New Disorders Workgroup Winter Webinar Series Part Three

On the Horizon: A Review of Up-and-Coming Disorders and the Future of the RUSP

Data Tools and Resources from the Newborn Screening Translational Research Network

Amy Brower, PhD
NBSTRN - Co-Principal Investigator
ACMG – Associate Project Director
abrower@acmg.net

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Objectives

- At the conclusion of the program, the participant will be able to:

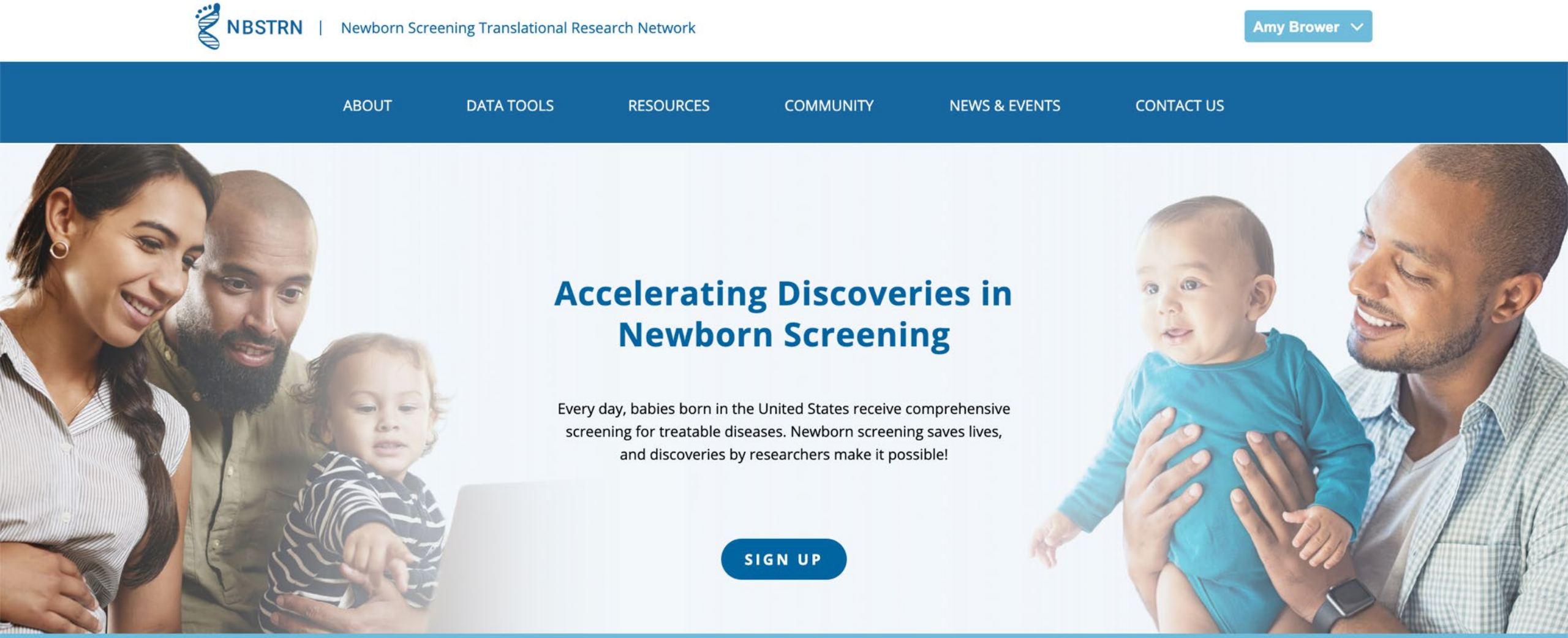
✓ • Review disorders on the horizon for RUSP nomination

✓ • Describe current research and pilot activities around these disorders

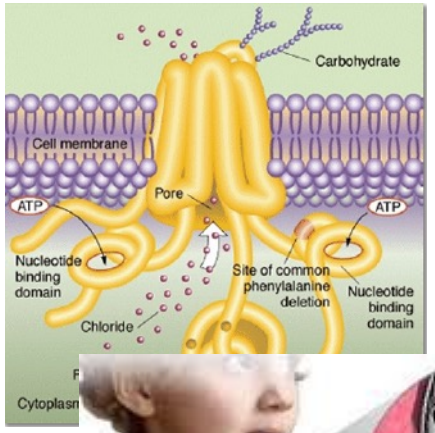
  • Review Metachromatic Leukodystrophy (MLD) RUSP nomination activities and ScreenPlus pilot activities

✓ • Discuss future recommendations for RUSP nomination

New Website Featuring Updated Resources and New Data Tools

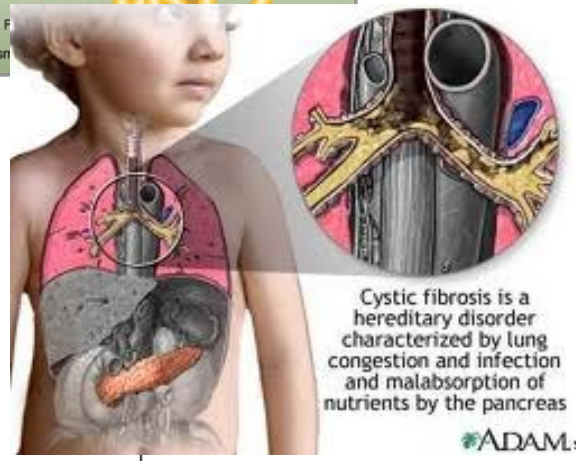


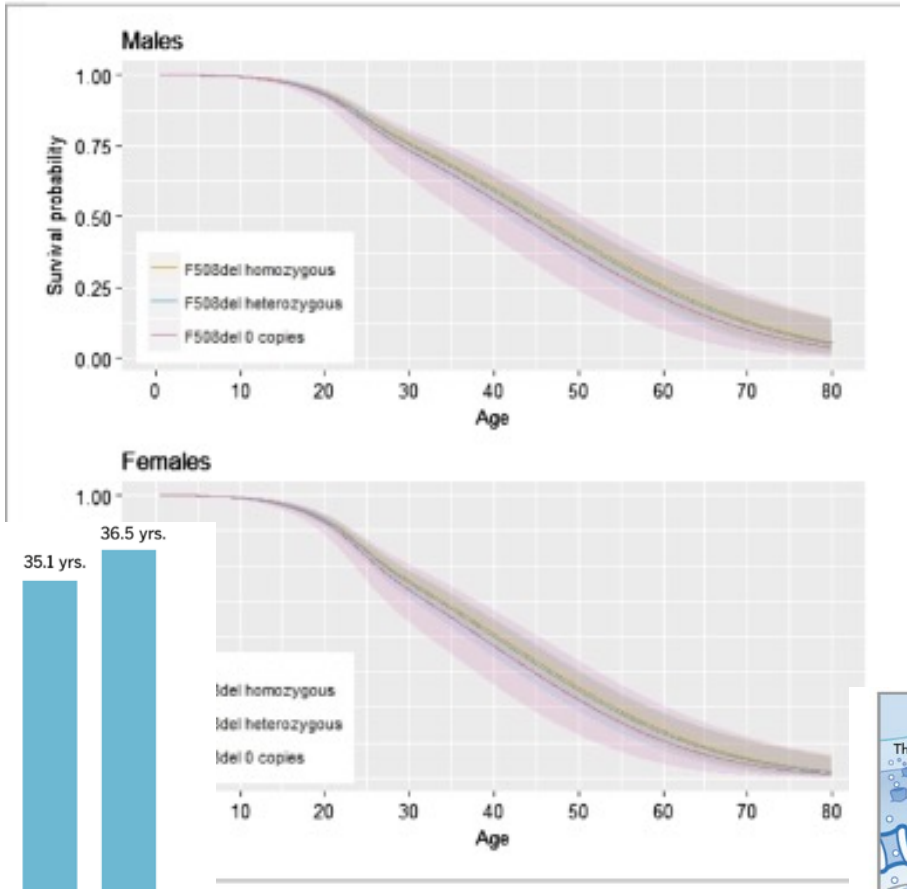
Evidence Based Expansion

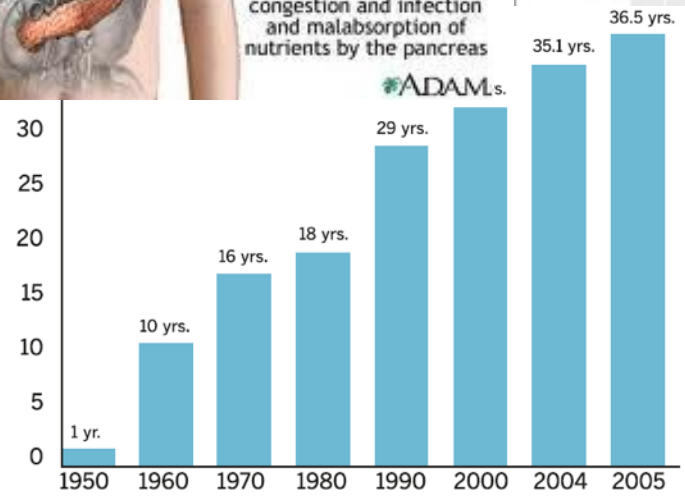


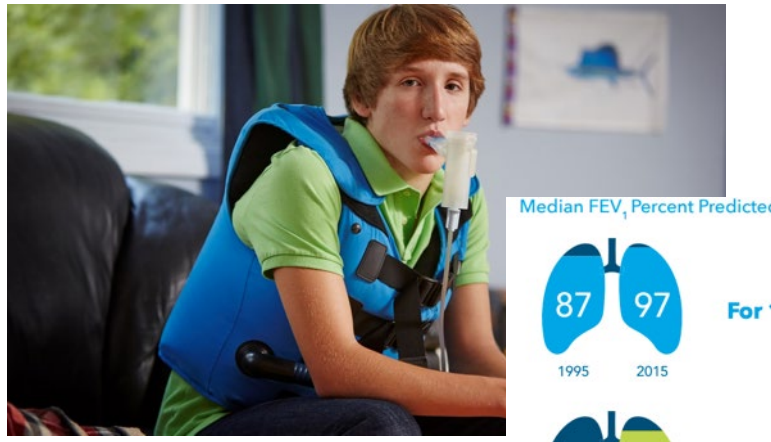
"Woe to the child which kissed on the forehead tastes salty. He is bewitched and will soon die."

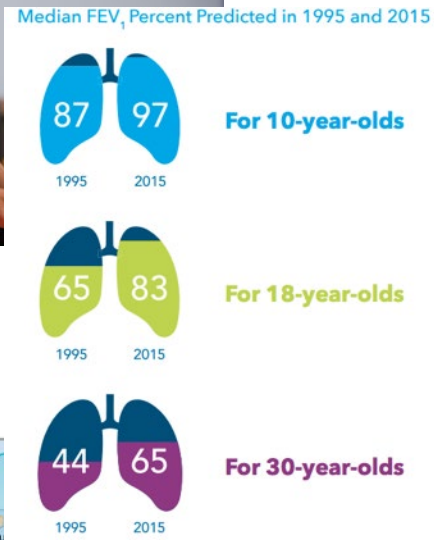
Northern European Folklore

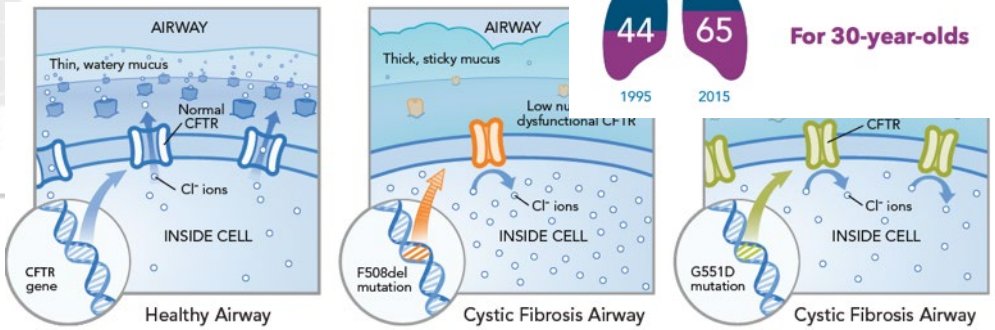




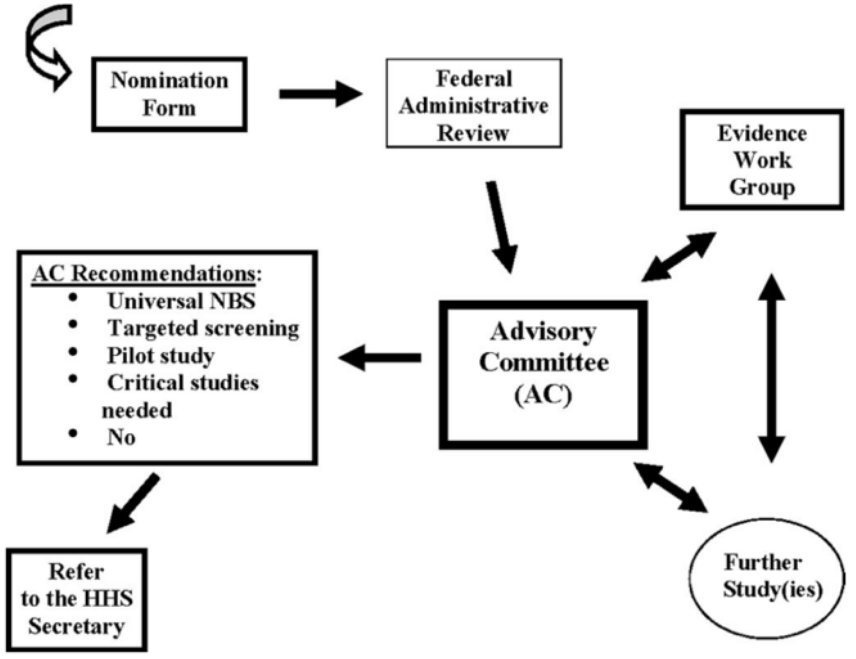








Recommended Uniform Screening Panel (RUSP)



SCID	Pompe	Niemann-Pick	Fabry	SMA	Hemoglobin H	Hyperbilirubinemia	CCHD	22q11 Deletion	MPSI	X-ALD	GAMT
9/07	10/07; 2/12	12/07	12/07	6/08; 8/16	4/09	7/09	10/09	01/11	2/12	8/12	5/15
1/10	5/13	Not Approved	Not Approved	Under Review	Not Approved	Not Approved	9/10	Not Approved	2/15	5/15	Not Approved

Nomination Process and Systematic Evidence Review

Clinical Effectiveness/Net Benefit to Individual/Family	• Magnitude/Strength of Evidence • Certainty of Evidence • Net Benefit of Early Detection, Diagnosis, and Treatment on Individual
Public Health Impact - Population	• Net Benefit of Newborn Screening on Population-level Health
Public Health Impact - System	• Feasibility of Population-based Screening • Readiness of States to Expand Screening • Cost of Expanding Screening

Research Informed by Evidence Review

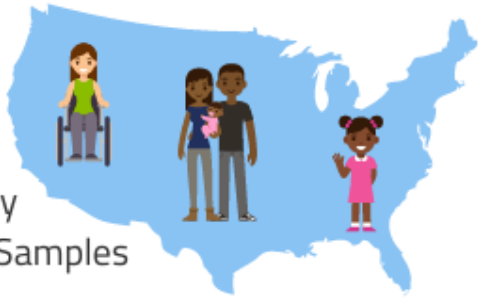
Clinical Effectiveness/Net Benefit to Individual/Family	• Population-Based Pilots • Data Collection – Common Data Elements • Treatment, Intervention, Timing
Public Health Impact - Population	• Published Literature on Health Outcomes • Case Definition • Expert Workgroups • Health Care Team - Subspecialists
Public Health Impact - System	• Analytical and Clinical Validation of Screening and Diagnostic Technology • Survey of NBS Programs

Research

LPDR
Longitudinal Pediatric Data Resource

NBS-CR
NBS Conditions Resource

NBS-VR
NBS Virtual Repository of States, Subjects & Samples



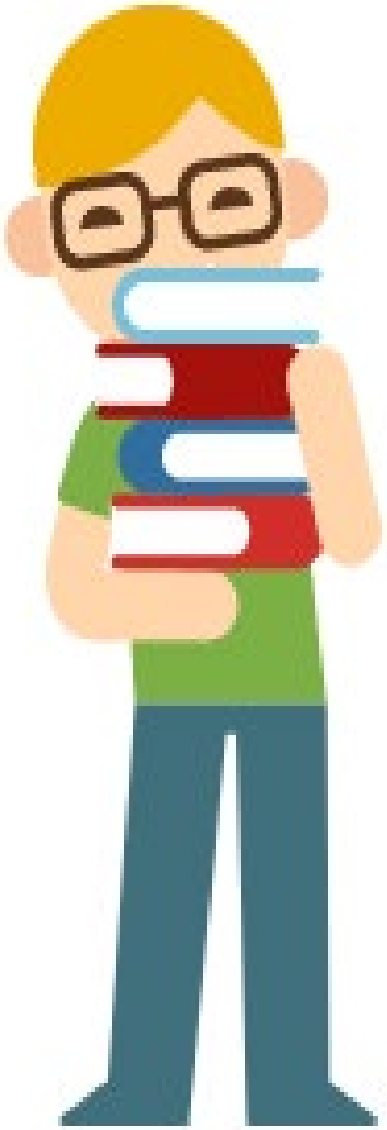
New Membership Site and Updated Tools

- De-identified Case Level Data Dashboards
- Expanded CDE Sets
- Disease Resource for RUSP, Pilot and Candidate Conditions
- State NBS Program Information for Investigators

nbstrn.org

NBS-CR

NBS Conditions Resource



118 Conditions

61 Recommended Uniform Panel (RUSP) Conditions

20 Conditions Screened by States

37 Conditions Identified as Pilot Candidates by NBSTRN

Key information on conditions that are part of, or candidates for newborn screening

MedGen

OMIM

Management

ACMG ACT Sheets

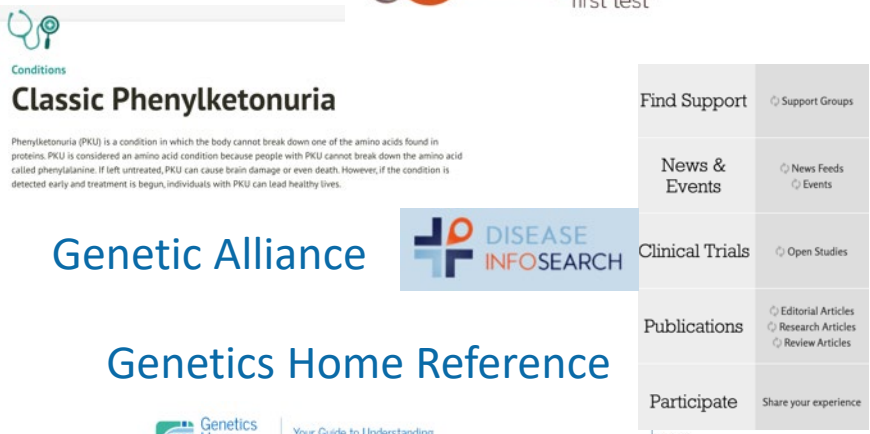
Diagnosis

Clinical Characteristics

NBS-CR

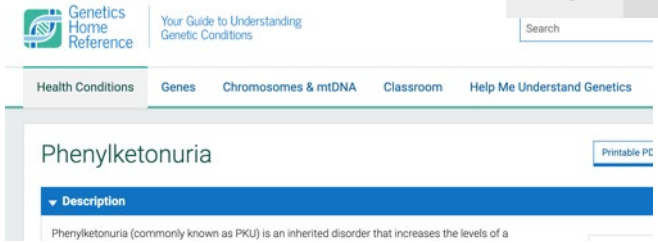
NBS Conditions Resource

Baby's First Test



Genetic Alliance

Genetics Home Reference



RUSP, Pilot and Candidate Disorders

nbstrn.org

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Amy Brower

ABOUT | DATA TOOLS | RESOURCES | COMMUNITY | NEWS & EVENTS | CONTACT US

DATA TOOLS / NBS CONDITION RESOURCE (NBS-CR)

NBS Condition Resource (NBS-CR)

Currently, newborns in the United States are screened for eighty-one disorders, sixty-one recommended by a federal advisory committee called the **Advisory Committee for Heritable Disorders in Newborns and Children (ACHDNC)**. These sixty-one conditions make up the Recommended Uniform Screening Panel (RUSP). The RUSP is divided into "core" and "secondary" conditions and grouped into the following categories: Organic Acid, Amnio Acid, Fatty Acid Oxidation, Hemoglobin, Endocrine, and Other.

118 Conditions

61 Recommended Uniform Panel (RUSP) Conditions

20 Conditions Screened by States

37 Conditions Identified as Pilot Candidates by NBSTRN

Last updated: 8/20/2020

Learn More >

Nomination Status

- [ ] RUSP - Core
- [ ] RUSP - Secondary
- [ ] Candidate

ACHDNC Classification

- [ ] Organic Acid
- [ ] Amino Acid
- [ ] Fatty Acid Oxidation
- [ ] Hemoglobin
- [ ] Endocrine
- [ ] Other

RESET & APPLY

Apply Filter

Quick Find

A B C D E F G H I J K L M N
O P Q R S T U V W X Y Z

gamt

Showing 1 Conditions

CANDIDATE

GAMT deficiency

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COVID-19 is an emerging, rapidly evolving situation.

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Get the latest research information from NIH: https://covid19.nih.gov
Learn more about COVID-19 and you from HHS: https://combatcovid.hhs.gov

Home → Genetics → Genetic Conditions → Guanidinoacetate methyltransferase deficiency

Guanidinoacetate methyltransferase deficiency

From Genetics Home Reference. Learn more

Description

Guanidinoacetate methyltransferase deficiency is an inherited disorder that primarily affects the brain and muscles. Without early treatment, people with this disorder have neurological problems that are usually severe. These problems include intellectual disability, speech development limited to a few words, and recurrent seizures (epilepsy). Affected individuals may also exhibit autistic behaviors that affect communication and social interaction or self-injurious behaviors such as head-banging. Other features of this disorder can include involuntary movements (extrapyramidal dysfunction) such as tremors or facial tics.

People with guanidinoacetate methyltransferase deficiency may have weak muscle tone and delayed development of motor skills such as sitting or walking. In severe cases they may lose previously acquired skills such as the ability to support their head or to sit unsupported.

Enlarge image

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Related Health Topics

Amino Acid Metabolism Disorders
Developmental Disabilities
Epilepsy

How Many Conditions are Candidates for Nomination?

How Many Conditions are Candidates for Pilots?

Growing Burden of Genetic Diseases

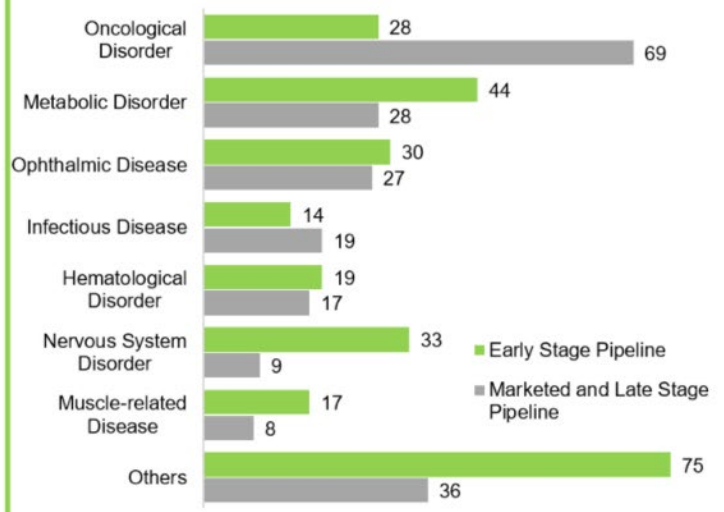
7,000+
Rare diseases have been identified, majority of them being genetic

350 Mn+
Individuals are reported to be living with some rare form of genetic disease

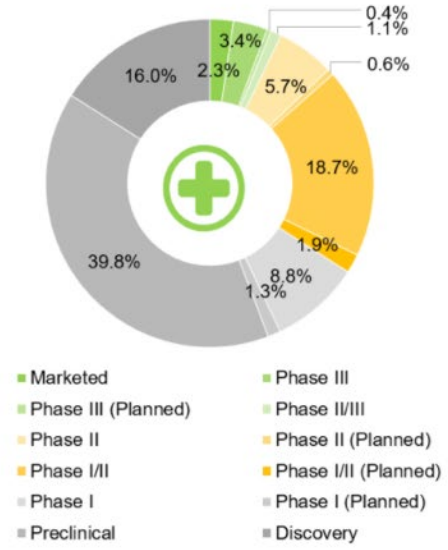
USD Billion 195+
Anticipated likely investment on the treatment of such disorders, till the year 2020

Most available treatment options fail to address the underlying genetic mutation that is responsible for causing such disorders

Gene Therapy: Development Pipeline
Distribution by Therapeutic Area



Gene Therapy: Development Pipeline
Distribution by Phase of Development



465+
Molecules in the clinical and preclinical stages

31,000 Patents
Filed / granted till date, indicating a heightened pace of research

Gene Therapy Market: A Strong Pipeline with $12 Billion Opportunity by 2030

https://www.rootsanalysis.com/blog/gene-therapy-market-a-strong-pipeline-with-12-billion-opportunity-by-2030/

Selection of Candidate Conditions

- Secondary RUSP
- Failed RUSP Nomination
- Screen by ≥ 1 NBS Program in the United States
- Focus of Advocacy Group
- Included in Differential Diagnosis of RUSP Condition
- Neonatal Onset with New Therapy/Intervention
- NBS Feasible with Childhood Onset

Assessment of Candidate Conditions

- Condition
- Screening Method
- Incidence
- Incidence Ref
- Treatment
- Modality – drug(s), diet, replacement therapy, transplant, etc
- Informative Markers for a Screening Test(s)
- Modality of Screening – DBS, physical or physiological assessment
- Analytical Method for Screening Test when DBS utilized
- Need for Second Tier Test and Modality
- Current or Planned Population-Based Pilot Study
  - Location of Prospective Pilot
  - Number of Newborns to be Screened
- Review of Previous Nomination to identify Evidence Gaps (if applicable)
- Review of clinicaltrials.gov
- Literature review – 2017 to present
- Current Screening in at least one NBS program
- Nomination status
- Survey of Experts to Assess Appropriateness for NBS Pilot Study
  - Understanding of Condition
  - Screening Test Efficacy
  - Treatment Efficacy

					APPROPRIATENESS FOR NBS PILOT STUDY		
CONDITION * Already in RUSP ** Already nominated for addition to RUSP	**INFORMATIVE MARKERS in DBS (High ↑ Low ↓)**	**ANALYTICAL METHOD in DBS**	**2nd TIER TEST(S) in DBS N/A, not available (High ↑ Low ↓)**	**AVAILABLE TREATMENT** (diet, drugs, procedures)	**UNDERSTANDING OF CONDITION** (Severity/Urgency) 0=no opinion (No) 1 - 5 (Yes)	**TEST EFFICACY** 0=no opinion (No) 1 - 5 (Yes)	**TREATMENT EFFICACY** 0=no opinion (No) 1 - 5 (Yes)
OTC deficiency	Cit ↓	MS/MS	NA	Diet Conjugating agent	0	0	0
CPS deficiency	Cit ↓	MS/MS	NA	Diet Conjugating agent	0	0	0
NAGS deficiency	Cit ↓	MS/MS	NA	Diet Conjugating agent	0	0	0
MTHFR deficiency (plus Cbl G, Cbl E)	Met ↓	MS/MS	Hcy ↑	Betaine Other	3	3	2
Cbl C,D deficiency*	C3 ↑, Met ↓	MS/MS	MMA ↑, Hcy ↑	Vit. B12 Carnitine	4	4	3
Arginase deficiency*	Arg ↑	MS/MS	N/A	Diet	4	4	5

Interested in Joining This Effort?

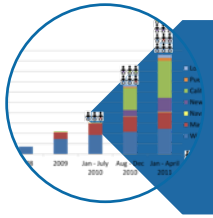
- Pilot Research & Implementation Workgroup
  - Chairs – Michele Caggana, ScD and Olad Bodamer, MD, PhD
  - Staff Lead – Jennifer Taylor, PhD
    - jtaylor@acmg.net

NBSTRN is funded by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

Hunter Kelly Newborn Screening Research Program

Identify, develop, and test the most promising screening technologies

Develop treatments and management strategies for conditions that can be detected through NBS



Generate and provide research findings and data for Conditions under review by the ACHDNC

Conduct pilots of conditions recommended or candidates for pilots or nationwide screening

NBSTRN Team at ACMG

Max Muenke, MD	Co-Principal Investigator
	ACMG CEO and ACMG Board of Directors
Amy Brower, PhD	Co-Principal Investigator
	Steering Committee
Kee Chan, PhD	Scientific Strategy Manager
	Marketing, Website, Clinical Integration Group
Mike Hartnett	Senior Research Assistant
	Duchenne NBS Pilot, REDCap Administrator, NY State LTFU
Jennifer Taylor, PhD	Genomic Scientist
	National Pilot Webinar, Pilot Workgroup, State NBS Program Liaison, Sickle Cell Project
Suzanne Houston, PhD	Data Scientist
	Data Governance, NLM Liaison, OHSU LTFU
LaStephanie Barnes	Administrative Assistant
	NBSTRN Calendar and Events
Ross Wiebenga	Marketing Intern
	Social Media, Blogs
Jill Miller	Intern
	HPO Mapping, Duchenne NBS Pilot

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