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MICHIGAN NEWBORN SCREENING PROGRAM

Annual Report 2016

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MDHHS
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RICK SNYDER, GOVERNOR | NICK LYON, DIRECTOR

MICHIGAN
Newborn
Screening

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Table of Contents

Executive Summary

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

Since the program began in 1965 with screening for phenylketonuria, over 50 disorders have been added to the screening panel. Through 2016, more than 7 million infants have been screened with more than 6,200 diagnosed with diseases included in the NBS blood spot panel.

Of the 111,685 infants screened in 2016, the vast majority were Michigan residents and 258 (0.2%) were diagnosed with a disease. Overall, one infant out of 433 screened was diagnosed with one of the disorders included in the NBS panel (see Table 1 for list of disorders).

Developments occurring in 2016:

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 in Lansing, Michigan
    - ◊ Association of Public Health Laboratories (APHL) Newborn Screening and Genetic Testing Symposium in St. Louis, Missouri
    - ◊ Public Health Informatics Conference in Atlanta, Georgia

Michigan continued to conduct NBS-related trainings:

- The NBS Follow-up Program held a centralized hospital training in Lansing in October 2016 that was attended in-person or via webinar by ~70 health professionals, representing 44 birthing hospitals across Michigan.
- The NBS Laboratory provided trainings for two residents from Wayne State University/Detroit Medical Center.

NBS laboratory personnel continued to serve on national NBS committees, including:

- A national APHL subcommittee
- The Clinical Laboratory Standards Institute (CLSI) Document Development Committee

New capacity was added for NBS:

- The NBS laboratory began using a molecular panel with 60 mutations for the second tier test for cystic fibrosis, replacing the 40 mutation panel it had been using.

- The NBS Program continued working towards implementing screening for Pompe disease, Mucopolysaccharidosis Type I (MPSI) disease, and X-linked adrenoleukodystrophy.[1]
- The Michigan NBS Laboratory was one of 20 laboratories that received a NewSTEPs 360 grant to improve turnaround time. The Michigan NBS lab will strive to improve turnaround time by implementing HL7 messaging.

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

- As of October 1, 2016, third party billing for metabolic formula is required for children and youth under 21 years of age. Families must use any benefits available through their private health plan, enroll in the Children's Special Health Care Services (CSHCS) Program, or pay out-of-pocket. The NBS Program continues to assist individuals during emergency or unusual situations when insurance benefits cannot be utilized to meet a patient's needs.

- A video was developed describing the lifelong treatment of specialized medical formulas for individuals with inborn errors of metabolism and the difficulty in attaining them because they are expensive and not all health plans cover the cost. The video can be viewed at www.michigan.gov/IEMTreatment

[1]Screening for Pompe disease and MPS1 began in Summer 2017 and more information will be provided in the 2017 Annual Report.

Listing of Figures & Tables

Figures

Tables

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 (SCD). The Act also permitted MDHHS's state laboratory to be 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 severe combined immunodeficiency (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.[2] 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 validation is completed[2].

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

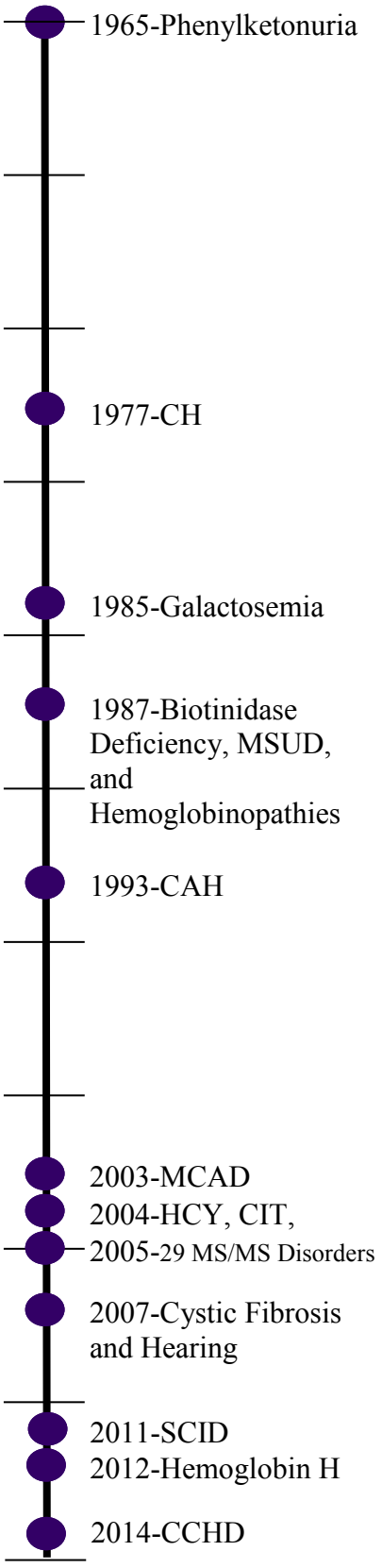

Figure 1. Implementation of Disorders on the NBS Panel, Michigan, 1965-2016

[1]More information about the newborn hearing screening program can be found at www.michigan.gov/ehdi.
[2]Screening for Pompe disease and MPS 1 began in Summer 2017 and more information will be provided in the 2017 Annual Report .

Table 1. Disorders included in the Newborn Screening Blood Spot Panel, Michigan, 2016

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.

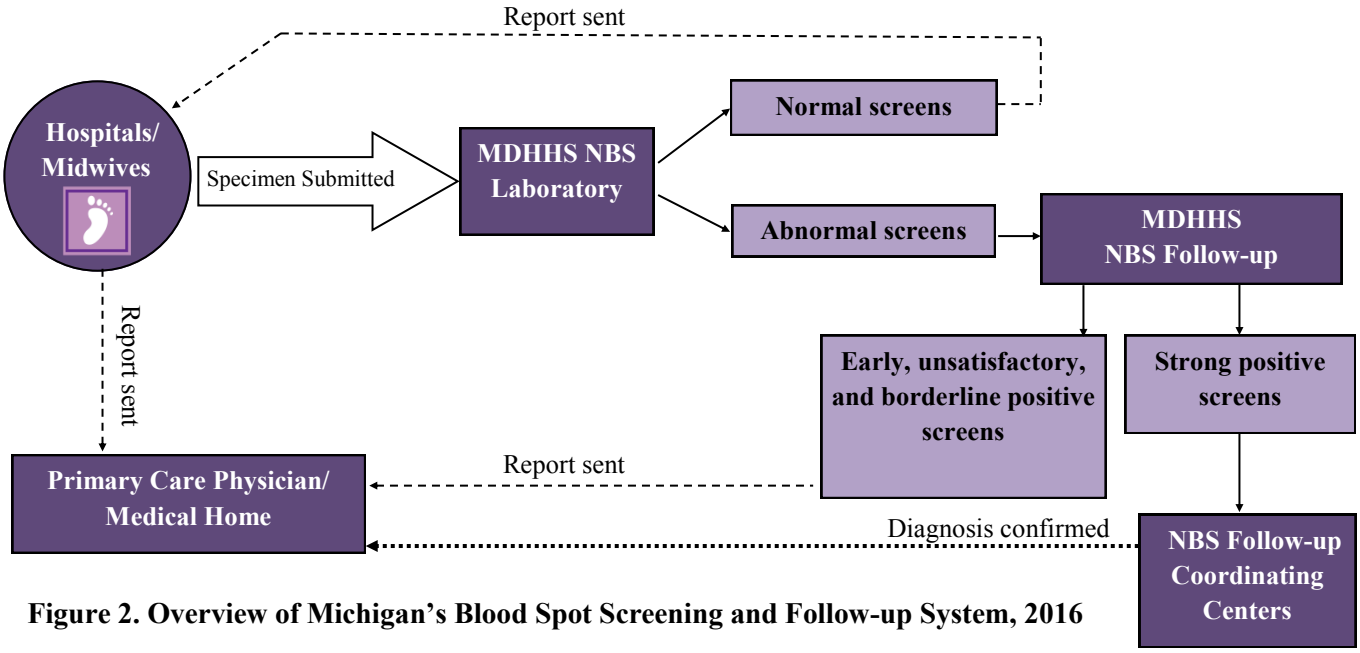

Figure 2. Overview of Michigan's Blood Spot Screening and Follow-up System, 2016

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

HOSPITALS

In 2016, 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 93 midwives registered with the NBS Program. Midwives are provided with individual assistance in meeting program 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 that were eligible for screening. The number of live births in 2016 (n=112,473) is a preliminary estimate based on the number of birth reported by September 2017.

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. Hospital quarterly reports contain QA indicators that focus on: 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 2016 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 2016, 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 112,473 live births that occurred in 2016, 375 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 112,098 remaining live births, the linkage algorithm successfully matched newborn screens for 110,957 infants (99.0%). The 1,141 unmatched records were sent to NBS Follow-up Program technicians for further investigation. This more in-depth follow-up revealed that 506 (44.3%) 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, 635 infants (0.6%) born in the state were not screened. Infants were not screened due to parental refusal of screening (n=238), transfer out of state (n=8), infant expired (n=17), child being screened in another state (n=9), or some other reason for not being screened (n=363). 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 2016, 40 infants born in hospitals are known to have missed being screened, and those hospitals were contacted. Of the 40, 11 have been screened to date and the remaining 29 screens were never submitted.

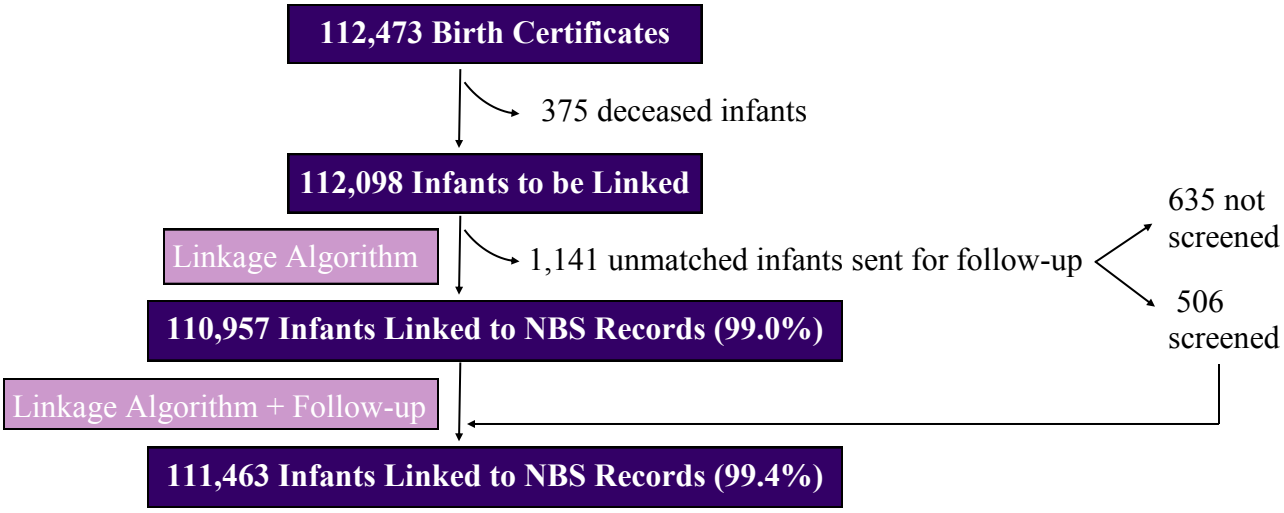

Figure 3. Newborn Screening and Live Births Records Linkage, Michigan, 2016

In total, NBS samples were received from 111,685 infants born in 2016. Of those, 307 (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 2016. 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, 10.5% of in-state infants screened were admitted to the NICU or special care nursery (SCN), 8.3% were low birth weight (<2,500 grams), and 9.5% were born preterm (<37 weeks gestational age). Black infants were over-represented among NICU, preterm, and low birth weight births.

Table 3: Demographics of Infants Screened by Race, Michigan, 2016, Excluding Out-of-State Residents

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	70,231	63.1	62,931	89.6	6,473	9.2	827	1.2	4,530	6.5	5,949	8.5
Black	20,006	18.0	16,788	83.9	3,210	16.0	8	0.04	2,760	14.0	2,676	13.4
Multi-Racial	6,845	6.1	6,141	89.7	664	9.7	40	0.6	574	8.5	650	9.5
Other	8,010	7.2	7,355	91.8	654	8.2	1	0.01	644	8.0	602	7.5
Missing	6,286	5.6	5,614	89.3	649	10.3	23	0.4	551	9.1	650	10.3
Column Total:	111,378	100	98,829	88.7	11,650	10.5	899	0.8	9,059	8.3	10,527	9.5

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 1,860 and 1,670 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 2016. The total numbers of cases detected both in and through 2016 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 centers 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 2016. 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, 1965-2016

Type of Disorder Classification (Year Screening Began)	Cases in 2016 (N)	Cases Through 2016 (N)	Cumulative Detection Rate
Galactosemia (1985)	8	200	1:20,760
Biotinidase Deficiencies (1987)	18	313	1:12,385
Amino Acid Disorders (1965)	19	748	1:9,506
Organic Acid Disorders (2005)	5	80	1:17,462
Fatty Acid Oxidation Disorders (2003)	21	253	1:6,551
Congenital Hypothyroidism (1977)	93	2,237	1:1,733
Congenital Adrenal Hyperplasia (1993)	3	156	1:19,242
Sickle Cell Disease (1987)	56	1,908	1:2,032
Hemoglobin H Disease (2012)	1	7	1:79,747
Cystic Fibrosis (October 2007)	20	258	1:4,065
Primary Immunodeficiencies (October 2011)	14	89	1:7,533
Total	258	6,249	-

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. 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 2016, while Hemoglobin H Disease, Congenital Adrenal Hyperplasia, and organic acid disorders were the least prevalent. Cystic fibrosis (CF) accounted for 8% of cases detected in 2016 and 4% of cases detected cumulatively. The cumulative percentage of CF cases is low compared to the 2016 percentage because screening began recently (October 2007) relative to the other disorders. Similarly, primary immunodeficiencies (PID) accounted for 5% 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 18% of cases in 2016 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 3% of all disorders detected in 2016 and 3% cumulatively. Biotinidase deficiency, including partial biotinidase deficiency, accounted for 7% of all cases detected in 2016 and 5% of all cases detected cumulatively. CAH accounted for 1% of all cases in 2016 and 3% of all cases detected cumulatively.

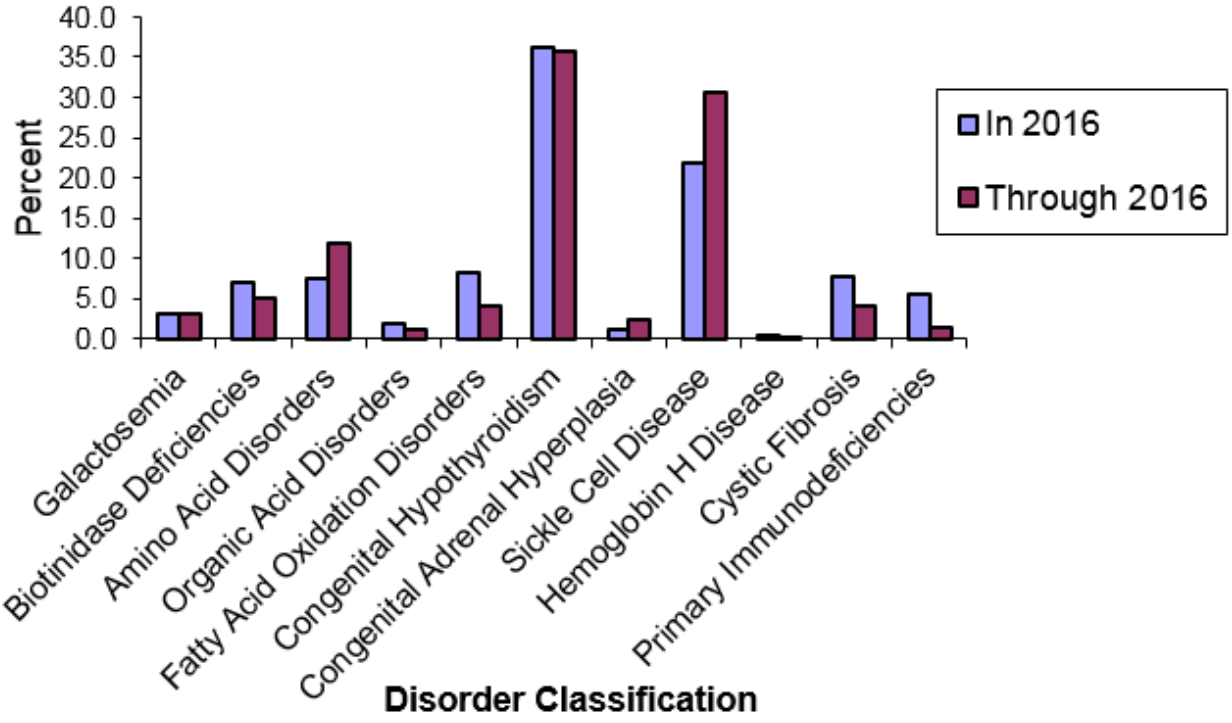

Figure 4. Percent Distribution of Disorders Identified in Newborns via Newborn Screening, Michigan Residents, in 2016 and through 2016

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 2016. Performance metrics for individual MS/MS disorders are provided in separate tables (see Tables 7-9).

GALACTOSEMIA, BIOTINIDASE DEFICIENCY & CYSTIC FIBROSIS

Five cases of Duarte D/G variant and three cases of classic galactosemia were detected in 2016, resulting in a FPR of 0.004% and PPV of 67%.

The biotinidase deficiency detection rate (including partial biotinidase deficiency) was 1:6,188; the FPR and PPV were 0.02% and 50%, respectively. Of the 18 cases detected, 16 were partial and two were profound.

Twenty cases of CF were detected in 2016 (detection rate-1:5,569; the associated FPR and PPV were 0.3% and 6%, respectively. Additionally, nine 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

Ninety-three cases of CH were detected in 2016. The CH screening FPR was 1.4%, and the PPV was 5.8%. The overall detection rate for CH was 1:1,198. Chapter IV of the 2007 Annual Report provides more detailed information describing CH screening in Michigan.

Three cases of CAH were detected in 2016, two were salt-wasting and one was non salt-wasting. The CAH screening FPR was 0.1%, and the PPV was 2.5%. The overall detection rate for CAH was 1:37,126.

HEMOGLOBINOPATHIES

Hemoglobinopathies include sickle cell disease (SCD) and Hemoglobin H disease. The Hemoglobin H disease FPR was 0.04% and the PPV was 2.5%. One case was identified in 2016, resulting in a detection rate for Hemoglobin H disease of 1:111,378.

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 89% of the cases in 2016. While the overall incidence of SCD is approximately one case per 1,989 screened, the incidence in African Americans is one in 400 screened in Michigan.

Table 5: Screening Results and Performance Metrics, Michigan, 2016

Disorder Type	Total N	Total + N (% NICU)	Confirmed + N	Positive Detection Rate	FPR %	PPV %
Galactosemia	111,378	12 (16.7)			0.004	66.7
Classic (GG)			3	1:37,126		
Duarte (DG)			5	1:22,276		
Total			*8*	*1:13,922*		
Biotinidase Deficiency		36 (11.1)			0.02	50.0
Profound			2	1:55,689		
Partial			16	1:6,961		
Total			*18*	*1:6,188*		
Cystic Fibrosis (CF)		335 (13.7)	20	1:5,569	0.3	6.0
Congenital Hypothyroidism (CH)		1,603 (24.0)	93	1:1,198	1.4	5.8
Congenital Adrenal Hyperplasias (CAH)		121 (94.2)			0.1	2.5
Salt wasting			2	1:55,689		
Non-Salt wasting			1	1:111,378		
Total			*3*	1:37,126		
Sickle Cell Disease (SCD)		72 (12.5)	56	1:1,989	0.01	77.8
Hemoglobin H Disease		40 (32.5)	1	1:111,378	0.04	2.5
Primary Immunodeficiencies		70 (84.3)			0.05	20.0
SCID			2	1: 55,689		
Syndromes with T-cell Impairment			6	1: 18,563		
Non-preterm Secondary T-cell Lymphopenias			6	1:18,563		
Total			*14*	*1:7,956*		
Amino Acid		38 (7.9)	19	1:5,862	0.02	50.0
Organic Acid		41 (29.3)	5	1:22,276	0.03	12.2
Fatty Acid Oxidation		97 (12.4)	21	1:5,304	0.1	21.7
*MS/MS Disorders Total**		168 (16.1)	45	1:2,475	0.1	26.8

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.*

In addition to sickle cell disease, variant hemoglobinopathies are identified through screening. In 2016, a total of 11 cases of other hemoglobinopathies were diagnosed, including cases of Hemoglobin C and E disease.

PRIMARY IMMUNODEFICIENCIES

In total, 14 cases of primary immunodeficiencies (PID) were identified, resulting in FPR of 0.05% and PPV of 20.0%. Of the 14 cases, 2 were classic SCID, 6 had syndromes with t-cell impairment, and 6 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 27%, and the detection rate was 1:2,475.

SCREENING PERFORMANCE METRICS-INDIVIDUAL MS/MS DISORDERS

AMINO ACID DISORDERS

Nineteen 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 8,568 newborns screened (thirteen newborns total). Chapter IV of the 2009 Annual Report provides more detailed information about PKU screening in Michigan. Three case of citrullinemia, two cases of maple syrup urine disease (MSUD) and one case of homocystinuria were also identified.

ORGANIC ACID DISORDERS

Five newborns were identified with organic acid disorders (Table 8) by MS/MS. Three were diagnosed with glutaric acidemia Type 1 (GA1) and two were diagnosed with 3-Methylcrotonyl-CoA carboxylase deficiency (3MCC).

FATTY ACID OXIDATION DISORDERS

Twenty-one children were identified with fatty acid oxidation disorders (Table 9); eight medium-chain acyl-CoA dehydrogenase deficiency (MCAD), six short-chain acyl-CoA dehydrogenase deficiency (SCAD), three very long-chain acyl-CoA dehydrogenase deficiency (VLCAD), two carnitine uptake defect (CUD), one carnitine palmitoyltransferase II deficiency (CPT II), and one glutaric acidemia Type II (GAII). Of the disorders detected, CPT II and GA II had the highest PPV(100%), followed by SCAD (75%) and VLCAD (75%).

Table 6: Hemoglobinopathy Screening Performance Metrics, Michigan, 2016

Disorder	Newborns (N)	Confirmed + (N)		Positive Detection Rate	
		Total	Among African Americans	Total	Among African Americans
Sickle Cell Anemia	111,378	23	20	1:4,843	1:1000
SC Disease		24	23	1:4,641	1:870
Sickle β thalassemia		7	5	1:15,911	1:4,001
SE Disease		2	2	1:55,689	1:10,003
Total		*56*	*50*	*1:1,989*	*1:400*

Notes: Out of the number of Michigan resident infants screened, total N=111,378, among African Americans N=20,006.

Table 7: Amino Acid Disorders Detected by Tandem Mass Spectrometry, Screening Performance Metrics, Michigan, 2016

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Phenylketonuria	111,378	18			0.004	72.2
Medically treated (PKU)			8	1:13,922		
Benign Hyperphenyl-alaninemia (H-PHE)			5	1:22,276		
Biopterin Cofactor Defects (BIOPT)			0	-		
Total			*13*	*1:8,568*		
Citrullinemia (CIT)/CIT II		4	3	1:37,126	0.001	75.0
Tyrosinemia II/III (TYR II/III)		11	0	-	0.01	0.0
Homocystinuria (HCY)/ Hypermethioninemia (MET)		1	1	1:111,378	0.0	100.0
Maple Syrup Urine Disease (MSUD)		2	2	1:55,689	0.0	100.0
Argininemia (ARG)		2	0	-	.002	0.0

Table 8: Organic Acid Disorders Detected by Tandem Mass Spectrometry, Screening Performance Metrics, Michigan, 2016

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Isobutyryl-CoA dehydro-genase deficiency (IBD)	111,378	8	0	-	0.01	0.0
3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC)		10	2	1:55,689	0.01	20.0
Glutaric Acidemia Type I (GA I)		8	3	1:37,126	0.004	37.5
Propionic Acidemia (PA)/ Methylmalonic Acidemia (MMA)		12	0	-	0.01	0.0
Beta-ketothiolase (BKT)		1	0	-	0.001	0.0
Isovaleric acidemia (IVA)		2	0	-	0.002	0.0

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 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, 2016

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Carnitine Uptake Defect (CUD)	111,378	71	2	1:55,689	0.06	2.8
Short-Chain Acyl-CoA Dehydrogenase deficiency (SCAD)		8	6	1:18,563	0.002	75.0
Carnitine/Acylcarnitine Translocase Deficiency-(CACT)/Carnitine Palmitoyltransferase II Deficiency (CPT II)		1	1	1:111,378	0.0	100.0
Glutaric Acidemia Type II (GA II)		1	1	1:111,378	0.0	100.0
Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD)		12	8	1:13,922	0.004	66.7
Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)		4	3	1:37,126	0.001	75.0

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 2016 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, 2016

Disorder Type	Among All +		Among Strong +	
	FPR	PPV	FPR	PPV
	%	%	%	%
Congenital Hypothyroidism (CH)	1.36	5.80	0.17	22.95
Congenital Adrenal Hyperplasia (CAH)	0.11	2.48	0.02	10.00
Phenylketonuria (PKU)	0.004	72.22	0.0	100.00
Galactosemia	0.004	66.67	0.0	100.00
Cystic Fibrosis (CF)	0.28	5.97	0.006	73.08
Primary Immunodeficiency	0.05	20.00	0.02	30.00
Biotinidase Deficiency	0.02	50.00	0.0	100.00
Carnitine Uptake Defect (CUD)	0.06	2.82	0.002	33.33
3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC)	0.007	20.00	0.003	25.00

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 approximately 8-fold for strong positive screens, and the PPV is increased approximately 4-fold compared to all positives. Among strong positives, the FPR for CAH is decreased by 6-fold and the PPV is increased by 4-fold compared to all positives.

Among strong positive screens for metabolic disorders, galactosemia, biotinidase, and PKU had the best screening performance metrics, with a 100% PPV and a 0% FPR.

Although cystic fibrosis does not have a strong positive category, children with compound heterozygote or homozygote DNA mutations were considered "strong positive" in Table 10. The FPR decreased 50-fold and the PPV increased from 6% to 73% when excluding children with a heterozygote DNA mutation.

For PID, the FPR decreased 3-fold and the PPV increased 10% for 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 2016, a total of 2,885 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=2,574) had a hemoglobin trait. Nearly 300 infants (n=293) were cystic fibrosis carriers, 14 were identified as hemoglobinopathy trait with Barts, 1 was identified as an MCAD carrier, 1 was identified as a citrullinemia carrier, one was identified as a glutaric acidemia Type I carrier, and one was identified as a VLCAD carrier.

Table 11: Carriers Identified from Newborn Screening, Michigan, 2016

Disorder	N
Hemoglobin Traits	2,574
Cystic fibrosis	293
Hemoglobinopathy Trait - Barts	14
Citrullinemia	1
Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD)	1
Glutaric acidemia Type I	1
Very long-chain acyl-CoA dehydrogenase deficiency	1

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, 2016

Maternal Disorder	N
Carnitine uptake defect (CUD)	2
Glutaric academia type 1 (GA1)	1

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 confirmatory diagnostic testing for infants, 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 2016, three maternal disorders were identified following an infant's positive screen (Table 12). Two mothers were identified with CUD and one mother was identified with GA 1.

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, 54% and 24% 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 (3.1%). 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 5,500 specimens required follow-up in 2016.

Table 13: Specimen Characteristics by Nursery Type, Michigan, 2016

Indicator	Type of Birth					
	Regular Nursery		NICU/SCN		Non-Hospital	
	N	%	N	%	N	%
Strong Positive Specimens	177	0.2	205	1.8	1	0.1
Borderline Positive Specimens	1,233	1.2	390	3.3	4	0.4
All Positive Specimens*	1,753	1.8	656	5.6	8	0.9
Isolated elevations of amino acids and acyl-carnitines	12	0.01	549	4.7	0	-
Unsatisfactory Specimens	887	0.9	251	2.2	28	3.1
Late (>6 days) Specimens	69	0.1	24	0.2	61	6.8
Early (<1 day) Specimens	298	0.3	947	8.1	3	0.3
Transfused Specimens	3	0.0	74	0.6	0	-
Specimens Missing Demographics **	1,677	1.7	164	1.4	26	2.9
Total Births Screened	98,829	88.7	11,650	10.5	899	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 2016, the hospital quarterly reports included five indicators related to blood spot screening. Table 14 lists the indicators and the performance goal for each indicator.

Table 14: Indicators and Performance Goals for Newborn Screening, Michigan, 2016

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 14 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, more than 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 measure based on specimen collection time and each hospital's courier pickup days and times. 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 2016, 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 six 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 63% of NICUs/SCNs and 71% of non-hospital births.

Table 15: Measures for Newborn Screening, by Nursery Type, Michigan, 2016

Measure	Nursery Type	N	%	Met Goal?
Late Screens: Less than 2% of screens collected greater than 36 hours after birth	Regular	794	0.8	Yes
	NICU/SCN	256	2.2	No
	Non-hospital	487	54.2	No
Appropriate Day: Greater than 90% of screens arrive in state laboratory on or before the appropriate day	Regular	87,242	88.3	No
	NICU/SCN	9,350	80.3	No
	Non-hospital*	NA		
Unsatisfactory Screens: Less than 1% of screens are unsatisfactory	Regular	878	0.9	Yes
	NICU/SCN	251	2.2	No
	Non-hospital	28	3.1	No
NBS Card Number: Greater than 95% of electronic birth certificates have the NBS card number recorded	Regular	99,216	96.4	Yes
	NICU/SCN**	NA		
	Non-hospital	266	17.0	No
Returned BioTrust for Health Consent Forms Completed Appropriately: At least 90% of specimens have a returned consent form that is completed appropriately	Regular	87,815	88.9	No
	NICU/SCN	7,293	62.6	No
	Non-hospital	634	70.5	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 15 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 15, time to treatment ranged from one to 267 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

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

BIOTINIDASE DEFICIENCY

Both cases of profound biotinidase deficiency had treatment started within seven days of life.

MS/MS DISORDERS

Six of the eight medically treated PKU cases were treated in the first week of life. Two of the three cases of CIT started treatment within the first week of life. Both cases of MSUD were treated during the first week of life.

Four of the five organic acid disorders started treatment within days of life. All three cases of GA1 were treated within 7 days of life. One cases of 3MCC was treated within the first week of life, while the other case was treated in the second week of life.

Of the 20 infants with fatty acid oxidation disorders and a treatment start date, 17 were treated within the first week of life. Of note, one of the CPT II patients was identified retrospectively after a laboratory analyte cut of change, thus treatment did not start until 267 days of life.

ENDOCRINE DISORDERS-CAH AND CH

The salt-wasting form of CAH is life-threatening in the first few weeks of life. Two infants were identified with salt-wasting CAH, one was treated within the first week of life and one began treatment at 12 days 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 56 CH cases with a strong positive screen, 46 (82%) 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, 2016

Disorder		Total	Treatment Time (days from birth) N			Treatment Time Range (days)
		N	1-7	8-14	>14	
Galactosemia	Classic (GG)	3	3			2-3
	Duarte (DG)	5		1	4	11-89
Biotinidase Deficiency	Partial	16	4	6	6	4-87
	Profound	2	2			3-6
Amino Acid Disorders	PKU-medically treated[1]	8	6		1	4-34
	CIT	3	2		1	2-18
	MSUD	2	2			4-5
	Total	*13*	*10*		*2*	*2-34*
Organic Acid Disorders	3MCC	2	1	1		3-13
	GA1	3	3			3-5
	Total	*5*	*4*	*1*		*3-13*
Fatty Acid Oxidation Disorders	SCAD	6	6			3-6
	MCAD	8	8			2-5
	GA II	1	1			3
	VLCAD[2]	3	2			1
	CPT II[3]	1			1	267
	CUD	2	2			4-5
	Total	*21*	*19*		*1*	*1-267*
Endocrine Disorders	CH					
	Borderline	37	1	2	34	7-115
	Strong	56	35	11	10	3-38
	CAH					
	Salt-wasting	2	1	1		1-12
	Non salt-wasting	1	1			
Total		*161*	*80*	*22*	*57*	*1-267*

Notes: Disorders that do not require treatment are excluded from the table.
[1] Missing treatment start date for one infant
[2] Missing treatment start date for one infant
[3] Identified retrospectively following a laboratory analyte cut off change

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 52 cases with a known penicillin initiation date, 90% were treated with penicillin within the first four months and 9% began treatment between four and five months of life.

Table 17: Time to Penicillin Initiation for Sickle Cell Disorders, Michigan, 2016

Disorder	Penicillin Prophylaxis Initiation Time	
	< 120 days	**120-149 days**
Sickle Cell Disorders*	47 (90.4%)	5 (9.6%)

*Three cases missing penicillin initiation date and one refused initiation.

V. Conclusions

NBS is a critical public health program that protects the lives of our state's newest residents. The NBS Laboratory screened 111,685 infants born in 2016, and the NBS Follow-up Program tracked approximately 5,500 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 258 newborns were identified with a disorder by NBS in 2016, as well as 2,885 carriers. Since blood spot screening began in Michigan in 1965, 6,249 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.