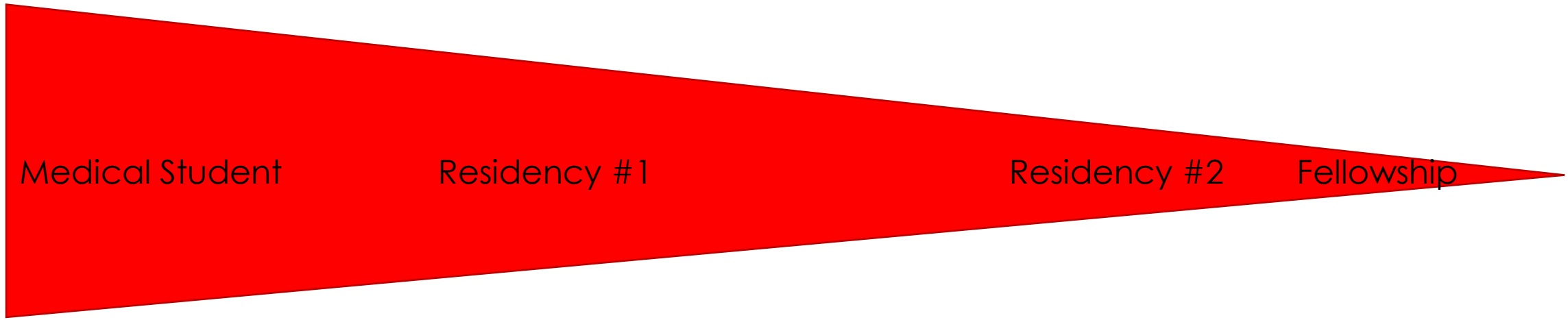
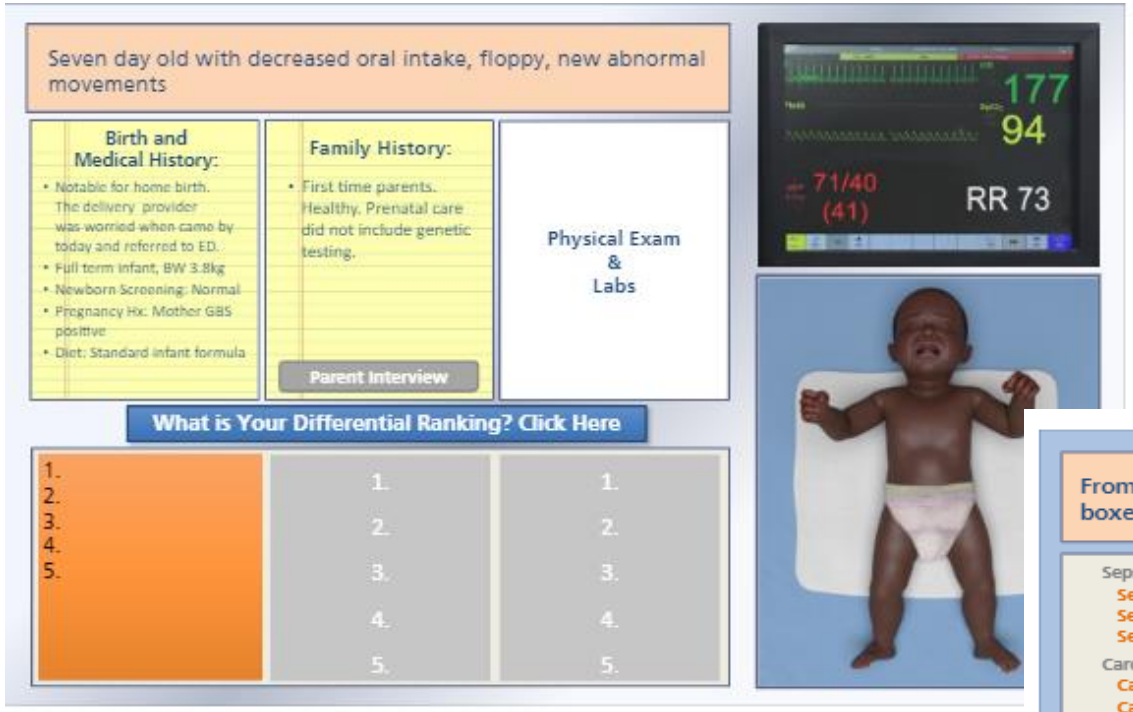
https://everylifefoundation.org/wp-content/uploads/2021/02/The_National_Economic_Burden_of_Rare_Disease_Study_Infographic_February_2021.pdf

How Can We Build The Rare Disease Clinical Community?



Sick Baby Program….Metabolism to the Broader Community



Funding provided by the George Washington University Pilot Project Grant for Education

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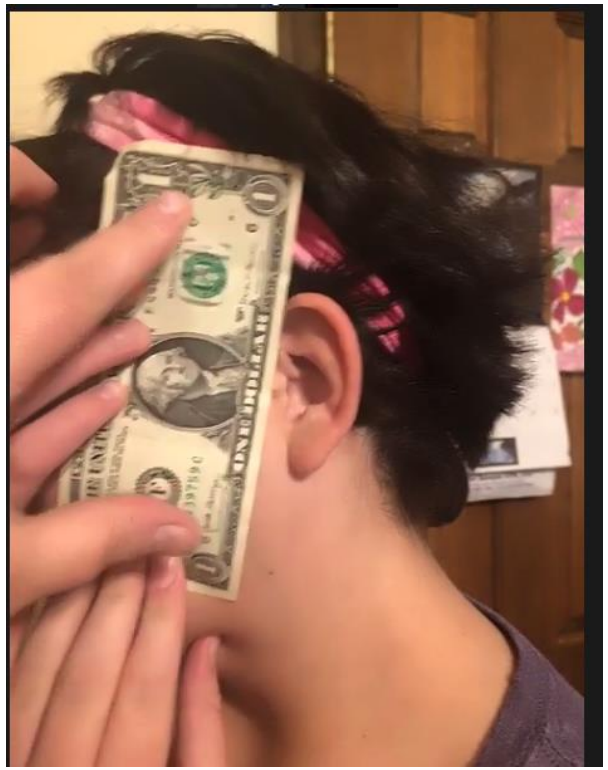
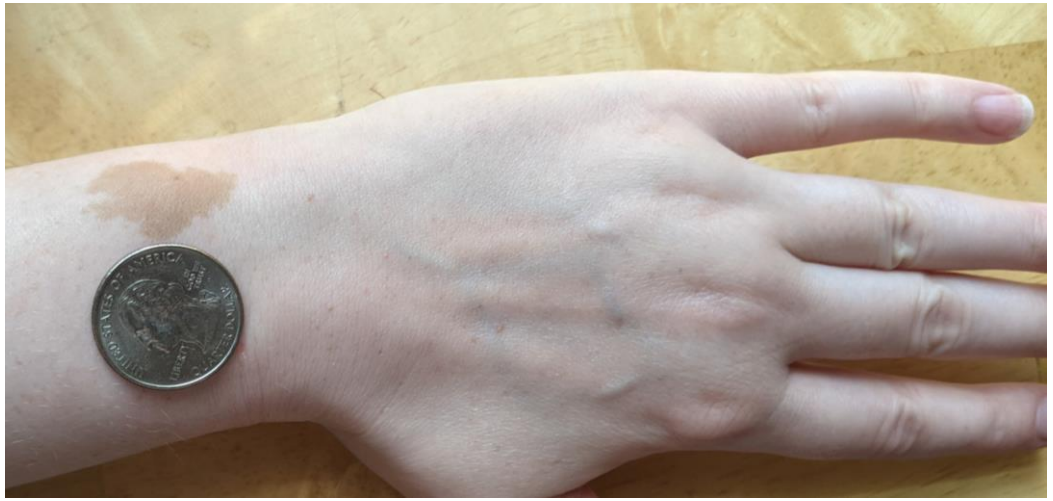
Household item	Length
US one dollar bill	6.14 in., 156 mm
US penny	0.75 in., 19 mm
US nickel	0.84 in., 21.2 mm
US dime	0.7 in., 17.9 mm
US quarter	0.96 in., 24.3 mm
20 oz soda lid	1.4 in., 3 cm
Credit card	3.7 in., 8.6 cm





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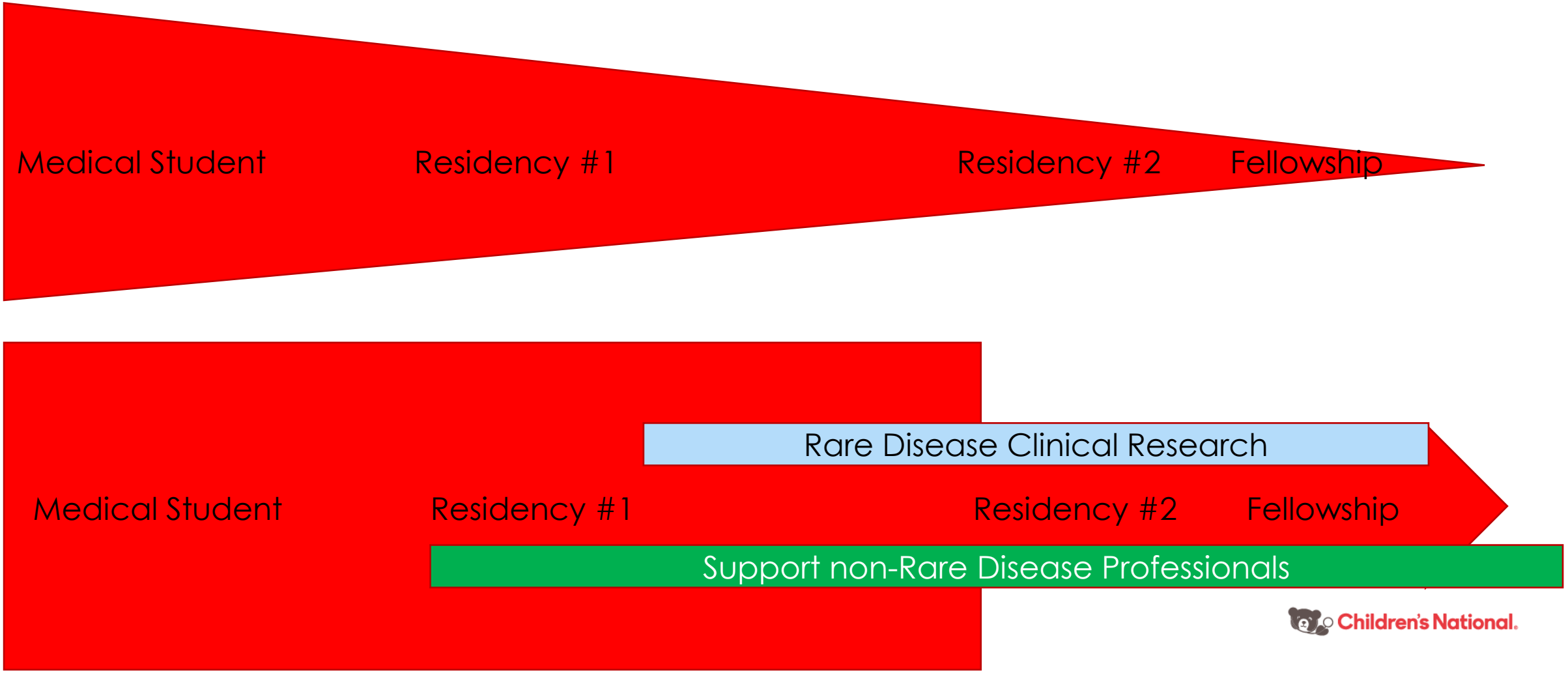
Cohen, et al. AJMG Part C. 2021

How Can We Build The Rare Disease Clinical Community?



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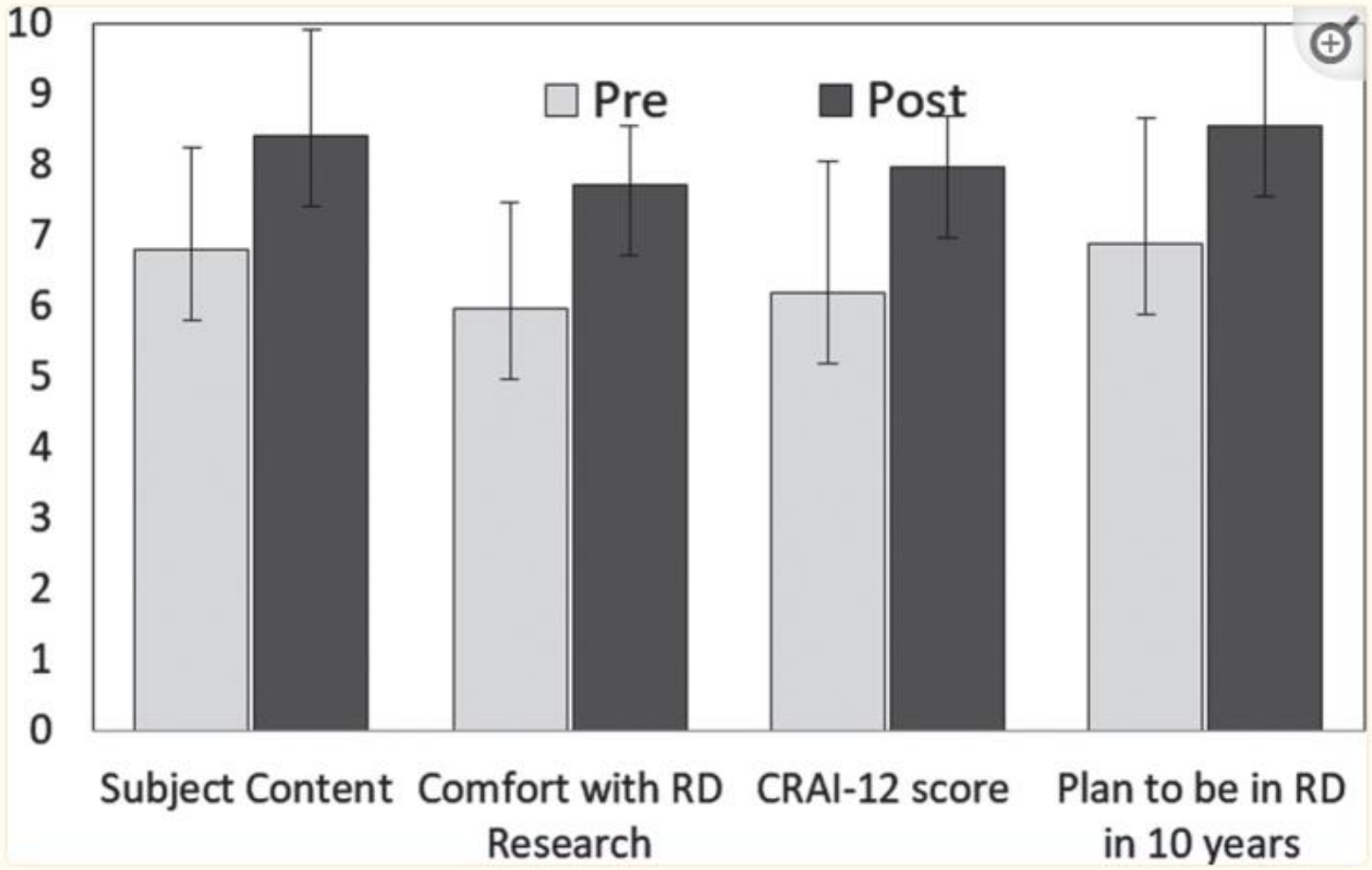

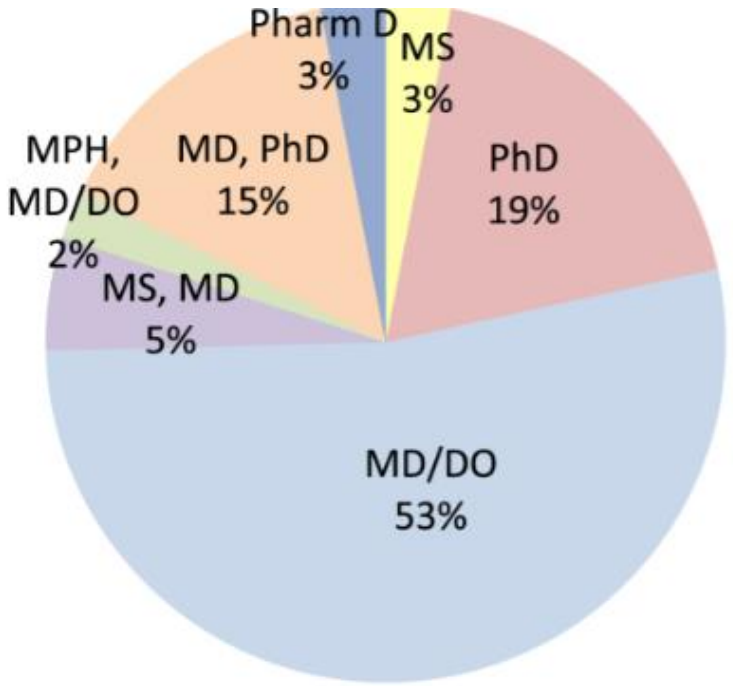

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Regier et al. Transl Sci Rare Dis 2022

Now expanded….

(and disaster science course launching Winter 2024!)

The Rare Disease Clinical Research Training Program

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- **Clinical research assistants**
- **Fellows in their final year of training**
- **Postdoctoral fellows**
- **Early career faculty with clinical research interests**

Topics Included: Small cohort statistics and study design; Grant writing and publishing in rare disease; Networking with the global rare disease community

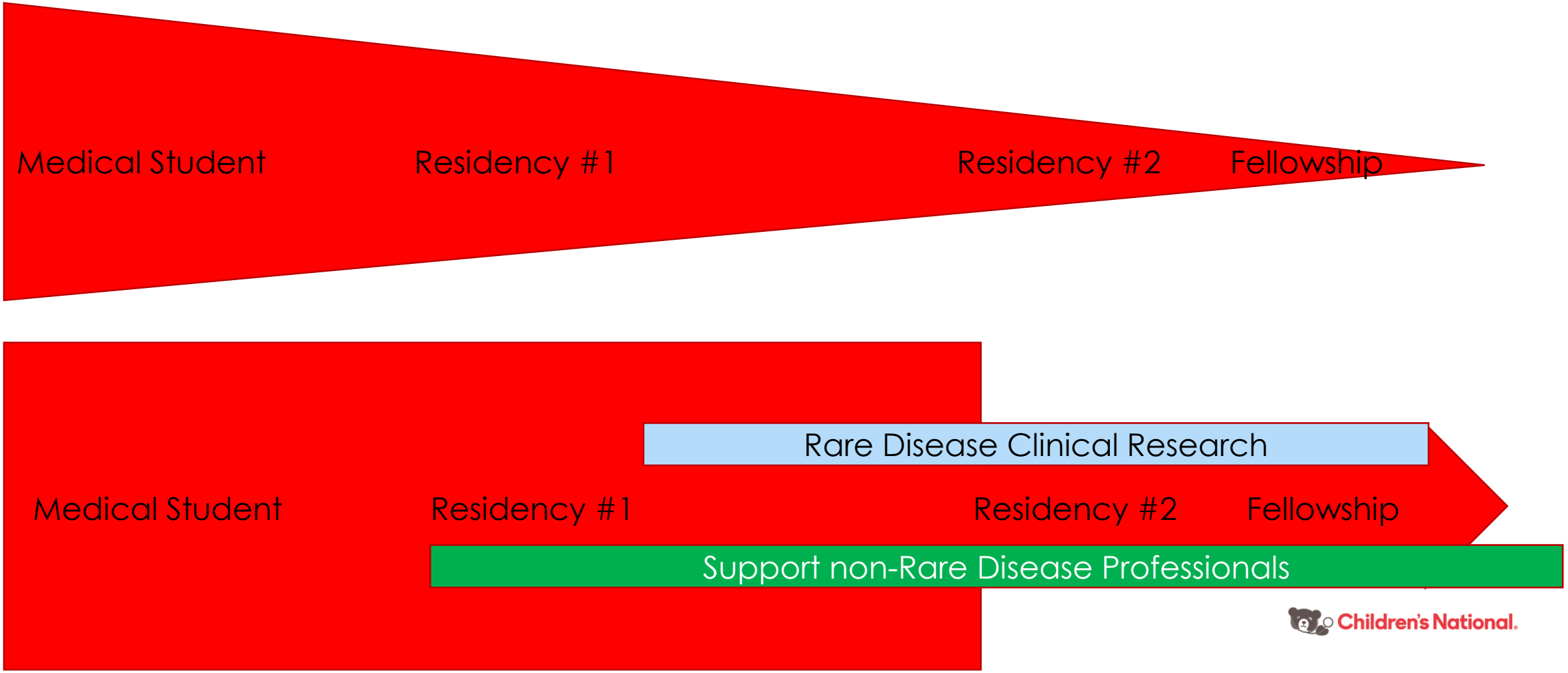
Program Beginning October 2023: Year-long course with Virtual sessions (in real time), In-Person sessions in Washington, DC; Twice monthly web-based sessions

Application Process: https://redcap.link/RDScholars (QR code). Limited travel funding available with priority for those from underrepresented in medicine groups. Rolling enrollment begins 8/15/2023

Questions??

Dr. Debra Regier, Course Director: dregier@childrensnational.org or Tiffany Swaringer, Course Coordinator: tswaringer@childrensnational.org

How Can We Build The Rare Disease Clinical Community?



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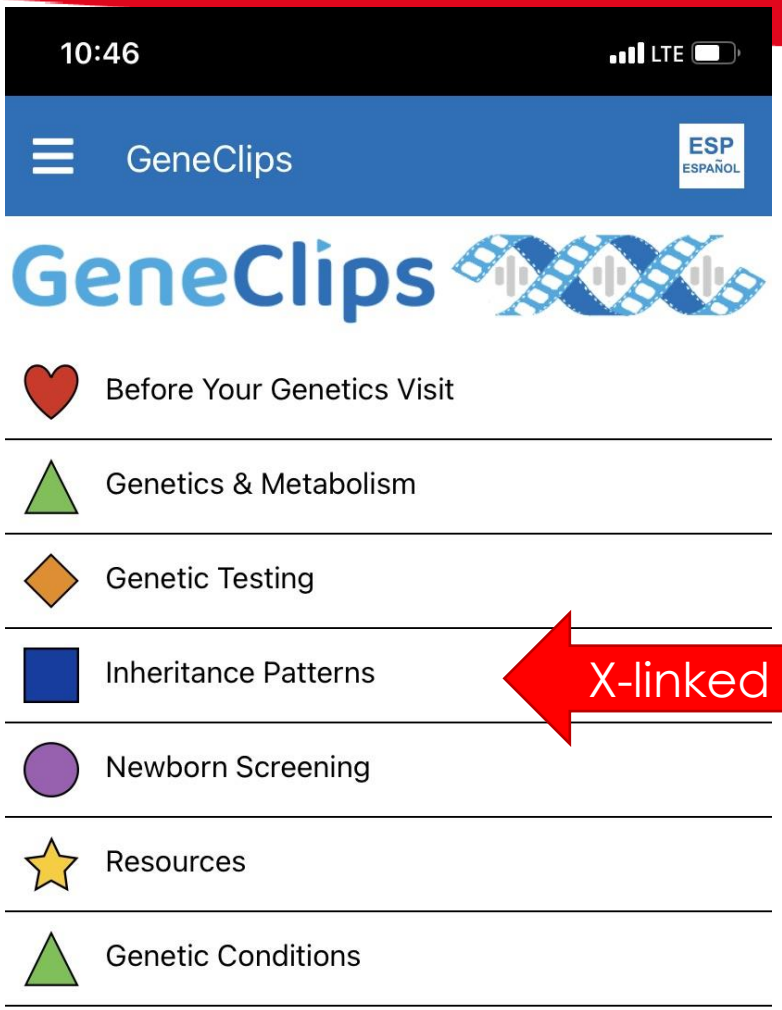

X-linked inheritance??

GeneClips

GeneClips is a smartphone app made for you to review the medical genetics information shared in your appointment.

Available for Download on:

App Store (iPhone)

Google Play Store (Android)

Please rate and review the app to let us know what you think!

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Now on Children's National Website: 1-5 minute videos: English and Spanish

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Chan Zuckerberg Initiative: How do we help primary care?

- Don't make toxic things (i.e. help them to use genetic testing in a way that won't lead to more frustrations)
- Give them what they can use (CME Credits)
- Don't give them what they cannot use (Busy Work)
- Scavenge toxic things (Help them identify supports in the community)
- Even if they are stellar primary care providers, they need support
- Know your friendly metabolist/geneticist (i.e. build a community)

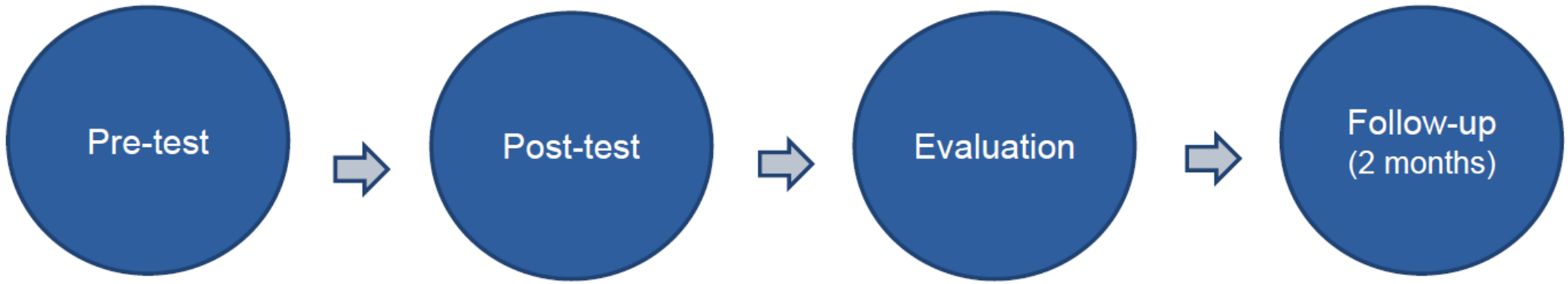
Rare Disease Diagnosis and Testing Strategies

Culturally Competent Care in Your Community

Creation of a Patient-centered Medical Rare Disease Home

Support Mechanisms for Providers of Rare Disease Care

Outcomes Methodology



Definitions

Starter – clicking through marketing materials or entering via website and landing on front matter/disclosure page for the activity, including learning objectives and short activity description
Learner – progressing beyond CME front matter and pre-test, and initiating educational content
Completer – responding to at least post-activity assessment
Credit seekers – completing post-activity eval and requesting certificate

Learner Engagement & Demographics

341
Learners*

59%
Clinician*
(MD/DO/NP/PA)

122
Treaters see an average of 30 patients weekly**

Specialty*

- **38%** PCP (FM/GM/IM/Peds/OBGYN)
- **6%** Critical Care/Emergency Medicine
- **5%** Endocrinology/Diabetes Medicine
- **4%** Neurology
- **3%** Genetics
- **3%** Cardiology
- **3%** Pharmacology
- **3%** Surgery

Years in Practice**

- **26%** <10 years
- **28%** 10 – 20 years
- **46%** >20 years

147	54	68	72
Activity 1	Activity 2	Activity 3	Activity 4

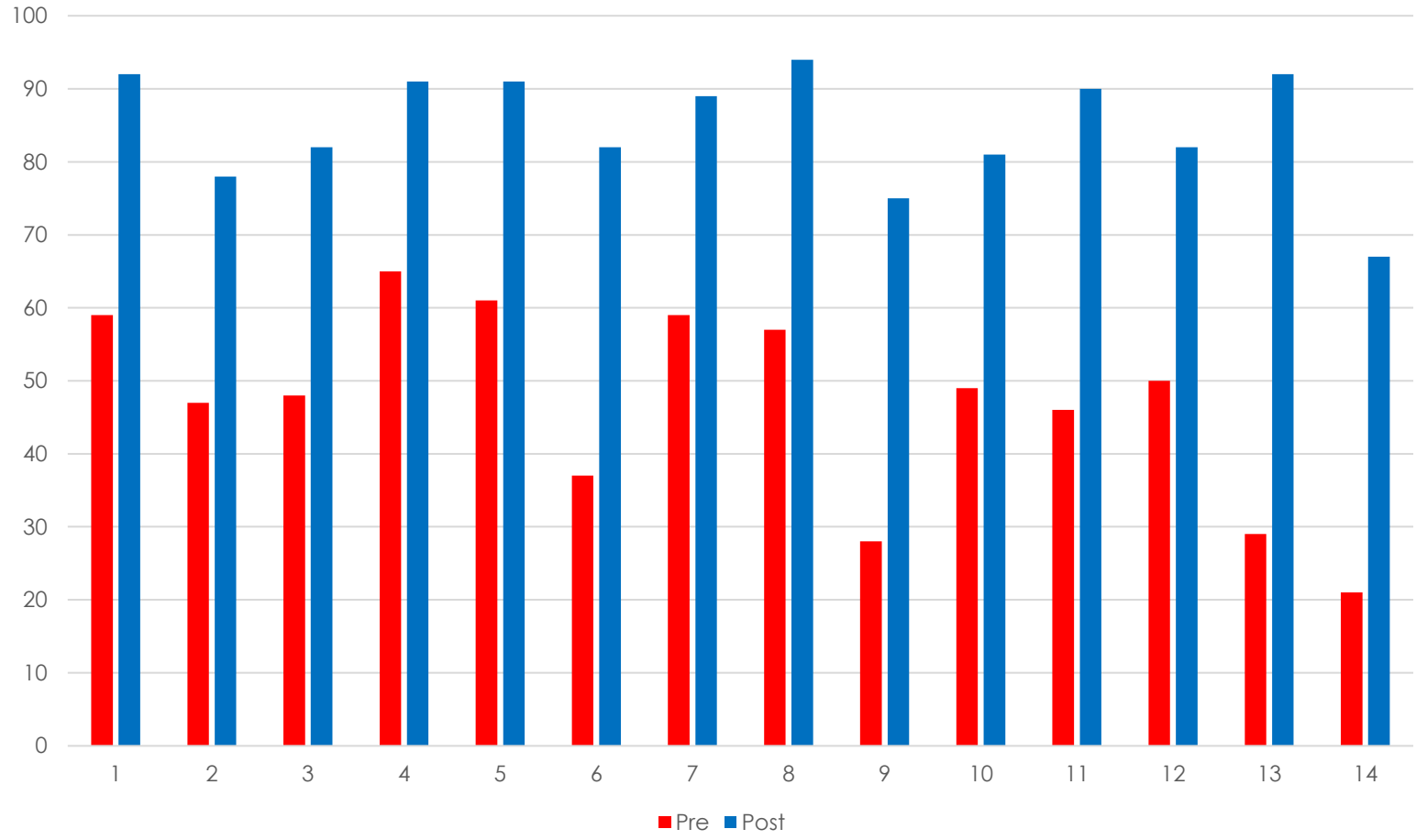
172
matched pre/post responses

52
slide downloads

160
follow-up survey responses

Source: *registration (n = 341) and **evaluation data (n = 168)

Outcomes from 14 Core Concepts



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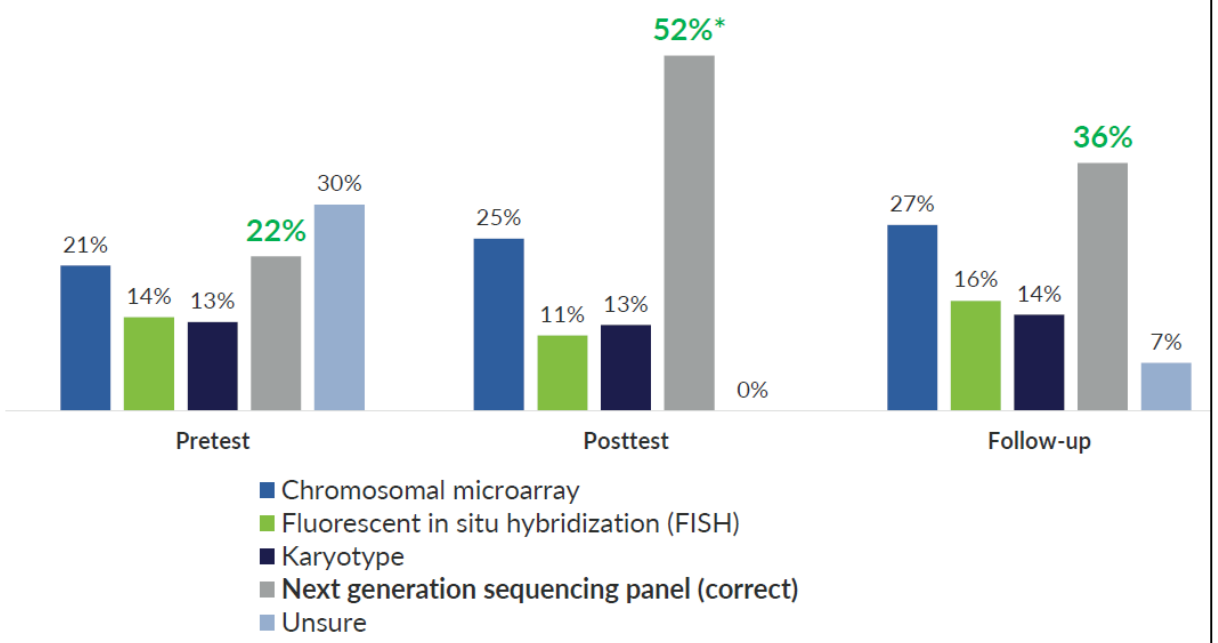
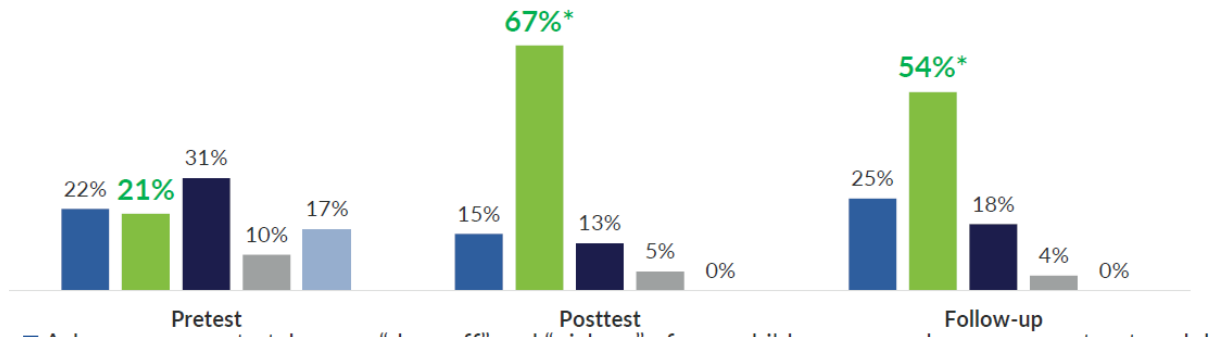
Which of the following genetic tests will identify a base pair change in the DNA leading to achondroplasia?



n = 147 pretest, n = 64 posttest, n = 56 follow-up survey

* p < 0.05 (significant)

You are attempting to increase appropriate boundaries in your life. Which of the following would be a reasonable first step?



n = 72 pretest, n = 39 posttest, n = 28 follow-up survey

* p < 0.05 (significant)

Unmet Need For Content

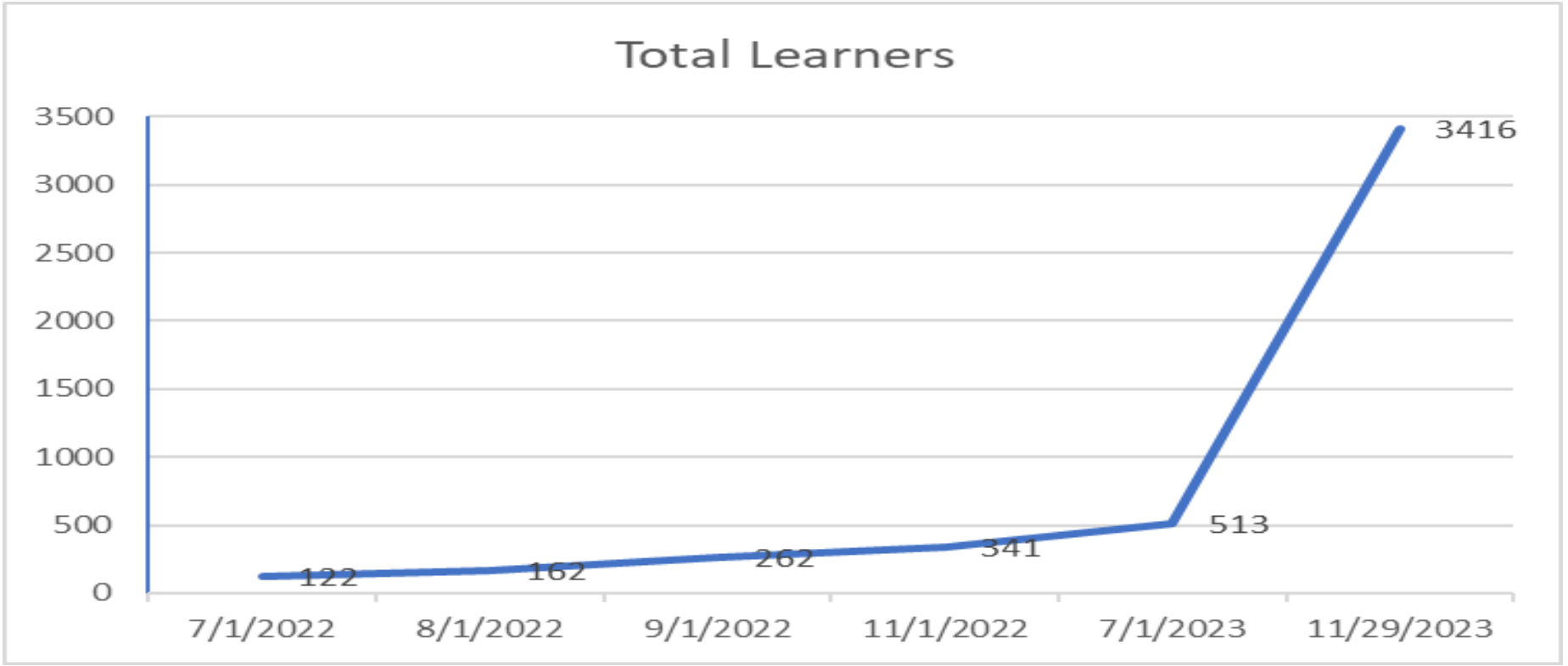


Figure 1: Total Learners Registered for Course: Each unique registered learner participated in 1-4 total sessions.

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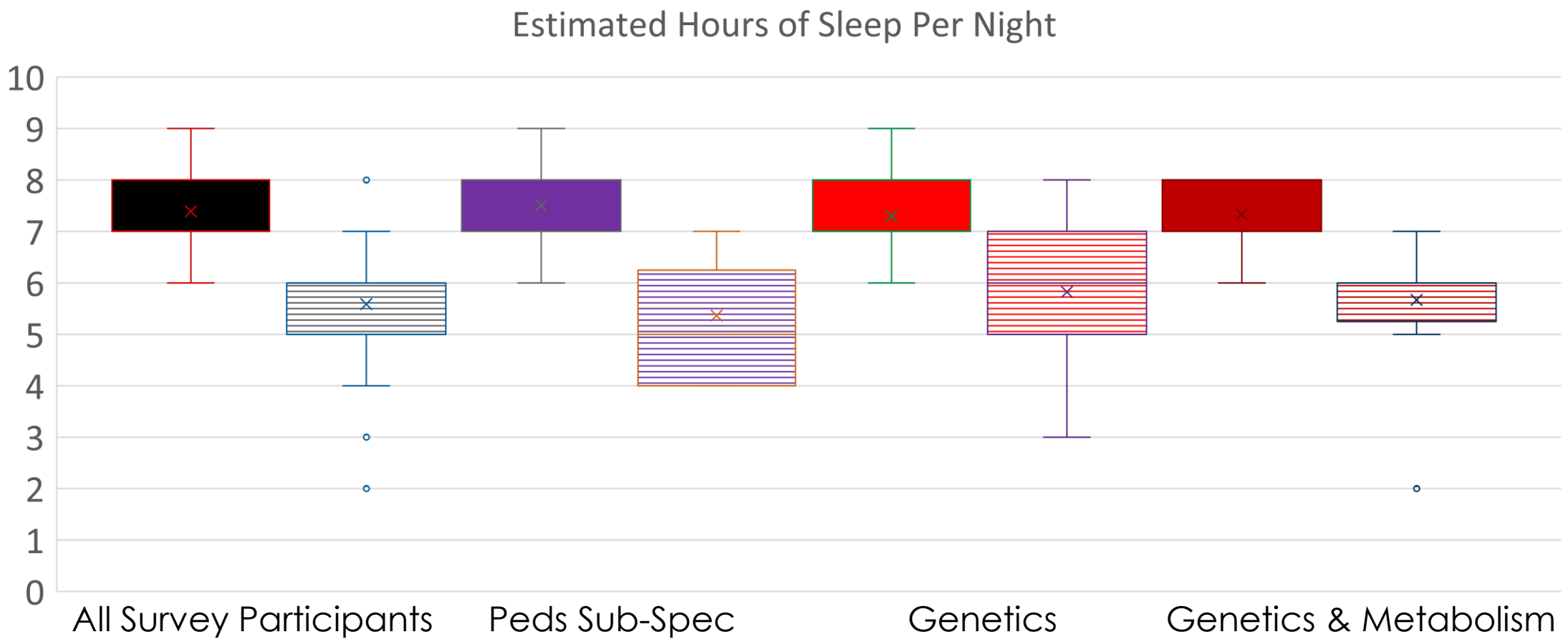
Improving Wellness in the RD Workforce



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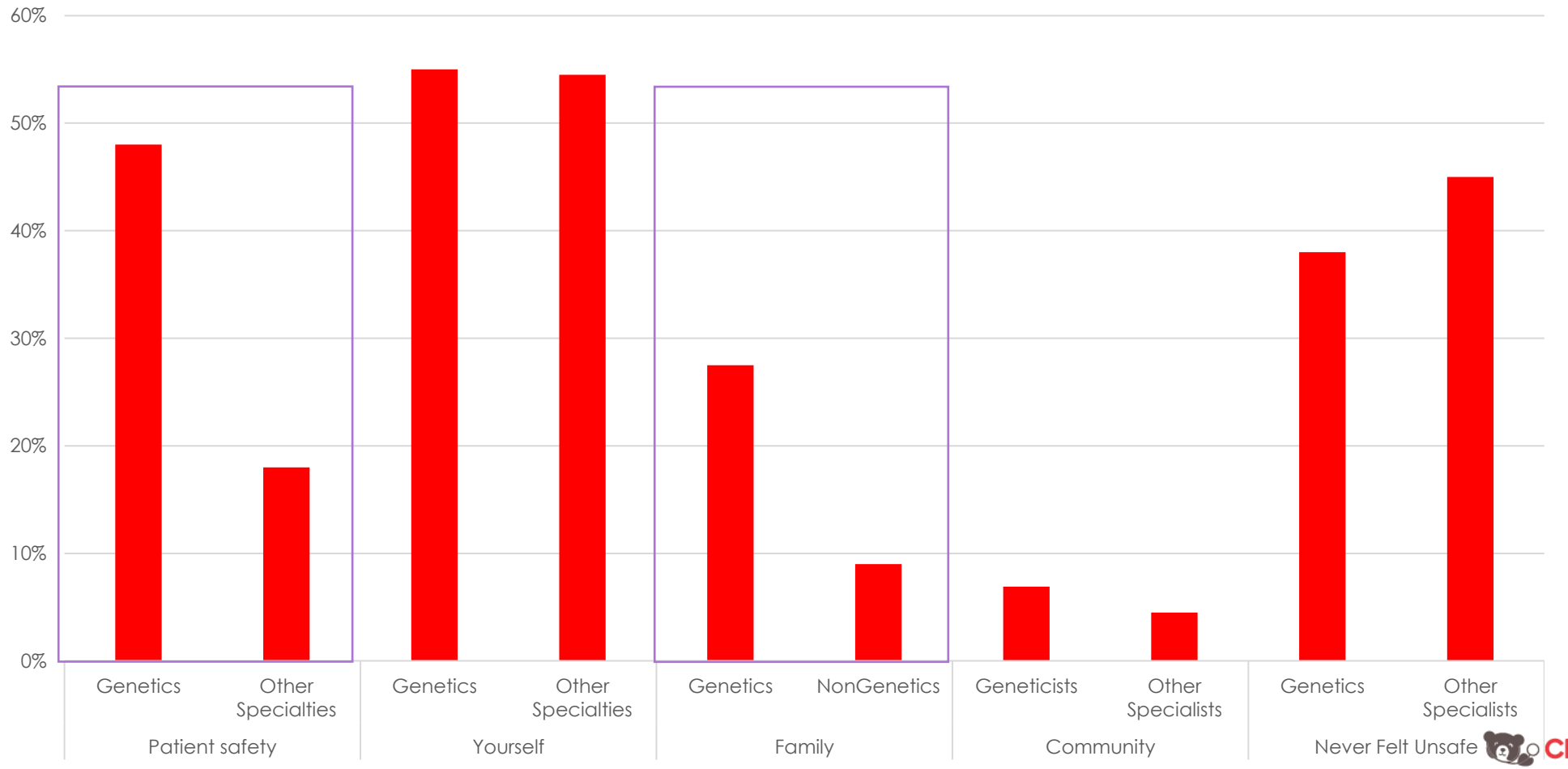
Unpublished data, Hot off of the RedCap!

Physician Worries After a Night of Home Call



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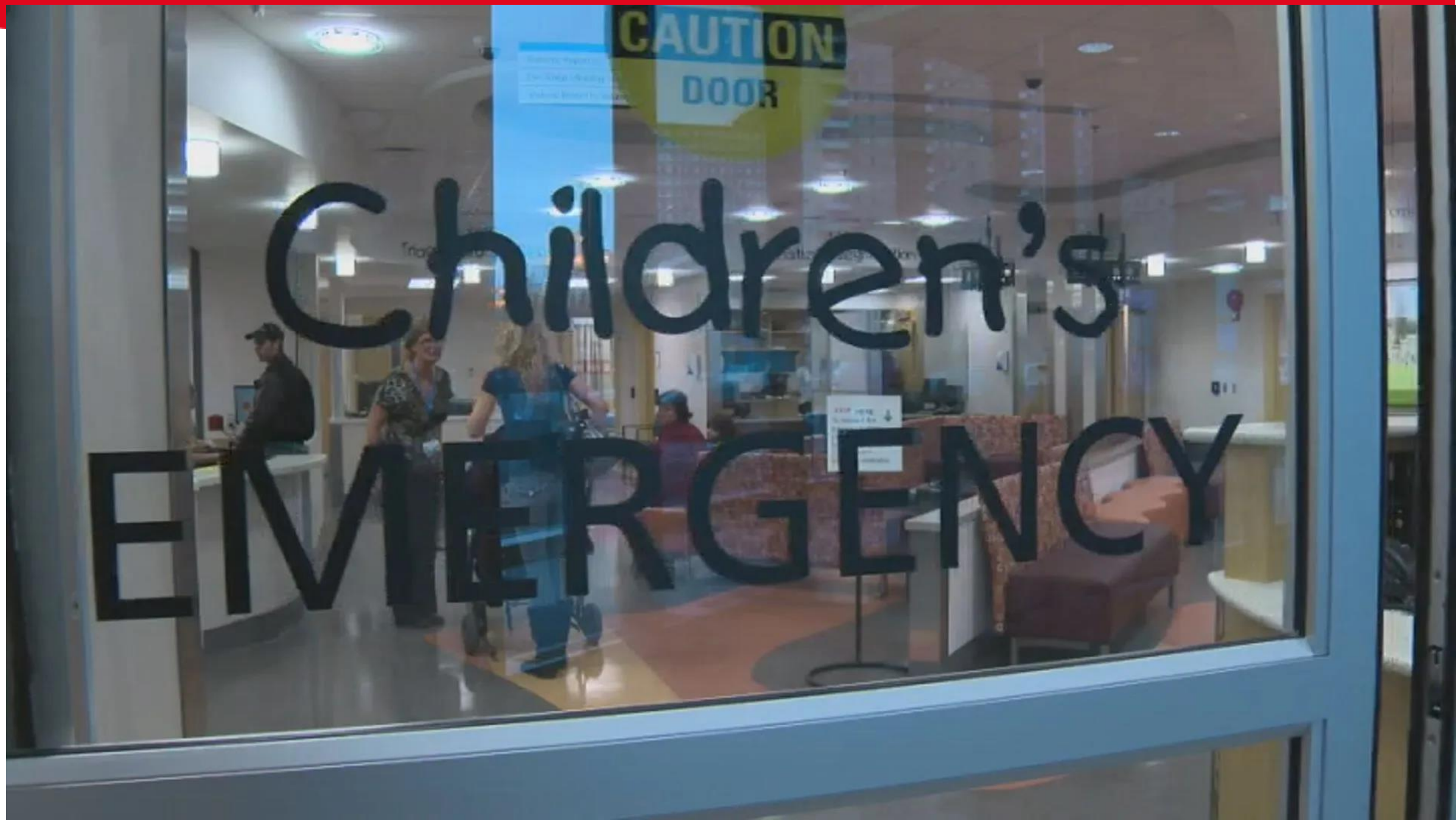
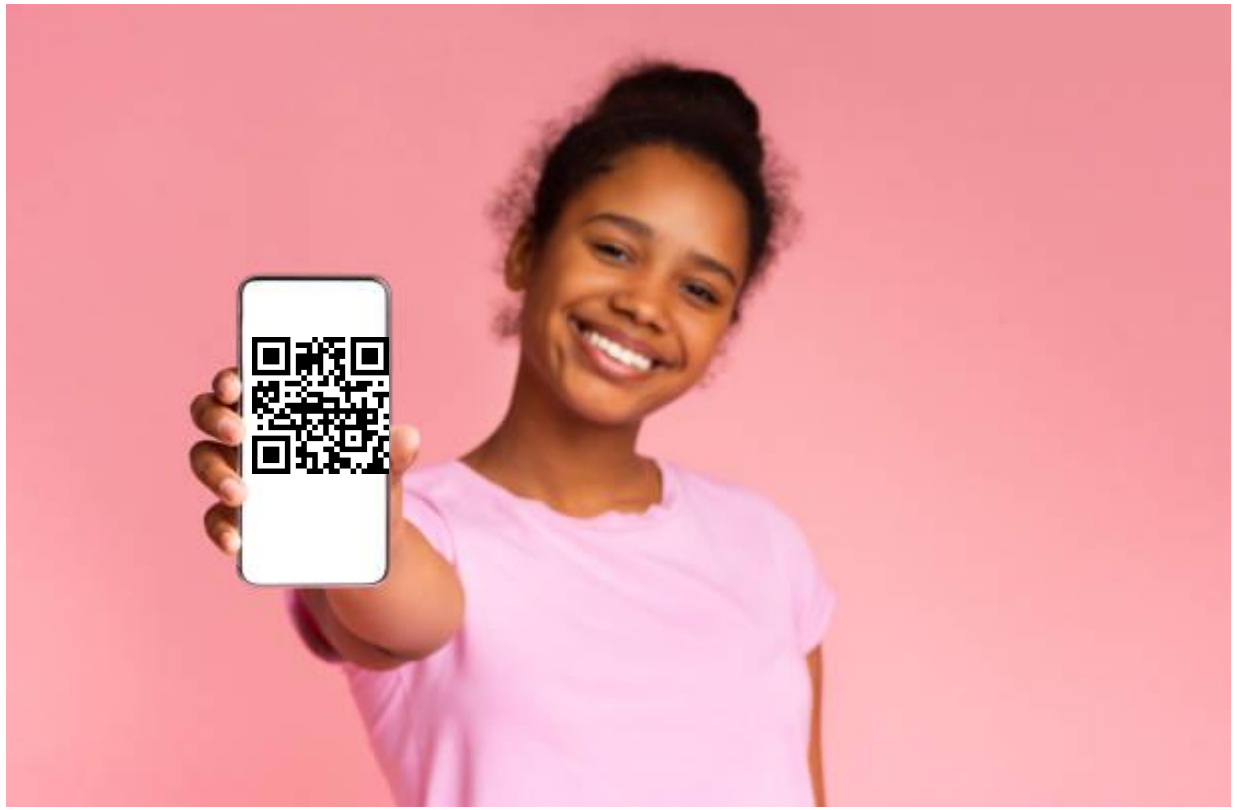

CAUTION
DOOR
Children's
EMERGENCY



- Emergency Providers
- Pediatrician
- Personal Rare Disease Physician
- World Expert in Their Rare Disease

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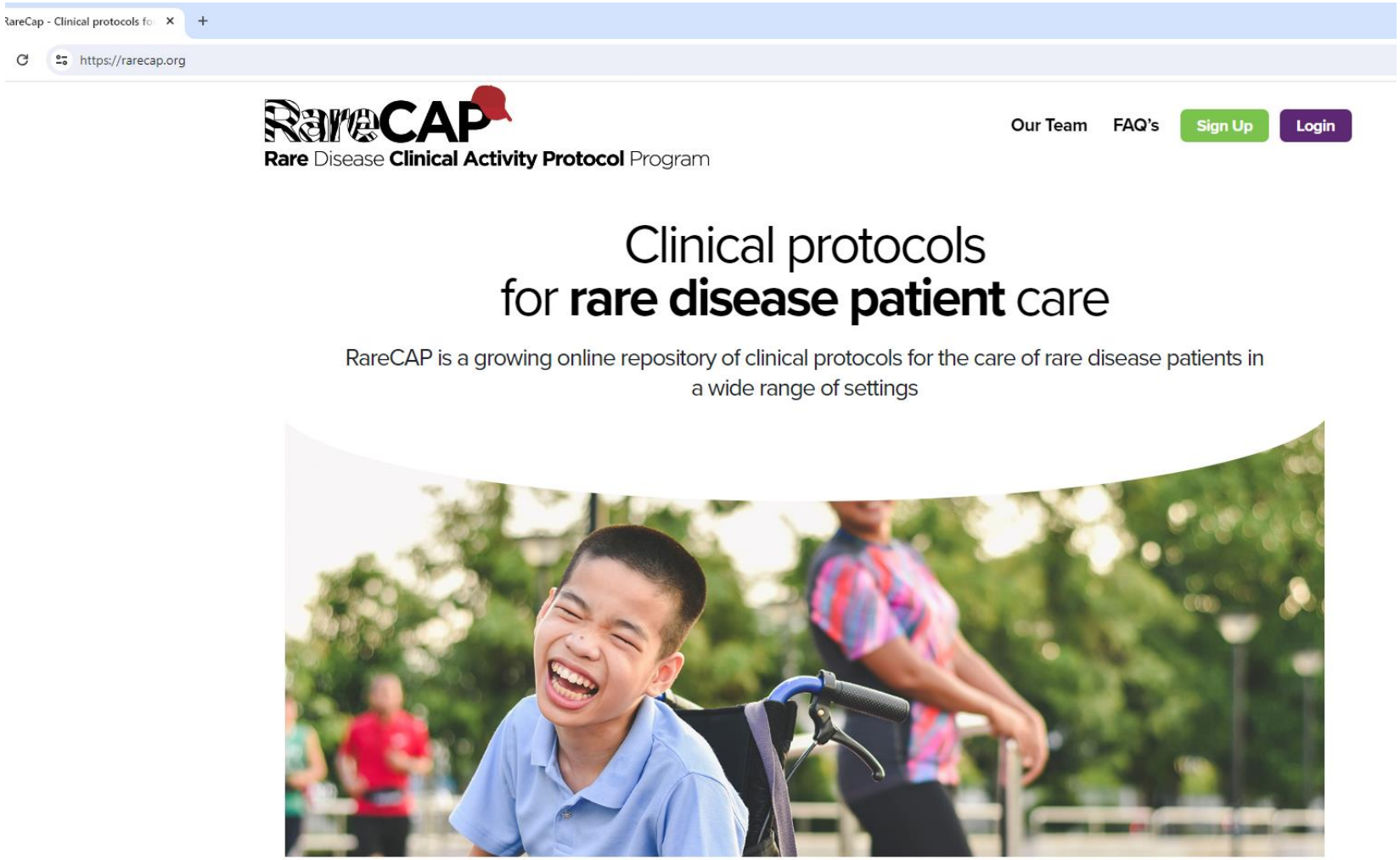
How Can We Support Primary Care and Urgent Care?



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Rare Disease Clinical Activity Protocol Program

guest [logout]

Search Diseases

Tay Sachs & Sandhoff Disease [Published: 2023-10-30 12:54]

Description:
A lysosomal storage disorder in which sphingolipids accumulate and lead to a progressive disorder affecting the nervous system and other organ systems. Infantile, juvenile, and adult forms have been described. Infantile and Juvenile forms lead to early death following progressive neurological disease. Late onset Tays Sachs (LOTS) can have symptoms as early as the second decade of life with lifelong progression, often without lethality.

Resources:

Owner(s): Jennifer Micham
Collaborator(s): Debra Regier

Alternate Disease Names:
GM2 gangliosidosis, TSD

Select a 'care setting' below to view topics (at right):

- Diagnosis
- Acute Management
  - Emergency
    - Hypotension
    - Swallowing Difficulties
    - Nausea/Vomiting
    - Altered Mental Status
    - Menstrual bleeding
    - Airway Management
  - Specialists/Systems
  - Therapies
    - Speech and Language Therapy
    - Physical Therapy
    - Medications - Contraindicated
  - Mental Health Care
- Non-Medical Setting
- Special Situations

Medications - Contraindicated

Disease Specific Scenario
In Tay Sachs and Sandhoff disease, use of antipsychotics has been associated with disease progression. Thus, currently these are considered contraindicated in this patient population.

Actions with Disease Specific Care Points
Antipsychotic medications (i.e. haloperidol, risperidone, chlorpromazine) should be avoided.
- Antidepressants and antiaxoltyics have been used successfully.

Disease Specific Scenario
In Tay Sachs and Sandhoff disease, use of antipsychotics has been associated with disease progression. Thus, currently these are considered contraindicated in this patient population.

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Primary Care 4 Hour CME

THANK YOU

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