Michigan Department of
Health and Human Services

MICHIGAN NEWBORN SCREENING PROGRAM

Annual Report 2015

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MDHHS
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RICK SNYDER, GOVERNOR | NICK LYON, DIRECTOR

MICHIGAN
Newborn
Screening

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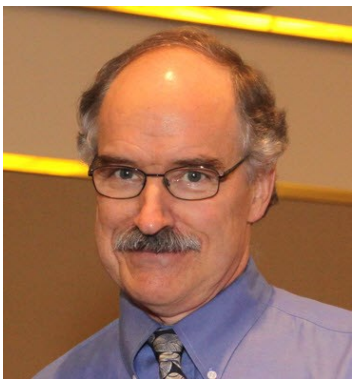
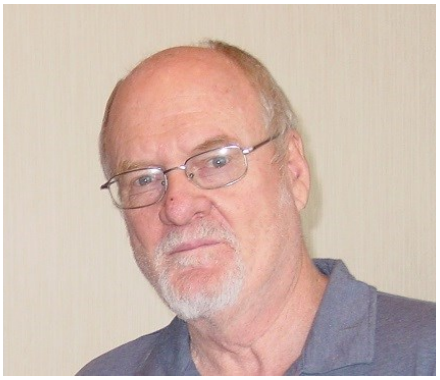
A Legacy of Saving Babies

Harry Hawkins and Bill Young



Harry Hawkins



Bill Young

Too often vital public health services are invisible to most state residents. While lifesaving research and medical science are translated into public health practice by state and local public health employees, most individuals do not realize such important work is keeping us safe from disease, injury, infection and more. Screening of newborns is an important public health program to detect babies with rare, but serious disorders that benefit from early treatment. Mr. Harry Hawkins and Dr. Bill Young are two individuals who have played a vital role in the progress that the Newborn Screening Program has seen since they started with the state health department in the 1970s.

Harry Hawkins started off working for the Michigan Department of Public Health in 1977 as a laboratory technologist, later becoming the Laboratory's Newborn Screening Section Manager. Over the years, he has been instrumental in the growth of the NBS laboratory from its infancy to current advanced state—evolving from a completely manual process using one computer and results figured on calculators for a single disorder—to a highly automated, high throughput facility that screens for over 50 disorders on a daily basis using over 30 instruments, more than 100 computers and a sophisticated Information System. Over the years, his contributions have included not only developing and standardizing assays, but implementing computers for data analysis, and writing programs for data reduction.

When Bill joined the Department in 1979 as manager of the Newborn Screening Follow-up Program, a role he held for more than 35 years, babies were being screened for two disorders: phenylketonuria (PKU) and congenital hypothyroidism (CH). He worked with birthing hospitals, primary care providers and medical specialists to develop a coordinated system for blood spot screening, follow-up, diagnosis and medical management of children identified by screening, collaborating with the laboratory to oversee expansion of the program. To prepare for adding

each new disorder to the panel, he acquired the expertise necessary for developing follow-up algorithms and medical management protocols. This meant assimilating scientific literature; finding the latest, often unpublished, research data; speaking with national and international experts; learning from public health colleagues in other states; and understanding new laboratory methods and how they impacted screening value cutoffs.

Today, in large part due to the efforts of Harry and Bill, Michigan screens for over 50 disorders that can lead to disability or death if not detected early. As each disorder was considered for addition to the screening panel, Bill provided scientific leadership to help assure Michigan babies always received "state of the art" screening and follow-up services while Harry ensured use of the best available laboratory technology. The advancements of the Michigan Newborn Screening Program would not be possible without the dedication of these two men, who were among the founding fathers of modern day screening programs, participating in national initiatives and networking with other state labs to help improve Michigan's program. Although most families are unaware of their efforts, over the last 3 ½ decades they have touched the lives of about 7 million newborns who received screening, and their work has directly benefitted almost 6,000 babies who have been identified with a disorder and referred for early treatment to help prevent serious health complications.

During this golden anniversary year of Michigan's Newborn Screening Program, we'd like to recognize Harry and Bill's passion for newborn screening, their many years of successful collaboration, and lifelong public health careers devoted to saving lives and improving the health of Michigan's newest infant citizens.

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Executive Summary

The Newborn Screening (NBS) annual report provides an overview of the Michigan NBS Program, screening performance metrics, and quality assurance information.

In 2015, the NBS Program celebrated its 50th anniversary. Since the program began in 1965 with screening for phenylketonuria, over 50 disorders have been added to the screening panel. Through 2015, nearly 7 million infants have been screened with almost 6,000 diagnosed with diseases included in the NBS bloodspot panel.

Of the 111,725 infants screened in 2015, the vast majority were Michigan residents and 270 (0.2%) were diagnosed with a disease. Overall, one infant out of 414 screened was diagnosed with one of the disorders included in the NBS panel (see Table 1 for list of disorders).

Developments occurring in 2015:

Michigan continued to disseminate findings at both the state and national level:

- The findings from different studies and analyses related to NBS were presented at the following meetings:
    - ◊ Michigan Epidemiology Conference
    - ◊ Region 4 Midwest Genetics Collaborative
- "Congenital Hypothyroidism Long-Term Follow-up Project: Navigating the Rough Waters of a Multi-Center, Multi-State Public Health Project" was published in *Journal of Genetic Counseling*.

New capacity was added for NBS:

- The NBS Program continued working towards implementing screening for Pompe disease. An FDA-approved laboratory method becomes available and is validated in Michigan.
- Mucopolysaccharidosis Type I (MPSI) disease and X-linked adrenoleukodystrophy were added to the mandatory screening panel. The Follow-up and Laboratory Programs began developing infrastructure for screening, and screening will commence when FDA-approved methods become available and is validated in Michigan.
- Clinics at the Children's Hospital of Michigan in Detroit and the University of Michigan in Ann Arbor were designated as NBS Follow-up Coordinating Centers for Pompe disease and MPS1.

Staff continued work on obtaining coverage for medical foods and formula:

- A work group focusing on diet for life for metabolic disorders and third party insurance coverage was formed January 2015 and developed a summary report available at: http://www.michigan.gov//documents/mdhhs/Metabolic_Formula_and_Food_Work_Group_Summary_v1-19-16_511139_7.pdf.

- Medicaid policy changes were put in effect April 1, 2015 to address the barriers identified by the Diet for Life Work Group convened in 2014. The updated policy is in regard to coverage of enteral nutrition administered orally. For further details regarding Medicaid changes, please go to: http://www.michigan.gov/mdhhs/0,5885,7-339-73971_4911_4916-323855--,00.html.

The NBS Program celebrated its 50th anniversary with activities throughout the year:

- Five press releases highlighting the importance of newborn screening were created.

- NBS staff attended 11 events for providers and 5 baby fairs for parents and families.

- On September 16, the NBS Program held a NBS Symposium with a variety of presentations about the past, present, and future of Michigan's NBS Program.

- A booklet about Michigan's NBS Program was developed.

- Individualized fact sheets for every birth hospital and every state legislator were distributed.

Listing of Figures & Tables

Figures

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Acronym Key

Acronym	Name
ACMG	American College of Medical Genetics and Genomics
CCHD	Critical Congenital Heart Disease
CDC	Centers for Disease Control and Prevention
CHM	Children's Hospital of Michigan
CHMMC	Children's Hospital of Michigan Metabolic Clinic
EBC	Electronic Birth Certificate
FIGLU	Formiminoglutamic acid disorder
FPR	False Positive Rate
HPLC	High Performance Liquid Chromatography
HRSA	Health Resources and Services Administration
MCIR	Michigan Care Improvement Registry
MDHHS	Michigan Department of Health and Human Services
MPSI	Mucopolysaccharidosis Type I Disease
MS/MS	Tandem Mass Spectrometry
NBS	Newborn Screening
NICU	Neonatal Intensive Care Unit
PCP	Primary Care Physician
PID	Primary Immunodeficiency Disorders
PPV	Positive Predictive Value
QA	Quality Assurance
QAAC	Quality Assurance Advisory Committee
SCDAA	Sickle Cell Disease Association of America
SCID	Severe Combined Immunodeficiency Disorder
SCN	Special Care Nursery
U of M	University of Michigan

I. Introduction

The Newborn Screening (NBS) Annual Report provides an overview of Michigan's NBS Program, screening performance metrics related to disorders included in the NBS panel, and quality assurance information. This report does not include appendices which have not changed, including the NBS research guidelines, supportive legislation, and NBS advisory committees.[1]

This report is intended to provide:

- An introduction and historical account of the development of NBS in Michigan
- Michigan screening performance metrics
- Quality assurance information

What is Newborn Screening?

NBS is the process of early identification of health conditions followed by their subsequent treatment before the onset of disease processes. Successfully screening, confirming, and treating newborns with disorders in a timely manner minimizes the risk of long-term sequelae. Depending on the condition, potential outcomes of disorders in the NBS panel include, but are not limited to, brain/neurological damage, intellectual disability, damage to the liver, eyes or spleen, or death if not detected early. To prevent these outcomes from occurring, NBS programs test blood spots collected from infants during the first few days of life and refer infants with abnormal screens for appropriate confirmatory testing and medical management.

NBS began in the 1960s when Dr. Robert Guthrie developed the bacterial inhibition assay to diagnose phenylketonuria (PKU) by determining the level of the amino acid phenylalanine in a drop of a baby's blood placed on a strip of filter paper. In 1965, Dr. K. Stanley Read at the Michigan Department of Public Health and Dr. Richard Allen at the University of Michigan introduced NBS for PKU to Michigan and almost immediately turned what had been a devastating, untreatable, genetic disorder into a condition readily manageable by a low protein diet (Figure 1).[2] In 1977, a test for congenital hypothyroidism (CH) was added to the NBS panel, and screening for galactosemia was initiated in 1985. Public Act 14 of 1987 mandated further expansion of screening with the addition of three disorders: biotinidase deficiency, maple syrup urine disease (MSUD), and hemoglobinopathies such as sickle cell disease. The Act also designated the state laboratory as the sole testing site and mandated a fee to fund the program. In 1993, another endocrine disorder, congenital adrenal hyperplasia (CAH), was added to the screening panel.

[1]All of these appendices can be found in previous annual reports, which are available at www.michigan.gov/newbornscreening.Reports for year 2009 and older are available here: http://www.michigan.gov/documents/mdch/NBS_Archived_Documents_314805_7.pdf

[2]For more information on the history of PKU and PKU-related NBS Program evaluations conducted in Michigan, see Chapter IV of the 2009 NBS Annual Report.

The introduction of tandem mass spectrometry (MS/MS) in 2003 enabled the state laboratory to efficiently screen for a large number of disorders using a single blood spot. This technology replaced Dr. Guthrie's bacterial inhibition assays previously used to detect PKU and MSUD. The first additional disorder screened with this method was medium chain acyl-CoA dehydrogenase deficiency (MCAD), a disorder of fatty acid oxidation that can result in sudden death during periods of fasting. MS/MS technology allowed further expansion of the NBS screening panel in 2004 to include an additional three amino acid disorders: homocystinuria (HCY), citrullinemia (CIT), and argininosuccinic aciduria (ASA).

In 2005, a pilot project was initiated to expand the screening panel to 48 disorders by including the 29 additional MS/MS disorders recommended by the American College of Medical Genetics and Genomics (ACMG) and the March of Dimes. Screening for cystic fibrosis began in Michigan on October 1, 2007, meeting another ACMG recommendation. Hearing screening was also added to the NBS panel in 2007, but this report does not include hearing screening results.[1] Screening for SCID began on October 1, 2011. Screening for Hemoglobin H disorder began in 2012. Pulse oximetry screening for critical congenital heart disease (CCHD) began in 2014, and information on this screening program will be released in a separate report once more data is compiled. Pompe disease was added to the panel in 2014, and screening will begin when an FDA-approved laboratory screening method becomes available and is validated. Mucopolysaccharidosis Type 1 and X-linked adrenoleukodystrophy were added to the panel in 2015, and screening will start when FDA-approved methods become available and is validated in Michigan.

Table 1 provides the complete list of disorders currently screened for in Michigan. The highlighted disorders are those that are screened for in Michigan, but no cases have ever been identified and confirmed through NBS. Detailed information about the disorders included in the screening panel, confirmation of diagnoses, and follow-up of positive tests can be found in the Michigan NBS Guide, which is available by clicking on the "Resources for Hospitals and Health Professionals" link on the NBS website (www.michigan.gov/newbornscreening).

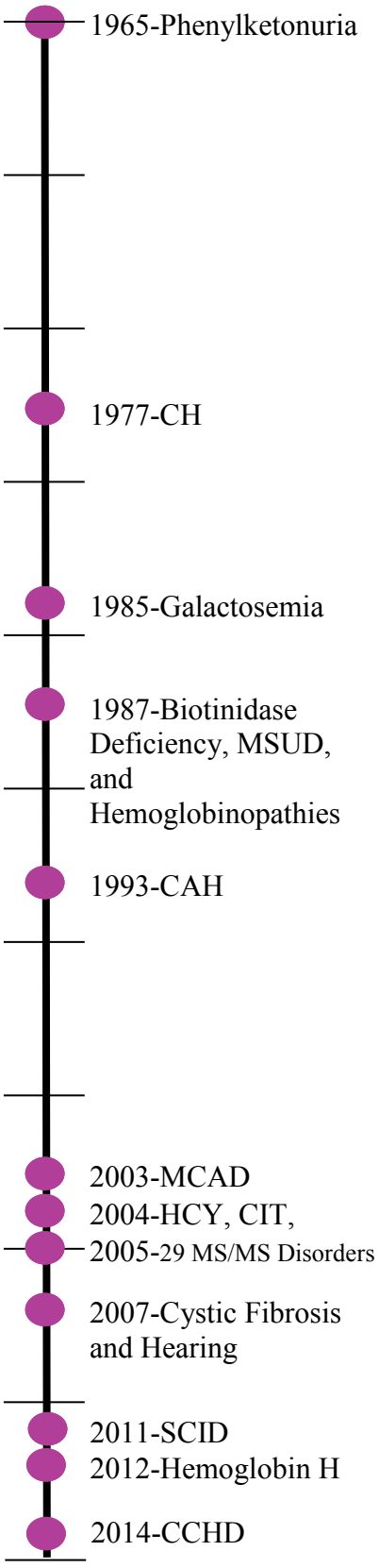

Figure 1. Implementation of Disorders on the NBS Panel, Michigan, 1965-2015

[1]More information about the newborn hearing screening program can be found at www.michigan.gov/ehdi.

Table 1. Disorders included in the Newborn Screening Blood Spot Panel, Michigan, 2015

Amino Acid Disorders	**Organic Acid Disorders**
1. Argininemia	28. 2-Methyl-3-hydroxy butyric aciduria
2. Argininosuccinic acidemia	29. 2-Methylbutyryl-CoA dehydrogenase deficiency
3. Citrullinemia	30. 3-Hydroxy 3-methylglutaric aciduria
4. Citrullinemia Type II	31. 3-Methylcrotonyl-CoA carboxylase deficiency
5. Homocystinuria	32. 3-Methylglutaconic aciduria
6. Hypermethioninemia	33. Beta-ketothiolase deficiency
7. Maple syrup urine disease	34. Glutaric acidemia Type I
8. Phenylketonuria	35. Isobutyryl-CoA dehydrogenase deficiency
9. Benign hyperphenylalaninemia defect	36. Isovaleric acidemia
10. Biopterin cofactor biosynthesis defect	37. Methylmalonic acidemia (Cbl A, B)
11. Biopterin cofactor regeneration defect	38. Methylmalonic acidemia (Cbl C, D)
12. Tyrosinemia Type I	39. Methylmalonic acidemia (mutase deficiency)
13. Tyrosinemia Type II	40. Multiple carboxylase deficiency
14. Tyrosinemia Type III	41. Propionic acidemia
Fatty Acid Oxidation Disorders	**Hemoglobinopathies**
15. Carnitine acylcarnitine translocase deficiency	42. S/Beta thalassemia
16. Carnitine palmitoyltransferase I deficiency	43. S/C disease
17. Carnitine palmitoyltransferase II deficiency	44. Sickle cell anemia
18. Carnitine uptake defect	45. Variant hemoglobinopathies
19. Dienoyl-CoA reductase deficiency	46. Hemoglobin H disease
20. Glutaric acidemia Type II	**Endocrine Disorders**
21. Long-chain L-3-hydroxyl acyl-CoA dehydrogenase deficiency	47. Congenital adrenal hyperplasia
22. Medium/short-chain L-3-hydroxyl acyl-CoA dehydrogenase deficiency	48. Congenital hypothyroidism
23. Medium-chain acyl-CoA dehydrogenase deficiency	**Other Disorders**
24. Medium-chain ketoacyl-CoA thiolase deficiency	49. Biotinidase deficiency
25. Short-chain acyl-CoA dehydrogenase deficiency	50. Galactosemia
26. Trifunctional protein deficiency	51. Cystic fibrosis
27. Very long-chain acyl-CoA dehydrogenase deficiency	52. Severe combined immunodeficiency
	53. T-cell related lymphocyte deficiencies

Notes: Highlighted disorders have never been detected in Michigan through NBS. The following disorders are reported together because the same analyte(s) is used for screening: #2-4, #5-6, #8-11, #13/#14, #15/#17, #21/#26, #29/#36, #41/ #37-39, #25/#35, #30-32/#40, #28/#33, #24/#34.

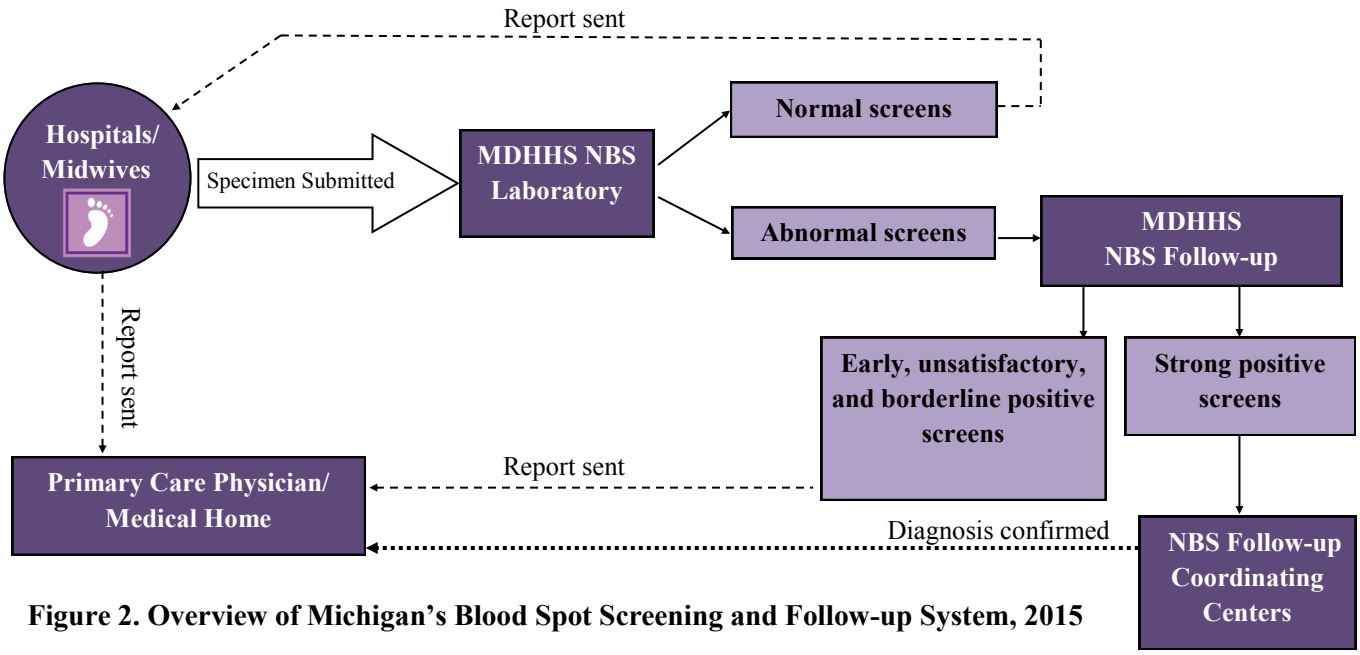

Figure 2. Overview of Michigan's Blood Spot Screening and Follow-up System, 2015

Abbreviations: MDHHS-Michigan Department of Health and Human Services; NBS-Newborn Screening;

HOSPITALS

In 2015, Michigan had 83 hospitals with birthing units. Each hospital has a designated NBS Coordinator who helps facilitate the screening process. Hospital coordinators receive a quarterly quality assurance report from the NBS Follow-up Program that includes information on hospital-specific performance indicators compared to the state overall. Hospitals receive periodic site visits by the NBS Nurse Consultant to evaluate the screening process and make recommendations for improvement.

MIDWIVES AND HOME BIRTH ATTENDANTS

There are approximately 80 midwives registered with the NBS Program. Midwives are provided with individual assistance in meeting standards. Although the number of midwife deliveries is small, they often occur in the Amish and Mennonite populations, which have a higher incidence of several disorders included in the NBS panel.

MICHIGAN DEPARTMENT OF HEALTH AND HUMAN SERVICES

The MDHHS NBS Program includes the NBS Laboratory, the Follow-up Program, and six medical management coordinating centers. More detailed descriptions of each entity are included in previous reports available on the NBS website (www.michigan.gov/newbornscreening).

II. Methods

This section describes the methods used to calculate: a) total number of newborns eligible for screening, b) total number of newborns diagnosed through the NBS process, c) the demographic characteristics of screened newborns, d) screening performance metrics, and e) quality assurance indicators.

TOTAL NUMBER OF NEWBORNS ELIGIBLE FOR SCREENING

We used vital statistics data collected by the Vital Records & Health Data Development Section within the Division for Vital Records and Health Statistics at MDHHS to determine the total number of live births statewide eligible for screening. The number of live births in 2015 (n=112,444) is a preliminary estimate as the final files have not been released yet.

TOTAL NUMBER OF NEWBORNS DIAGNOSED BY NEWBORN SCREENING

We used the MDHHS laboratory information system (PerkinElmer Life Sciences, Inc.) to identify positive cases. We also used data collected at the coordinating centers and managed by the NBS Follow-up Program to determine the total number of cases identified by NBS and to describe the population screened. Cases referred to in this report have the following characteristics: a) they were identified by NBS, b) they were Michigan residents, and c) they were identified and diagnosed through established laboratory and clinical protocols.

DEMOGRAPHIC CHARACTERISTICS OF SCREENED NEWBORNS

The demographic characteristics of screened newborns are presented for Michigan residents screened in Michigan. This report focuses on cases and screening results among Michigan residents only since out-of-state infants born within the state are followed-up and diagnosed elsewhere.

SCREENING PERFORMANCE METRICS

Table 2 provides a description of screening performance metrics included in subsequent tables. These indicators are commonly used to assess the performance of screening tests and allow for comparisons both over time and with other screening programs. Ideal screening tests have a high positive predictive value (perfect=100%) and a low false positive rate (perfect=0%); a perfect screening test correctly identifies all cases of a disorder with no false positives. Detection rates, the total number of cases identified out of the total number of newborns screened, are based on the total number of screens for in-state residents. Cases are defined as newborns identified with disorders via NBS. Maternal disorders and carriers identified by NBS are not included as confirmed cases in the performance metrics, though they are presented in separate tables in this report.

Table 2. Screening Performance Indicator Descriptions

Indicator	Description
Newborns (N)	The total number of screened live births among in-state residents
Total + (% NICU)	Total number of positive screens among in-state residents (the percentage of infants with positive screens who were admitted to the NICU among all infants with positive screens)
Positive	Screening value exceeds cutoff
Strong +	Strong positive screen (in most cases considered a medical emergency and referred immediately for diagnostic testing)
Borderline +	Borderline positive screen (not a medical emergency and repeat screen requested)
Confirmed +	A diagnosis of a disorder that has been confirmed
False +	A positive screen that is not confirmed as a case of a disease included in the NBS panel
Detection Rate	The number of infants having a confirmed disorder out of the total number of infants screened, depicted as a ratio. One case per 'X' number of infants screened depicted as 1: 'X'
FPR	False positive rate: the number of infants with false positive screens divided by the total number of infants screened, expressed as a percentage (%)
PPV	Positive predictive value: the number of infants confirmed with a disorder divided by the number of infants having positive screens, expressed as a percentage (%)

QUALITY ASSURANCE INDICATORS

Quality assurance (QA) data were obtained from NBS cards and information recorded by the state NBS laboratory and coordinating centers. QA indicators on the hospital quarterly reports prepared by the NBS Follow-up Program include: a) time from birth to specimen collection, b) specimen arrival at the state NBS laboratory by the appropriate day, c) number of specimens that are unsatisfactory, d) number of birth certificates with NBS kit number recorded, e) number of screened births with BioTrust consent form returned that is completed appropriately, and f) number of screened births with pulse oximetry values. Time from birth to start of treatment is another QA indicator used by the NBS Program.

III. Screening Results

DEMOGRAPHIC CHARACTERISTICS OF SCREENED NEWBORNS

This section describes the population of screened infants born in 2015 in terms of race, birth weight, gestational age, and birth place (hospital regular nursery, NICU/SCN, or non-hospital). These data are helpful in understanding the epidemiology (distribution of disease cases among the population) of the disorders covered in subsequent sections of this report. For example, sickle cell disease is predominantly found in African Americans, so the number of cases will fluctuate with the birth rate of African Americans.

The Michigan NBS Program screened 99.4% of the live births occurring in Michigan in 2015, as determined by the linkage of NBS records to preliminary live births records received from the Vital Records & Health Data Development Section and follow-up of unmatched records (Figure 3). Of the 112,468 live births that occurred in 2015, 338 were listed as deceased on the birth certificate. Many of these infants are not screened due to their short life spans, so they are excluded from the linkage calculations. Of the 112,130 remaining live births, the linkage algorithm successfully matched newborn screens for 110,993 infants (99.0%). The 1,137 unmatched records were sent to NBS Follow-up Program technicians for further investigation. This more in-depth follow-up revealed that 495 (43.5%) of the unmatched records were screened. For these infants, the linkage algorithm failed to create the match for a variety of reasons, including data recording errors, data entry errors, or name changes due to adoptions. Overall, 642 infants (0.6%) born in the state were not screened. Infants may not have been screened due to parental refusal of screening (n=302), transfer out of state (n=8), infant expired (n=29), child being screened in another state (n=20), or some other reason for not being screened (n=283). For all infants who are missed, the NBS Follow-up technicians either contact the nurse coordinator for hospital births or send a parental notification letter for home births. In 2015, 45 infants born in hospitals are known to have missed being screened, and those hospitals were contacted. Of the 45, 20 have been screened to date and the remaining 25 are pending.

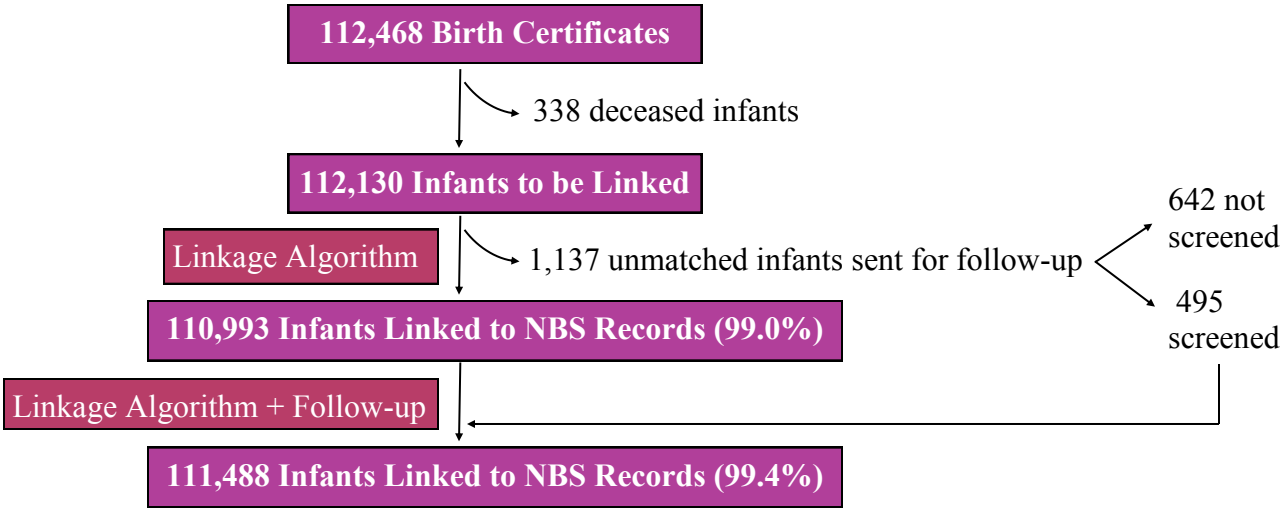

Figure 3. Newborn Screening and Live Births Records Linkage, Michigan, 2015

In total, NBS samples were received from 111,725 infants born in 2015. Of those, 290 (0.3% of screens) belonged to out-of-state residents or were collected out-of-state. Table 3 reports the demographic and perinatal characteristics by race of screened in-state residents born in 2015. This report details the screening results for in-state residents only since non-residents are typically followed in their home state. As indicated in Table 3, the majority of in-state infants screened were white, born in hospital nurseries, term (≥37 weeks gestational age), and of normal birth weight (>2,500 g). Overall, 11% of in-state infants screened were admitted to the NICU or special care nursery (SCN), 8% were low birth weight (<2,500 grams), and 9% were born preterm (<37 weeks gestational age). African Americans were over-represented among NICU, preterm, and low birth weight births.

Table 3: Demographics of Infants Screened by Race, Michigan, 2015, Excluding Out-of-State Residents, N=111,435

Race	Column Total		Nursery Type						Birth Weight (g)		Gestational Age (wks)	
			Regular Hospital		NICU/SCN		Non-Hospital		<2500		<37	
	N	%	N	%	N	%	N	%	N	%	N	%
White	70,209	63.0	62,880	63.8	6,550	54.6	779	90.2	4,553	6.6	5,809	8.4
African American	20,237	18.2	16,794	17.0	3,429	28.6	14	1.6	2,788	14.0	2,663	13.5
American Indian	464	0.4	410	0.4	50	0.4	4	0.5	21	4.6	31	6.8
Asian/Pac Islander	2,810	2.5	2,572	2.6	234	2.0	4	0.5	242	8.7	202	7.3
Middle Eastern	4,048	3.6	3,724	3.8	323	2.7	1	0.1	307	7.7	293	7.4
Multi-Racial	7,000	6.3	6,198	6.3	750	6.3	52	6.0	599	8.7	656	9.5
Missing	6,667	6.0	5,987	6.1	670	5.6	10	1.2	540	8.4	632	9.9
Column Total:	111,435	100	98,565	88.4	12,006	10.8	864	0.8	9,050	8.3	10,286	9.4

Notes: All percentages are row percentages except for Column Total which is a column percentage. All characteristics are as recorded on the newborn screening card. A total of 1,846 and 2,108 newborns were missing birth weight and gestational age on the card, respectively. Non-hospital nursery type includes home births, births that occurred at birthing centers, and all other births that did not occur at a hospital.

SCREENING OUTCOME INFORMATION

In the following sub-sections, outcome information is provided for the disorders included in the NBS panel in 2015. The total numbers of cases detected both in and through 2015 are presented along with screening performance metrics. The disorders are organized into five categories: metabolic, endocrine, cystic fibrosis, sickle cell disease and Hemoglobin H disease, and primary immunodeficiency disorders, corresponding to the five NBS follow-up coordinating programs responsible for assessing diagnosis and initiation of treatment.

CUMULATIVE DETECTION RATE

Table 4 reports the cumulative detection rate of disorders identified via NBS by classification both in and through 2015. The metabolic disorders detected by MS/MS are grouped by category (amino acid, organic acid, and fatty acid oxidation disorders). Two metabolic disorders, galactosemia and biotinidase deficiency, are detectable by enzyme assay screening rather than MS/MS and are listed separately. The galactosemia cumulative detection rate includes both Duarte compound heterozygotes (D/G) and classic galactosemia (G/G). However, only D/G cases that have been detected since 2004, the year that CHMMC began short-term treatment of this disorder, are included in the cumulative detection rate. Similarly, the biotinidase deficiency cumulative detection rate includes both partial and profound biotinidase deficiency. Treatment of partial biotinidase deficiency did not begin until 2000.

Table 4: Disorders Identified in Newborns via Newborn Screening, Michigan Residents, 1965-2015

Type of Disorder Classification (Year Screening Began)	Cases in 2015 (N)	Cases Through 2015 (N)	Cumulative Detection Rate
Galactosemia (1985)	4	192	1:21,044
Biotinidase Deficiencies (1987)	24	292	1:12,893
Amino Acid Disorders (1965)	13	729	1:9,601
Organic Acid Disorders (2005)	4	73	1:17,607
Fatty Acid Oxidation Disorders (2003)	22	230	1:6,721
Congenital Hypothyroidism (1977)	94	2,144	1:1,756
Congenital Adrenal Hyperplasia (1993)	5	153	1:18,890
Sickle Cell Disease (1987)	64	1,849	1:2,036
Hemoglobin H Disease (2012)	1	6	1:74,428
Cystic Fibrosis (October 2007)	19	238	1:3,937
Primary Immunodeficiencies (October 2011)	20	75	1:7,450
Total	270	5,981	-

Notes: Denominators for the cumulative detection rates, the number of live births eligible to have been screened, are calculated from the year screening began onward; thus, if screening commenced other than at the start of the year the denominator will be slightly larger than the true denominator. The CF detection rate denominator includes births from October 2007-2011. See Table 1 for a list of all disorders included in each disorder classification.

As indicated in Table 4 and Figure 4, CH and sickle cell disease were the most prevalent disorders in 2015, while Hemoglobin H Disease, galactosemia, and organic acid disorders were the least prevalent. Cystic fibrosis (CF) accounted for 7% of cases detected in 2015 and 4% of cases detected cumulatively. The cumulative percentage of CF cases is low compared to the 2015 percentage because screening began recently (October 2007) relative to the other disorders. Similarly, primary immunodeficiencies (PID) accounted for 7% of cases and 1% of cumulative cases since screening began in October 2011. Disorders detected by MS/MS (amino acid, organic acid, and fatty acid oxidation disorders) accounted for 14% of cases in 2015 and 17% cumulatively. However, PKU, the first disorder screened in Michigan, is now screened by MS/MS, meaning the overall proportion of cases detected by MS/MS is an overestimate because it includes cases detected prior to 2003 when MS/MS screening was initiated. The cumulative detection rate for fatty acid oxidation disorders is an underestimate because MCAD screening began in 2003, while other conditions were not screened until 2005. This means that births included in the denominator from 2003-2005 were not eligible for being diagnosed with fatty acid oxidation disorders other than MCAD leading to an artificially low cumulative detection rate. The MS/MS detection rate does not include cases of formiminoglutamic acid disorder (FIGLU) detected because the disorder is not included in the NBS panel. Galactosemia, including Duarte compound heterozygotes, accounted for 1.5% of all disorders detected in 2015 and 3% cumulatively. Biotinidase deficiency, including partial biotinidase deficiency, accounted for 9% of all cases detected in 2015 and 5% of all cases detected cumulatively. CAH accounted for 2% of all cases in 2015 and 3% of all cases detected cumulatively.

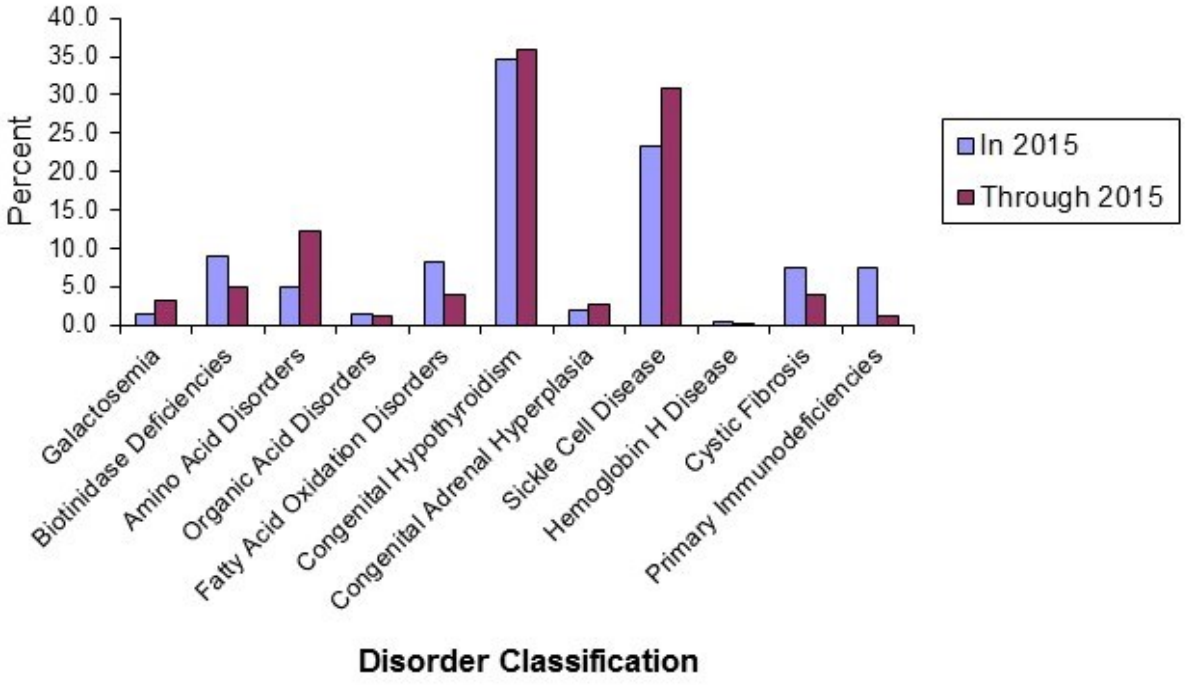

Figure 4. Percent Distribution of Disorders Identified in Newborns via Newborn Screening, Michigan Residents, in 2015 and through 2015

SCREENING PERFORMANCE METRICS

Screening performance metric targets are available in previous annual reports. Screening performance metrics include the detection rate, false positive rate (FPR), and positive predictive value (PPV). Table 5 reports screening performance metrics for all disorders in 2015. Performance metrics for individual MS/MS disorders are provided in separate tables (see Tables 7-9).

GALACTOSEMIA, BIOTINIDASE DEFICIENCY & CYSTIC FIBROSIS

Two cases of Duarte D/G variant and two cases of classic galactosemia were detected in 2015, resulting in a FPR of 0.004% and PPV of 44%.

The biotinidase deficiency detection rate (including partial biotinidase deficiency) was 1:4,643; the FPR and PPV were 0.03% and 43%, respectively. Of the 24 cases detected, 23 were partial and 1 was profound. One newborn with homozygous D444H was also identified.

Nineteen cases of CF were detected in 2015 (detection rate-1:5,865; the associated FPR and PPV were 0.3% and 6%, respectively. Additionally, seven cases of CFTR-related metabolic syndrome were detected. Chapter IV of the 2008 Annual Report provides more detailed information describing CF screening in Michigan.

ENDOCRINE DISORDERS-CH AND CAH

The CH screening FPR was 1.1%, and the PPV was 7%. The overall detection rate for CH was 1:1,185. Chapter IV of the 2007 Annual Report provides more detailed information describing CH screening in Michigan.

The CAH screening FPR was 0.1%, and the PPV was 4%. The overall detection rate for CAH was 1:22,287. Four cases detected were salt-wasting and one was non salt-wasting.

HEMOGLOBINOPATHIES

Hemoglobinopathies include sickle cell disease (SCD) and Hemoglobin H disease. The Hemoglobin H disease FPR was 0.03% and the PPV was 3.3%. One case was identified in 2015, resulting in a detection rate for Hemoglobin H disease of 1:111,435.

Additional SCD screening outcome information is reported in Table 6. SCD screening differs from screening for the other disorders because the purpose is to identify the presence or absence of abnormal hemoglobins and not to quantify selected analytes. There is no screening reference range, and the results of screening are essentially considered a confirmatory diagnosis. Confirmatory testing is primarily for differentiating sickling genotypes.

As depicted in Table 6, SCDs are quite common among African Americans, who accounted for 91% of the cases in 2015. While the overall incidence of SCD is approximately one case per 1,741 screened, the incidence in African Americans is one in 349 screened in Michigan.

In addition to sickle cell disease, variant hemoglobinopathies are identified through screening. In

Table 5: Screening Results and Performance Metrics, Michigan, 2015

Disorder Type	Total N	Total + N (% NICU)	Confirmed + N	Positive Detection Rate	FPR %	PPV %
Galactosemia	111,435	9 (22.2)			0.004	44.44
Classic (GG)			2	1:55,718		
Duarte (DG)			2	1:55,718		
Total			*4*	*1:27,859*		
Biotinidase Deficiency		56 (7.1)			0.03	42.86
Profound			1	1:111,435		
Partial			23	1:4,845		
Total			*24*	*1:4,643*		
Cystic Fibrosis		339 (13.6)	19	1:5,865	0.29	5.60
Congenital Hypothyroidism		1305 (25.6)	94	1:1,185	1.09	7.20
Congenital Adrenal Hyperplasias		116 (98.3)			0.10	4.31
Salt wasting			4	1:27,859		
Non-Salt wasting			1	1:111,435		
Total			*5*	*1:22,287*		
Sickle Cell Disease		91(19.8)	64	1:1,741	0.02	70.33
Hemoglobin H Disease		30 (33.3)	1	1:111,435	0.03	3.33
Primary Immunodeficiencies		73 (80.8)			0.05	27.40
SCID			3	1: 37,145		
Syndromes with T-cell Impairment			5	1: 22,287		
Non-preterm Secondary T-cell Lymphopenias			12	1:9,287		
Total			*20*	*1:5,572*		
Amino Acid		37 (24.3)	13	1:8,572	0.02	35.14
Organic Acid		30 (20.0)	4	1:27,859	0.02	13.33
Fatty Acid Oxidation		103 (15.5)	22	1:5,065	0.07	21.36
*MS/MS Disorders Total**		*161 (19.2)*	*39*	*1:2,857*	*0.11*	*24.22*

Notes: Maternal cases and carriers identified following an abnormal newborn screen are not included as confirmed cases in the screening performance indicators (i.e., considered false positives).
**SCAD and IBG are screened using the same analyte. The infants with elevated levels are included in both the organic acid and fatty acid oxidation total positive screens, but counted only once for the MS/MS Disorders total.*

2015, a total of 7 cases of other hemoglobinopathies were diagnosed, including cases of Hemoglobin C and E disease.

PRIMARY IMMUNODEFICIENCIES

In total, 20 cases of primary immunodeficiencies (PID) were identified, resulting in FPR of 0.05% and PPV of 27%. Of the 20 cases, 3 were classic SCID, 5 had syndromes with t-cell impairment, and 12 had non-preterm secondary T-cell lymphopenias. Chapter IV of the 2011 Annual Report provides more detailed information about PID screening in Michigan.

MS/MS DISORDERS

The overall FPR for MS/MS disorders was 0.1%. The PPV was 24%, and the detection rate was 1:2,857.

SCREENING PERFORMANCE METRICS-INDIVIDUAL MS/MS DISORDERS

AMINO ACID DISORDERS

Thirteen newborns were identified with amino acid disorders (Table 7) by MS/MS. Phenylketonuria (PKU) was the most frequent amino acid disorder identified, found in one of every 10,130 newborns screened (eleven newborns total). Chapter IV of the 2009 Annual Report provides more detailed information about PKU screening in Michigan. One case of citrullinemia and one case of homocystinuria were also identified. One case of pyruvate carboxylase deficiency was identified following an abnormal screen, but that disorder is not on Michigan's panel of NBS disorders.

ORGANIC ACID DISORDERS

Four newborns were identified with organic acid disorders (Table 8) by MS/MS. One infant was diagnosed with beta-ketothiolase deficiency (BKT), the first case identified in Michigan through NBS. One was diagnosed with glutaric acidemia Type 1 (GA1); one was diagnosed with isobutyryl-CoA dehydrogenase deficiency (IBD); and one was diagnosed with methylmalonic acidemia (MMA).

FATTY ACID OXIDATION DISORDERS

Twenty-two children were identified with fatty acid oxidation disorders (Table 9); ten medium-chain acyl-CoA dehydrogenase deficiency, seven short-chain acyl-CoA dehydrogenase deficiency, two carnitine palmitoyltransferase I deficiency (CPT I), one very long-chain acyl-CoA dehydrogenase deficiency (VLCAD), one long-chain L-3-hydroxy acyl-CoA dehydrogenase deficiency (LCHAD), and one carnitine palmitoyltransferase II deficiency (CPT II). Of the disorders detected, CPT I and II had the highest PPV (100%), followed by SCAD (78%) and MCAD (77%).

Table 6: Hemoglobinopathy Screening Performance Metrics, Michigan, 2015

Disorder	Newborns (N)	Confirmed + (N)		Positive Detection Rate	
		Total	Among African Americans	Total	Among African Americans
Sickle Cell Anemia	111,435	33	29	1:3,377	1:698
SC Disease		30	28	1:3,715	1:723
Sickle β thalassemia		1	1	1:111,435	1:20,237
SE Disease		0	0	-	-
Total		*64*	*58*	*1:1,741*	*1:349*

Notes: Out of the number of Michigan resident infants screened, total N=111,435, among African Americans N=20,237

Table 7: Amino Acid Disorders Detected by Tandem Mass Spectrometry, Screening Performance Metrics, Michigan, 2015

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Phenylketonuria	111,435	23			0.011	47.8
Diet-treated (PKU)			6	1:18,573		
Benign Hyperphenyl-alaninemia (H-PHE)			5	1:22,287		
Biopterin Cofactor Defects (BIOPT)			0	-		
Total			*11*	*1:10,130*		
Citrullinemia (CIT)/CIT II		3	1	1:111,435	0.002	33.3
Tyrosinemia I (TYR I)		1	0	-	0.001	-
Tyrosinemia II/III (TYR II/III)		4	1	1:111,435	0.005	-
Homocystinuria (HCY)/ Hypermethioninemia (MET)		1	0	-	0.0	-
Maple Syrup Urine Disease (MSUD)		1	0	-	0.0	-
Argininemia (ARG)						

Table 8: Organic Acid Disorders Detected by Tandem Mass Spectrometry, Screening Performance Metrics, Michigan, 2015

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Isobutyryl-CoA dehydro-genase deficiency (IBD)	111,435	9	1	1:111,435	0.007	11.1
3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC)		11	0	-	0.01	-
Glutaric Acidemia Type I (GA I)		4	1	1:111,435	0.003	25.0
Propionic Acidemia (PA)/ Methylmalonic Acidemia (MMA)		4	1	1:111,435	0.003	25.0
Multiple Carboxylase Deficiency (MCD)		1	0	-	0.001	-
Beta-ketothiolase (BKT)		1	1	1:111,435	0.0	100
Isovaleric acidemia (IVA)		1	0	-	0.001	-

Notes: Maternal cases and carriers identified following an abnormal newborn screen are not included as confirmed cases in the screening performance indicators (i.e., considered false positives). IBD and SCAD are screened using the same analyte. Thus, the FPR is slightly elevated and the PPV is slightly reduced for IBD since infants confirming with SCAD are considered false positives.

Table 9: Fatty Acid Oxidation Disorders Detected by Tandem Mass Spectrometry, Screening Performance Metrics, Michigan, 2015

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Carnitine Uptake Defect (CUD)	111,435	70	0	-	0.06	0.0
Short-Chain Acyl-CoA Dehydrogenase deficiency (SCAD)		9	7	1:15,919	0.002	77.8
Carnitine/Acylcarnitine Translocase Deficiency-(CACT)/Carnitine Palmitoyltransferase II Deficiency (CPT II)		1	1	1:111,435	0.0	100.0
Glutaric Acidemia Type II (GA II)		2	0	-	0.002	0.0
Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD)		13	10	1:11,144	0.003	76.9
Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)		5	1	1:111,435	0.004	20.0
Carnitine Palmitoyltransferase I Deficiency (CPT I)		2	2	1:55,718	0.0	100.0
Long-chain L-3-hydroxy acyl-CoA dehydrogenase deficiency (LCHAD)		1	1	1:111,435	0.0	100.0

Notes: Maternal cases and carriers identified following an abnormal newborn screen are not included as confirmed cases in the screening performance indicators (i.e., considered false positives). IBD and SCAD are screened using the same analyte. Thus, the FPR is slightly elevated and the PPV is slightly reduced for SCAD since infants confirming with IBG are considered false positives.

SCREENING PERFORMANCE METRICS AMONG STRONG POSITIVE SCREENS

This section provides screening performance metrics (FPR and PPV) among strong positive screens relative to those among total positive screens (strong and borderline positives). Disorders lacking a borderline positive category are not reported in Table 10 because their performance metrics have been previously reported in Tables 5-10. Disorders not detected in 2015 and detected disorders with no borderline positive screens are also excluded from Table 10, as there would be no change in screening performance overall compared to strong positive screens only.

Performance metrics among strong positive screens are particularly useful clinically in that they report the risk of a strong positive being a true case (PPV) or a false positive (FPR). When evaluating the significance of a strong positive screen, the performance metrics below should be considered. As indicated in Table 10, the FPRs and PPVs among strong positive screens are significantly improved relative to the overall screening performance metrics among all positive screens. Maternal cases and carriers identified through NBS are not included in Table 10.

Table 10: Screening Performance Metrics (FPR and PPV) among Strong Positive Screens compared to All Positive Screens, Michigan, 2015

Disorder Type	Among All +		Among Strong +	
	FPR	PPV	FPR	PPV
	%	%	%	%
Congenital Hypothyroidism (CH)	1.087	7.20	0.157	24.24
Congenital Adrenal Hyperplasia (CAH)	0.100	4.31	0.027	11.76
Phenylketonuria (PKU)	0.011	47.83	0.001	90.91
Galactosemia	0.004	44.44	0	100
Cystic Fibrosis (CF)	0.287	5.61	0.004	73.68
Primary Immunodeficiency	0.048	27.40	0.020	42.11
Biotinidase Deficiency	0.029	42.86	0	100
Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)	0.004	20.00	0.001	50.00

Notes: Maternal cases and carriers identified following an abnormal newborn screen are not included as confirmed cases in the screening performance metrics (i.e., considered false positives).

The FPR for CH is reduced nearly 7-fold for strong positive screens, and the PPV is increased approximately 3.5-fold compared to all positives. The FPR and PPV for CAH are each decreased and increased by 4-fold and 3-fold among strong positives, respectively.

Among strong positive screens for metabolic disorders, galactosemia and biotinidase had the best screening performance metrics, with 100% PPV and 0% FPR. VLCAD had a 4-fold increase in PPV and 2.5 fold decrease in FPR among strong positive screens compared to all positive screens. The PPV for PKU nearly doubled among strong positive screens and the FPR had a 12-fold decrease compared to all positive screens for PKU.

Although cystic fibrosis does not have a strong positive category, children with compound heterozygote or homozygote DNA mutations were considered "strong positive" in Table 11. The FPR decreased 64-fold and the PPV increased from 6% to 74% when excluding children with a heterozygote DNA mutation.

For PID, the FPR decreased and the PPV increased approximately 2-fold among strong positive screens compared to all positive screens.

Overall, strong positive screens are far less likely to be false positives and far more likely to be indicative of true disease compared to positive screens overall (i.e., both strong and borderline).

CARRIERS, MATERNAL DISORDERS, AND OTHER DISORDERS DETECTED

Although the overarching goal of NBS is to detect disorders in newborns, carriers and maternal disorders are also identified. For disorders in the NBS panel, carriers have one normal gene and one mutated gene and typically do not display any clinical symptoms. On a routine basis, the NBS Follow-up Program refers all newborns with positive screens to the appropriate medical management coordinating center that will follow-up to determine the final diagnosis: no disease, disease, carrier, or maternal disorder. NBS will only detect carriers or maternal disorders following an abnormal screen. Thus, NBS will not identify all carriers or all maternal disorders.

In 2015, a total of 3,026 infants were identified as carriers of a disease included in the NBS panel, following an abnormal screen (Table 11). The majority of these infants (n=2,717) had sickle cell trait. Nearly 300 infants (n=296) were cystic fibrosis carriers, 9 were identified as hemoglobinopathy trait with Barts, 2 were identified as VLCAD carriers, 1 was identified as an MCAD carrier, and 1 was identified as a GAI carrier.

Table 11: Carriers Identified from Newborn Screening, Michigan, 2015

Disorder	N
Cystic Fibrosis	296
Very long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)	2
Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD)	1
Glutaric Acidemia Type I (GAI)	1
Sickle Cell Trait	2,717
Hemoglobinopathy Trait - Barts	9

Notes: All of these infants were identified following an abnormal screen. Not all carriers will have abnormal screens, so not all carriers will be detected through newborn screening.

Table 12: Maternal Disorders Identified from Newborn Screening, Michigan, 2015

Maternal Disorder	N
Carnitine uptake defect (CUD)	2
3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC)	3

Notes: These maternal disorders were identified following their infant's abnormal screen. Not all infants of women with disorders will have abnormal screens, so not all maternal disorders will be detected through newborn screening.

Besides the confirmatory diagnostic testing for infants, the medical management centers also offer diagnostic testing for mothers. Since mothers may have the disease rather than the infant, they could possibly be identified through NBS for a few disorders.

In 2015, five maternal disorders were identified following an infant's positive screen (Table 12). Two mothers were identified with CUD, and three were identified with 3MCC.

IV. Quality Assurance Information

This section includes quality assurance (QA) information about NBS specimen characteristics and indicators included in the quarterly reports that are distributed to hospitals.

SPECIMEN CHARACTERISTICS

Table 13 reports specimen characteristics by nursery type where the specimen was collected. Although 11% of infants were admitted to the NICU or SCN, 53% and 25% of strong and borderline positive screens were received from infants in the NICU, respectively. Isolated elevations of one or more amino acids and/or acyl-carnitines were also more prevalent among specimens received from infants in the NICU; these elevations are commonly associated with infants receiving total parenteral nutrition or transfusions, or low birth weight or preterm infants. While the overall number of unsatisfactory specimens was greatest among hospital nurseries, the proportion of unsatisfactory specimens was greatest among non-hospital samples (5%). Early (collected before 24 hours of life) and transfused specimens were more common among infants from the NICU, while late specimens, those collected after six days of life, were most common among non-hospital deliveries. The NBS Follow-up Program tracks all strong and borderline positive, isolated elevation, unsatisfactory, early, and transfused specimens; approximately 5,300 specimens required follow-up in 2015.

Table 13: Specimen Characteristics by Nursery Type, Michigan, 2015

Indicator	Type of Birth					
	Regular Nursery		NICU/SCN		Non-Hospital	
	N	%	N	%	N	%
Strong Positive Specimens	179	0.2	203	1.7	1	0.1
Borderline Positive Specimens	990	1.0	341	2.8	8	0.9
All Positive Specimens*	1,553	1.6	618	5.1	11	1.3
Isolated elevations of amino acids and acyl-carnitines	6	0.01	533	4.4	0	-
Unsatisfactory Specimens	867	0.9	297	2.5	41	4.8
Late (>6 days) Specimens	87	0.1	30	0.3	46	5.3
Early (<1 day) Specimens	249	0.3	967	8.1	1	0.1
Transfused Specimens	4	0.0	112	1.0	0	0.0
Specimens Missing Demographics **	1,739	1.8	167	1.4	19	2.2
Total Births Screened	98,565	85.4	12,006	10.8	864	0.8

**Includes all strong and borderline specimens plus specimens positive for cystic fibrosis or hemoglobinopathies*
***Defined as missing race, specimen collection time, or birth weight*
Notes: Percentages expressed in the above table are column percentages, except for Total Births Screened which is a row percentage.

PERFORMANCE INDICATORS

During 2015, the quarterly reports included six indicators. Table 14 lists the indicators and the performance goal for each indicator.

Table 14: Indicators and Performance Goals for Newborn Screening, Michigan, 2015

Measure	Performance Goal
Late Screens	Less than 2% of screens collected greater than 36 hours after birth
Appropriate Day	Greater than 90% of screens arrive in state laboratory on or before the appropriate day
Unsatisfactory Screens	Less than 1% of screens are unsatisfactory
NBS Card Number	Greater than 95% of electronic birth certificates have the NBS card number recorded
Returned BioTrust for Health Consent Forms	At least 90% of specimens have a returned BioTrust for Health consent form that is completed appropriately

Table 15 lists the statistics for each performance measure and whether the goal was met, by nursery type. For late screens, only regular nurseries met the goal with approximately 1% of screens being collected more than 36 hours after birth. Of note, nearly 50% of non-hospital births had screens collected more than 36 hours after birth. Timely collection of specimens is critical for ensuring prompt screening and referral to medical management. Receipt by appropriate day is a new measure. Hospital-specific cutoffs based on specimen collection time and each hospital's courier pickup days and times were created. Any specimen collected more than five hours before the designated pickup time for that day should be sent out the same day and received in the state laboratory the next day. For appropriate day, neither regular nurseries nor NICUs met the goal, although regular nurseries were close with 88% of specimens arriving on or before the appropriate day. Regular nurseries met the goal for unsatisfactory specimens for 2015, while NICUs and non-hospital births did not meet the goal. For recording of the NBS card number on birth certificates, regular nurseries met the goal, while non-hospital births did not meet the goal. Birth certificates coming from regular nurseries were approximately three times more likely to have the NBS kit number recorded than certificates for non-hospital births. Although none of the nursery types met the BioTrust for Health measure, regular nurseries were the closest; 89% of regular nursery births had a BioTrust for Health consent form returned that was appropriately completed compared to approximately 64% of NICUs/SCNs and 72% of non-hospital births.

Table 15: Measures for Newborn Screening, by Nursery Type, Michigan, 2015

Measure	Nursery Type	N	%	Met Goal?
Late Screens: Less than 2% of screens collected greater than 36 hours after birth	Regular	881	0.9	Yes
	NICU/SCN	341	2.6	No
	Non-hospital	430	49.8	No
Appropriate Day: Greater than 90% of screens arrive in state laboratory on or before the appropriate day	Regular	90,320	88.0	No
	NICU/SCN	6,453	76.2	No
	Non-hospital*	NA		
Unsatisfactory Screens: Less than 1% of screens are unsatisfactory	Regular	867	0.9	Yes
	NICU/SCN	297	2.5	No
	Non-hospital	41	4.8	No
NBS Card Number: Greater than 95% of electronic birth certificates have the NBS card number recorded	Regular	98,278	95.6	Yes
	NICU/SCN**	NA		
	Non-hospital	502	33.1	No
Returned BioTrust for Health Consent Forms Completed Appropriately: At least 90% of specimens have a returned consent form that is completed appropriately	Regular	87,614	88.9	No
	NICU/SCN	7,707	64.2	No
	Non-hospital	622	72.0	No

*Receipt by appropriate day is not calculated for non-hospital births because they do not have a designated courier pick-up time for each day like birthing facilities have.
**Recording of NBS card number is not a performance measure for NICUs since the birth hospital is asked to draw the NBS specimen before transferring the infant to the NICU. Infants transferred to NICUs (as recorded on the birth certificate) are not included in the performance measure for regular nurseries.

SCREENING TURN-AROUND TIME

Turn-around time in NBS refers to the time from birth to initiation of treatment. The target turn-around time for initiating treatment for the early-onset life-threatening disorders (CAH, galactosemia and disorders detected by MS/MS) is no later than the seventh day of life. The goals for other disorders vary.

TIME TO TREATMENT

Table 16 reports the time to treatment for disorders other than hemoglobinopathies and cystic fibrosis. Penicillin prophylaxis, the treatment for hemoglobinopathies, is initiated later than treatment for other disorders and is reported in a separate table (Table 17). As indicated in Table 16, time to treatment ranged from 2 to 104 days of life among all disorders. Certain disorders often require one or more retests before being referred for confirmatory diagnosis. For that reason, CH is presented separately by initial screening result (strong or borderline) in the table.

GALACTOSEMIA

Both cases of classic galactosemia had treatment started within seven days of life.

BIOTINIDASE DEFICIENCY

The case of profound biotinidase deficiency identified had treatment started within seven days of life.

MS/MS DISORDERS

All newborns identified with amino acid, fatty acid oxidation, and organic acid disorders had treatment started within seven days of life.

ENDOCRINE DISORDERS-CAH AND CH

The salt-wasting form of CAH is life-threatening in the first few weeks of life. All four salt-wasting cases of CAH were treated within the first week of life.

The target for CH is treatment by 14 days of life for newborns with initial TSH values greater than 50 (i.e., strong positives). Of the 50 CH cases with a strong positive initial screen, 47 (94%) were treated by the 14th day of life.

Table 16: Time to Treatment of Amino Acid Disorders, Organic Acid, Fatty Acid Oxidation, and Endocrine Disorders, Michigan, 2015

Disorder		Total	Treatment Time (days from birth) N			Treatment Time Range (days)
		N	1-7	8-14	>14	
Galactosemia	Classic (GG)	2	2			2-3
	Duarte (DG)[1]	2			1	27
Biotinidase Deficiency	Partial[2]	23	7	11	3	3-22
	Profound	1	1			4
Amino Acid Disorders	PKU-Diet treated	6	6			3-6
	CIT	1	1			5
	Total	*7*	*7*			*3-6*
Organic Acid Disorders	BKT	1	1			4
	GA1	1	1			4
	MMA	1	1			4
	IBD	1	1			5
	Total	*4*	*4*			*4-5*
Fatty Acid Oxidation Disorders	SCAD	7	7			3-6
	MCAD	10	10			3-5
	VLCAD	1	1			3
	CPT II	1	1			3
	LCHAD	1	1			4
	CPT I	2	2			3
	Total	*22*	*22*			*3-6*
Endocrine Disorders	CH					
	Borderline[3]	32		3	27	11-104
	Strong	50	32	15	3	4-24
	CAH					
	Salt-wasting	4	4			3-5
	Non salt-wasting	1			1	21
Total		*159*	*79*	*31*	*44*	*2-104*

Notes: Disorders that do not require treatment are excluded from the table.
[1]One child had parents refuse treatment
[2]Two children had parents refuse treatment
[3]Missing treatment start date on two infants.

HEMOGLOBINOPATHIES

Table 17 reports the time to treatment among newborns with hemoglobinopathies. The target is to initiate penicillin prophylaxis by four months of life (120 days). Of the 64 cases having a penicillin start date reported, 93% were treated with penicillin within the first four months, 3% began treatment between four and five months of life, 2% began treatment between five and six months, and 2% began treatment beyond six months of age.

Table 17: Time to Penicillin Initiation for Sickle Cell Disorders, Michigan, 2015

Disorder	Penicillin Prophylaxis Initiation Time			
	< 120 days	**120-149 days**	**150-179 days**	**≥ 180 days**
Sickle Cell Disorders*	59 (92.9%)	2 (3.1%)	1 (1.6%)	1 (1.6%)

*1 case missing penicillin initiation date.

V. Conclusions

NBS is a critical public health program protecting the lives of our State's newest residents. The NBS Laboratory screened 111,725 infants born in 2015, and the NBS Follow-up Program tracked approximately 5,300 strong and borderline positive, isolated elevation, unsatisfactory, early, and transfused specimens; newborns with strong positive screening results were immediately referred to the appropriate NBS follow-up coordinating center for evaluation. A total of 270 newborns were identified with a disorder by NBS in 2015, as well as 3,025 carriers. Since blood spot screening began in Michigan in 1965, 5,981 newborns have been diagnosed and treated. We are continuing to both expand and refine the NBS Program in order to better protect the health of infants born in Michigan.