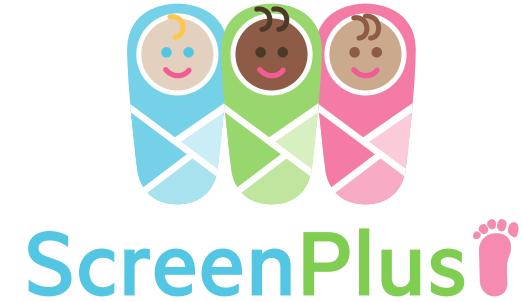
Update from the NPC Newborn Screening Initiative

Allison May Rosen
3D Communications for Firefly Fund

NNPDF Family Support & Medical Conference
July 12, 2020

Key Initiatives Linked to Meeting Recommended Uniform Screening Panel Criteria

RUSP Criteria	Firefly Fund Initiatives
→ Validated screening test acceptable sensitivity, specificity →Labs' ability to perform test	→NBS Pilot Study →Supporting ScreenPlus
→ A public health problem, without easily identified symptoms at birth →Significant risk if babies not treated promptly	→Clinical Roundtable →Demonstrating that treating earlier is better for health outcomes
→ Benefits outweigh risks and burdens of screening and treatment	→Public Health Benefits →Identifying how intervening earlier can benefit public health



A Comprehensive, Flexible, Multi-Disorder Newborn Screening Program

Melissa Wasserstein, MD

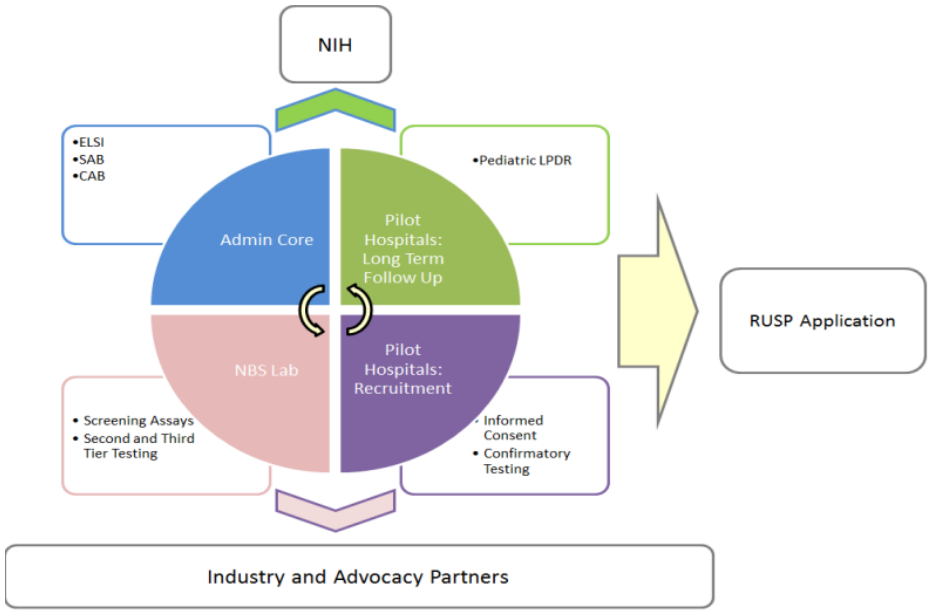
NNPDF 2020

The Children's Hospital at Montefiore

THE PEDIATRIC HOSPITAL FOR:
EINSTEIN
Albert Einstein College of Medicine
OF YESHIVA UNIVERSITY

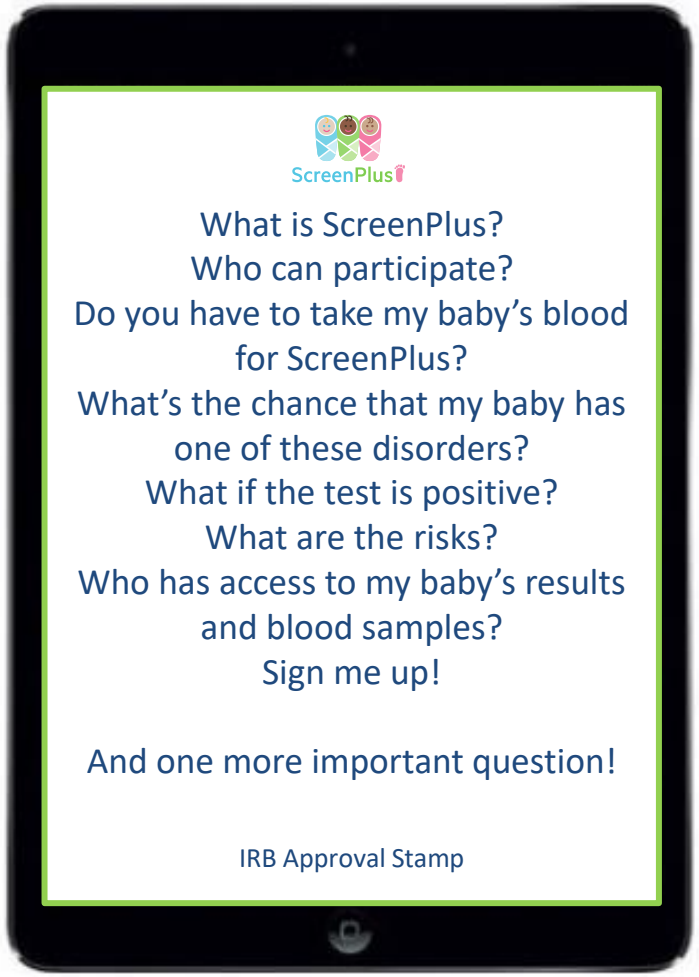
Goals of ScreenPlus

- Evaluate the analytic and clinical validity of multi-tiered newborn screening assays, and define disease incidence in a diverse population
- Determine the impact of NBS on clinical outcome through longitudinal follow up of true positive infants
- Examine the ethical, legal, and social issues (ELSI) associated with screening newborns for complex disorders



Anticipated Recruitment and Timing

- ~ 175,000 babies from 8 high birth rate, ethnically diverse pilot hospitals over 5 years will be enrolled, assuming 73% consent rate*
- One-on-one e-consenting model
  - We are making contingency plans for virtual recruitment in case of COVID-19 resurgence
- Initial start date for live recruitment (May 2020) delayed until fall 2020 because of COVID-19



*Wasserstein, MP, Caggana M, Bailey SM, Desnick RJ, Edelmann L, Estrella L, Holzman I, Kelly NR, Kornreich R, Kupchik SG, Martin M, Wasserman R, Yang A, Yu C, Orsini JJ. The New York Pilot Newborn Screening Program for Lysosomal Storage Diseases: Report of the First 65,000 Infants. Genet Med 2018 Aug 10.

ScreenPlus Disorders

- Criteria to be on ScreenPlus Panel
  - A DBS screening assay that can be multiplexed, and that is high-throughput, reasonably priced, and has had positive baseline validation studies;
  - Significant morbidity or mortality if untreated;
  - A pediatric phenotype; and
  - FDA approved treatment(s), or treatment(s) currently in clinical trial.
- Panel is fluid; disorders may be removed if added to RUSP, or added if meet criteria

ScreenPlus Panel	
ASMD	Acid sphingomyelinase deficiency
CLN2	Ceroid lipofuscinosis type 2
CTX	Cerebrotendonous xanthomatosis
Gaucher	Gaucher disease
Fabry	Fabry disease
LAL-D	Lysosomal acid lipase deficiency
MLD	Metachromatic leukodystrophy
MPS II	Mucopolysaccharidosis type II/ Hunter
MPS IIIB	Mucopolysaccharidosis type IIIb/ Sanfilippo IIIb
MPS IVA	Mucopolysaccharidosis type IVa/Morquio IVa
MPS VI	Mucopolysaccharidosis type VI/ Maroteaux Lamy
MPS VII	Mucopolysaccharidosis type VII/ Sly
NPC	Niemann Pick C

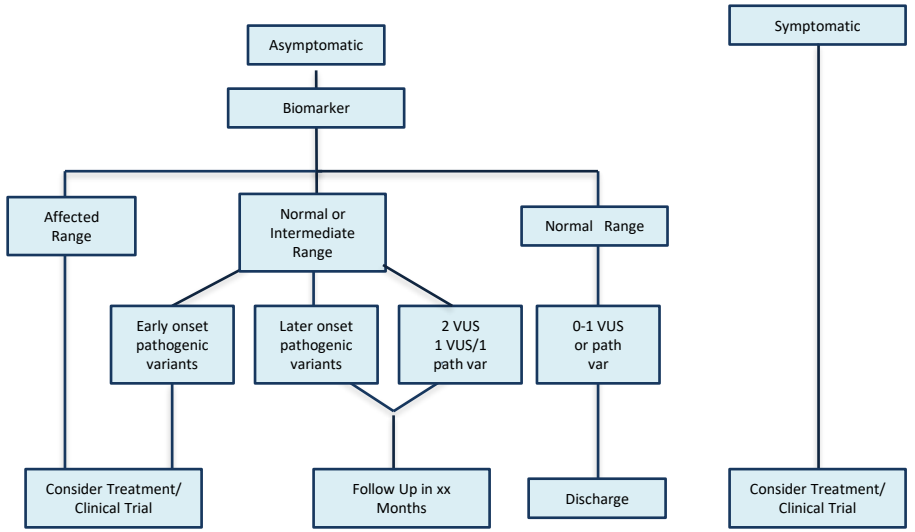
Using ScreenPlus to Enhance the Accuracy of Screening

Disorder	First Tier	Second Tier	Third Tier
ASMD	ASM	Lyso SM	DNA
CLN2	TPP1	-	DNA
CTX	Bile tetrol glucoronide	-	DNA
Fabry	GLA	Lyso Gb3	DNA
Gaucher	GBA	Lyso Gb1	DNA
LALD	LAL	-	DNA
MLD	Sulfatides	Enzyme	DNA
MPS II	I2S	DBS GAG	DNA
MPS IIIb	NAGLU	DBS GAG	DNA
MPS IVa	GALNS	DBS GAG	DNA
MPS VI	ARSB	DBS GAG	DNA
MPS VII	GUSB	DBS GAG	DNA
NPC	Bile Acid B	COT	DNA

- Screening assays will be performed at the NYS Department of Health using samples from the already-collected NBS filter paper
- We will use at least two tiers per disorder in an effort to
  - Reduce false positives?
  - Predict phenotypic severity?

Long Term Follow Up

- We will establish standardized follow up protocols and data collection forms for each disorder
  - These are being developed with help from ScreenPlus advisory boards
  - Algorithms will include guidelines for treatment referral or access to clinical trials
- Longitudinal data on affected and indeterminate children will be collected uniformly across sites, used to evaluate impact of early diagnosis on outcome



In Conclusion

- ScreenPlus is largest multi-disorder, consented, NBS pilot program in US
- It is a comprehensive program that extends from screening assay development to long term follow up and treatment
- The multi-tiered approach may improve NBS accuracy
- It includes uniform data collection that may be used to support RUSP applications

Acknowledgements

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Others, Pending Contract Completion

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NPC Clinical Roundtable – Consensus Building Regarding Timing for Treatment Initiation Following NBS

- Successful RUSP applications require research to support need for NBS
  - Why is earlier intervention a clinical benefit for patients?
  - How soon after birth must treatment be initiated to be effective?
  - How will earlier intervention benefit public health?
- Initial 2019 meeting prompted initiation of a “Sibling Study”

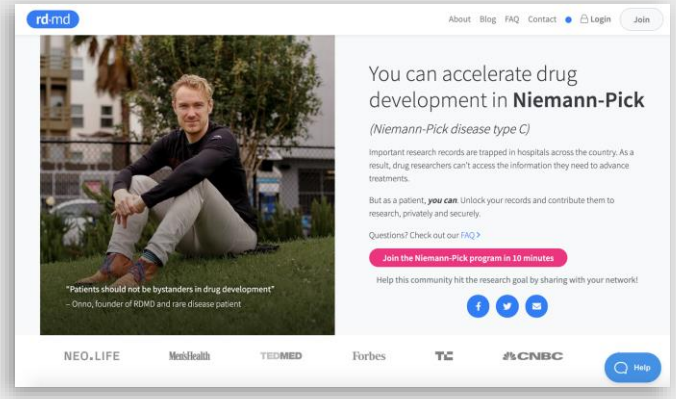
“Sibling Study” to Demonstrate Significance of Intervening Earlier for Improved Health Outcomes

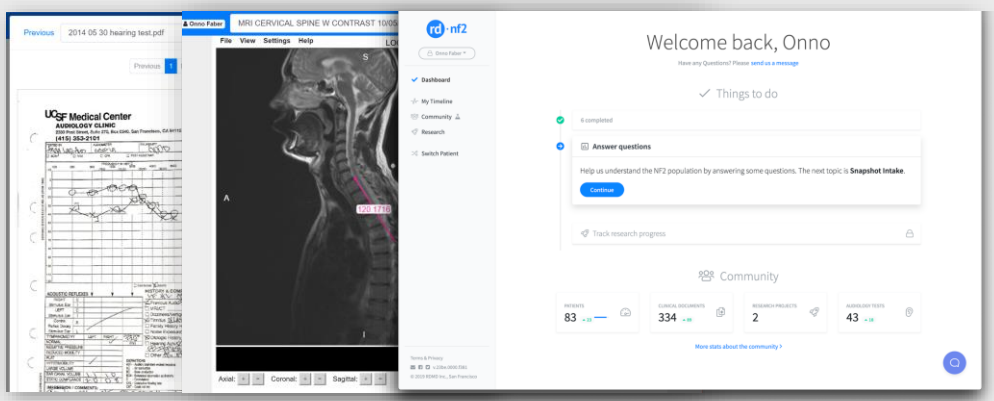
- Leading NPC experts believe families with multiple affected children may show differences in outcomes based on earlier intervention
  - One child diagnosed ***following*** onset of symptoms
  - Diagnosis triggers NPC testing of another child
    - Diagnosed ***before*** onset of visible symptoms
- Possible evidence demonstrating differential outcomes based on timing of intervention
- Proving importance of screening for NPC at birth, and criticalness of earlier intervention

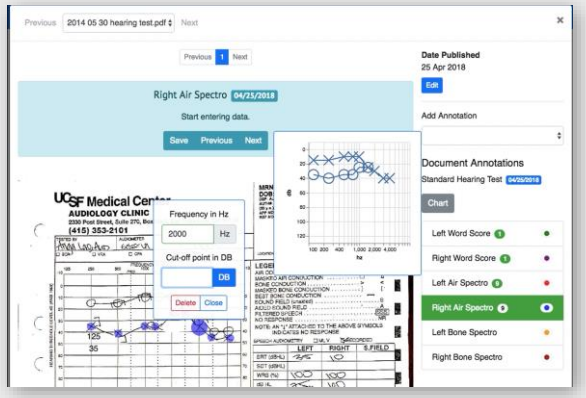
Partnership with RDMD Can Accelerate NPC Research

rd·md

1	2	3	4
RDMD hosts an online platform for the NPC community, at no cost to patients & families.	Parents accept RDMD's consent & authorize RDMD to retrieve their children's records from healthcare facilities.	RDMD retrieves all records on patients' behalf. Each family can easily access all their records in a secure account.	RDMD extracts de-identified medical data in a structured way to speed research.







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NPC Experts Will Analyze De-Identified Data

- Led by Newborn Screening Working Group Clinical Leaders: Elizabeth Berry-Kravis, Rush University Medical Center; Marc Patterson, Mayo Clinic; Denny Porter, NIH
- Analysis to help determine
  - How closely course of disease is similar
  - What affect timing of intervention has on disease progression
- Examples of clinical variables for possible analysis (if available)
  - Diagnosis and symptomatic onset
  - Genetic testing and labs
  - Seizure history
  - Swallowing
  - Cognitive functioning
  - Hearing loss
  - Medications

NOTE: This slide **NOT** shown at NNPDF. Hope to include in future presentations.

Participating in NPC Sibling Study: Involving Families with Multiple Children Affected with NPC

- Recruitment goal: 30 sibling pairs/groups in the US and Canada
- Sign-up process:
  - Visit rdmd.com/npc
  - 10–15 minutes per child to enroll
  - Parents can sign up multiple children under one master account
- Families can access their children's medical records and participate in research at no cost

*Note: Families of **all individuals with NPC in the US & Canada** can contribute to other research efforts through the broader RDMD NPC Research Program*

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2020 Expanded Stakeholder Support

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DART Dana's Angels Research Trust ...aiming to cure Niemann-Pick Type C

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Inpda International Niemann-Pick Disease Alliance

NP CANADA Niemann-Pick Canada

np uk

Johnathan's Dreams

K4K KURE for KAMRYN

Australian NPC Disease Foundation Inc

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Marc Patterson
- Mayo Clinic

Dan Ory and Xuntian Jiang
- Wash University in St. Louis

Denny Porter
- National Institutes of Health

Cindy Powell
- University of North Carolina

Ray Wang
- Children's Hospital of California

Melissa Wasserstein
- Children's Hospital at Montefiore

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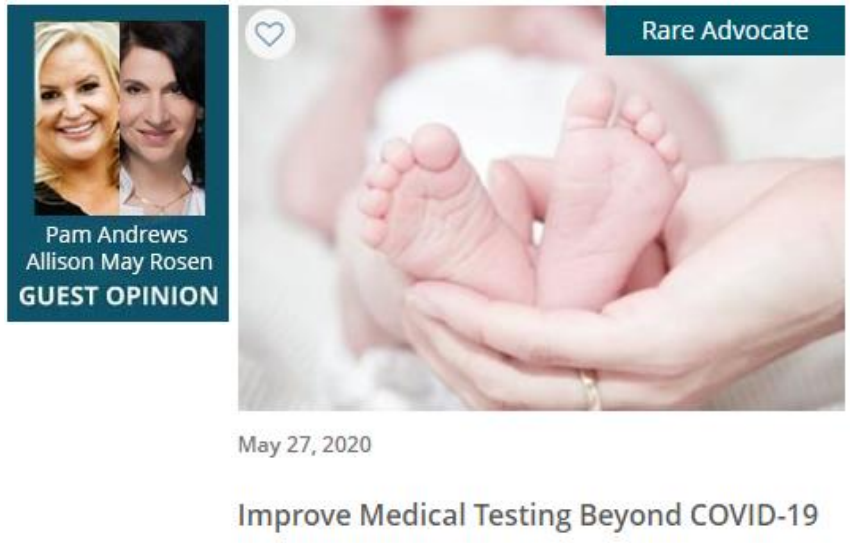
Continuing to Generate Awareness

- World Orphan Drug Conference – August, Virtual
- NPC NBS Clinical Roundtable – November, Virtual
- NPC NBS Annual Stakeholder Meeting – November, Virtual

- Check Out: *RARE Daily* column on parallels between testing for covid-19 and NBS testing for NPC



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