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Newborn Screening: An Introduction

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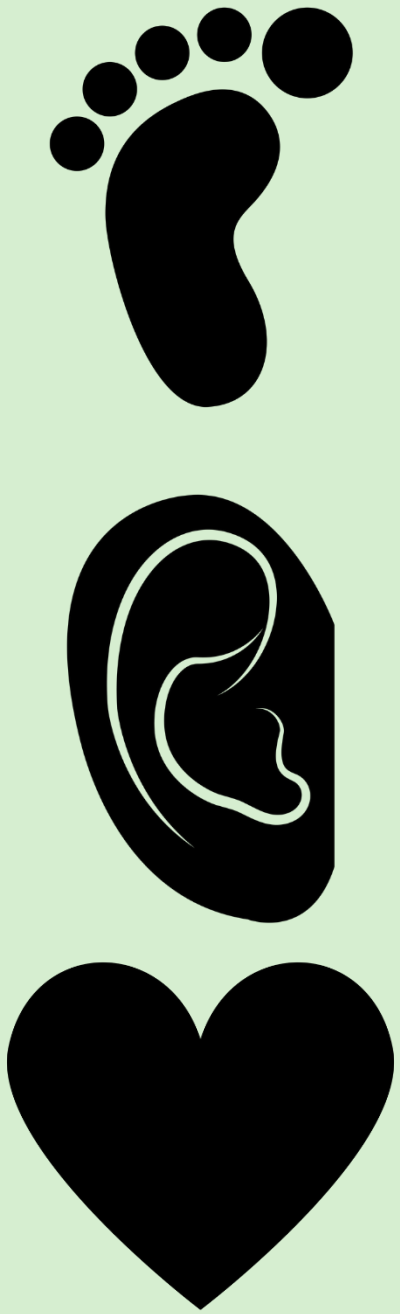
Learning Objectives

Objective 1: Understand the newborn screening process in the United States and variations amongst individual state programs.

Objective 2: Differentiate between screening and diagnostic testing.

Objective 3: Identify provider and family resources related to newborn screening both at the Federal and State Levels.



What is Newborn Screening?

Blood spot: Screens for more than 50 metabolic, endocrine, blood, pulmonary/digestive, lysosomal storage disorders, and immune disorders.

Hearing: Screens for congenital hearing loss in the range where speech is heard.

Pulse oximetry: Screens for critical congenital heart disease.

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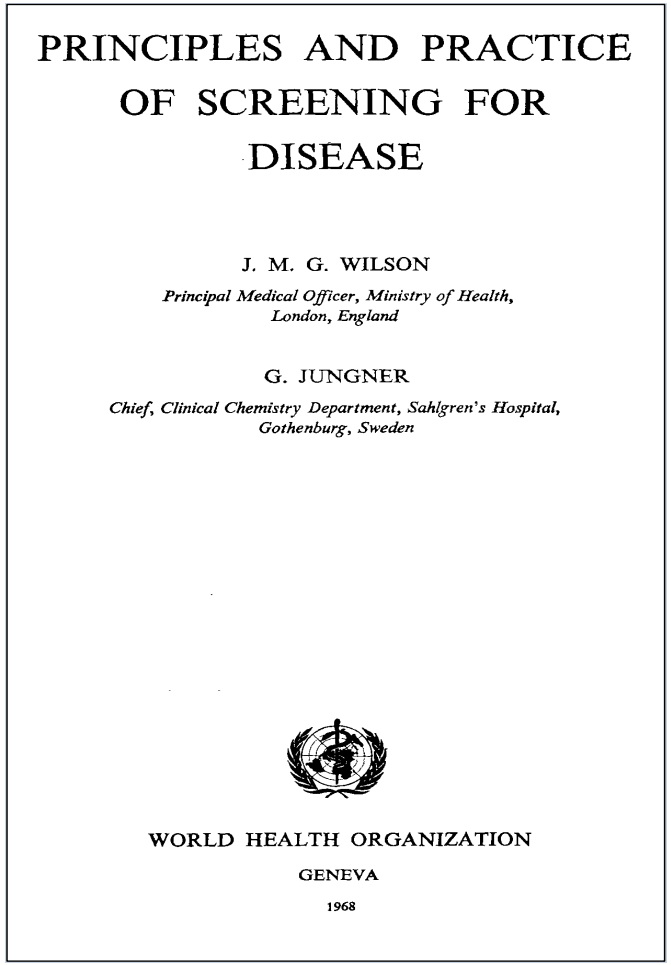
Background

- **Newborn Screening Programs are PUBLIC HEALTH programs**
  - Successful programs require knowledge and coordination from multiple stakeholders, including primary care providers, who play a critical role in the screening process.
- **Newborn screening Programs are STATE-BASED**
  - Variations between Newborn Screening Programs exist from state-to-state.
- **Newborn Screening Programs are OPT-OUT programs**
  - In nearly all states, parents can refuse newborn screening.
- **Newborn Screening Programs are designed to detect TREATABLE conditions**
  - Disorders on the newborn screening panel have to meet certain criteria (e.g., affect children, not be clinically obvious, and have treatment).



PRINCIPLES AND PRACTICE OF SCREENING FOR DISEASE

J. M. G. WILSON

Principal Medical Officer, Ministry of Health, London, England

G. JUNGNER

Chief, Clinical Chemistry Department, Sahlgren's Hospital, Gothenburg, Sweden

WORLD HEALTH ORGANIZATION

GENEVA

1968

In 1968, criteria for selecting suitable conditions for population-based screening was developed…and these are still in use today.

Andermann, et al., 2008. *Revisiting Wilson and Jungner in the genomic age: a review of screening criteria over the past 40 years.* Bulletin of the World Health Organization: 86(4)241-320.

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Wilson-Jungner Criteria for Population-Based Screening

1. **Important health problem**
2. **Accepted treatment**
3. **Available centers for diagnosis and treatment**
4. **Recognizable latent or early symptomatic stage**
5. **Suitable test or examination**
6. **Acceptable to the population**
7. **Natural history should be understood**
8. **Agreed policy on whom to treat**
9. **Cost of screening/diagnosis/treatment should be weighed against possible expenditure on medical care**
10. **Case-finding should be a continuing process and not "once and for all"**

Wilson, JMG, Jungner G. *Principles and practice of screening for disease*. Geneva: WHO; 1968.

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Screening vs. Diagnostic Testing

	Screening Test	Diagnostic Test
Population (offered the test)	• Those **without symptoms** of disease where early detection is important	• Those **with symptoms** • Those undergoing further work-up **after a positive screening test**
Results	• Result is an **estimate of level of risk** • Determines whether a diagnostic test is warranted	• Result provides a **definitive diagnosis**
Test Metrics	• Cutoffs set towards high **sensitivity** • Acceptance of **false positive** results	• Cutoffs set towards high **specificity** • Higher **precision and accuracy**
Invasiveness	• Usually **non-invasive**	• May be **invasive**

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Federal Recommended Uniform Screening Panel (RUSP)

- List of disorders recommended by the Secretary of the Department of Health and Human Services for states to screen as part of their screening program.
  - *Recommended, not required*
- Disorders are approved for inclusion on the RUSP based on the following criteria:
  - Support potential net benefit of screening
  - Public health readiness to screen
  - Availability of effective treatment
- Establishes a standardized list of approved disorders for newborn screening in the United States.

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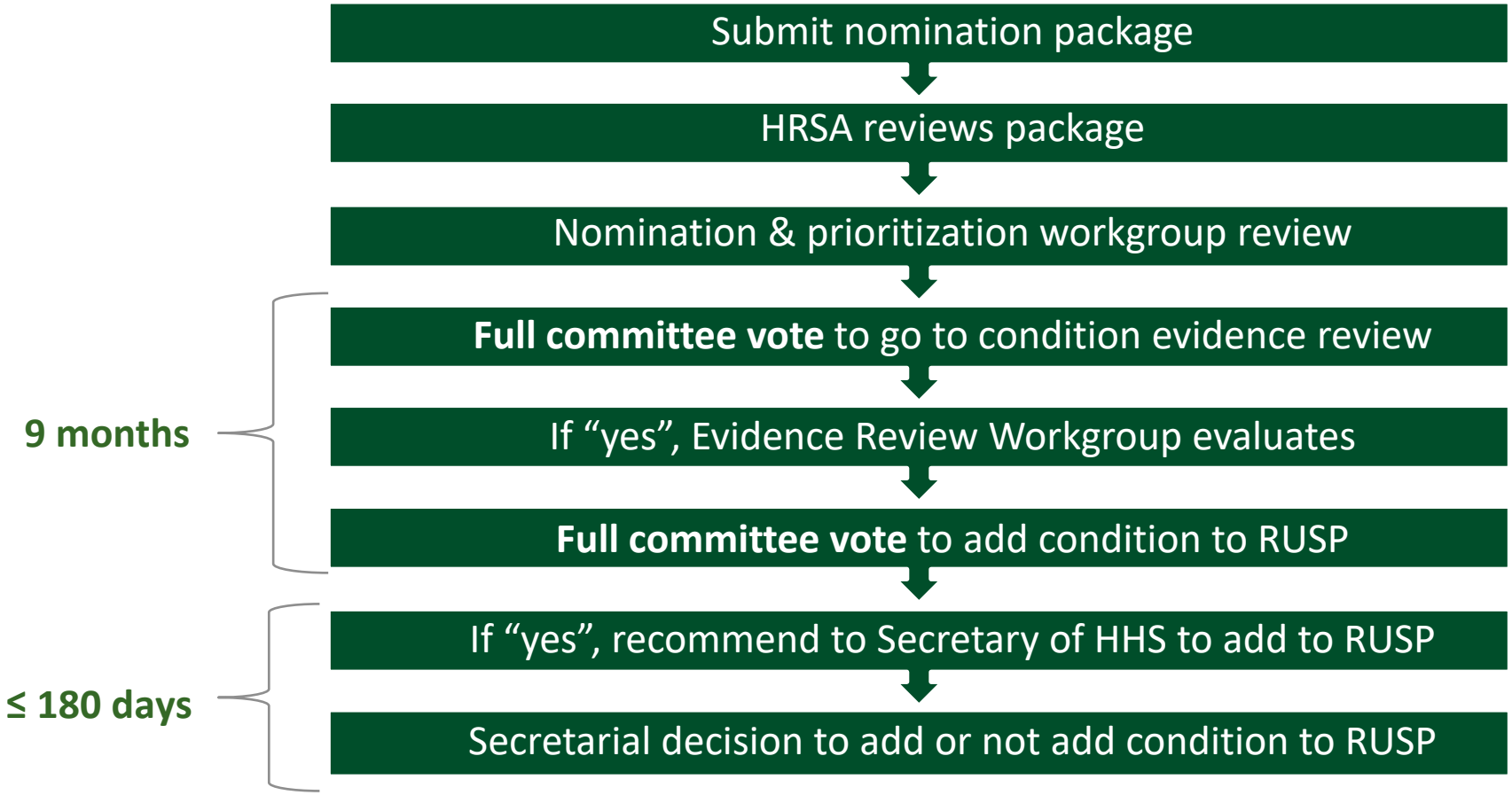
How Disorders Get on the RUSP



Disorder/ Disorder Category	Prevalence in United States	Time-Critical	When States Began Screening/ When Added to RUSP*
Phenylketonuria	1:10,000 – 1:15,000	N	1960s
Congenital Hypothyroidism	1:2,000 – 1:4,000	N	1960s-1970s
Galactosemia	1:30,000 – 1:60,000	Y	1960s-1970s
Hemoglobinopathies (e.g., sickle cell disease)	1:1,500 – 1:1,680	N	1980s
Congenital Adrenal Hyperplasia	1:10,000	Y	1990s
Amino Acidemias		Some Y; Some N	2000-2009
Fatty Acid Oxidation Disorders	1:5,000 – 1:10,000	Some Y; Some N	2000-2009
Organic Acidemias		Some Y; Some N	2000-2009
Biotinidase Deficiency	1:61,000	N	2000-2009
Cystic Fibrosis	1:3,400	N	2000-2009
Severe Combined Immunodeficiency	1:58,000	N	2011*
Pompe disease	1:28,000	Y/N	2015*
Mucopolysaccharidosis, type I	1:100,000	N	2016*
X-linked Adrenoleukodystrophy	1:20,000	N	2016*
Spinal Muscular Atrophy	1:6,000 – 1:10,000	N	2018*

** Denotes when added to RUSP; states may or may not have begun screening for this disorder at this time.*

How Disorders Become a part of State Legislation

- A mandate by legislature may require states to screen for one or more disorders.
- Often sparked by family advocates.
- Often unfunded, which can result in implementation delays.

NJSPOTLIGHT
WHERE ISSUES MATTER

» BUDGET » EDUCATION » ENERGY & ENVIRONMENT » HEALTHCARE » MORE ISSUES » OPINION » ABOUT

Fine Print: Emma's Law

Legislature asked to approve $1.6M to implement screening of newborns for certain genetic disorders

By **Andrew Kitchenman**, **March 21, 2013** in **Healthcare** | *Post a Comment* print | email | share

What it is: A law, **S-1999**, signed by Gov. Chris Christie in January 2012, requiring that newborns be screened for a series of genetic disorders that attack the nervous systems of infants. The law didn't include funding to implement testing.

Its goal: To allow babies to be treated as quickly as possible. Early treatment can reduce the negative consequences of the diseases, in which nerve cell insulation is underdeveloped, affecting the child's mental and physical development. Early cord blood and bone marrow transplants, as well as physical therapy, can benefit the children. There is no effective treatment once the symptoms have started to appear, and the diseases are fatal.

Related Links
S-1999, Emma's Law

Who Emma was: Emma Daniels was an infant born with Krabbe disease in 2009. While she grew normally at first, her symptoms began at the age of 2 months, beginning with fussiness and irritability. She was not tested for the disorder until she was 4 months old, at which time it was too late for her to be treated. She died at the age of 2 in March 2012. Her family lobbied for the law's enactment.

What's new: Christie proposed $1.6 million to fund the screening tests – which cover Krabbe and five similar diseases, known as lysosomal storage disorders -- for the budget year starting on July 1. This will increase the total number of disorders for which newborns are screened from 54 to 60, at a total annual cost to the state of $25 million. Christie mentioned the law during his February 26 budget message to the Legislature and has repeatedly referred to it at health-related public appearances since the speech.

How newborn screenings work: Doctors take a few drops of blood from each newborn's heel to test for genetic, endocrine and metabolic disorders. According to the federal Centers for Disease Control, early detection, diagnosis and intervention can prevent death or disability and enable children to reach their full

e state

PA Governor Corbett Signs Bill Expanding Newborn Screening Requirements

Oct 15, 2014, 12:46 ET from Pennsylvania Office of the Governor

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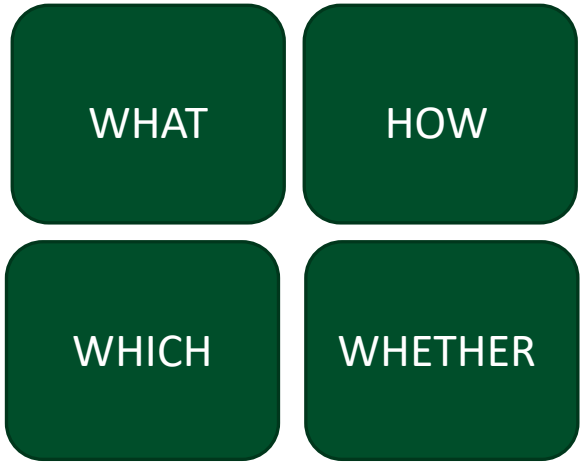
State Variations Exist

Newborn Screening Programs are **STATE-BASED** programs with federal guidance and support.

- This means that variations exist in:
- **WHAT** disorders are screened for in each state
- **HOW** disorders are added to the state's screening panel
- **WHICH** method/assay is used to screen for the disorders
- **WHETHER** parents can refuse screening or exercise other parental options



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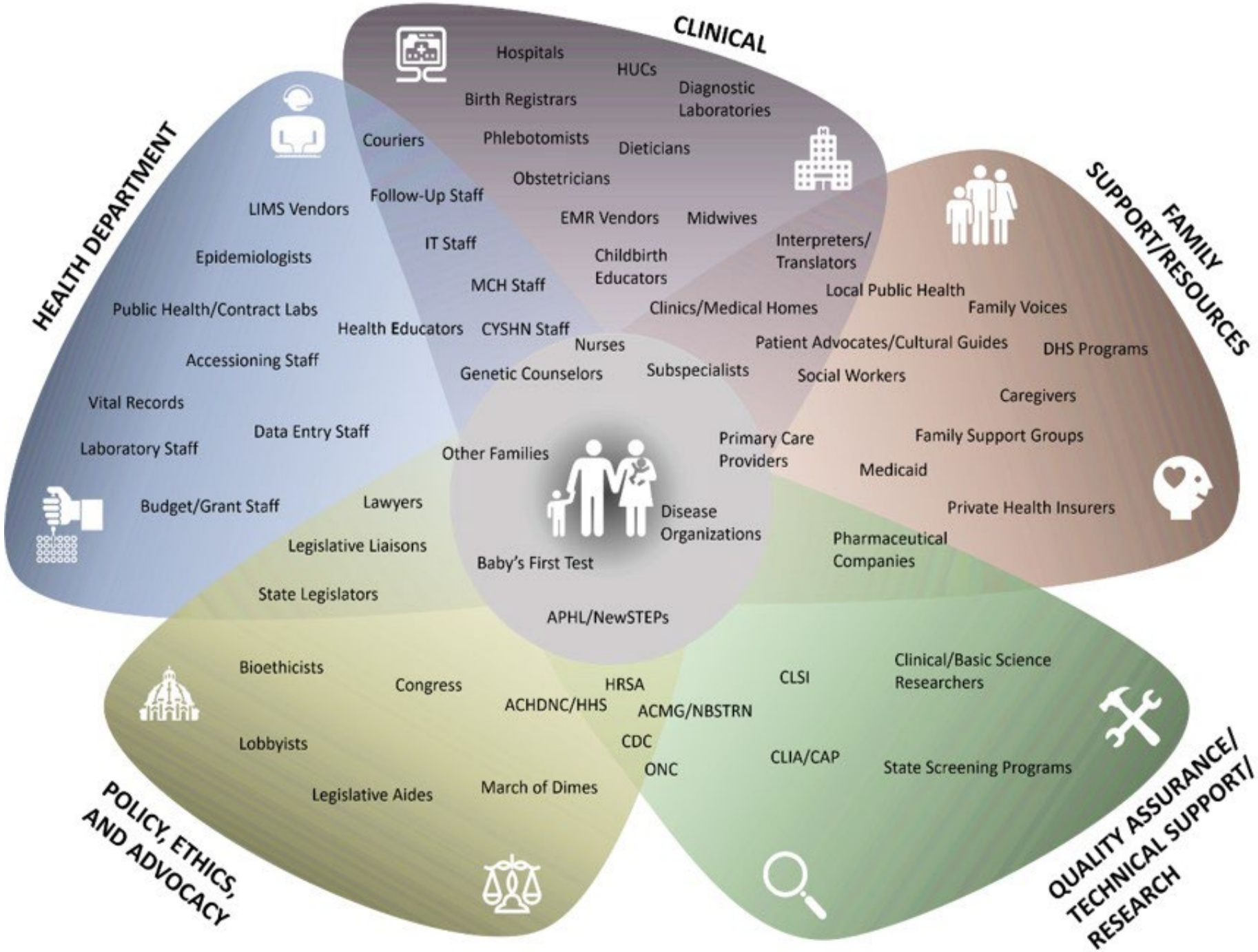
Your state's screening panel

For information on disorders on your state's screening panel and information about options available to parents in your state, go to:

- Baby's First Test: https://www.babysfirsttest.org
- New Steps: https://www.newsteps.org/
- State Health Department website
- HRSA's Newborn Screening Information Center: https://newbornscreening.hrsa.gov/


CLINICAL
Hospitals
HUCs
Diagnostic Laboratories
Birth Registrars
Couriers
Phlebotomists
Dieticians
Obstetricians
Follow-Up Staff
EMR Vendors
Midwives
IT Staff
Childbirth Educators
MCH Staff
Clinics/Medical Homes
Nurses
Genetic Counselors
Subspecialists
Other Families
Primary Care Providers
Disease Organizations
Baby's First Test
APHL/NewSTEPs
HEALTH DEPARTMENT
LIMS Vendors
Epidemiologists
Public Health/Contract Labs
Health Educators
CYSHN Staff
Accessioning Staff
Vital Records
Data Entry Staff
Laboratory Staff
Budget/Grant Staff
Lawyers
Legislative Liaisons
State Legislators
FAMILY SUPPORT/RESOURCES
Interpreters/ Translators
Local Public Health
Family Voices
Patient Advocates/Cultural Guides
DHS Programs
Social Workers
Caregivers
Family Support Groups
Medicaid
Private Health Insurers
Pharmaceutical Companies
POLICY, ETHICS, AND ADVOCACY
Bioethicists
Congress
HRSA
ACHDNC/HHS
ACMG/NBSTRN
Lobbyists
CDC
ONC
Legislative Aides
March of Dimes
QUALITY ASSURANCE/ TECHNICAL SUPPORT/ RESEARCH
CLSI
Clinical/Basic Science Researchers
CLIA/CAP
State Screening Programs

The Newborn Screening Process

Hearing screening is conducted through objective testing to determine hearing loss in the range where speech is heard.

Pulse oximetry screening examines the presence of hypoxemia, which may indicate an undetected critical congenital heart disease.

Blood spot specimens are collected by the birth facility and sent to the state public health screening laboratory.

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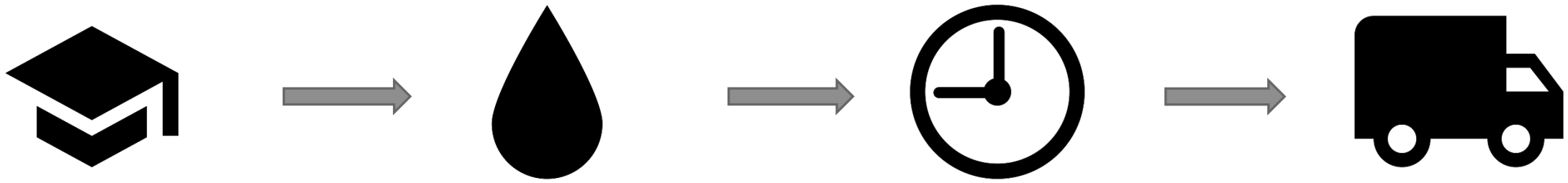
Blood Spot Process: Pre-Analytical

Families should be provided education about screening BEFORE the sample is collected, including the prenatal period.

Blood spot samples are recommended to be collected between 24 – 48 hours of age.

Specimens are dried horizontally for at least 3 hours prior to submission.

Specimens should be sent to the state screening program within 24 hours of collection.



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Types of Newborn Screening Results

Result Interpretation	Result Meaning	For Further Information
Normal/Negative/Within Normal Limits	• The child is at low-risk for having the condition. • All values were within the expected range for unaffected newborns.	Newborn Screening Virtual Learning Collaborative Session 2
Unsatisfactory/Invalid	• The specimen was deemed invalid for accurate screening. • Results cannot be accurately interpreted.	Newborn Screening Virtual Learning Collaborative Session 3
Borderline/Inconclusive	• The child is at low to medium-risk for having the condition. • A repeat screen is usually requested and often (but not always!) resolves the result.	Newborn Screening Virtual Learning Collaborative Session 3
Abnormal/Positive/Out-of-Range	• The child is at moderate to high-risk for having the condition. • Clinical evaluation and specialty referral are recommended.	Newborn Screening Virtual Learning Collaborative Session 3

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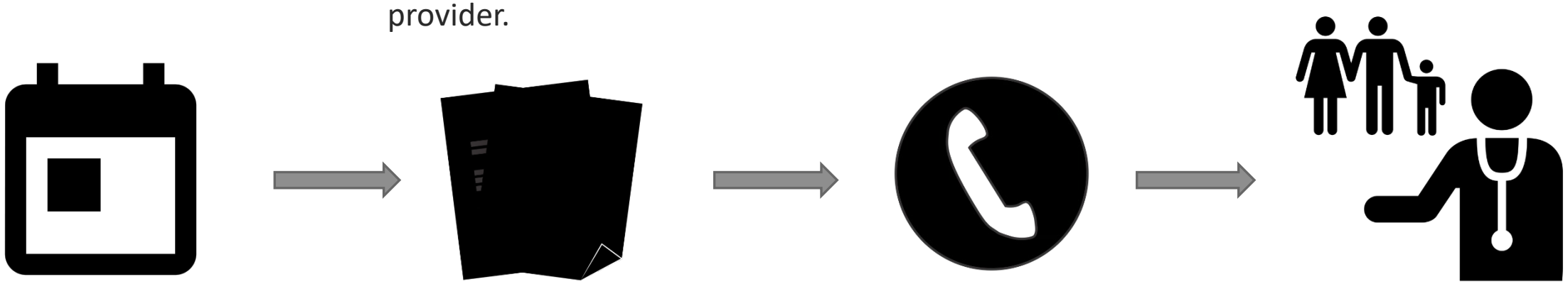
Blood Spot Process: Post-Analytical

Results should be available around 7 days after birth (positive results may be available sooner).

Normal results will be provided back to the submitting birth facility and should be forwarded to the primary care provider.

Positive results will be called out to the primary care provider and/or specialist.

Family should be notified by the primary care provider/specialist as soon as possible.



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Primary Care Provider Role in Newborn Screening Documentation

- Newborn screening results should be available by the first well-child check
- Ensure that screening results are obtained, communicated, and documented for all newborn patients by their 2-week visit.
- Primary Care Providers are often the first person to notify families for out-of-range results and may be the **ONLY** way parents receive their child's newborn screening results.

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Primary Care Provider Role in Provision of Newborn Screening Results

- Many families may not remember having newborn screening done due to timing of specimen collection shortly after birth.
- Key messages to share with families (which we will review in detail in later VLC sessions):
  - Remind family what newborn screening **IS** and **IS NOT**
  - Remind family what types of conditions newborns screening **DOES** and **DOES NOT** look for

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So much more than a “PKU test”…

- The term “PKU test” is no longer accurate, can cause confusion, and leads to unnecessary and/or inappropriate testing.
- References to the “PKU test” should be updated to the term “Newborn Screen” wherever this language is found.

OUTDATED MEDICAL TERMS	MODERN MEDICAL TERMS
Mental Retardation	Intellectual Disability
Cretinism	Congenital Hypothyroidism
Estimated Date of Confinement	Estimated Date of Delivery
Geriatric Pregnancy	Advanced Maternal Age
PKU Test	**Newborn Screen**

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Challenges in Newborn Screening

Parents **MAY NOT** be told about newborn screening or remember that it happened

- Family education is important in the prenatal period, before the screening occurs, and after the results are available

Parents are often “blind-sided” by out-of-range results or don’t know to ask for results.

- In a study completed in one state, nearly 40% of parents surveyed reported that they **DID NOT** receive their newborn screening results

Transparency from primary care physicians is vital both in terms of:

- Education of parents before and after newborn screening
- Provision of screening results back to family regardless of results

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Newborn Screening Resources

FAMILY & PROVIDER-SPECIFIC RESOURCES

Resource	Link
ACMG ACT Sheets (more provider focused)	https://www.acmg.net/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms.aspx
STAR-G (more family specific)	https://www.newbornscreening.info/
Baby's First Test	https://www.babysfirsttest.org/
Medline Plus (formerly Genetics Home Reference)	https://medlineplus.gov/
State Newborn Screening Program Website	See your State's Newborn Screening Program Website
HRSA's Newborn Screening Information Center	https://newbornscreening.hrsa.gov/