

Ensuring Our Children have Access to Quality, Accurate Laboratory Testing

February 4, 2026

Snapshot of Children in the United States

- 73 million children under the age of 18 in the United States
- 22 million children under the age of 5
- 3 billion laboratory tests performed on children annually
- 72% of rare disorders begin in childhood

Ensuring Our Children have Access to Quality, Accurate Laboratory Testing

- Newborn Screening
- Reference Intervals
- Laboratory developed tests (LDTs)

Speakers



Danyel Tacker, PhD

Clinical Professor,
West Virginia
University Hospitals;
Section Director –
Special Chemistry &
Mass Spectrometry

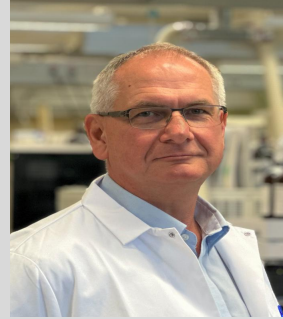
WVU Clinical
Laboratory



Stanley Lo, PhD

Professor,
Pathology,
Medical College
of Wisconsin;
Associate Director

Children's
Wisconsin Clinical
Laboratories



Hubert Vesper, PhD

Director, Clinical
Standardization
Program, Centers for
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Moderator/Speaker



Dennis Dietzen, PhD

Chief, Pathology &
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Division
Phoenix Children's
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Newborn Screening



- **Danyel Hermes Tacker, PhD**
- Clinical Professor of Pathology, West Virginia University;
- Section Director – Special Chemistry & Mass Spectrometry, WVU Hospital
- Medical Director, WVU Medicine Fairmont Medical Center Laboratory

What is Newborn Screening?

- Blood spot, hearing, and congenital heart disease
- Process for adding new tests
- State-to-state variation
- Current recommended screenings



Newborn Screening Saves Lives Act

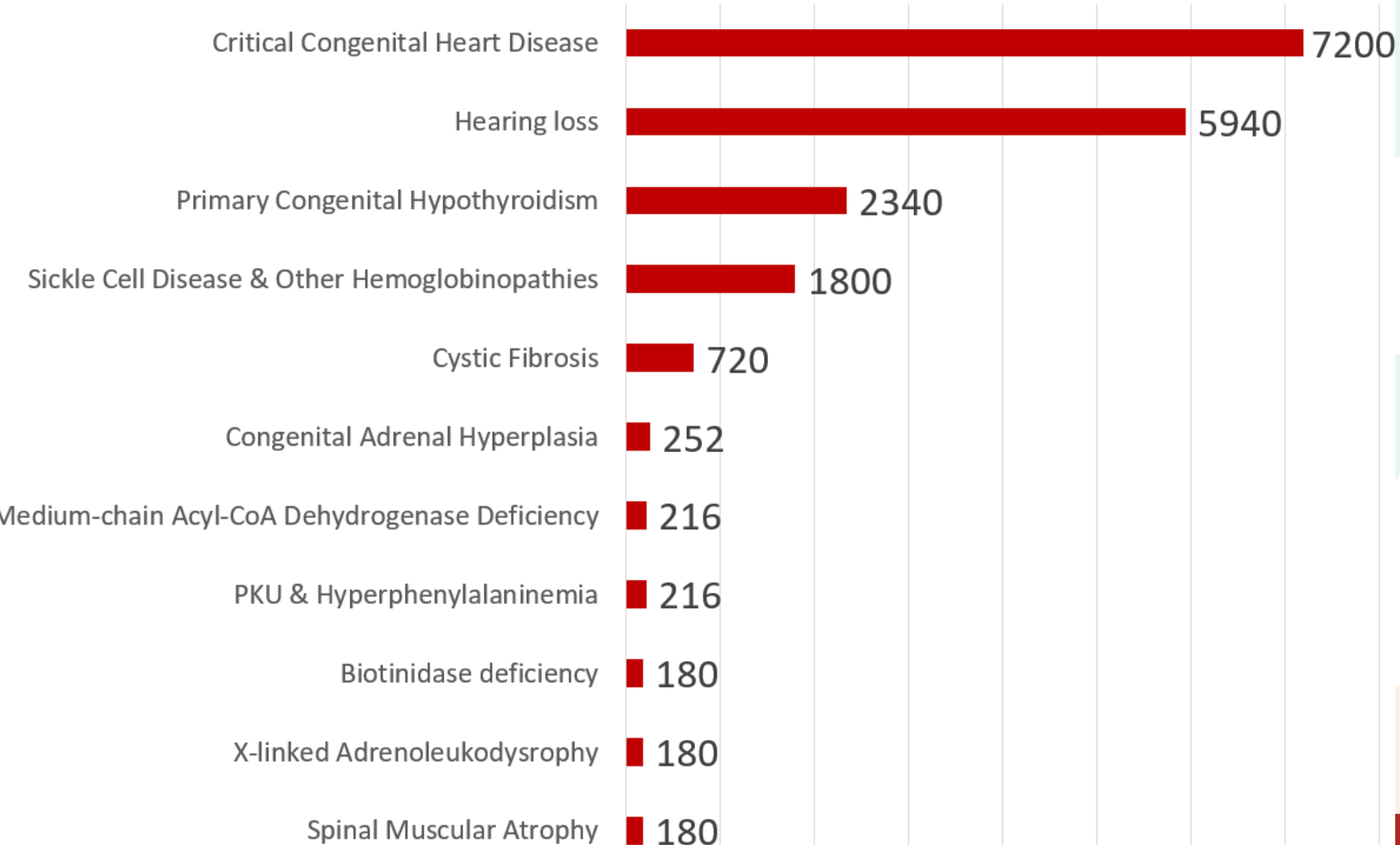
HISTORY

- First passage – 2007 [110-204]
- Renewed – 2014 [110-240]
- Authorization expired in 2019. Congress continues to fund as it considers changes to legislation

FUNCTIONS

- Established grant programs to help states expand screening programs/efforts
- Supported education & outreach
- Enabled quality and surveillance oversight
- Solidified the role of ACHDNC → Recommended Uniform Screening Panel (RUSP)
 - 40 Core Conditions
 - 26 Secondary Conditions

Projected Frequencies of Common & Moderately Common Disorders in 3.6M Births (~1 year; based on CDC data)



Screening for 38 core conditions yields ~19,500 disorder diagnoses in a year.

>98% are represented by the 11 conditions (19,224 diagnoses) shown.

Based on CDC data expressed as rates per 10k or 50k live births & extrapolated to 3.6M.

NBS Value Equation

- Hard to quantify some benefits of early detection...because it's hard to count what you *don't* know.
- Cost of 379 rare diseases, US 2019 data¹: **\$997B/year from 15.5M affected children & adults**
- Benefit-Cost Ratio of newborn screening = 3.97 in USD²
 - Cost of NBS vs quality adjusted life years
 - Probability of cost-effectiveness: **100% for NBS** if comparing program costs to per capita GDP per WHO recommendation of 3xGDP

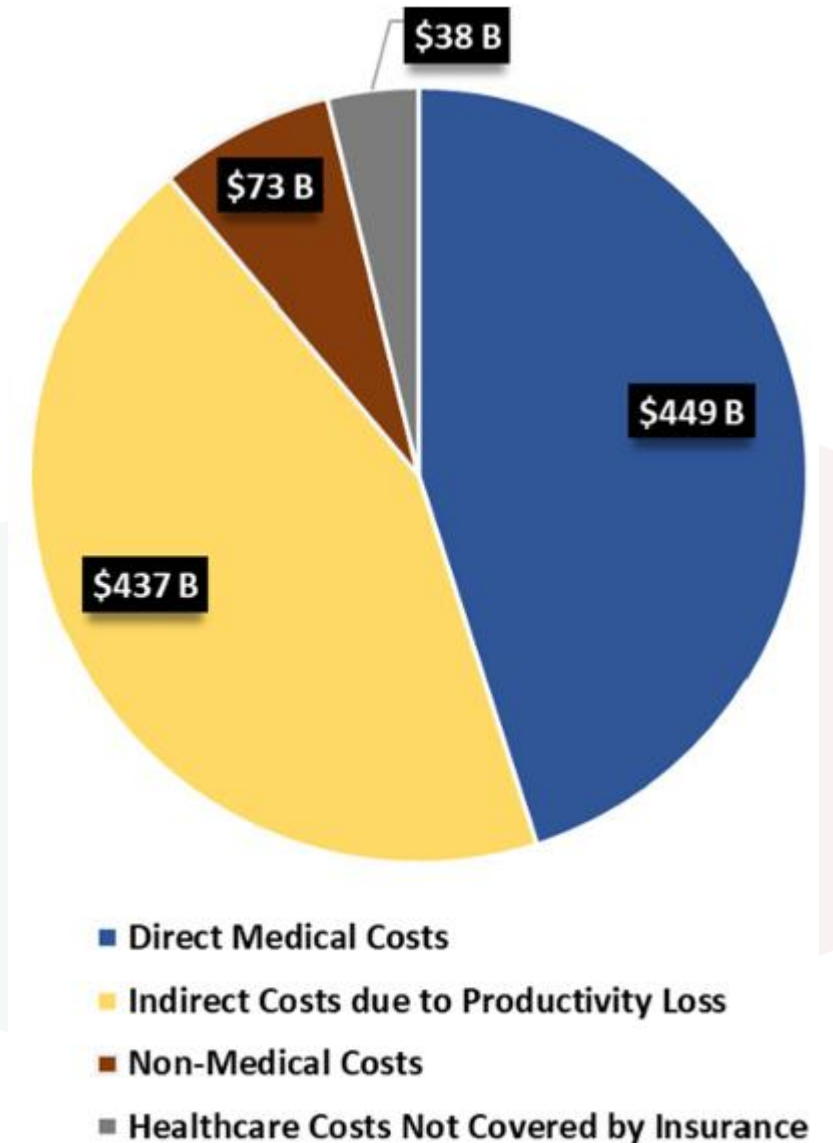


Fig. 1 Total Economic Burden of Rare Disease in the U.S. in 2019: \$997 Billion

Newborn Screening – congressional action needed:

- Pass the Newborn Screening Saves Lives Reauthorization Act
- Maintain stable funding for newborn screening programs in FY27
- Reinstate or reconstitute federal Advisory Committee on Heritable Disorders for Newborns and Children



Pediatric Reference Intervals – The Need for Better Diagnostic Tools

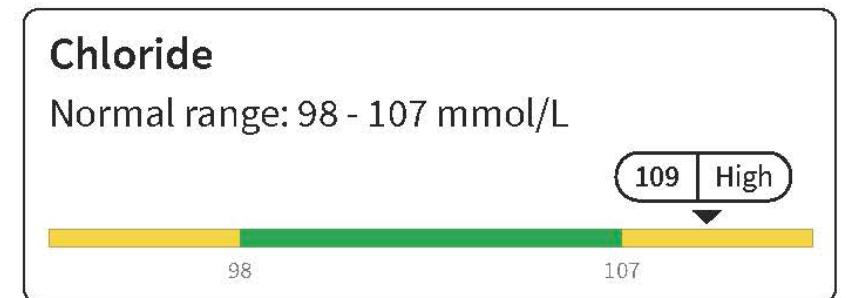
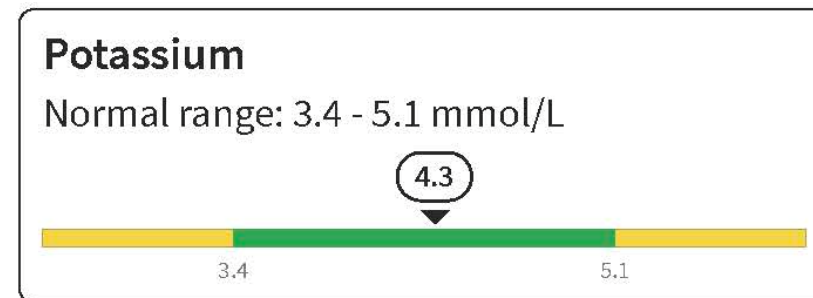
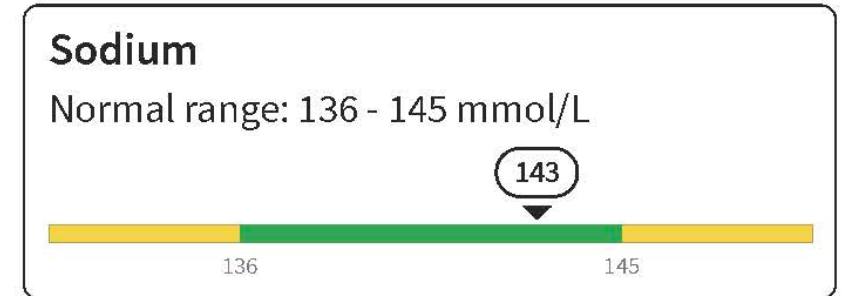
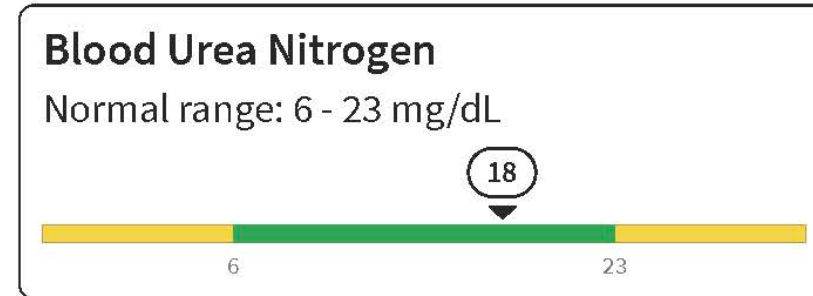


- **Stanley Lo, PhD**
- Professor, Pathology, Medical College of Wisconsin;
- Associate Director Children's Wisconsin Clinical Laboratories

What are Pediatric Reference Intervals (PRIs)?

- Well vs NOT Well
- Normal Ranges
- Tied to clinical picture

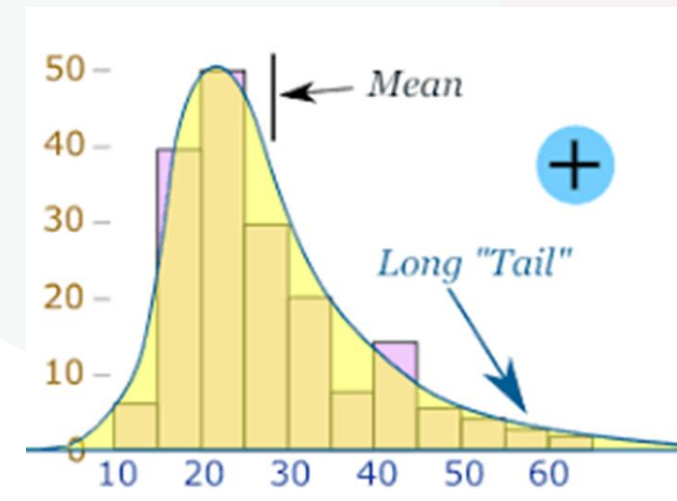
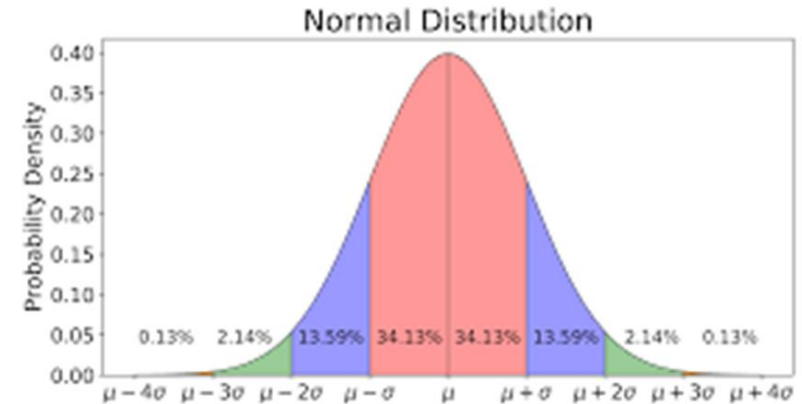
Results



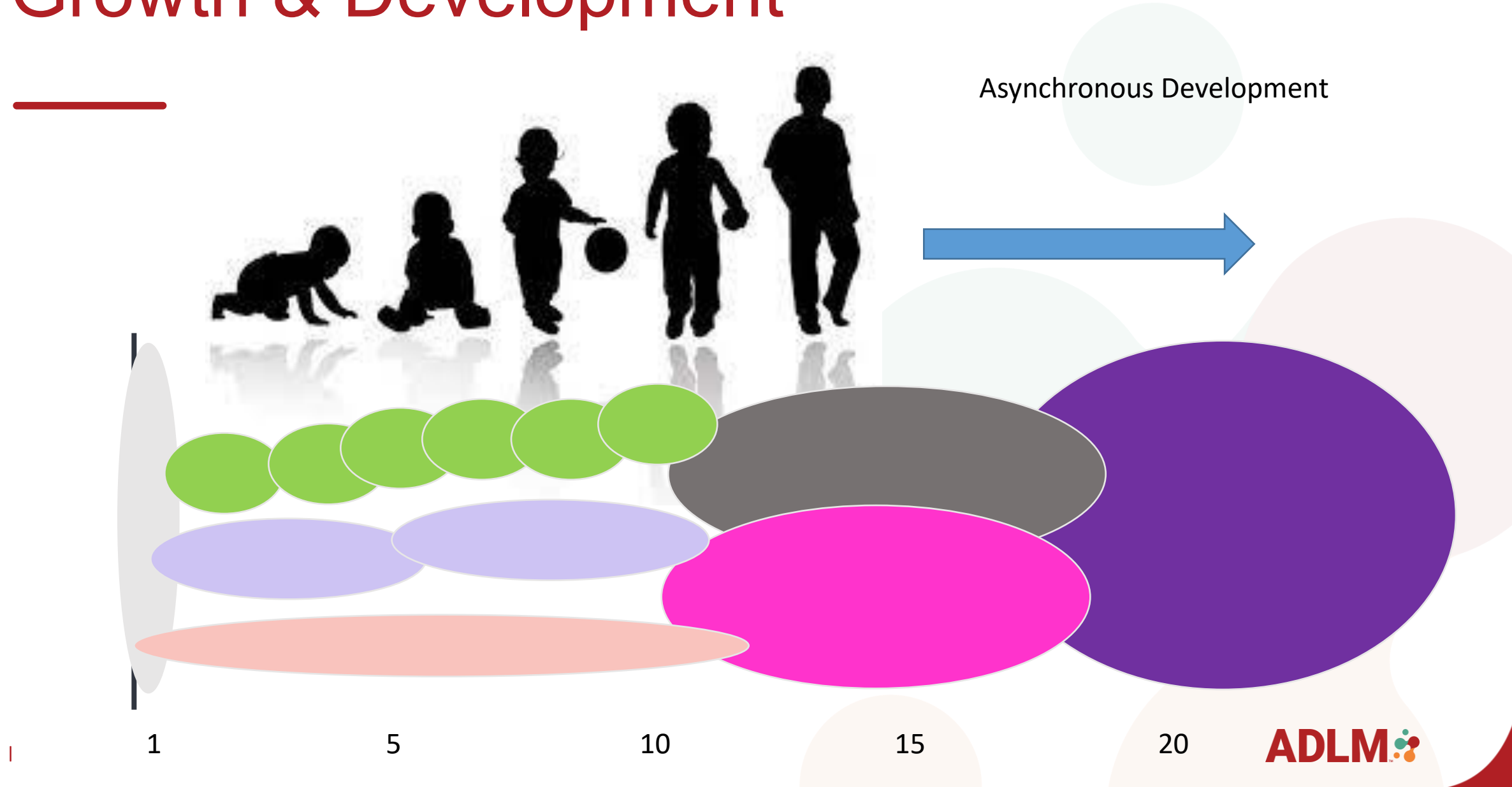
Issues in Developing Accurate PRIs

PROBLEMS

- “healthy”
- Rapid development
- Asynchronous development
- Limited blood volumes
- Large number of participants
- Parental consent
- Geographic diversity
- Ethnic diversity
- Instrumentation differences



Growth & Development



Current State

Adult

FT4 0.8-1.9 ng/dL

TSH 0.5-5mIU/L

Pediatrics

9 Pediatric, Academic, Tertiary Care Centers

FT4 - Bins: 1-6

TSH – Bins: 3-7

Neonate Upper Limit: 7.60– 25.0

Neonate Lower Limit: 0.40-1.00

Laboratory	FT4		TSH	
	Age Group	PRI (ng/dL)	Age Group	PRI (mIU/L)
1	0 - 3 days	1.00 - 3.00	0 - 3 days	1.00 - 25.00
	4 - 30 days	0.80 - 2.20	4 - 30 days	0.50 - 10.00
	1 month - 18 years	0.90 - 1.70	1 month - 18 years	0.30 - 4.20
2	0 - 3 days	2.00 - 5.00	0 - 3 days	1.00 - 20.00
	4 - 30 days	0.90 - 2.20	4 - 30 days	0.50 - 6.50
	1 month - 18 years	0.90 - 1.70	1 - 5 months	0.70 - 4.80
			6 months - 14 years	0.70 - 4.10
3	0 - 6 days	0.86 - 2.49	0 - 6 days	0.70 - 15.20
	7 days - 3 months	0.92 - 1.99	7 days - 3 months	0.72 - 11.00
	4 - 23 months	0.92 - 1.99	4 - 23 months	0.72 - 8.35
	2 - 6 years	0.96 - 1.77	2 - 6 years	0.70 - 5.97
	7 - 11 years	0.97 - 1.67	7 - 11 years	0.60 - 4.84
	12 - 18 years	0.98 - 1.63	12 - 18 years	0.98 - 4.30
4	0 - 2 days	1.80 - 3.90	0 - 3 days	0.70 - 16.00
	3 - 30 days	1.10 - 2.00	4 days - 6 months	0.70 - 4.80
	1 month - 18 years	1.0 - 1.80	6 months - 14 years	0.70 - 4.20
			15 - 18 years	0.50 - 3.40
5	0 - 3 days	2.00 - 5.00	0 - 3 days	1.00 - 20.00
	4 - 30 days	0.90 - 2.20	4 - 30 days	0.50 - 6.50
	1 month - 18 years	0.80 - 2.00	1 - 5 months	0.50 - 6.00
			5 months - 18 years	0.50 - 4.50
6	0 - 18 years	0.89 - 1.76	0 - 23 months	0.40 - 7.59
			2 - 3 years	0.40 - 6.96
			4 - 7 years	0.40 - 6.05
			8 - 10 years	0.40 - 5.56
			11 - 13 years	0.40 - 5.34
			14 - 15 years	0.40 - 5.02
			16 - 18 years	0.40 - 5.14
7	0 - 3 days	2.00 - 5.00	0 - 3 days	1.00 - 20.00
	4 - 30 days	0.90 - 2.20	4 days - 1 month	0.50 - 6.50
	1 month - 18 years	0.70 - 2.00	2 - 5 months	0.50 - 6.00
			6 months - 18 years	0.50 - 4.50
8	0 - 6 days	1.50 - 3.00	0 - 6 days	0.9 - 13.50
	7 - 29 days	0.90 - 2.10	7 - 29 days	0.90 - 10.00
	1 - 11 months	0.70 - 1.80	1 - 11 months	0.70 - 6.60
	1 - 18 years	0.70 - 2.10	1 - 10 years	0.60 - 4.50
			11 - 18 years	0.40 - 4.00
9	0 - 18 years	0.8 - 1.9	0 - 1 year	0.35 - 7.60
			2 - 4 years	0.35 - 6.00
			5 - 6 years	0.35 - 6.00
			7 - 18 years	0.35 - 5.50

Abbreviations: PRI, pediatric reference interval; FT4, free thyroxine; TSH, thyroid stimulating hormone

Different PRIs

6 groups

Laboratory	FT4		TSH	
	Age Group	PRI (ng/dL)	Age Group	PRI (mIU/L)
3	0 - 6 days	0.06 - 2.49	0 - 6 days	0.70 - 15.20
	7 days - 3 months	0.92 - 1.99	7 days - 3 months	0.72 - 11.00
	4 - 23 months	0.92 - 1.99	4 - 23 months	0.72 - 8.35
	2 - 6 years	0.96 - 1.77	2 - 6 years	0.70 - 5.97
	7 - 11 years	0.97 - 1.67	7 - 11 years	0.60 - 4.84
	12 - 18 years	0.98 - 1.63	12 - 18 years	0.98 - 4.30

3&4 groups

4	0 - 2 days	2.00 - 5.00	0 - 3 days	0.70 - 16.00
	3 - 30 days	1.10 - 1.80	4 days - 6 months	0.70 - 4.80
	1 month - 18 years	1.0 - 1.80	6 months - 14 years	0.70 - 4.20
			15 - 18 years	0.50 - 3.40

1&7 groups

6	0 - 18 years	0.89 - 1.76	0 - 23 months	0.40 - 7.59
			2 - 3 years	0.40 - 6.96
			4 - 7 years	0.40 - 6.05
			8 - 10 years	0.40 - 5.56
			11 - 13 years	0.40 - 5.34
			14 - 15 years	0.40 - 5.02
			16 - 18 years	0.40 - 5.14

Why Better PRIs are Critical

- **Inaccurate PRIs can lead to:**
 - Misdiagnosis
 - Inappropriate or unnecessary medical interventions
 - Unnecessary healthcare costs
 - Less than optimal health outcomes
- **Accurate PRIs can lead to:**
 - Better diagnoses
 - Reduced healthcare costs
 - Improved health outcomes



Congressional Action on PRIs

On several occasions Congress and key committees have recognized the importance of better PRIs through report language urging CDC to address the issue:

- FY20 - Congress attached report language to the budget asking CDC to develop and submit a plan on how it would accomplish this task and a cost estimate
- FY22 - Congress attached report language to the budget urging CDC to initiate efforts to improve the accuracy of PRIs
- FY25 - House and Senate appropriation committees attached report language urging CDC to improve PRIs and provide information on the cost of moving forward with the initiative
- FY26 – House and Senate appropriation committees attached similar report language asking CDC to initiate efforts and provide cost estimates for improving PRIs

CDC needs \$10 million annually to develop better PRIs

The CDC's role in addressing Pediatric Reference Intervals



- **Hubert Vesper, PhD**
- Director, Clinical Standardization Program, Centers for Disease Control and Prevention

Laboratory Developed Tests – Critical to Ensuring Healthy Children



- **Dennis Dietzen, PhD, DABCC, FADLM**
- Chief, Pathology & Laboratory Medicine
- Megan K Dishop Endowed Chair
- Phoenix Children's Hospital

- Professor of Child Health and Pathology
- University of Arizona College of Medicine - Phoenix

What is a Laboratory Developed Test (Procedure), LDT

What are LDTs?



Waived



Moderate
Complexity



High
Complexity



How many LDTs exist? How many impact children?

- Approximately 12,000 High Complexity Laboratories are eligible to build and perform LDTs.
- Approximately 3-5% of total testing volumes are LDTs.
- Individual LDTs are low volume.
- Fill niches where FDA-approved tools don't exist or are inadequate.
- Pediatric laboratory medicine relies heavily on LDTs.
 - Impact on Newborn Screening is immense (4,000,000 annual births).
 - Rare genetic, endocrine, and metabolic conditions diagnosed using LDTs.

Regulatory Landscape



Engineering Controls
Design Controls
Manufacturing Controls
Shipping Controls
Raw materials
Complaint Tracking
Labeling
Recalls
510k
De novo
PMA

Rigorous but imperfect: 280 recalls from July 2023 to June 2024

Regulatory Landscape

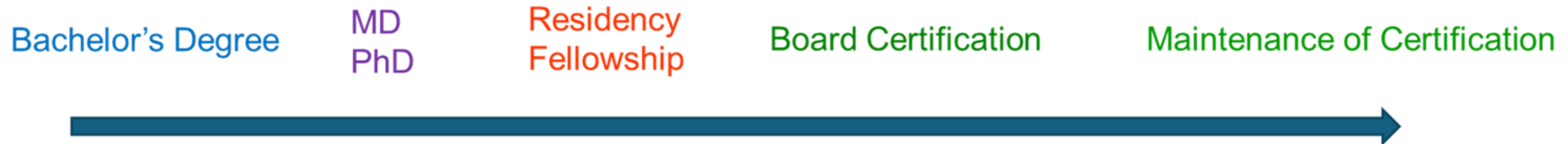


Laboratory Practice: Freezer Temps, SOPs, Personnel Requirements, Proficiency Testing, Pipette Calibration, Balance Calibration, Quality Control, Quality Assurance



Who builds LDTs? People, not “Manufacturers.”

- Highly qualified/trained MDs & PhDs
- Limited to high complexity labs
- Approximately 4% of labs eligible
- Considerable monetary, time investment



Areas of Potential Improvement

- Clinical validity
- Adverse event reporting
- Corrective action documentation
- Transparency of performance data
- Comprehensive LDT Directory
- Personnel Qualifications

Where are we now that the “Final Rule” is no longer final?

- Lawsuit challenging FDA authority over LDTs filed by American Clinical Laboratory Association (ACLA) and the Association for Molecular Pathology (AMP)
- Amicus Briefs from ADLM, CAP, ASCP, ASM, AAB, IDSA
- March 31, 2025; final rule set aside and vacated.
- Regulatory authority remains with CMS/CLIA.
- Pathway to reform via CLIA. FDA reform independent from LDT reform.
- Reform should address both advances in technology and software applications.

Summary and Out



- LDTs are vital laboratory tools
- LDTs are particularly crucial in the care of children with rare disorders
- The kids will not go away; the need will not go away
- LDTs are highly regulated via CLIA
- LDT performance needs more transparency
- Regulations need to be consistent
- Regulations need to adapt to medical science and technology
- Engagement of stakeholders is essential

Take Home Messages

- Support continued funding for NBS in FY27
- Include funding for PRI in CDC's Environmental Health Laboratory appropriation for FY27
- Monitor activities regarding changes to LDT oversight

— **Questions?**

