TIMELINESS OF NEWBORN SCREENING – DACHDNC LABORATORY STANDARDS AND PROCEDURES SUBCOMMITTEE DRAFT FINDINGS AND PROPOSED RECOMMENDATIONS

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PURPOSE

- To report on best practices to alleviate gaps and identify barriers to timely newborn screening (NBS) and assess whether current goals for timely specimen collection, transit and testing are appropriate for the current NBS system.

DACHDNC RECOMMENDED THE FOLLOWING TIMEFRAMES RELATED TO NBS – JAN 2014

- Initial NBS specimens should be collected at 24 to 48 hours of life.
- NBS specimens should be received at the Laboratory within 24 hours of collection.
- Newborn screen results for time-critical conditions should be available within 5 days of life.
- All NBS results should be available within 5 days of collection.

THE LABORATORY STANDARDS AND PROCEDURES SUBCOMMITTEE TASKS

1. Outline the NBS system
2. Investigate existing gaps and barriers in NBS systems
3. Identify best practices to achieving these goals
4. Develop a list of critical conditions that require urgent follow-up
5. Review the recommendations in light of new technologies
6. Suggest revisions, if needed.

ACTIVITIES

- Convened steering workgroup made up of Lab SC members:

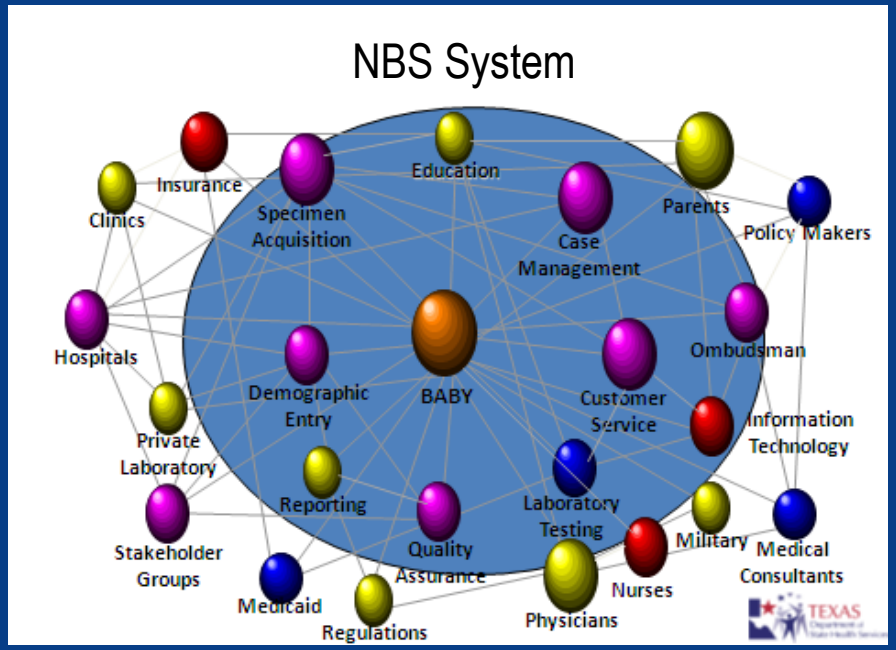
Stan Berberich	Dieter Matern	Michele Caggana
Mei Baker	George Dizikes	Bill Slimak
APHL	Debi Sarkar	Tina Turgel
Susan Tanksley	Kellie Kelm	Ed McCabe

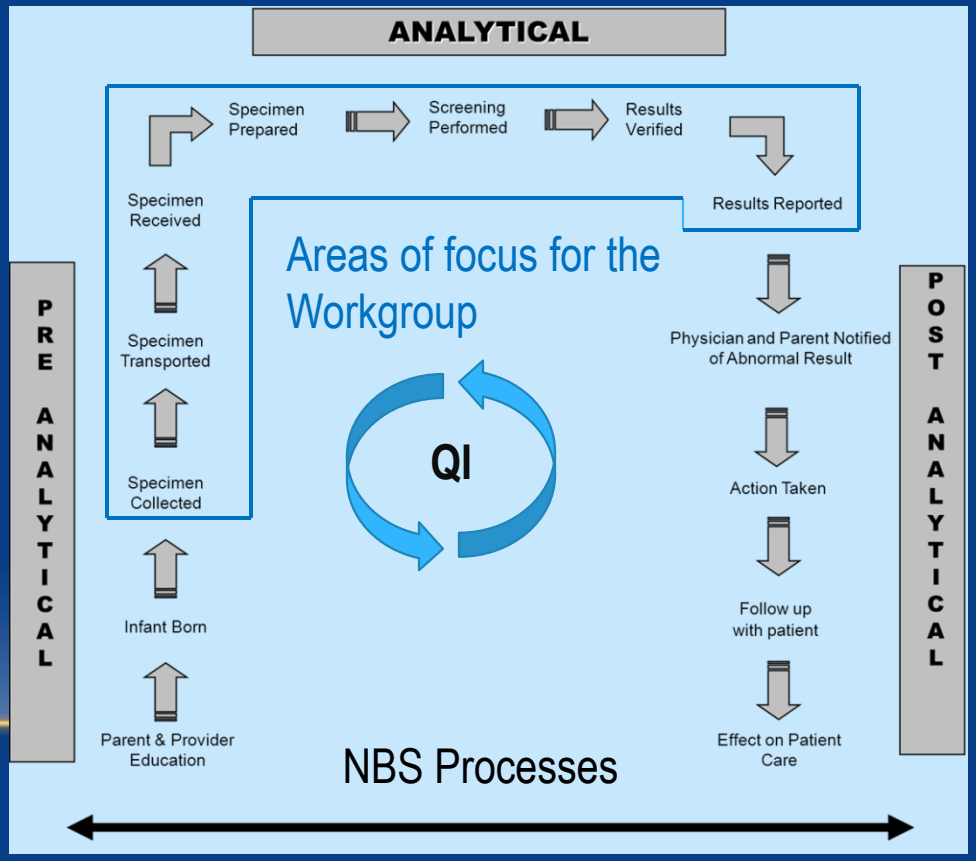
- Held bi-weekly calls
- Developed an outline of the NBS system
- Developed discussion guide
- Using discussion guide, workgroup members held focus groups at 2 regional collaboratives meetings

ACTIVITIES

- Surveyed States
  - Used focus group results and common themes to guide development of survey questions and answer choices.
- Critical conditions discussions
  - Society of Inherited Metabolic Diseases– metabolic disorders
  - In the process of convening additional expert groups –Endocrinology, pulmonology, hematology and immunology.
- Reaching out to the Joint Commission and American Hospital Association (via ACMG and March of Dimes)

OUTLINE THE NBS SYSTEM





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DEVELOP LIST OF CRITICAL CONDITIONS THAT REQUIRE URGENT FOLLOW-UP

- Hemoglobinopathies
  - Experts utilized in case definitions project
  - General consensus within group that these conditions do not require urgent follow-up (i.e. not critical conditions)
- Endocrine Disorders
  - Endocrinologists utilized in case definitions project
  - CAH is time critical, results within 5-7 days
  - CH is time sensitive, results within 7-14 days
- Cystic Fibrosis
  - Experts utilized in case definitions project
  - Discussion to be held with experts next week
- Metabolic conditions
  - SIMD work group

CRITICAL CORE METABOLIC CONDITIONS

- Critical Condition: A condition on the RUSP in which acute symptoms or potentially irreversible damage could develop in the first week of life, and for which early recognition and treatment can reduce risk of morbidity and mortality.

Organic Acid Conditions	**Fatty Acid Oxidation Disorders**
Propionic Acidemia (PROP)	Medium Chain Acyl-CoA-dehydrogenase deficiency (MCAD)
Methylmalonic Acidemia (methylmalonyl-CoA mutase) (MUT)	Very Long chain acyl-CoA dehydrogenase deficiency (VLCAD)
Isovaleric Acidemia (IVA)	Long chain L-3-hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)
3-Hydroxy-3-methyglutaric aciduria (HMG)	Trifunctional protein deficiency (TFP)
Holocarboxylase synthase deficiency (MCD)	
β-Ketothiolase deficiency (BKT)	
Glutaric Aciduria, Type 1 (GA1)	
Amino Acid Disorders	**Other**
Argininosuccinic Aciduria (ASA)	Classic Galactosemia (GALT)
Citrullinemia type 1 (CIT)	
Maple syrup urine disease (MSUD)	

- Source: SIMD Position Statement August 21, 2014

SIMD POSITION STATEMENT: CRITICAL CONDITIONS

- Critical conditions can present with acute crisis in the first week of life
  - Maintain appropriate standards of collection
  - Important to have presumptive positive results ASAP
  - I**mmediate** referral for appropriate evaluation and management
- These conditions can also present with potentially lethal crisis in the first hours or days of life.
  - "It is not possible, even in the most ideal system, to have results of NBS available before clinical presentation of all affected babies"
  - "some babies will present even before it is proper to collect the NBS sample."
- Clinicians must include IEM in the differential diagnosis of an ill newborn.

SIMD POSITION STATEMENT: CONSIDERATIONS

- Be aware of clinical variability.
  - Clinical response may depend on the analyte level, analyte patterns or ratio of analytes.
  - There is heterogeneity in the severity of conditions with a spectrum of clinical manifestations.
  - Each condition listed has a significant risk of catastrophic presentation in the first week of life though many babies with a critical condition may be asymptomatic in the first weeks of life.
  - Some babies with conditions on the RUSP that are not included on the critical conditions list may present in the first week of life.

Association of Public Health Laboratories

SURVEY TO STATES

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SURVEY INSTRUMENT

- 31 questions
- Format of survey
  - Section 1 – Communication between State NBS Programs and birth facilities
  - Section 2 – State NBS Programs and the 4 recommendations related to timeliness
  - Section 3 – New technology/new tests and their impact on timeliness
- Number of respondents

	Number of Completed Surveys
All respondents	62
NBS Laboratory Director version	47
NBS Follow-up Coordinator version	15

- For purposes of this survey: Birth is used as the reference point and data presented per state/territory (multiple responses per state combined)
- Survey open: July 8 – 31, 2014

COMMUNICATION BETWEEN STATE NBS PROGRAMS AND BIRTH FACILITIES

- All NBS programs provide feedback to individual birthing facilities.
  - Unsatisfactory specimens, transit time, completion of essential information, age at specimen collection
  - Feedback is generally provided monthly, quarterly or as needed.
- Technical assistance and/or training to birthing facilities is provided by 50/51 programs.
  - Typically upon request or upon recognition of an issue based on monitoring

DOES YOUR NBS PROGRAM HAVE A MECHANISM TO ENSURE THAT ALL NEWBORNS IN YOUR STATE ARE SCREENED?

Answer	Response	%
Yes	30	58.8%
No	16	31.4%
I don't know	5	9.8%
Total	51	100.0%

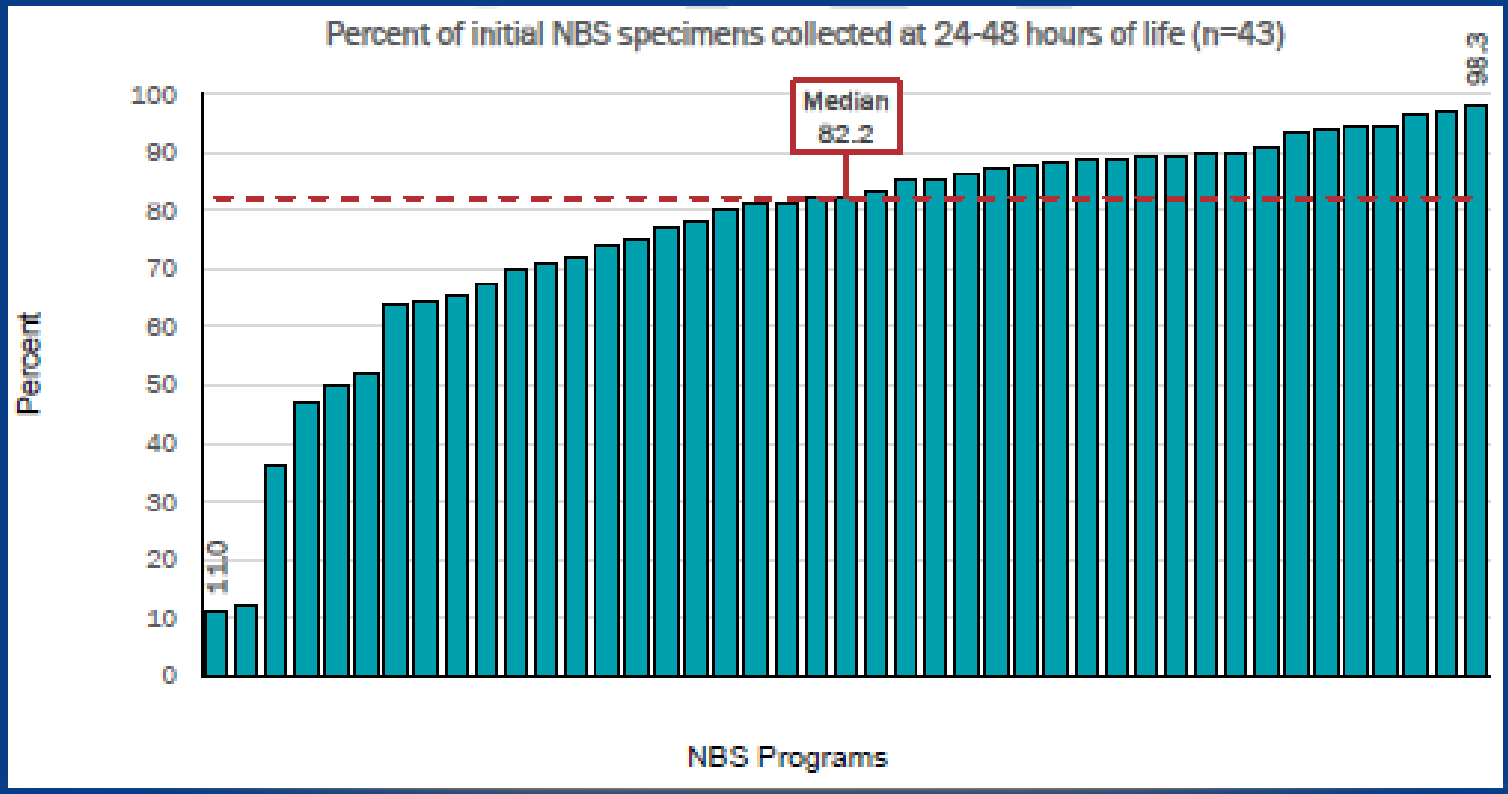
Mechanisms include matching NBS specimens to vital records/birth certificates daily, weekly or monthly and NBS specimens card kit numbers submitted with birth certificate request linking the two

Barriers:

- Lack of a data linkage between NBS records and vital statistics.
- Failure to link directly to Amish populations, other home deliveries, and babies born out of state
- Availability of birth certificate data at the time of screening
- No way to capture parent refusals

INITIAL NBS SPECIMENS SHOULD BE COLLECTED AT 24 TO 48 HOURS OF LIFE

- % of responses that met this goal



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INITIAL NBS SPECIMENS SHOULD BE COLLECTED AT 24 TO 48 HOURS OF LIFE

- The factors that NBS programs rated as having a major impact on their ability to meet the goal:
  - Compliance with collection from premature/sick infants (23.5%)
  - Transfer of newborn before specimen is collected (15.7%)
  - Release of newborn prior to 24 hours of life (13.7%)
  - High turnover of staff performing DBS collection (11.8%)
- Other Gaps/Barriers Noted:
  - Midwifery centers/out-of-hospital births (11/49 or 22%)
  - Lack of education to submitters & parents due to low staffing; high turnover at birthing facilities (7/49 or 14%)
  - State regulations allow collection for NBS specimens at different times than what is in the recommendation. (5/49 or 10%)

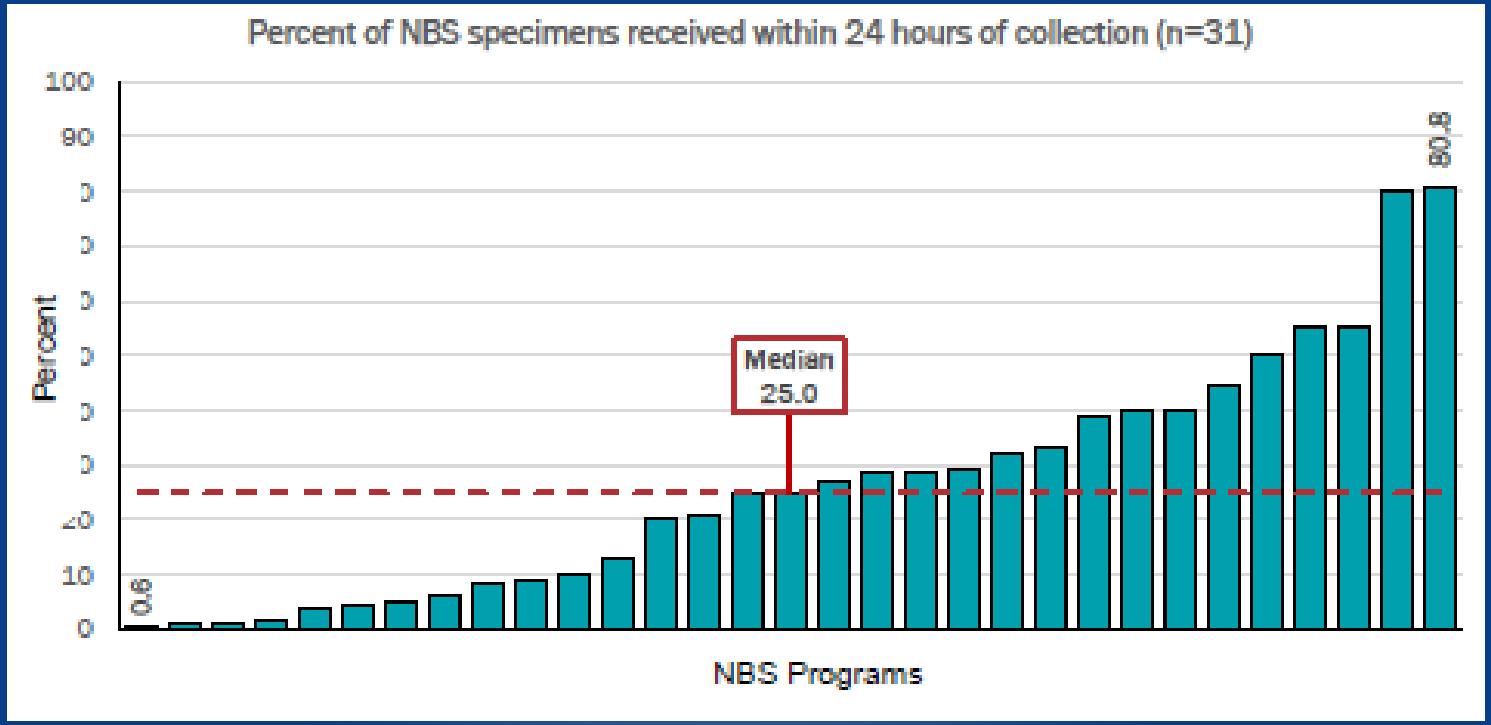
INITIAL NBS SPECIMENS SHOULD BE COLLECTED AT 24 TO 48 HOURS OF LIFE

- Best Practices
  - Provide education and outreach to individuals involved in NBS processes (from parents to providers)
  - Monitor performance and provide feedback and technical assistance to birthing facilities
  - Make legislative changes/revise state regulations to match recommendations and to provide regulatory authority to ensure compliance

"Make it (the recommendation) a Joint Commission Standard."

NBS SPECIMENS SHOULD BE RECEIVED AT THE LABORATORY WITHIN 24 HOURS OF COLLECTION

- % of responses that met this goal



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NBS SPECIMENS SHOULD BE RECEIVED AT THE LABORATORY WITHIN 24 HOURS OF COLLECTION

- The factors that NBS programs rated as having a major impact on their ability to meet the goal:
  - Geographic distance from birthing facility to NBS lab (37.3%)
  - Laboratory not accessioning specimens on weekends or holidays (29.4%)
  - Operating hours of the laboratory (27.5%)
  - Operating hours of courier system (27.5%)
  - Lack of dedicated courier system (25.5%)
  - Batching by birthing facilities (19.6%)
- Other Gaps/Barriers Noted
  - Courier services and other mail delivery challenges (27/51 or 52%)
  - Birthing facilities/submitter challenges in getting specimens sent out (9/51 or 18%)
  - Lack of timely feedback to birthing facilities/ submitters on performance (6/51 or 12%)

NBS SPECIMENS SHOULD BE RECEIVED AT THE LABORATORY WITHIN 24 HOURS OF COLLECTION

- Best practices
  - Utilize courier and/or overnight delivery services
  - Provide educational activities to birthing facility staff, laboratory staff & parents
  - Continuous quality improvement activities with birthing facilities/submitters
  - Performance monitoring and feedback
  - Expansion of NBS laboratory operating hours

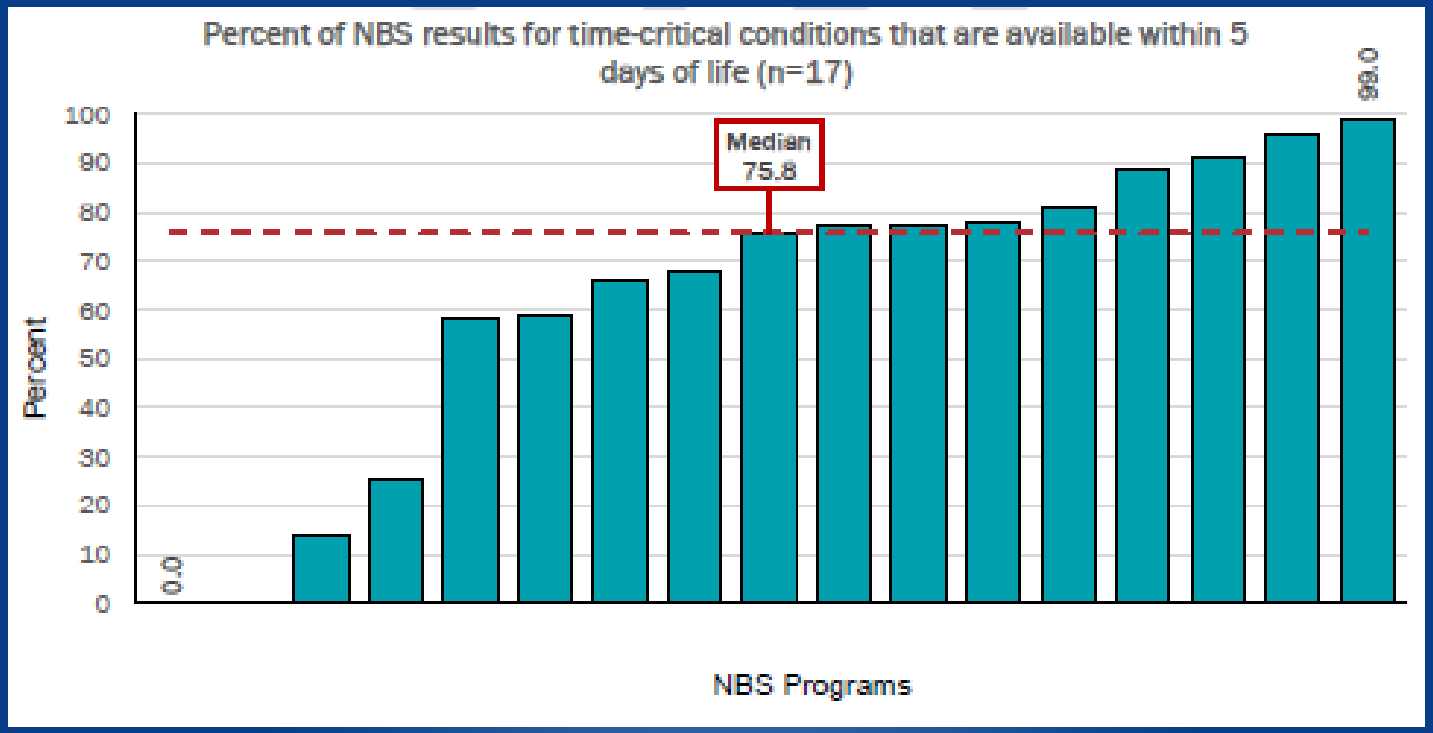
NEWBORN SCREEN RESULTS FOR TIME-CRITICAL CONDITIONS SHOULD BE AVAILABLE WITHIN 5 DAYS OF LIFE

- **Does your NBS program differentiate conditions based on how time-critical they are?**

Answer	Response	%
Yes (Ask q15-q20)	37	72.5%
No (Got to q21)	14	27.5%
Total	51	100.0%

NEWBORN SCREEN RESULTS FOR TIME-CRITICAL CONDITIONS SHOULD BE AVAILABLE WITHIN 5 DAYS OF LIFE

What percent of NBS results for time-critical conditions are available within 5 days of life?



NEWBORN SCREEN RESULTS FOR TIME-CRITICAL CONDITIONS SHOULD BE AVAILABLE WITHIN 5 DAYS OF LIFE

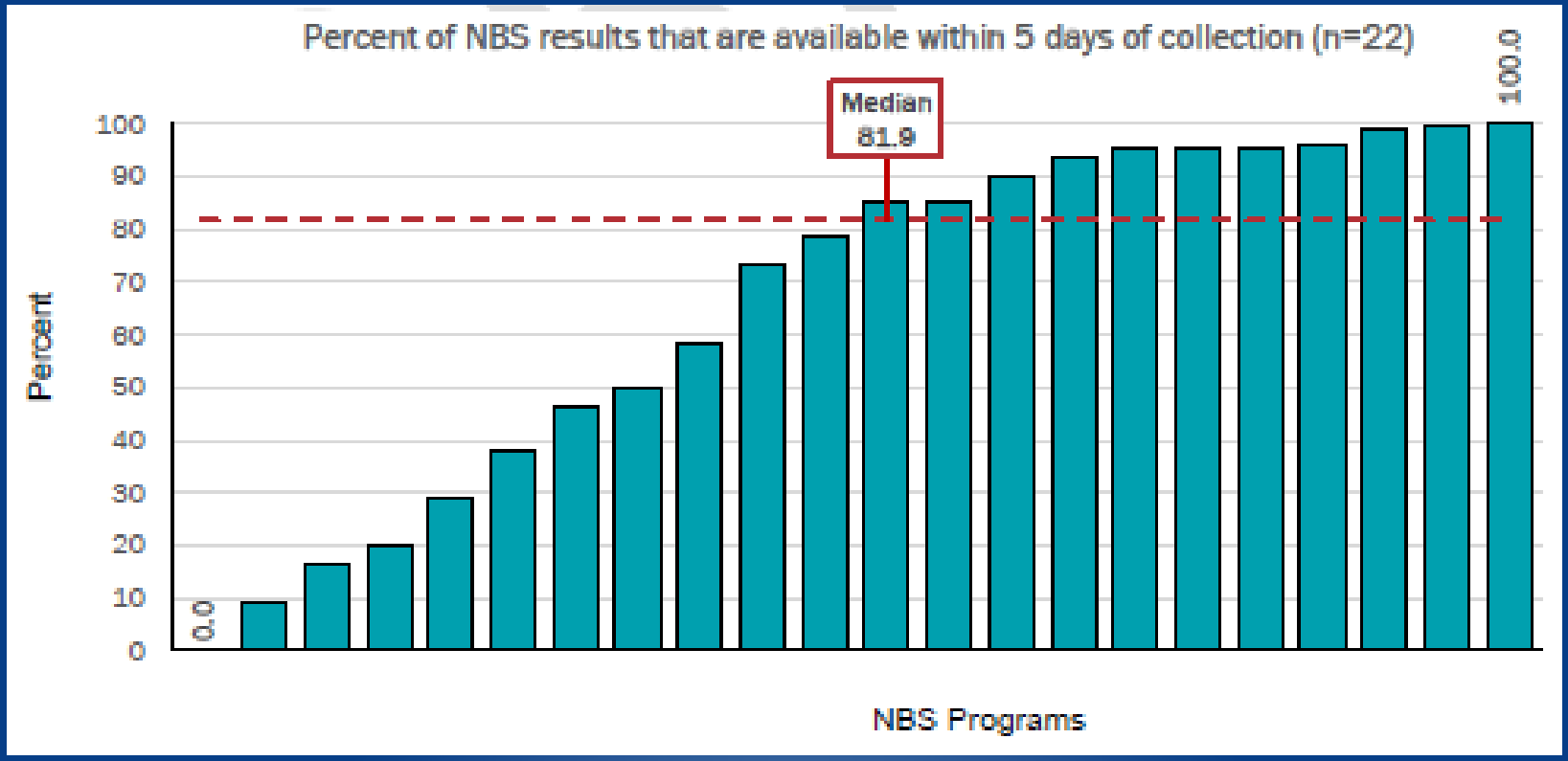
- The factors that NBS programs rated as having a major impact on their ability to meet the goal:
  - Specimen receipt time falls outside recommended time frame (40.5%)
  - Operating hours of courier (27.0%)
  - Operating hours of NBS lab; lab not accessioning specimens on weekends/holidays (18.9%)
  - Home births not reported (16.2%)
  - Second tier testing is performed; current system does not allow parsing of specific conditions (13.5%)
- Other Gaps/Barriers Noted
  - Delay in receipt of specimens in NBS laboratory (14/37 or 37%)
  - Use of out of state NBS laboratory (2/37 or 5%)

NEWBORN SCREEN RESULTS FOR TIME-CRITICAL CONDITIONS SHOULD BE AVAILABLE WITHIN 5 DAYS OF LIFE

- Best Practices
  - Provide education to birthing facilities on specimen collection and submission
  - Increase NBS program operating hours (laboratory & follow-up)
  - Provide courier/overnight delivery services or encourage their use
  - Monitor performance and provide feedback to birthing facilities, couriers and laboratory
  - Focus on NBS program improvement (e.g. capacity, turnaround time, technology)

ALL NBS RESULTS SHOULD BE AVAILABLE WITHIN 5 DAYS OF COLLECTION

- % of responses that meant this goal



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ALL NBS RESULTS SHOULD BE AVAILABLE WITHIN 5 DAYS OF COLLECTION

- The factors that NBS programs rated as having a major impact on their ability to meet the goal:
  - Delays in the processes that lead up to release of NBS results (35.3%)
  - Operating hours of NBS lab (29.4%)
  - Nature of the test itself (23.5%)
  - Ability to implement change (17.6%)
  - Release of paper NBS results to submitters via USPS (17.6%)
- Other Gaps/Barriers Noted
  - Limitations within NBS laboratory (14/51 or 28%) or of Laboratory Information Management Systems (LIMS) functionality (12/51 or 24%)
  - Delayed specimen receipt at NBS laboratory (10/51 or 20%)

ALL NBS RESULTS SHOULD BE AVAILABLE WITHIN 5 DAYS OF COLLECTION

- Best practices
  - Expand operating hours of NBS program
  - Ensure timely specimen collection and transit to the NBS laboratory (previously listed)
  - Improve reporting and communications mechanisms (e.g. ELO/ELR)
  - Provide education to birthing facility staff on importance of timely NBS
  - Provide cross-training to NBS laboratory staff
  - Monitor performance and provide feedback
  - NBS program improvement activities

NEW TECHNOLOGY IN THE LABORATORY AND ITS IMPACT ON TIMELINESS

Has the use of new technology or adding new tests in your newborn screening program improved and/or hindered your ability to perform timely newborn screening? (n=45) Check all that apply

Answer	Response	%
Improved	9	20.0%
Hindered	15	33.3%
Neither	24	53.3%

Improvements (n=9)

- New instrument allows for continuous loading of test plates
- Automated instruments and assays that run anytime during the day and overnight with minimal supervision
- Deployment of new computer system
- Ability to add DNA results and tandem mass spectrometry for quicker results
- Greater precision and accuracy which can lead to faster turnaround times

NEW TECHNOLOGY IN THE LABORATORY AND ITS IMPACT ON TIMELINESS

Hindrances (n=15)

- Increase in number of disorders increases testing time e.g., DNA testing for Cystic fibrosis
- High costs of reagents
- Limited resources and capacities of NBS program: e.g., staffing challenges – same number of staff running more tests
- Pressures to reduce false positives leads to more testing before release of results and thus a delay is observed
- Second tier testing e.g. CF second tier testing delays notification of presumptive positive NBS results

SURVEY LIMITATIONS

- Lack of definitions of terms
  - i.e. how the program interpreted the timeframes in question and calculated the quantitative data
- Lack of ability to collect appropriate data fields
  - E.g. No time of receipt, just date of receipt
- Software limitations
  - E.g. Inability of program staff to quickly pull data for ad hoc requests

REVISITING THE RECOMMENDATIONS

A NEW APPROACH

Placing the emphasis on the goal of the NBS program:

- moving recommendations 3 and 4 upfront as the overall goals for the NBS programs
- recommendations 1 and 2 providing the means to achieve these goals

RECOMMENDATION 3: NEWBORN SCREEN RESULTS FOR TIME-CRITICAL CONDITIONS SHOULD BE AVAILABLE WITHIN 5 DAYS OF LIFE.

- Issue – definition of “available”
  - Scope limited in this project from collection thru testing and reporting
  - Timeframes were left open to interpretation & thus calculations may vary
  - Timeframes must be defined and data must be captured to compute the calculation.

- New wording:
  - *Presumptive positive* results for time-critical conditions should be *reported to the child’s healthcare provider* within 5 days of life.
  - However, this recommendation may not be measurable at this time

RECOMMENDATION 4: ALL NBS RESULTS SHOULD BE AVAILABLE WITHIN 5 DAYS OF COLLECTION

- Issue - definition of “available”
  - Timeframes were left open to interpretation & thus calculations may vary
  - Timeframes must be defined and data must be captured to compute the calculation
  - Important for providers to receive results on any out-of-range results for time sensitive disorders in timely manner for follow-up purposes. We use *time sensitive disorders* to indicate the disorders we screen for that aren’t time critical; this definition captures that timely screening for these disorders is also important.
  - Important for providers to receive ‘normal’ results in timely manner as well

- Now two recommendations with new wording:
  - *All presumptive positive results for time sensitive conditions should be reported to the healthcare provider within 7 days of life.*
  - *All NBS results should be reported within 7 days of life.*

RECOMMENDATION 1: INITIAL NBS SPECIMENS SHOULD BE COLLECTED AT 24 TO 48 HOURS OF LIFE

- Considerations:
  - Different recommendations exist for specimens collected from pre-term, low birth weight and sick newborns[1]
  - Some states have different timeframes in their regulations (ranges included 12 hours to 72 hours).
  - Balancing false negatives & false positives – esp. endocrine disorders

- New wording:
  - *Initial NBS specimens should be collected in the appropriate time frame for the baby's condition but no later than 48 hours after birth*

[1]CLSI Guideline NBS03-A

RECOMMENDATION 2: NBS SPECIMENS SHOULD BE RECEIVED AT THE LABORATORY WITHIN 24 HOURS OF COLLECTION.

- Considerations:
  - Courier, geography and weather limitations
  - Routine second screens

- New wording:
  - NBS specimens should be received at the Laboratory *ideally* within 24 hours of collection *but no later than 72 hours after collection*.

NEW RECOMMENDATIONS

In order to achieve the best outcomes for babies:

- Presumptive positive results for time-critical conditions should be reported to the child's healthcare provider within 5 days of life.
- All presumptive positive results for time sensitive conditions should be reported to the healthcare provider within 7 days of life.
- All NBS results should be reported within 7 days of life

In order to achieve these goals (and reduce delays in newborn screening):

- Initial NBS specimens should be collected in the appropriate time frame for the baby's condition but no later than 48 hours after birth
- NBS specimens should be received at the Laboratory ideally within 24 hours of collection but no later than 72 hours after collection.

QUESTIONS/DISCUSSION