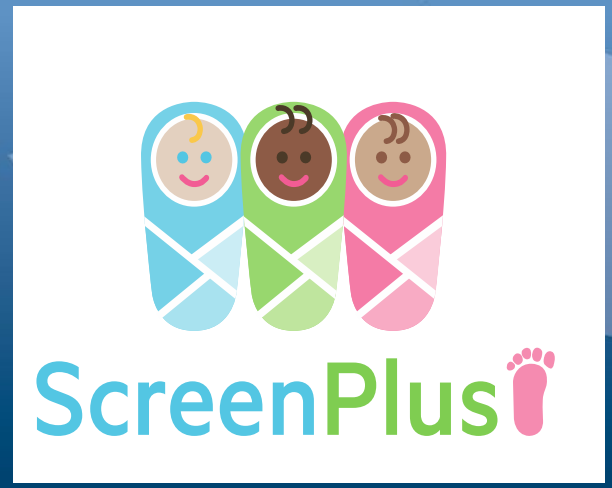

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THE PEDIATRIC HOSPITAL FOR:
EINSTEIN
Albert Einstein College of Medicine
OF YESHIVA UNIVERSITY

	Key Opinion Leader/ Consultant Fees	Travel Reimbursement	Research Support
Sanofi Genzyme	x	x	x
Takeda			x
NNPDF			x
Ara Parseghian Medical Research Fund			x
BioMarin			x
Cure Sanfilippo Foundation			x
Dana's Angels Research Trust			x
Firefly Fund			x
Noah's Hope			x
Orchard Therapeutics			x
PassageBio			x
Sio Therapeutics			x
Travere Therapeutics			x
Ultragenyx			x

ScreenPlus Support

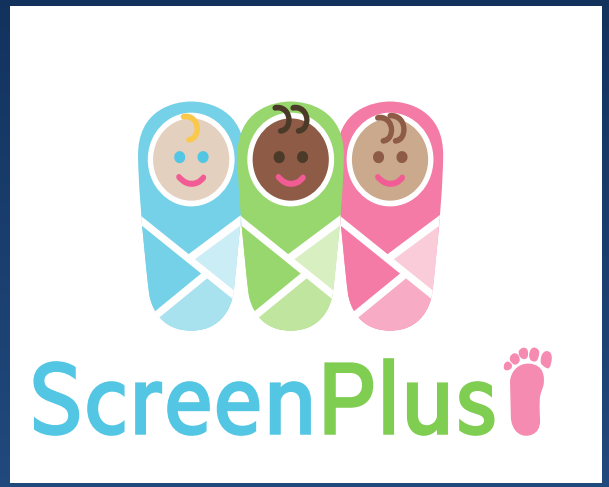
ScreenPlus: A Comprehensive, Flexible, Multi-disorder Pilot Newborn Screening Program

Contents

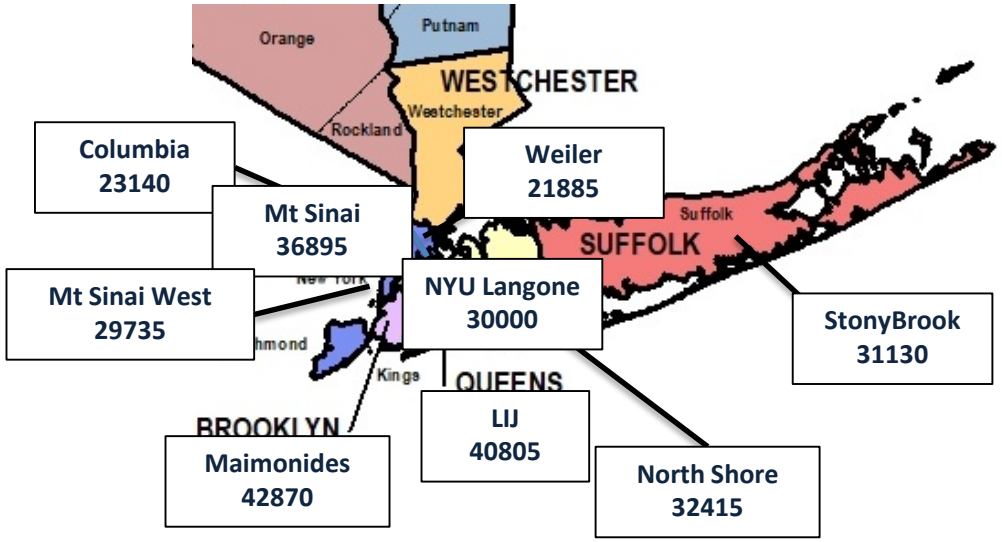
- Overview and logistics of pilot screen
- Programmatic infrastructure
- ELSI studies
- Current status

ScreenPlus

Overview and Logistics



Pilot Hospitals and Recruitment



Pilot Hospital Criteria

- High birth rate
- Ethnically diverse community
- NYS NBS referral site

Recruitment Goal

- 175,000 babies over five years
- Total estimated births: ~290,000
- Estimated consent rate: ~73%

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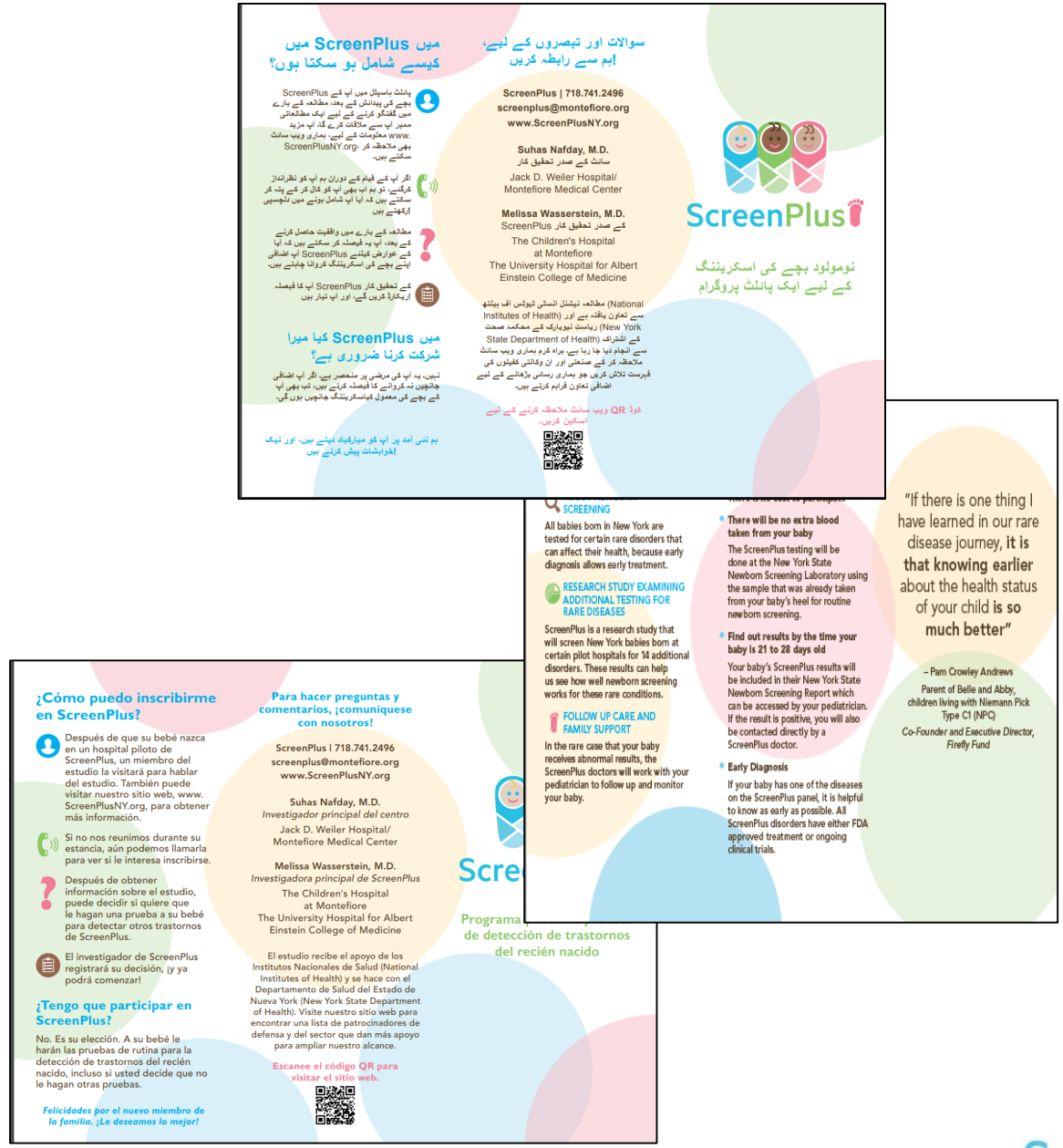
Informed Consent

- Direct, in person one-on-one conversation between recruiter and parents shortly after birth
- Coordinators are bilingual and brochures are translated into 8 languages
- Parental consent automatically creates RedCap form and emails parents a copy of the consent/brochure



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ScreenPlus Panel

- Panel is fluid; disorders may be removed if added to RUSP, or added if meet criteria

- 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.

Initial Panel	
ASMD	Acid sphingomyelinase deficiency
CLN2	Ceroid lipofuscinosis type 2
CTX	Cerebrotendonous xanthomatosis
Gaucher	Gaucher disease
GM1	GM1 gangliosidosis
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

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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
GM1	GM1	-	DNA
LALD	LAL	-	DNA
MLD	Sulfatides	ARSA	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

- We will use at least two tiers per disorder prior to call out
- Can biomarkers and DNA testing on the DBS enhance accuracy?
  - Reduce false positives?
  - Predict phenotypic severity?

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Longitudinal follow up

- For new and complex disorders, capturing long term follow up data is critical
  - NBS lab may not be able to assess accuracy of their assay if/until patient expresses phenotype
  - Confirmatory testing results may be unclear until patient does or does not express phenotype
  - Children with later onset disease usually do not need immediate treatment; inability to predict if/when obligates monitoring
  - How do we know if there is a benefit to early detection?

MLD, Positive and Uncertain, 0-36 m

	Baseline (~3-4 wks of age)	Q 4 m
Neuro exam	x	x
Brain MRI*	x	x
U sulfatides	x	x
Mullen Dev Assessment	x	x
NCV		x
Ophthalmologic Exam		x
VEP		x
BAER		x
Clinical feeding assessment		x

Indications to Refer for Clinical Trial or BMT

Genotype:	Known late infantile variants (refer to leukodystrophy center immediately)
Clinical status:	Reproducible NCV or MRI change abnormalities Worsening in clinical status

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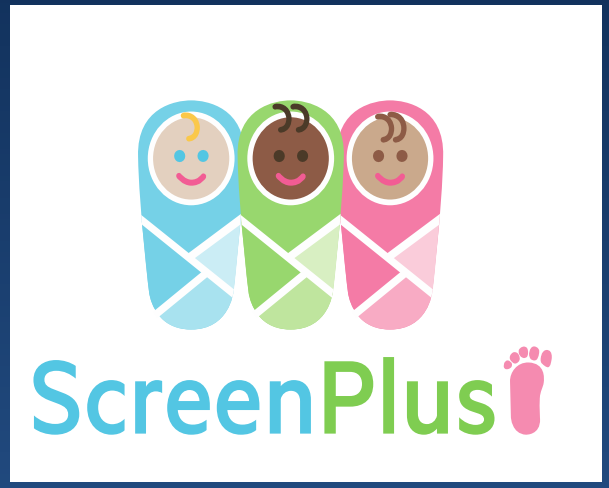
Infrastructure



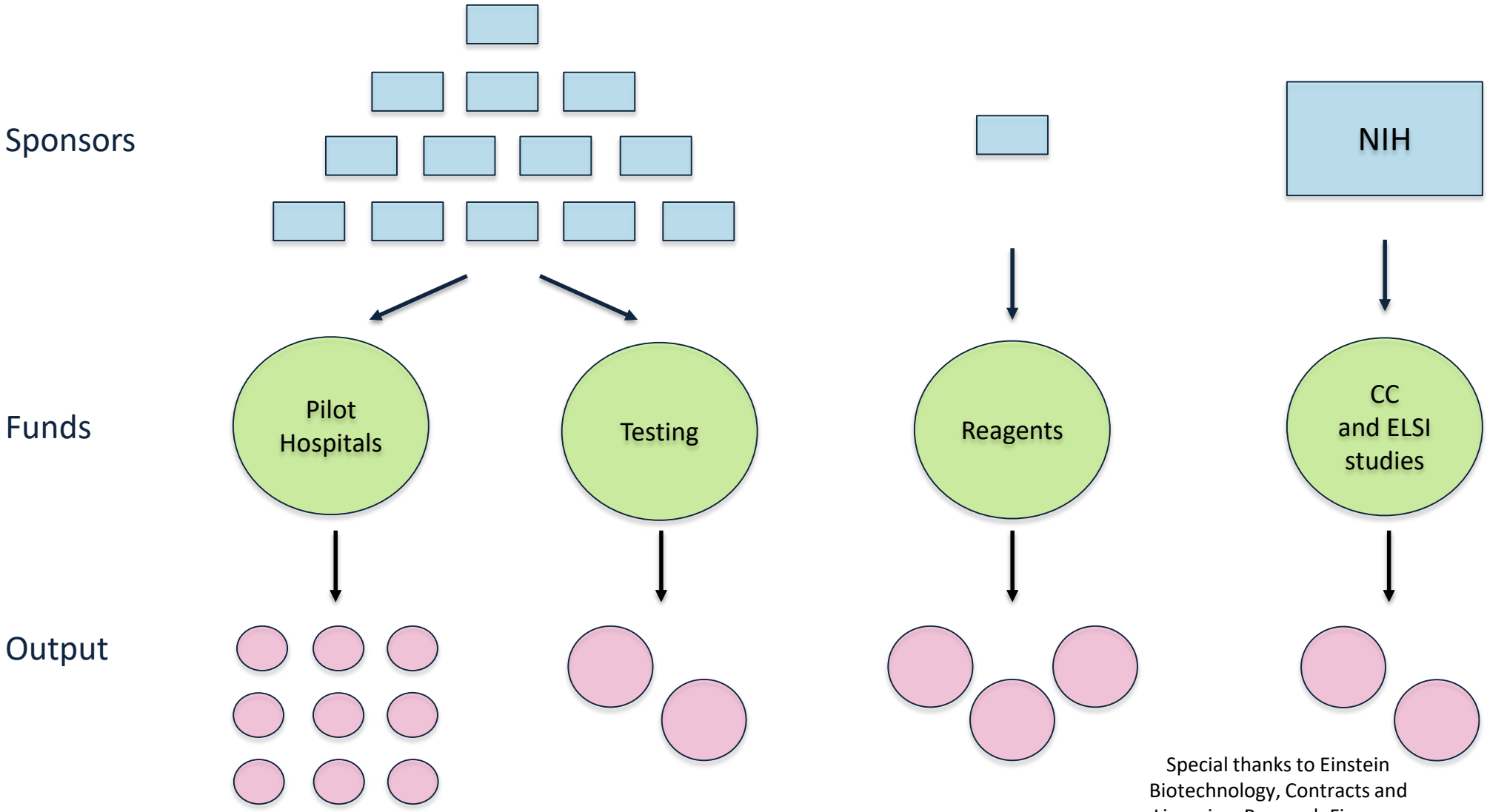
Cost-Sharing

- We have created a unique cost-sharing infrastructure with NIH, Industry Sponsors and Patient Advocacy Groups

- All parties have a vested interest in NBS for a particular disorder(s) because they have an FDA approved therapy, are sponsoring a clinical trial, or are advocating for a RUSP nomination.

- This cooperative plan will streamline costs, while enabling the program to function at maximal efficiency

ScreenPlus Organizational and Financial Infrastructure



Special thanks to Einstein Biotechnology, Contracts and Licensing, Research Finance, and Legal

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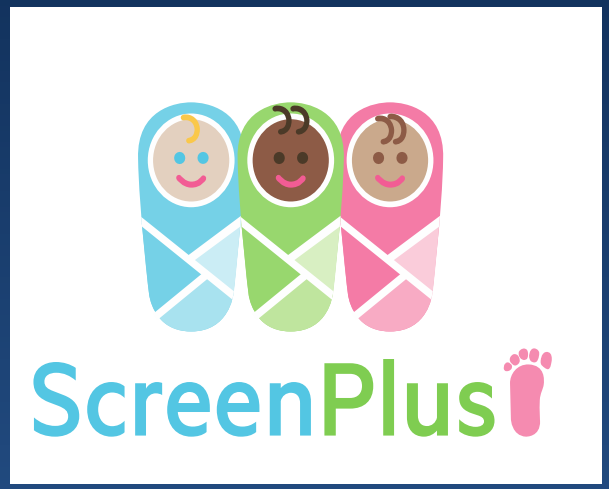
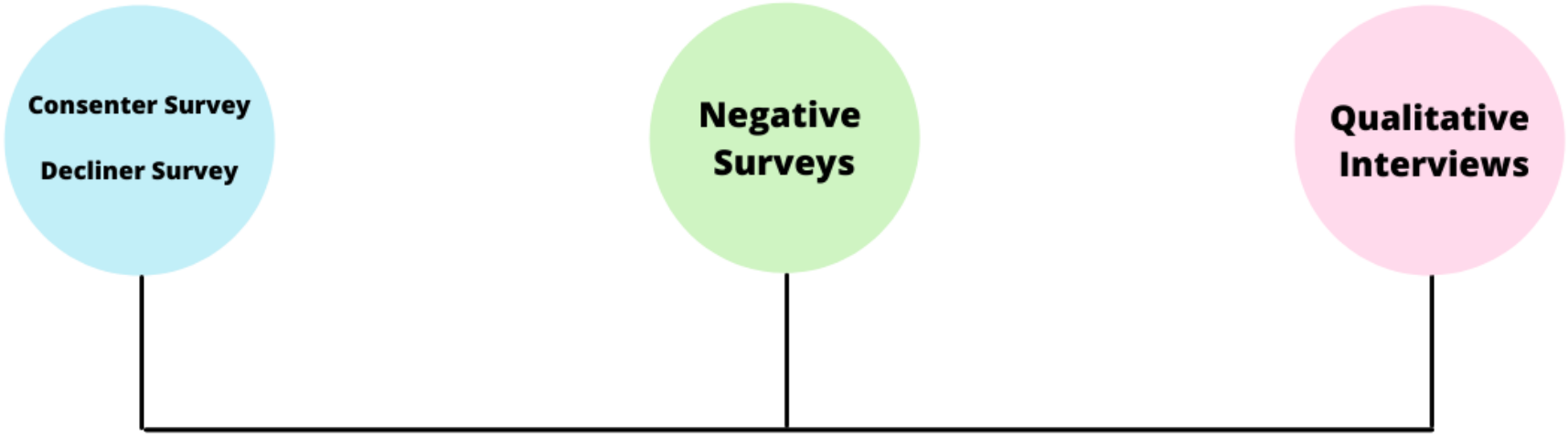
Ethical, Legal, and Social Implications Studies



ELSI Surveys/Interviews



Immediately after birth

- Consent process
- Understanding of information
- Reason for participating/declining
- Sociodemographic factors

Approx. 1 month after results

Opinions about:

- NBS for expanded panel of disorders
- Whole genome sequencing
- Informed consent for NBS

Approx. 6 months - 2 years after results

- Newborn screening narrative
- Impact of screening on mental health, finances, relationship w partner, other children, etc.
- Parent bonding
- Support systems/resources needed

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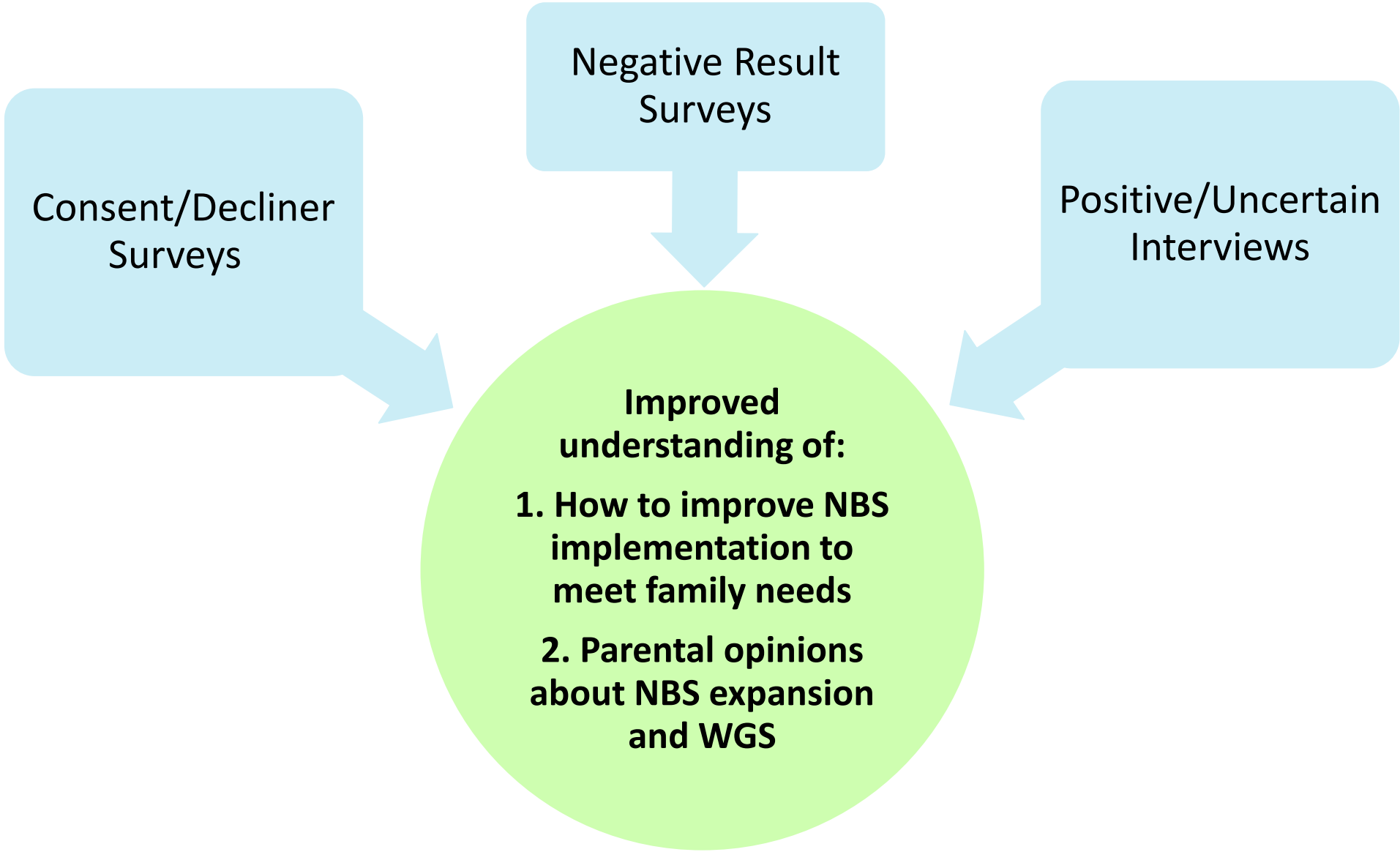
Consent/Decliner Surveys
Negative Result Surveys
Positive/Uncertain Interviews
Improved understanding of:
1. How to improve NBS implementation to meet family needs
2. Parental opinions about NBS expansion and WGS

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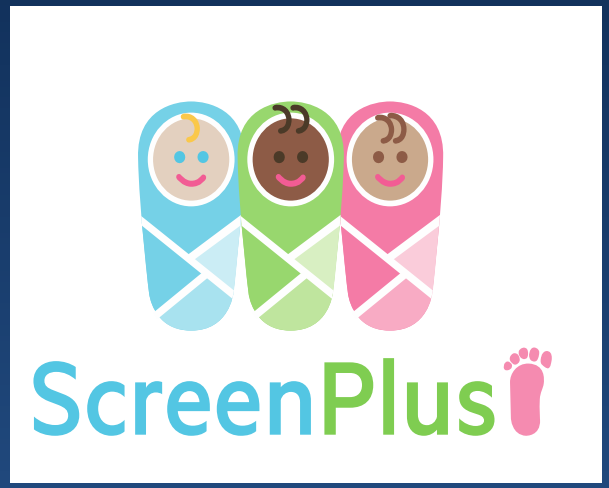
Current Status



May 10, 2021: First Baby In!

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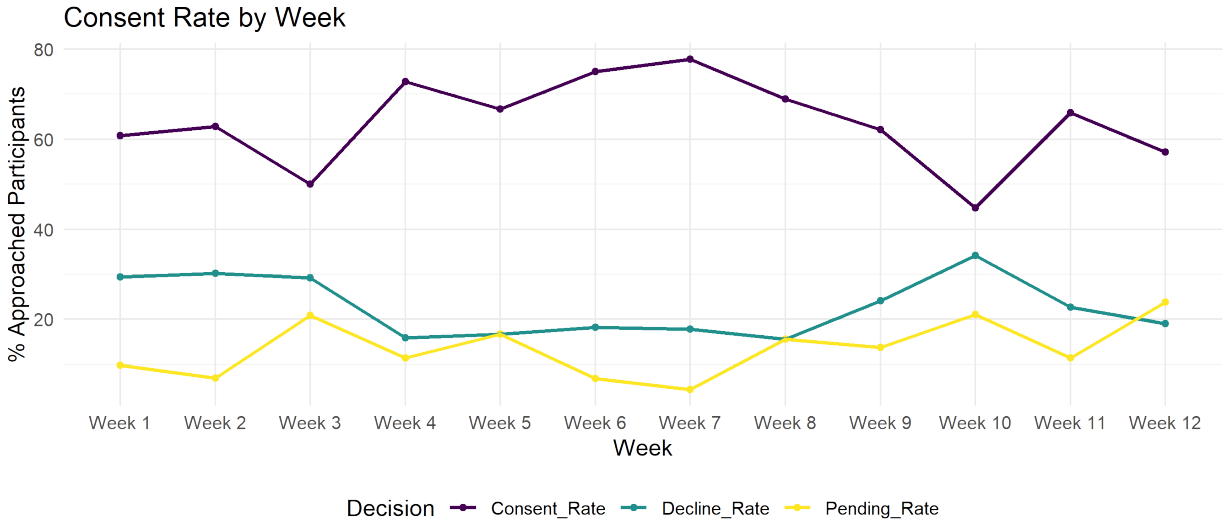
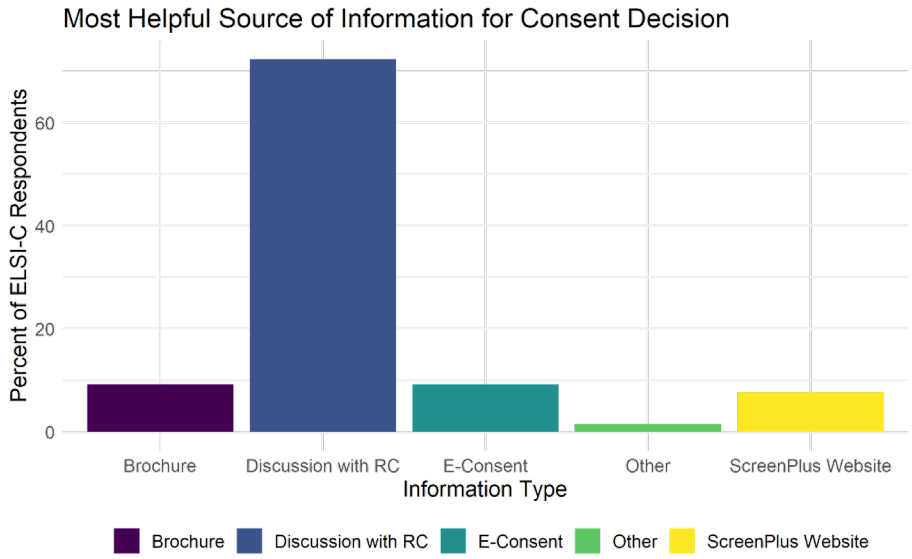
Early Recruitment Experience

- Parental surveys about consenting experience
  - Amount and clarity of information?
  - What materials did you use?
  - How was the e-consent?
  - What was the most helpful in your decision to participate?
  - What was the main reason why you participated?
  - Demographic information
- Decliner surveys
  - What were your reasons for choosing to not participate in ScreenPlus?
  - Demographic information





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Next Steps

- We are in the process of contracting with other pilot hospitals
  - We hope to have other hospitals live within next few months
- Based on early feedback:
  - We are continuing to refine recruitment script and materials
  - We are developing passive e-consent for discharged parents to use at home
- ELSI surveys and qualitative studies
  - We are seeking feedback from our Community Advisory Board on study materials and will continue to refine our instruments to ensure they are appropriate for parents

ScreenPlus

Acknowledgements

ScreenPlus Team

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