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MICHIGAN NEWBORN SCREENING PROGRAM

Annual Report 2017

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GRETCHEN WHITMER, GOVERNOR | ROBERT GORDON, DIRECTOR

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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.

Since the program began in 1965 with screening for phenylketonuria, more than 50 disorders have been added to the screening panel. Through 2017, more than 7.2 million infants have been screened with almost 6,600 diagnosed with diseases included in the NBS blood spot panel.

Of the 109,740 infants screened in 2017, the vast majority were Michigan residents and 305 (0.3 percent) were diagnosed with a disease. Overall, one infant out of 360 screened was diagnosed with one of the disorders included in the NBS panel (see Table 1 for list of disorders).

Developments occurring in 2017:

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 Grand Rapids, Michigan
    - ◊ Association of Public Health Laboratories (APHL) Newborn Screening and Genetic Testing Symposium in New Orleans, Louisiana

Michigan continued to conduct NBS-related trainings:

- The NBS Follow-up Program held two hospital trainings in Lansing and Detroit in October 2017 that were attended in-person or via webinar by about 120 health professionals, representing 44 birthing hospitals across Michigan.

NBS follow up staff presented or participated as an exhibitor at numerous educational events:

- WIC Conference.
- Beaumont Baby Fair.
- Michigan Midwives Conference.
- American Academy of Pediatrics, Michigan Chapter, Novi.
- March of Dimes Health Walk, University of Michigan, Ann Arbor.

NBS laboratory personnel and follow up staff continued to serve on national NBS committees, including:

- Education and Training workgroup for the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC).
- The Clinical Laboratory Standards Institute (CLSI) Document Development Committee.
- CCHD Technical Assistance Workgroup.
- State Education Workgroup.

New screening developments:

- The NBS laboratory began screening for Mucopolysaccharidosis I (MPS I) and Pompe disease in August, 2017.
- The NBS Program continued working towards implementing screening for X-linked Adrenoleukodystrophy.
- Short-chain acyl-CoA dehydrogenase deficiency (SCAD) and Isobutyryl-CoA dehydrogenase deficiency (IBD) were removed from Michigan's NBS panel, effective October, 2017.

Continuing work:

- In the second year of the NewSTEPs 360 grant, the Michigan NBS lab continued to work on improving turnaround time by implementing HL7 messaging for inbound demographics and outbound NBS results.

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.

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.

[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 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 31 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. Information on pulse oximetry screening can be found in a separate annual report[2]. Pompe disease and Mucopolysaccharidosis Type 1 (MPS 1) were added to the panel in 2014 and 2015, respectively. Screening for these conditions began in August 2017, after an FDA-approved laboratory screening method became available.
X-linked adrenoleukodystrophy (X-ALD) was added to the panel in 2015, and screening will start when FDA-approved methods become available and validation is complete, which is expected in 2019. GAMT deficiency was voted to be added to Michigan's NBS panel in November 2017, and was officially added in October 2018. Screening is expected to begin in 2019.
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).

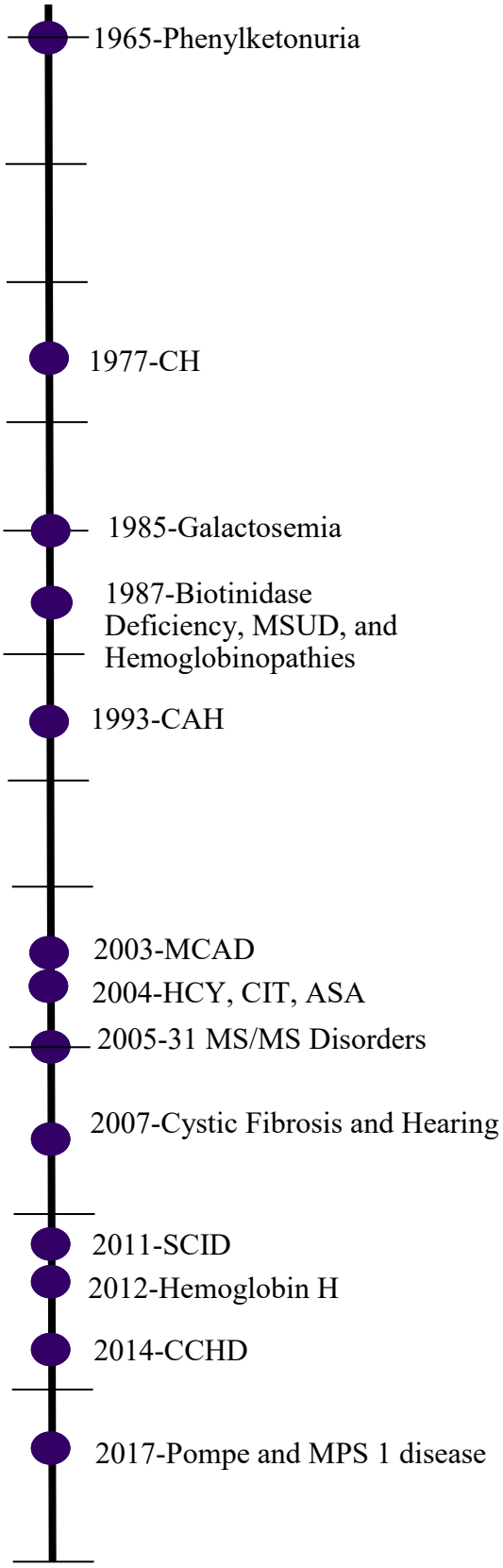

Figure 1. Implementation of Disorders on the NBS Panel, Michigan, 1965-2017

[1]More information about the newborn hearing screening program can be found at www.michigan.gov/ehdi.
[2] The critical congenital heart disease Annual reports can be found in the "Resources for Hospitals and Health Professionals" link on the NBS website (www.michigan.gov/newbornscreening).

Table 1. Disorders included in the Newborn Screening Blood Spot Panel, Michigan, 2017

Amino Acid Disorders	**Organic Acid Disorders**
1. Argininemia	30. 2-Methyl-3-hydroxy butyric aciduria
2. Argininosuccinic acidemia	31. 2-Methylbutyryl-CoA dehydrogenase deficiency
3. Citrullinemia	32. 3-Hydroxy 3-methylglutaric aciduria
4. Citrullinemia Type II	33. 3-Methylcrotonyl-CoA carboxylase deficiency
5. Homocystinuria	34. 3-Methylglutaconic aciduria
6. Hypermethioninemia	35. Beta-ketothiolase deficiency
7. Maple syrup urine disease	36. Glutaric acidemia Type I
8. Phenylketonuria	37. Isobutyryl-CoA dehydrogenase deficiency
9. Benign hyperphenylalaninemia defect	38. Isovaleric acidemia
10. Biopterin cofactor biosynthesis defect	39. 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
Lysosomal Storage Disorders	53. T-cell related lymphocyte deficiencies
28. Pompe Disease	
29. Mucopolysaccharidosis I (MPS I)	

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.

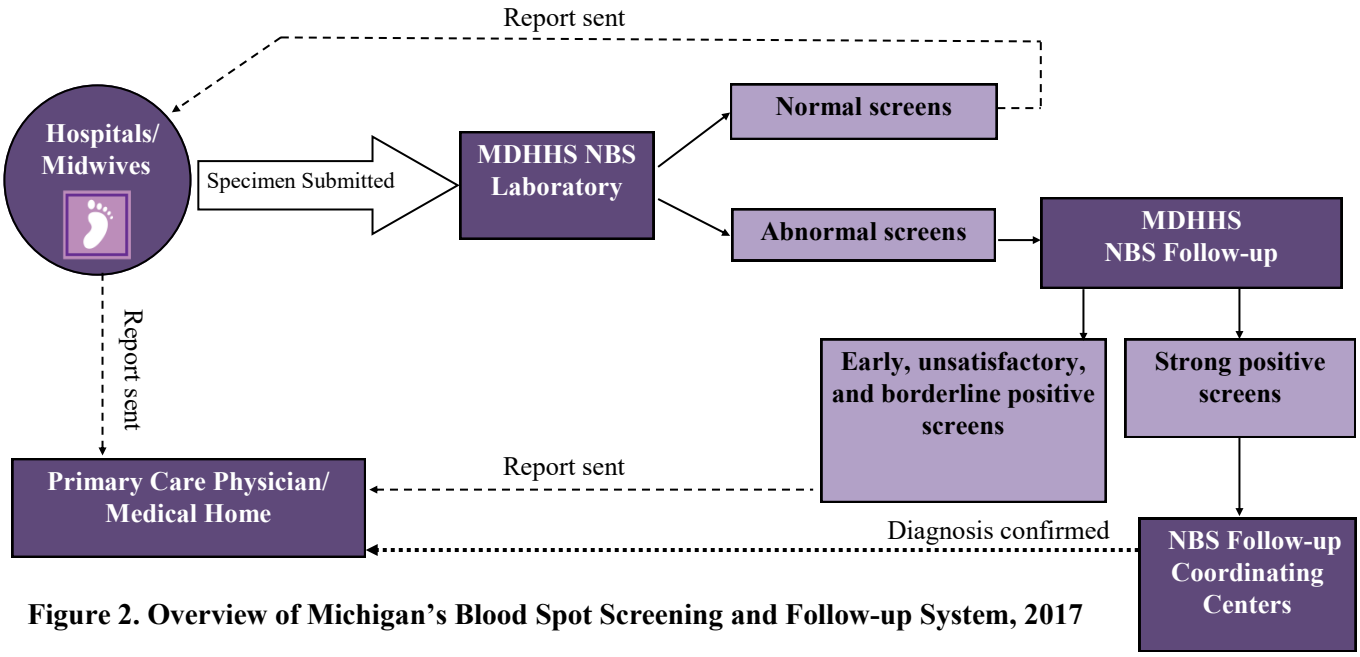

Figure 2. Overview of Michigan's Blood Spot Screening and Follow-up System, 2017

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

HOSPITALS

In 2017, 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 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 2017 (n=110,519) is a preliminary estimate based on the number of birth reported by August 2018.

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.

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

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 percent) and a low false positive rate (perfect= 0 percent); 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.

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, and e) number of screened births with BioTrust consent form returned that is completed appropriately, 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 2017 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 percent of the live births occurring in Michigan in 2017, 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 110,519 live births that occurred in 2017, 357 were listed as deceased on their 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 110,162 remaining live births, the linkage algorithm successfully matched newborn screens for 109,017 infants (98.9 percent). The 1,145 unmatched records were sent to NBS Follow-up Program technicians for further investigation. This more in-depth follow-up revealed that 493 (43.0 percent) 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, 652 infants (0.6 percent) born in the state were not screened. Infants were not screened due to parental refusal of screening (n=212), transfer out of state (n=2), infant expired (n=12), child being screened in another state (n=10), or some other reason for not being screened (n=417). 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 2017, 84 infants born in hospitals are known to have missed being screened, and those hospitals were contacted. Of the 84, 14 have been screened to date and the remaining 70 screens were never

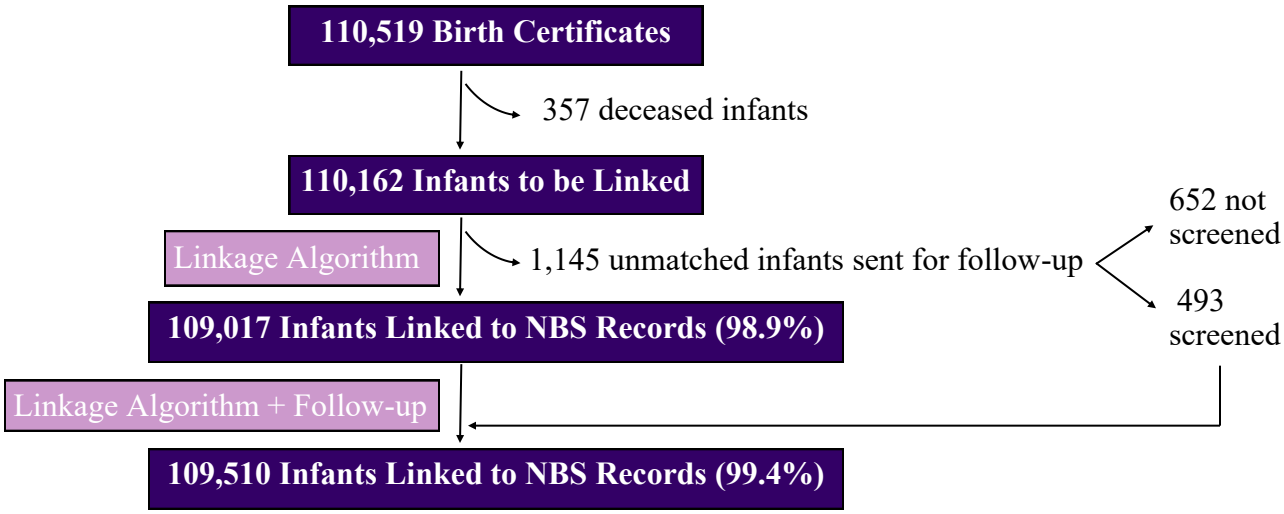

Figure 3. Newborn Screening and Live Births Records Linkage, Michigan, 2017

submitted.
In total, 109,740 NBS samples were received from infants born in 2017. Of those, 297 (0.3 percent 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 2017. 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, 10.8 percent of in-state infants screened were admitted to the NICU or special care nursery (SCN), 8.4 percent were low birth weight (<2,500 grams), and 9.5 percent were born preterm (<37 weeks gestational age). Black infants were over-represented

Table 3: Demographics of Infants Screened by Race, Michigan, 2017, 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	67,882	62.0	60,617	89.3	6,435	9.5	830	1.2	4,587	6.8	5,771	8.5
Black	20,255	18.5	16,774	82.8	3,462	17.1	19	0.1	2,850	14.1	2,872	14.2
Multi-Racial	6,785	6.2	6,099	89.9	643	9.5	43	0.6	559	8.2	589	8.7
Other	8,352	7.6	7,673	91.9	675	8.1	4	0.05	699	8.4	622	7.4
Missing	6,169	5.6	5,574	90.4	584	9.5	11	0.2	507	8.2	586	9.5
Column Total:	109,443	100.0	96,737	88.4	11,799	10.8	907	0.8	9,202	8.4	10,440	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 1,726 and 1,281 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.

among NICU, preterm, and low birth weight births.

SCREENING OUTCOME INFORMATION

In the following sub-sections, outcome information is provided for the disorders included in the NBS panel in 2017. The total numbers of cases detected both in and through 2017 are presented along with screening performance metrics.
The disorders are organized into six categories: metabolic, endocrine, cystic fibrosis, hemoglobinopathies, primary immunodeficiency disorders, and lysosomal storage disorders.

CUMULATIVE DETECTION RATE

Table 4 reports the cumulative detection rate of disorders identified via NBS by classification both in and through 2017. 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. As indicated in Table 4 and Figure 4, CH and sickle cell disease were the most prevalent disorders in 2017, while lysosomal storage disorders and hemoglobin H Disease were the least prevalent.

Table 4: Disorders Identified in Newborns via Newborn Screening, 1965-2017

Type of Disorder Classification (Year Screening Began)	Cases in 2017 (N)	Cases Through 2017 (N)	Cumulative Detection Rate
Galactosemia (1985)	5	205	1:20,788
Biotinidase Deficiencies (1987)	22	335	1:11,898
Amino Acid Disorders (1965)	21	769	1:9,389
Organic Acid Disorders (2005)	6	86	1:17,516
Fatty Acid Oxidation Disorders (2003)	15	268	1:6,593
Congenital Hypothyroidism (1977)	121	2,358	1:1,690
Congenital Adrenal Hyperplasia (1993)	9	165	1:18,856
Sickle Cell Disease (1987)	64	1,972	1:2,021
Hemoglobin H Disease (2012)	2	9	1:74,186
Cystic Fibrosis (2007)	26	284	1:4,078
Primary Immunodeficiencies (2011)	12	101	1:7,721
Lysosomal Storage Disorders (August 2017)	2	2	1:22,984
Total	305	6,554	-

Notes: The CF and LSD detection rate denominator includes only infants born after screening commenced. For the other disorders, the number of live births eligible to have been screened was 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.

Figure 4 displays detection rates in 2017 and overall. CH accounted for 40 percent of cases diagnosed in 2017 and 36 percent cumulatively. Sickle cell disease accounted for 21 percent of cases detected in 2017 and 30 percent detected cumulatively. Cystic fibrosis (CF) was the third most commonly diagnosed disorder in 2017 and accounted for 9 percent of cases detected in 2017 and 4 percent of cases detected cumulatively. The cumulative percentage of CF cases is low compared to the 2017 percentage because screening began recently (October 2007) relative to the other disorders. Similarly, primary immunodeficiencies (PID) accounted for 4 percent of cases and 2 percent 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 percent of cases in 2017 and 17 percent 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 (5 percent) is an underestimate because MCAD screening began in 2003, while screening for other conditions did not begin until 2005. This means that births included in the denominator from 2003-2005 were not eligible for diagnosis of a fatty acid oxidation disorders other than MCAD leading to an artificially low cumulative detection rate. The MS/MS detection rate does not include detected cases of formiminoglutamic acid disorder (FIGLU) because the disorder is not included in the NBS panel. Galactosemia, including Duarte compound heterozygotes, accounted for 2 percent of all disorders detected in 2017 and 3 percent cumulatively. Screening for lysosomal storage disorders started in August 2017 and accounted for 0.3 percent of cases diagnosed in 2017, but only 0.03 percent of cases detected cumulatively, which is to be expected since screening recently began.

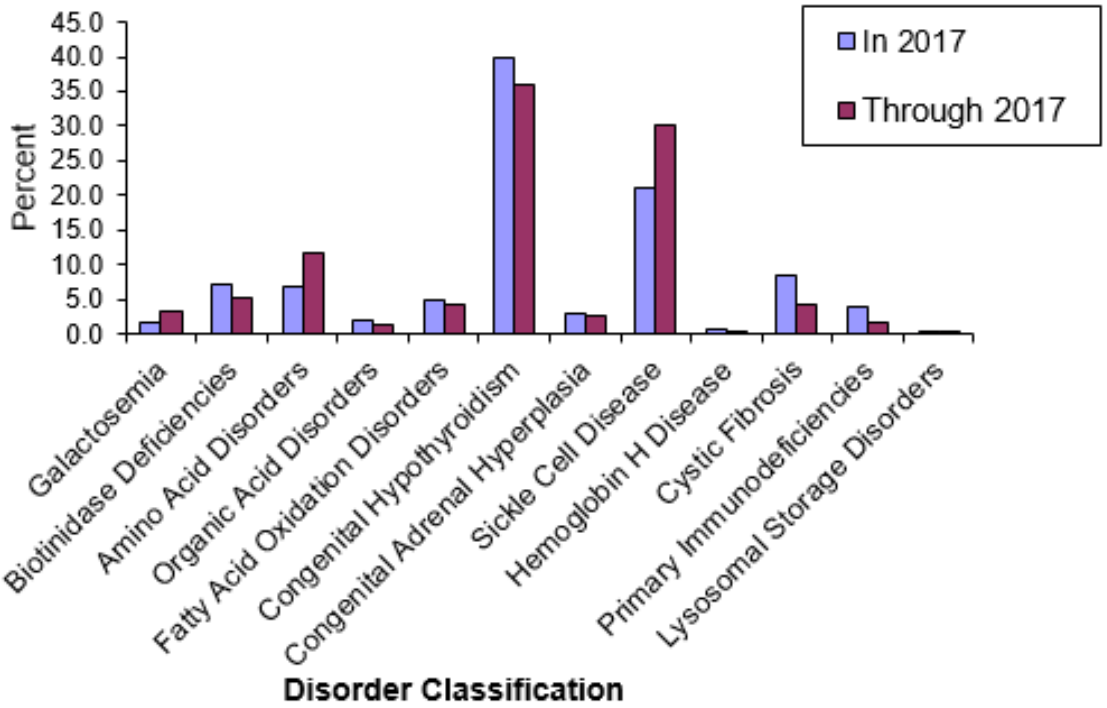

Figure 4. Percent Distribution of Disorders Identified in Newborns via Newborn Screening, Michigan Residents, in 2017 and through 2017

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 2017. Performance metrics for individual MS/MS disorders are provided in separate tables (see Tables 7-9).

GALACTOSEMIA, BIOTINIDASE DEFICIENCY & CYSTIC FIBROSIS

Four cases of Duarte D/G variant and one case of classic galactosemia were detected in 2017, resulting in a FPR of 0.003 percent and PPV of 62.5 percent.

The biotinidase deficiency detection rate (including partial biotinidase deficiency) was 1:4,975. The FPR and PPV were 0.03 percent and 43.1 percent, respectively. Of the 22 cases detected, 19 were partial and 3 were profound.

Twenty-six cases of CF were detected in 2017 (detection rate-1:4,209). The associated FPR and PPV were 0.4 percent and 5.5 percent, respectively. Additionally, fourteen 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

One hundred and twenty-one cases of CH were detected in 2017. The CH screening FPR was 1.8 percent, and the PPV was 5.9 percent. The overall detection rate for CH was 1:904. Chapter IV of the 2007 Annual Report provides more detailed information describing CH screening in Michigan.

Nine cases of CAH were detected in 2017, seven were salt-wasting and two were non salt-wasting. The CAH screening FPR was 0.1 percent, and the PPV was 9.6 percent. The overall detection rate for CAH was 1:12,160.

HEMOGLOBINOPATHIES

Hemoglobinopathies include sickle cell disease (SCD) and Hemoglobin H disease. Two cases of Hemoglobin H were detected in 2017, resulting in a detection rate of 1:54,722. The Hemoglobin H disease FPR was 0.03 percent and the PPV was 6.5 percent.

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 94 percent of the cases in 2017. While the overall incidence of SCD is approximately one case per 1,710 screened, the incidence in African Americans is one in 337 screened in Michigan. In addition to sickle cell disease, variant hemoglobinopathies are identified through screening. In 2017, a total of seven cases of other hemoglobinopathies were diagnosed, including cases of Hemoglobin C and E disease.

Table 5: Screening Results and Performance Metrics, Michigan, 2017

Disorder Type	Total N	Total + N (% NICU)	Confirmed + N	Positive Detection Rate	FPR %	PPV %
Galactosemia	109,443	8 (25.0)			0.003	62.5
Classic (GG)			1	1:109,443		
Duarte (DG)			4	1:27,361		
Total			*5*	*1:21,889*		
Biotinidase Deficiency		51 (0.0)			0.03	43.1
Profound			3	1:36,481		
Partial			19	1:5,760		
Total			*22*	*1:4,975*		
Cystic Fibrosis (CF)		470 (28.3)	26	1:4,209	0.4	5.5
Congenital Hypothyroidism (CH)		2,043 (18.8)	121	1:904	1.8	5.9
Congenital Adrenal Hyperplasias (CAH)		94 (95.7)			0.1	9.6
Salt wasting			7	1:15,635		
Non-Salt wasting			2	1:54,722		
Total			*9*	1:12,160		
Sickle Cell Disease (SCD)		77 (11.7)	64	1:1,710	0.01	83.1
Hemoglobin H Disease		31 (32.3)	2	1:54,722	0.03	6.5
Primary Immunodeficiencies		39 (71.8)			0.02	30.8
SCID			1	1: 109,443		
Syndromes with T-cell Impairment			3	1: 36,481		
Non-preterm Secondary T-cell Lymphopenias			8	1:13,680		
Total			*12*	*1:9,120*		
Amino Acid		44 (27.3)	21	1:5,212	0.02	47.7
Organic Acid		30 (33.3)	6	1:18,241	0.02	20.0
Fatty Acid Oxidation		84 (7.1)	15	1:7,296	0.1	17.9
*MS/MS Disorders Total**		152 (19.1)	42	1:2,606	0.1	27.6

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.*

PRIMARY IMMUNODEFICIENCIES

In total, 12 cases of primary immunodeficiencies (PID) were identified, resulting in FPR of 0.02 percent and PPV of 30.8 percent. Of the 12 cases, 1 were classic SCID, 3 had syndromes with t-cell impairment, and 8 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

In total, 42 disorders were detected by MS/MS. The overall FPR for MS/MS disorders was 0.1 percent. The PPV was 27.6 percent, and the detection rate was 1:2,606.

SCREENING PERFORMANCE METRICS-INDIVIDUAL MS/MS DISORDERS

AMINO ACID DISORDERS

Twenty one 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 7,296 newborns screened (15 newborns total). Chapter IV of the 2009 Annual Report provides more detailed information about PKU screening in Michigan. Two case of citrullinemia, two cases of tyrosinemia, one case of argininemia, and one case of hypermethio-ninemia were also identified.

ORGANIC ACID DISORDERS

Six newborns were identified with organic acid disorders (Table 8) by MS/MS. Four were diagnosed with 3-Methylcrotonyl-CoA carboxylase deficiency (3MCC), one was diagnosed with methylmalonic acidemia (MMA), and one was diagnosed with propionic acidemia (PA).

FATTY ACID OXIDATION DISORDERS

Fifteen children were identified with fatty acid oxidation disorders (Table 9); seven medium-chain acyl-CoA dehydrogenase deficiency (MCAD), four short-chain acyl-CoA dehydrogenase deficiency (SCAD), two very long-chain acyl-CoA dehydrogenase deficiency (VLCAD), two carnitine uptake defect (CUD), and one glutaric acidemia Type II (GAII). One of these infants was diagnosed with two fatty acid disorders.

LYSOSOMAL STORAGE DISORDERS

Screening for Pompe and Mucopolysaccharidosis I (MPS 1) disease began August 7, 2017. Between August 2017 and December 2017, two case of Pompe disease was identified through NBS, resulting in a FPR of 0.3 percent and a PPV of 1.6 percent. (Table 10). No cases of MPS 1 were diagnosed in 2017, resulting in a FPR of 0.4 percent.

Table 6: Hemoglobinopathy Screening Performance Metrics, Michigan, 2017

Disorder	Newborns (N)	Confirmed + (N)		Positive Detection Rate	
		Total	Among African Americans	Total	Among African Americans
Sickle Cell Anemia	109,443	42	38	1:2,606	1:532
SC Disease		14	14	1:7,817	1:1,445
Sickle β thalassemia		8	8	1:13,680	1:2,528
SE Disease		0	-	-	-
Total		64	60	1:1,710	1:337

Notes: Out of the number of Michigan resident infants screened, total N=109,443 among African Americans N=20,255

Table 7: Amino Acid Disorders Detected by Tandem Mass Spectrometry, Screening Performance Metrics, Michigan, 2017

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Phenylketonuria	109,443	21			0.01	71.4
Medically treated (PKU)			5	1:21,889		
Benign Hyperphenyl-alaninemia (H-PHE)			10	1:10,944		
Biopterin Cofactor Defects (BIOPT)			0	-		
Total			*15*	*1:7,296*		
Citrullinemia (CIT)/CIT II		4	2	1:54,722	0.002	50.0
Tyrosinemia I (TYR I)		3	2	1:54,722	0.003	66.7
Tyrosinemia II/III (TYR II/III)		9	0	-	0.01	0.0
Homocystinuria (HCY)		1	1	1:109,443	0.0	100.0
Argininemia (ARG)		2	1	1:109,443	0.001	50.0
Maple Syrup Urine Disease (MSUD)		4	0	-	0.004	0.0

Table 8: Organic Acid Disorders Detected by Tandem Mass Spectrometry, Screening Performance Metrics, Michigan, 2017

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Isobutyryl-CoA dehydrogenase deficiency (IBD)	109,443	6	0	-	0.01	0.0
3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC)		14	4	1:27,361	0.01	28.5
Glutaric Acidemia Type I (GA I)		2	0	-	0.002	0.0
Propionic Acidemia (PA)/ Methylmalonic Acidemia (MMA)		6	2	1:54,722	0.004	33.3
Multiple Carboxylase Deficiency (MCD)		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

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Carnitine Uptake Defect (CUD)	109,443	57	2	1:54,722	0.05	3.5
Short-Chain Acyl-CoA Dehydrogenase deficiency (SCAD)		6	3	1:36,481	0.003	50.0
Long-chain L-3-hydroxyl acyl-CoA dehydrogenase deficiency (LCHAD)		2	0	-	0.002	0.0
Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD)		10	7	1:15,634	0.003	70.0
Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)[1]		8	2	1:54,722	0.005	25.0
Medium/shot-chain L-3 Hydroxyacyl– CoA Dehydrogenase Deficiency (MSCHAD)		1	0	-	0.001	0.0
Carnitine palmitoyltransferase II deficiency (CPT II)		1	0	-	0.001	0.0

[1]One infant screened positive for VLCAD, but was diagnosed with two different fatty acid disorders after confirmatory testing. This infant is not included in this table, but is including in the total number of diagnosed infants in table 4.

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 10: Lysosomal Storage Disorders, Screening Performance Metrics, Michigan, 2017

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Pompe	45,968	125	2	1:22,984	0.3	1.6
Mucopolysaccharidosis I (MPS 1)		164	0	-	0.4	0.0

Notes: Screening for LSDs began in August 2017, thus only 45,968 infants were screened for LSDs in 2017. This number was used to calculate all screening performance metrics for LSDs.

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 11 because their performance metrics have been previously reported in Tables 5-10. Disorders not detected in 2017 and detected disorders with no borderline positive screens are also excluded from Table 11, 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 11.

Table 11: Screening Performance Metrics (FPR and PPV) among Strong Positive Screens compared to All Positive Screens, Michigan, 2017

Disorder Type	Among All +		Among Strong +	
	FPR	PPV	FPR	PPV
	%	%	%	%
Congenital Hypothyroidism (CH)	1.76	5.92	0.18	23.66
Congenital Adrenal Hyperplasia (CAH)	0.08	9.57	0.02	25.00
Phenylketonuria (PKU)	0.01	71.43	0.00	100.00
Galactosemia	0.00	62.50	0.00	100.00
Cystic Fibrosis (CF)	0.41	5.53	0.01	80.77
Primary Immunodeficiency (PID)	0.02	30.77	0.01	50.00
Biotinidase Deficiency	0.03	43.14	0.00	87.50
Carnitine Uptake Defect (CUD)	0.05	3.51	0.00	100.00
3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC)	0.01	28.57	0.00	42.86
Very Long-chain Acyl-CoA Dehydro-genase Deficiency (VLCAD)	0.01	25.00	0.00	28.57
Citrullinemia (CIT)	0.00	50.00	0.00	66.67

The FPR for CH is reduced approximately 10-fold for strong positive screens, and the PPV is increased approximately 4-fold compared to all positives.

Among strong positive screens for metabolic disorders, PKU, galactosemia, and CUD had the best screening performance metrics, with a 100 percent PPV and a 0 percent 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 11. The FPR decreased 89-fold and the PPV increased from 6 percent to 81 percent when excluding children with a heterozygote DNA mutation.

For PID, the FPR decreased 5-fold and the PPV increased from 43 percent to 88 percent 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 2017, a total of 3,050 infants were identified as carriers of a disease included in the NBS panel, following an abnormal screen (Table 12). The majority of these infants (n=2,724) had a hemoglobin trait. More than 300 infants (n=316) were cystic fibrosis carriers, 3 were identified as V-LCAD carriers, 2 were identified as hemoglobinopathy trait with Barts, 2 were identified as MMA carriers and 3 were identified as MPS1 carriers.

Table 12: Carriers Identified from Newborn Screening, Michigan, 2017

Disorder	N
Hemoglobin Traits	2,724
Cystic fibrosis (CF)	316
Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)	3
Hemoglobinopathy Trait - Barts	2
Methylmalonic Acidemia (MMA)	2
Mucopolysaccharidosis I (MPS1)	3

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 13: Maternal Disorders Identified from Newborn Screening, Michigan, 2017

Maternal Disorder	N
Carnitine uptake defect (CUD)	2

Notes: 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 2017, two mothers were identified with CUD following their infant's positive screen (Table 13).

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 14 reports specimen characteristics by nursery type where the specimen was collected. Although 11 percent of infants were admitted to the NICU or SCN, 46 percent and 20 percent 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 (4.1 percent). Early (collected before 24 hours of life) and transfused specimens were more common among infants from the NICU (8.1 percent), while late specimens, those collected after six days of life, were most common among non-hospital deliveries (7.5 percent). The NBS Follow-up Program tracks all strong and borderline positive, isolated elevation, unsatisfactory, early, and transfused specimens; approximately 6,500 specimens required follow-up in 2017.

Table 14: Specimen Characteristics by Nursery Type, Michigan, 2017

Indicator	Type of Birth					
	Regular Nursery		NICU/SCN		Non-Hospital	
	N	%	N	%	N	%
Strong Positive Specimens	262	0.3	220	1.9	1	0.1
Borderline Positive Specimens	1,740	1.8	446	3.8	7	0.8
All Positive Specimens*	2,418	2.5	824	7.0	12	1.3
Isolated elevations of amino acids and acyl-carnitines	14	0.0	512	4.3	4	0.4
Unsatisfactory Specimens	1,077	1.1	270	2.3	37	4.1
Late (>6 days) Specimens	52	0.1	19	0.2	68	7.5
Early (<1 day) Specimens	257	0.3	957	8.1	1	0.1
Transfused Specimens	4	0.0	72	0.6	0	-
Specimens Missing Demographics **	1,554	1.6	150	1.3	26	2.9
Total Births Screened	96,737	88.4	11,799	10.8	907	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 2017, the hospital quarterly reports included five indicators related to blood spot screening. Table 15 lists the indicators and the performance goal for each indicator.

Table 15: Indicators and Performance Goals for Newborn Screening, Michigan, 2017

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

Table 16 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 percent of screens being collected more than 36 hours after birth. Of note, more than 50 percent 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, regular nurseries met the goal with 91.2 percent of specimens arriving on or before the appropriate day. NICUs had 84.3 percent of specimens arrive by the appropriate day and thus did not meet the goal of 90 percent. None of the groups met the goal for unsatisfactory specimens for 2017, though regular nurseries were close to 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 five 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 percent of regular nursery births had a BioTrust for Health consent form returned that was appropriately completed compared to approximately 63 percent of NICUs/SCNs and 65 percent of non-hospital births.

Table 16: Measures for Newborn Screening, by Nursery Type, Michigan, 2017

Measure	Nursery Type	N	%	Met Goal?
Late Screens: Less than 2 percent of screens collected greater than 36 hours after birth	Regular	764	0.8	Yes
	NICU/SCN	241	2.0	No
	Non-hospital	515	56.8	No
Appropriate Day: Greater than 90 percent of screens arrive in state laboratory on or before the appropriate day	Regular	88,222	91.2	Yes
	NICU/SCN	9,931	84.3	No
	Non-hospital*	NA		
Unsatisfactory Screens: Less than 1 percent of screens are unsatisfactory	Regular	1077	1.1	No
	NICU/SCN	270	2.3	No
	Non-hospital	37	4.1	No
NBS Card Number: Greater than 95 percent of electronic birth certificates have the NBS card number recorded	Regular	95,689	95.8	Yes
	NICU/SCN**	-	-	-
	Non-hospital	299	20.3	No
Returned BioTrust for Health Consent Forms Completed Appropriately: At least 90 percent of specimens have a returned consent form that is completed appropriately	Regular	86,299	89.2	No
	NICU/SCN	7,482	63.5	No
	Non-hospital	597	65.8	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 17 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 18). As indicated in Table 17, time to treatment ranged from zero to 181 days among all disorders. Since borderline positive screens require one of more retests before being referred for confirmatory testing, CH is presented separately by initial screening result (strong or borderline) in the table.

GALACTOSEMIA

The classic galactosemia case had treatment started within seven days of life.

BIOTINIDASE DEFICIENCY

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

MS/MS DISORDERS

Five of the five medically treated PKU cases were treated in the first week of life. Both cases of CIT started treatment within the first week of life. The ARG case was treated on the fourth day of life. The two TYR cases were treated in the first week of life

One of the three infants with organic acid disorders and a known treatment start date started treatment within the first week of life, the other two cases began treatment in the second week of life. One of these infants was referred after a repeat borderline screen and the other was referred after second tier testing came back positive.

Of the 14 infants with fatty acid oxidation disorders and a known treatment start date, 11 were treated within the first week of life. Of the three infants that started treatment after a week of life, two had an initial borderline screen and thus had a repeat screen before they were referred and one infant screened positive for VLCAD, but confirmed with two other fatty acid disorders after confirmatory testing.

ENDOCRINE DISORDERS-CAH AND CH

The salt-wasting form of CAH is life-threatening in the first few weeks of life. Five infants were identified with salt-wasting CAH, three were treated within the first week of life and the remaining two began treatment at eight 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 71 CH cases with a strong positive screen, 55 (77 percent) were treated by the 14th day of life.

Table 17: Time to Treatment of Amino Acid Disorders, Organic Acid, Fatty Acid Oxidation, and Endocrine Disorders, Michigan, 2017

Disorder		Total	Treatment Time (days from birth)			Treatment Time Range (days)
			N			
		N	1-7	8-14	>14	
Galactosemia	Classic (GG)	1	1			2
	Duarte (DG)	4			4	24-66
Biotinidase Deficiency	Partial	19	8	5	6	4-99
	Profound	3	3			5-6
Amino Acid Disorders	PKU-medically treated	5	5			3-6
	CIT	2	2			5-6
	ARG	1	1			4
	TYR 1	2	2			5
	Total	10	10			3-6
Organic Acid Disorders	3MCC[1]	4	1	1		2-10
	PA/MMA[2]	2		1		9
	Total	6	1	2		2-10
Fatty Acid Oxidation Disorders	SCAD	3	3			4-5
	MCAD	7	7			2-3
	GA II	1		1		9
	VLCAD	2	2			4-5
	CUD[3]	2		1		8
	Total	15	12	2		2-9
Endocrine Disorders	CH					
	Strong[4]	62	40	12	9	1-107
	Borderline	31	0	8	23	9-181
	Inconclusive/normal	28	0	3	25	10-73
	CAH					
	Salt-wasting	7	6	1		0-8
	Non salt-wasting	2	2			1-6
Total		188	83	33	67	0-181

Notes: Disorders that do not require treatment are excluded from the table. Time to treatment categories for CH are based on the results of the first screen. Infants who screened borderline or inconclusive on their first screened required a repeat screen before referral to medical management. Some infants screened normal on their first screen and were not positive until a repeat screen.

[1] Two infants diagnosed with 3MCC had a missing time to treatment.
[2] One infant diagnosed with PA/MMA had a missing tine to treatment
[3] One infant diagnosed with CUD had a missing time to treatment.
[4] One infant diagnosed with CH had a missing time to treatment.

HEMOGLOBINOPATHIES

Table 18 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 63 cases with a known penicillin initiation date, 84 percent were treated with penicillin within the first four months. Eleven percent began treatment between four and five months of life and 5 percent began treatment after five months of life.

Table 18: Time to Penicillin Initiation for Sickle Cell Disorders, Michigan, 2017

Disorder	Penicillin Prophylaxis Initiation Time		
	< 120 days	**120-149 days**	**> 150 days**
Sickle Cell Disorders*	53 (84.1%)	7 (11.1%)	3 (4.7%)

*One case was missing a penicillin initiation date.

V. Conclusions

NBS is a critical public health program that protects the lives of our state's newest residents. The NBS Laboratory screened 109,740 infants born in 2017, and the NBS Follow-up Program tracked approximately 6,500 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 305 newborns were identified with a disorder by NBS in 2017, as well as 3,050 carriers. Since blood spot screening began in Michigan in 1965, 6,554 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.