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Health and Human Services

MICHIGAN NEWBORN SCREENING PROGRAM

Annual Report 2014



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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, over 50 disorders have been added to the screening panel. Through 2014, nearly 6.9 million infants have been screened with almost 5,700 diagnosed with diseases included in the NBS panel.

Of the 112,790 infants screened in 2014, the vast majority were Michigan residents and 259 (0.2%) were diagnosed with a disease. Overall, one infant out of 435 screened was diagnosed with one of the disorders included in the NBS panel (see Table 1 for list of disorders).

Developments occurring in 2014:

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 Home Visiting Conference
 - ◊ Region 4 Midwest Genetics Collaborative
- “Improving the Rate of Sufficient Sweat Collected in Infants Referred for Sweat Testing in Michigan” was published in *Global Pediatric Health*.

The Michigan Department of Health and Human Services (MDHHS) continued to provide educational outreach and training:

- The NBS Program held 5 regional trainings to educate hospital and birth attendant staff. Presentation topics included an update on critical congenital heart disease (CCHD) and medical management information and case presentations on metabolic disorders.

NBS Program staff met with individuals with disorders and families to learn more about improving delivery of services:

- Focus groups of individuals with sickle cell disease and a stakeholder strategic planning meeting were held to inform a strategic plan (http://www.michigan.gov/documents/mdhhs/MDHHS_Final_SCD_Strategic_Plan_504325_7.pdf).
- A workgroup focusing on diet for life for metabolic disorders was formed and developed a summary report (http://www.michigan.gov/MDHHS/0,4612,7-132-2942_4911_4916-323855--,00.html).

New capacity was added for NBS:

- The NBS Program implemented pulse oximetry screening for critical congenital heart disease (CCHD) on April 1, 2014.
- Pompe disease was added to the mandatory screening panel on October 1, 2014. The Follow-up and Laboratory Programs began developing infrastructure for screening at that time. Implementation will begin when an FDA-approved method becomes available.

The NBS Laboratory activities include:

- Sara Tomechko, PhD was appointed Chemistry and Toxicology Division Director over the Newborn Screening Laboratory.
- Laboratory renovations were completed without interrupting testing to prepare the facility for equipment updates and to comply with CDC recommendations for molecular testing.
- Installations were started for new Panthera blood spot punching machines and Genetic Screening Processor (GSP) instruments for CAH, CH, CF, galactosemia, and biotinidase deficiency testing.

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Acronym Key

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

I. Introduction

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

This report is intended to provide:

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

What is Newborn Screening?

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

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

¹All 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

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

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

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

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).

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

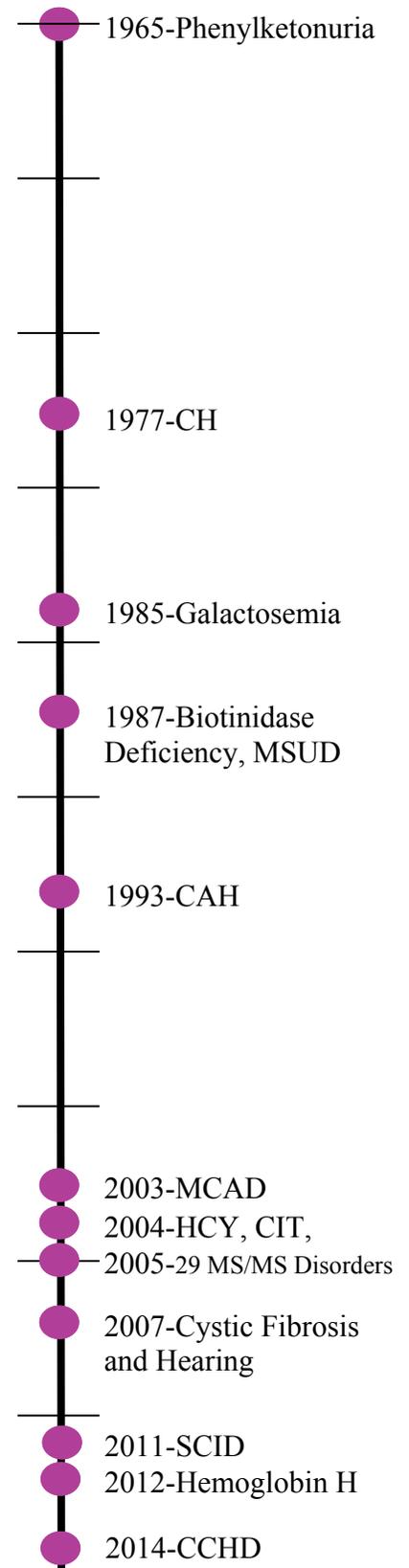


Figure 1. Implementation of Disorders to the NBS Panel, Michigan, 1965-2014

Table 1. Disorders included in the Newborn Screening Blood Spot Panel, Michigan, 2014

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.

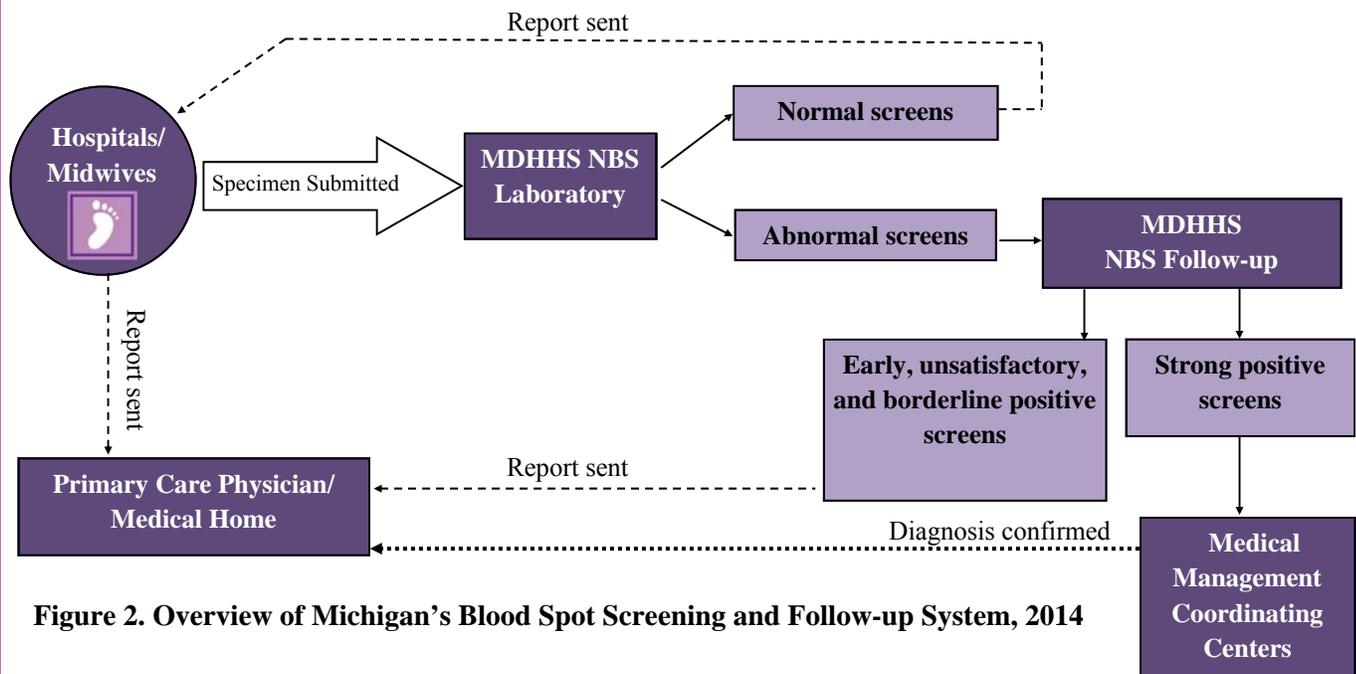


Figure 2. Overview of Michigan’s Blood Spot Screening and Follow-up System, 2014

Abbreviations: MDHHS-Michigan Department of Community Health; NBS-Newborn Screening;

HOSPITALS

In 2014, Michigan had 84 hospitals with birthing units. Each hospital has a designated NBS Coordinator who helps facilitate the screening process. Hospital coordinators receive a quarterly quality assurance report from the NBS Follow-up Program that includes information on hospital-specific performance indicators compared to the state overall. Hospitals receive periodic site visits by the NBS Nurse Consultant to evaluate the screening process and make recommendations for improvement.

MIDWIVES AND HOME BIRTH ATTENDANTS

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

MICHIGAN DEPARTMENT OF HEALTH AND HUMAN SERVICES

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

II. Methods

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

TOTAL NUMBER OF NEWBORNS ELIGIBLE FOR SCREENING

We used vital statistics data collected by the Vital Records & Health Data Development Section within the Division for Vital Records and Health Statistics at MDHHS to determine the total number of live births statewide eligible for screening. The number of live births in 2014 (n=113,637) is a preliminary estimate as the final files have not been released yet.

TOTAL NUMBER OF NEWBORNS DIAGNOSED BY NEWBORN SCREENING

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

DEMOGRAPHIC CHARACTERISTICS OF SCREENED NEWBORNS

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

SCREENING PERFORMANCE METRICS

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

Table 2. Screening Performance Indicator Descriptions

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

QUALITY ASSURANCE INDICATORS

Quality assurance (QA) data were obtained from NBS cards and information recorded by the state NBS laboratory and coordinating centers. QA indicators on the hospital quarterly reports prepared by the NBS Follow-up Program include: a) time from birth to specimen collection, b) time from specimen collection to arrival at the state NBS laboratory, c) number of specimens that are unsatisfactory, d) number of envelopes containing specimens with a collection date range of more than two days (i.e., batched envelopes), e) number of birth certificates with NBS kit number recorded, and f) 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 2014 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 99.5% of the live births occurring in Michigan in 2014, 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 113,637 live births that occurred in 2014, 502 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 113,135 remaining live births, the linkage algorithm successfully matched newborn screens for 112,106 infants (99.1%). The 1,029 unmatched records were sent to NBS Follow-up Program technicians for further investigation. This more in-depth follow-up revealed that 427 (41.5%) of the unmatched records were screened. For these infants, the linkage algorithm failed to create the match for a variety of reasons, including data recording errors, data entry errors, or name changes due to adoptions. Overall, 602 infants (0.5%) born in the state were not screened. Infants may not have been screened in Michigan due to parental refusal of screening (n=292), transfer out of state (n=23), infant expired (n=15), or some other reason for not being screened (n=272). 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 2014, 41 infants born in hospitals are known to have been missed by NBS, and hospitals were contacted. Of the 41, 16 have been screened to date and the remaining 25 are pending.

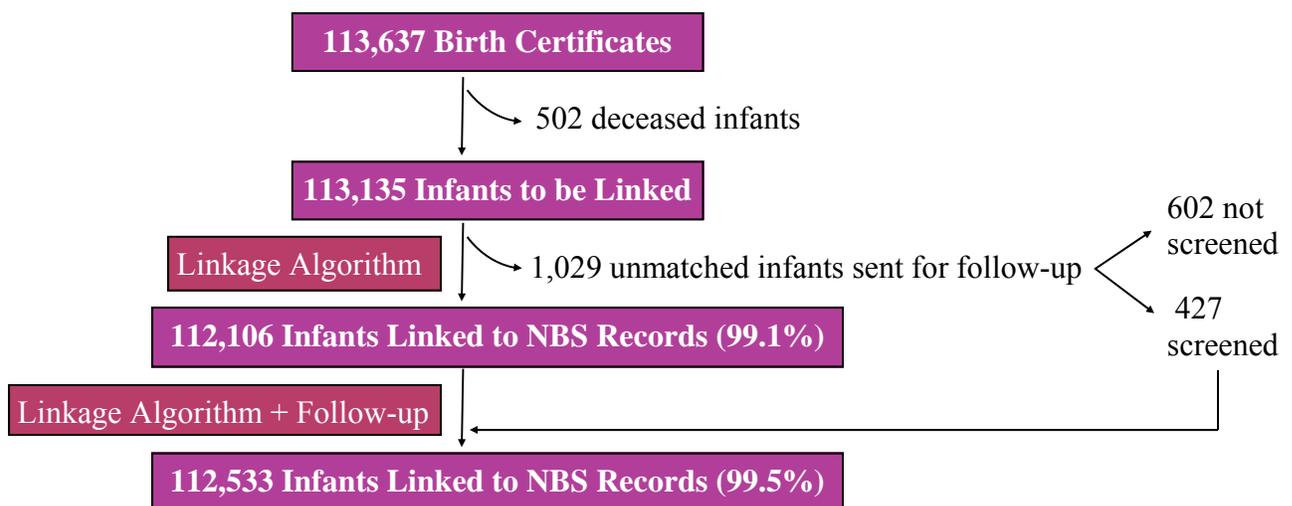


Figure 3. Newborn Screening and Live Births Records Linkage, Michigan, 2014

In total, NBS samples were received from 112,790 infants born in 2014. Of those, 277 (0.2% of screens) belonged to out-of-state residents. Table 3 reports the demographic and perinatal characteristics by race of screened in-state residents born in 2014. This report details the screening results for in-state residents only since non-residents are typically followed in their home state. As indicated in Table 3, the majority of in-state infants screened were white, born in hospital nurseries, term (≥ 37 weeks gestational age), and of normal birth weight ($> 2,500$ g). Overall, 11% of in-state infants screened were admitted to the NICU or special care nursery (SCN), 8% were low birth weight ($< 2,500$ grams), and 9% were born preterm (< 37 weeks gestational age). African Americans were over-represented among NICU, preterm, and low birth weight births.

Table 3: Demographics of Infants Screened by Race, Michigan, 2014, Excluding Out-of-State Residents, N=112,513

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	71,433	63.5	63,873	89.4	6,763	9.5	797	1.1	4,651	6.6	5,920	8.4
African American	19,815	17.6	16,447	83.0	3,361	17.0	7	0.1	2,635	13.5	2,606	13.4
American Indian	460	0.4	395	85.9	57	12.4	8	1.7	25	5.6	33	7.3
Asian/Pac Islander	2,662	2.4	2,455	92.2	204	7.7	3	0.1	207	7.8	184	7.0
Middle Eastern	3,891	3.5	3,559	91.5	332	8.5	0	-	304	7.9	282	7.4
Multi-Racial	6,568	5.8	5,847	89.0	684	10.4	37	0.6	477	7.4	583	9.0
Missing	7,684	6.8	6,931	90.2	731	9.5	22	0.3	634	8.5	725	9.9
Column Total:	112,513	100	98,507	88.4	12,132	10.8	874	0.8	8,933	8.1	10,333	9.4

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

SCREENING OUTCOME INFORMATION

In the following sub-sections, outcome information is provided for the disorders included in the NBS panel in 2014. The total numbers of cases detected both in and through 2014 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 medical management coordinating programs responsible for assessing diagnosis and initiation of treatment.

CUMULATIVE DETECTION RATE

Table 4 reports the cumulative detection rate of disorders identified via NBS by classification both in and through 2014. 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 Newborn Residents, 1965-2014

Type of Disorder Classification (Year Screening Began)	Cases in 2014 (N)	Cases Through 2014 (N)	Cumulative Detection Rate
Galactosemia (1985)	7	188	1:20,904
Biotinidase Deficiencies (1987)	23	268	1:13,636
Amino Acid Disorders (1965)	14	716	1:9,621
Organic Acid Disorders (2005)	9	69	1:17,028
Fatty Acid Oxidation Disorders (2003)	16	208	1:6,901
Congenital Hypothyroidism (1977)	84	2,050	1:1,783
Congenital Adrenal Hyperplasia (1993)	11	148	1:18,782
Sickle Cell Disease (1987)	52	1,785	1:2,047
Hemoglobin H Disease (2012)	1	5	1:67,242
Cystic Fibrosis (October 2007)	27	219	1:3,775
Primary Immunodeficiencies (October 2011)	15	55	1:8,182
Total	259	5,711	-

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

As indicated in Table 4 and Figure 4, CH and sickle cell disease were the most prevalent disorders in 2014, while Hemoglobin H Disease, galactosemia, and organic acid disorders were the least prevalent. Cystic fibrosis (CF) accounted for 10% of cases detected in 2014 and 4% of cases detected cumulatively. The cumulative percentage of CF cases is low compared to the 2014 percentage because screening began recently (October 2007) relative to the other disorders. Similarly, primary immunodeficiencies (PID) accounted for 6% 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 15% of cases in 2014 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 2014 and 3% cumulatively. Biotinidase deficiency, including partial biotinidase deficiency, accounted for 9% of all cases detected in 2014 and 5% of all cases detected cumulatively. CAH accounted for 4% of all cases in 2014 and 3% of all cases detected cumulatively.

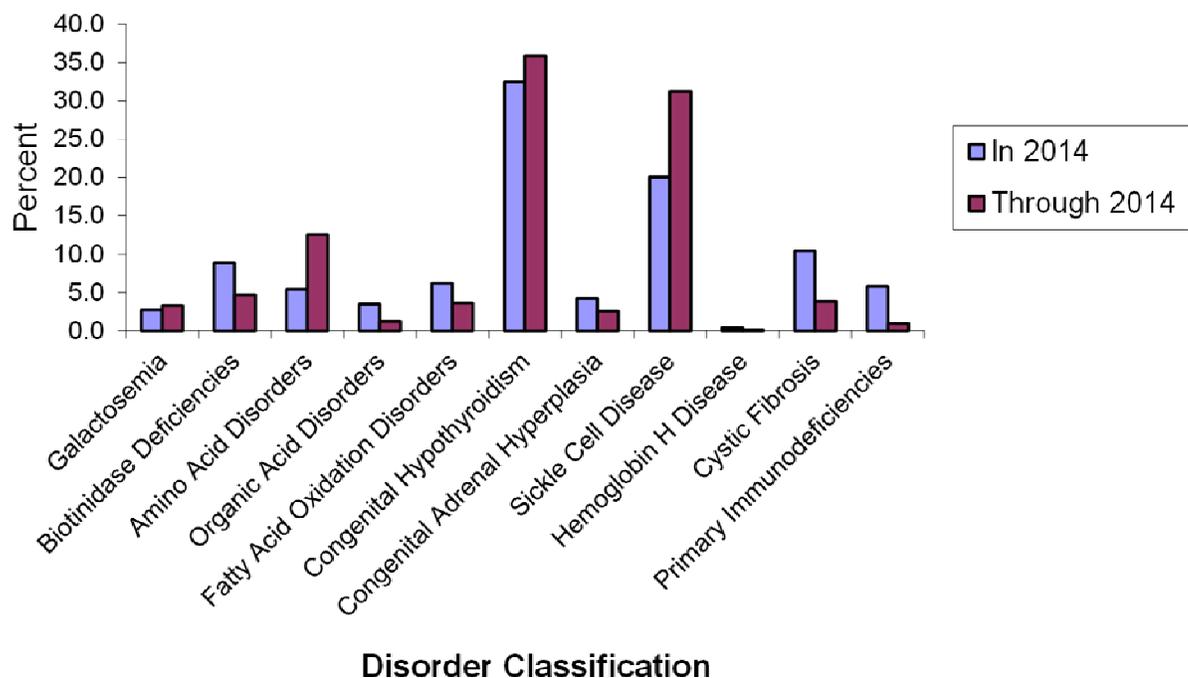


Figure 4. Percent Distribution of Disorders Identified in Newborns via Newborn Screening, Michigan Residents, in 2014 and through 2014

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 2014. Performance metrics for individual MS/MS disorders are provided in separate tables (see Tables 7-9).

GALACTOSEMIA, BIOTINIDASE DEFICIENCY & CYSTIC FIBROSIS

Two cases of Duarte D/G variant and five cases of classic galactosemia were detected in 2014, resulting in a FPR of 0.007% and PPV of 47%.

The biotinidase deficiency detection rate (including partial biotinidase deficiency) was 1:4,892; the FPR and PPV were 0.05% and 31%, respectively. Of the 23 cases detected, 21 were partial and 2 were profound. Five newborns with homozygous D444H were also identified.

Twenty-seven cases of CF were detected in 2014 (detection rate-1:4,167); the associated FPR and PPV were 0.3% and 8%, respectively. Additionally, 7 cases of CFTR-related metabolic syndrome were detected. Chapter IV of the 2008 Annual Report provides more detailed information describing CF screening in Michigan.

ENDOCRINE DISORDERS-CH AND CAH

The CH screening FPR was 0.95%, and the PPV was 7%. The overall detection rate for CH was 1:1,339. Chapter IV of the 2007 Annual Report provides more detailed information describing CH screening in Michigan.

The CAH screening FPR was 0.10%, and the PPV was 9%. The overall detection rate for CAH was 1:11,251. All eleven cases detected were salt-wasting.

HEMOGLOBINOPATHIES

Hemoglobinopathies include sickle cell disease (SCD) and Hemoglobin H disease. The Hemoglobin H disease FPR was 0.05% and the PPV was 1.8%. One case was identified in 2014, resulting in a detection rate for Hemoglobin H disease of 1:112,513.

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 85% of the cases in 2014. While the overall incidence of SCD is approximately one case per 2,164 screened, the incidence in African Americans is one in 450 screened in Michigan.

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

Table 5: Screening Results and Performance Metrics, Michigan, 2014

Disorder Type	Total N	Total + N (% NICU)	Confirmed + N	Positive Detection Rate	FPR %	PPV %
Galactosemia	112,513	15 (26.7)			0.007	46.67
Classic (GG)*			5	1:22,503		
Duarte (DG)			2	1:56,257		
<i>Total</i>		7	1:16,073			
Biotinidase Deficiency		74 (8.1)			0.05	31.08
Profound			2	1:56,257		
Partial			21	1:5,358		
<i>Total</i>		23	1:4,892			
Cystic Fibrosis		341 (14.1)	27	1:4,167	0.28	7.92
Congenital Hypothyroidism		1155 (28.0)	84	1:1,339	0.95	7.27
Congenital Adrenal Hyperplasias		121 (90.1)			0.10	9.09
Salt wasting			11	1:10,228		
Non-Salt wasting			0	-		
<i>Total</i>		11	1:10,228			
Sickle Cell Disease		59 (22.0)	52	1:2,164	0.01	88.14
Hemoglobin H Disease		56 (30.4)	1	1:112,513	0.05	1.79
Primary Immunodeficiencies		71 (77.5)			0.05	21.13
SCID			4	1: 28,128		
Syndromes with T-cell Impairment			4	1: 28,128		
Non-preterm Secondary T-cell Lymphopenias			7	1:16,073		
<i>Total</i>		15	1:7,501			
Amino Acid		42 (23.8)	14	1:8,037	0.02	33.33
Organic Acid		34 (26.5)	9	1:12,501	0.02	26.47
Fatty Acid Oxidation		83 (15.7)	16	1:7,032	0.06	19.28
<i>MS/MS Disorders Total**</i>	150 (21.3)	39	1:2,885	0.10	26.00	

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).

*One confirmed galactosemia case is a variant, but is being followed like a classic case.

**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.

2014, a total of 13 cases of other hemoglobinopathies were diagnosed, including cases of Hemoglobin C, D, and E disease.

PRIMARY IMMUNODEFICIENCIES

In total, 15 cases of primary immunodeficiencies (PID) were identified, resulting in FPR of 0.05% and PPV of 21%. Of the 15 cases, 4 were classic SCID, 4 had syndromes with t-cell impairment, and 7 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 1:2,813.

SCREENING PERFORMANCE METRICS-INDIVIDUAL MS/MS DISORDERS

AMINO ACID DISORDERS

Fourteen newborns were identified with amino acid disorders (Table 7) by MS/MS. Phenylketonuria (PKU) was the most frequent amino acid disorder identified, found in one of every 10,228 newborns screened (eleven newborns total). Chapter IV of the 2009 Annual Report provides more detailed information about PKU screening in Michigan. As indicated in the table, maple syrup urine disease (MSUD) screening had the highest PPV (100%) among amino acid disorders (one confirmed out of one positive screen). Two Tyrosinemia Type 1 cases were also identified. These were the first Tyrosinemia Type 1 cases identified through NBS in Michigan. Additionally, one pyruvate carboxylase deficiency case (screened positive for citrullinemia) was identified, but not included in the final count because that disorder is not on the NBS panel.

ORGANIC ACID DISORDERS

Nine newborns were identified with organic acid disorders (Table 8) by MS/MS. One infant was diagnosed with 3-methylcrotonyl-CoA carboxylase deficiency (3MCC); one was diagnosed with glutaric acidemia Type 1 (GA1); three were diagnosed with isobutyryl-CoA dehydrogenase deficiency (IBG); and four were diagnosed with methylmalonic acidemia (MMA). Three infants were identified as carriers of 3MCC and another as a carrier of GA1.

FATTY ACID OXIDATION DISORDERS

Sixteen children were identified with fatty acid oxidation disorders (Table 9); nine medium-chain acyl-CoA dehydrogenase deficiency, five short-chain acyl-CoA dehydrogenase deficiency, one very long-chain acyl-CoA dehydrogenase deficiency (VLCAD), and one carnitine palmitoyltransferase II deficiency (CPT II). Of the disorders detected, CPT II had the highest PPV (100%), followed by MCAD (75%). Two maternal cases of carnitine uptake defect were found following an infant's positive screen, and two MCAD carriers were identified.

Table 6: Hemoglobinopathy Screening Performance Metrics, Michigan, 2014

Disorder	Newborns (N)	Confirmed + (N)		Positive Detection Rate	
		Total	Among African Americans	Total	Among African Americans
Sickle Cell Anemia	112,513	30	25	1:3,750	1:793
SC Disease		18	15	1:6,251	1:1,321
Sickle β thalassemia		4	4	1:28,128	1:4,954
SE Disease		0	0	-	-
<i>Total</i>		52	44	1:2,164	1:450

Notes: Out of the number of Michigan resident infants screened, total N=112,513, among African Americans N=19,815

Table 7: Amino Acid Disorders Detected by Tandem Mass Spectrometry, Screening Performance Metrics, Michigan, 2014

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Phenylketonuria	112,513	21	8	1:14,064	0.009	52.4
Diet-treated (PKU)			3	1:37,504		
Benign Hyperphenylalaninemia (H-PHE)			0	-		
Biopterin Cofactor Defects (BIOPT)			11	1:10,228		
<i>Total</i>			4	0		
Citrullinemia (CIT)/CIT II	7	2	1:56,257	0.006	28.6	
Tyrosinemia I (TYR I)	9	0	-	0.008	-	
Homocystinuria (HCY)/Hypermethioninemia (MET)	1	1	1:112,513	0.0	100.0	
Maple Syrup Urine Disease (MSUD)						

Table 8: Organic Acid Disorders Detected by Tandem Mass Spectrometry, Screening Performance Metrics, Michigan, 2014

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Isobutyryl-CoA dehydrogenase deficiency (IBG)	112,513	9	3	1:37,504	0.005	33.3
3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC)		7	1	1:112,513	0.004	14.3
Glutaric Acidemia Type I (GA I)		7	1	1:112,513	0.005	14.3
Propionic Acidemia (PA)/ Methylmalonic Acidemia (MMA)		10	4	1:28,128	0.005	40.0
Multiple Carboxylase Deficiency (MCD)		1	0	-	0.001	-

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

Table 9: Fatty Acid Oxidation Disorders Detected by Tandem Mass Spectrometry, Screening Performance Metrics, Michigan, 2014

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Carnitine Uptake Defect (CUD)	112,513	52	0	-	0.046	-
Short-Chain Acyl-CoA Dehydrogenase deficiency (SCAD)		9	5	1:22,503	0.004	55.6
Carnitine/Acylcarnitine Translocase Deficiency-(CACT)/Carnitine Palmitoyltransferase II Deficiency (CPT II)		1	1	1:112,513	0.0	100.0
Glutaric Acidemia Type II (GA II)		3	0	-	0.003	-
Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD)		12	9	1:12,501	0.003	75.0
Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)		3	1	1:112,513	0.002	33.3
Carnitine Palmitoyltransferase I Deficiency (CPT I)		3	0	-	0.003	-

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). IBG 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 2014 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, 2014

Disorder Type	Among All +		Among Strong +	
	FPR	PPV	FPR	PPV
	%	%	%	%
Congenital Hypothyroidism (CH)	0.95	7.27	0.14	24.64
Congenital Adrenal Hyperplasia (CAH)	0.10	9.09	0.03	25.00
Phenylketonuria (PKU)	0.009	52.38	0.002	84.62
Galactosemia	0.01	46.67	0.0	100.0
Cystic Fibrosis (CF)	0.28	7.92	0.006	79.41
Primary Immunodeficiency	0.05	21.13	0.02	33.3
Biotinidase Deficiency	0.045	31.08	0.001	85.71
3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC)	0.004	14.29	0.001	50.00
Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)	0.002	33.33	0.0	100.0
Tyrosinemia Type I (TYR I)	0.006	28.57	0.0	100.0
Citrullinemia (CIT)	0.003	25.00	0.001	50.00
Glutaric Acidemia Type I (GA I)	0.005	14.29	0.004	20.00

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

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

Among MS/MS disorders, galactosemia, VLCAD, and TYR I all had 100% PPV and 0% FPR among strong positive screens. The rest of the disorders had roughly 2-3 fold increase in PPV and 2-5 fold decrease in FPR among strong positive screens compared to all positive screens.

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 45-fold and the PPV increased from 8% to 79% when excluding children with a heterozygote DNA mutation.

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

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

CARRIERS, MATERNAL DISORDERS, AND OTHER DISORDERS DETECTED

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

In 2014, a total of 2,961 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=2,654) had sickle cell trait. Nearly 300 infants (n=296) were cystic fibrosis carriers, 5 were identified as hemoglobinopathy trait with Barts, 2 were identified as MCAD carriers, 3 were identified as 3MCC carriers, and 1 was identified as a GA I carrier.

Table 11: Carriers Identified from Newborn Screening, Michigan, 2014

Disorder	N
3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC)	3
Cystic fibrosis	296
Glutaric Acidemia Type I (GA I)	1
Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD)	2
Sickle Cell Trait	2,654
Hemoglobinopathy Trait - Barts	5

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, 2014

Maternal Disorder	N
Carnitine uptake defect (CUD)	2

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

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

In 2014, two maternal disorders were identified following an infant's positive NBS (Table 12). Two mothers were identified with CUD.

V. 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, 52% and 27% 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 (6%). 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 5,800 specimens required follow-up in 2014.

Table 13: Specimen Characteristics by Nursery Type, Michigan, 2014

Indicator	Type of Birth					
	Regular Nursery		NICU/SCN		Non-Hospital	
	N	%	N	%	N	%
Strong Positive Specimens	171	0.17	192	1.58	3	0.34
Borderline Positive Specimens	881	0.89	335	2.76	3	0.34
All Positive Specimens*	1,427	1.43	605	4.99	9	1.03
Isolated elevations of amino acids and acyl-carnitines	5	0.01	434	3.56	1	0.11
Unsatisfactory Specimens	1,424	1.27	367	3.03	53	6.06
Late (>6 days) Specimens	67	0.07	34	0.28	53	6.06
Early (<1 day) Specimens	252	0.25	765	6.31	3	0.34
Transfused Specimens	4	0.00	107	0.99	0	0.00
Specimens Missing Demographics **	1,663	1.67	184	1.52	16	1.83
Total Births Screened	99,507	88.4	12,132	10.8	874	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 2014, the quarterly reports included six indicators. Table 14 lists the indicators and the performance goal for each indicator.

Table 14: Indicators and Performance Goals for Newborn Screening, Michigan, 2014

Measure	Performance Goal
Late Screens	Less than 2% of screens collected greater than 36 hours after birth
Courier Time	Greater than 90% of screens arrive in state laboratory less than or equal to 3 days after collection
Unsatisfactory Screens	Less than 1% of screens are unsatisfactory
Batching	Less than 2% of envelopes are batched*
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

*Batched envelopes are those containing specimens with a collection date range of more than 2 days.

Table 15 lists the statistics for each performance measure and whether the goal was met, by nursery type. For late screens, only regular nurseries met the goal with approximately 1.3% of screens being collected more than 36 hours after birth. Of note, nearly 51% 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. For courier time, both regular nurseries and NICUs met the goal, with over 93% of specimens received in the state laboratory within three days of collection. Non-hospital births did not meet the goal. None of the nursery types met the goal for unsatisfactory specimens for 2014, while all nursery types met the batching 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 4 times more likely to have the NBS kit number recorded than certificates coming from non-hospital births. Although none of the nursery types met the BioTrust for Health measure, regular nurseries were the closest; 86% of regular nursery births had a BioTrust for Health consent form returned that was appropriately completed compared to approximately 62% of NICU/SCN and 74% of non-hospital births.

Table 15: Measures for Newborn Screening, by Nursery Type, Michigan, 2014

Measure	Nursery Type	N	%	Met Goal?
Late Screens: Less than 2% of screens collected greater than 36 hours after birth	Regular	1,307	1.3	Yes
	NICU/SCN	447	3.7	No
	Non-hospital	444	50.8	No
Courier Time: Greater than 90% of screens arrive in state laboratory less than or equal to 3 days after collection	Regular	95,629	96.5	Yes
	NICU/SCN	11,258	93.2	Yes
	Non-hospital	548	63.4	No
Unsatisfactory Screens: Less than 1% of screens are unsatisfactory	Regular	1,424	1.4	No
	NICU/SCN	367	3.0	No
	Non-hospital	53	6.1	No
Batching: Less than 2% of envelopes are batched	Regular	244	1.1	Yes
	NICU/SCN	36	0.5	Yes
	Non-hospital	2	0.2	Yes
NBS Card Number: Greater than 95% of electronic birth certificates have the NBS card number recorded	Regular	99,161	96.0	Yes
	NICU/SCN*	NA		
	Non-hospital	418	28.9	No
Returned BioTrust for Health Consent Forms Completed Appropriately: At least 90% of specimens have a returned consent form that is completed appropriately	Regular	85,183	85.6	No
	NICU/SCN	7,496	61.8	No
	Non-hospital	647	74.0	No

*Recording of NBS card number is not a performance measure for NICUs since the birth hospital is asked to draw the NBS specimen before transferring the infant to the NICU. Infants transferred to NICUs (as recorded on the birth certificate) are not included in the performance measure for regular nurseries.

SCREENING TURN-AROUND TIME

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

TIME TO TREATMENT

Table 16 reports the time to treatment for disorders other than hemoglobinopathies and cystic fibrosis. Penicillin prophylaxis, the treatment for hemoglobinopathies, is initiated later than treatment for other disorders and is reported in a separate table (Table 17). As indicated in Table 16, time to treatment ranged from 1 to 113 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 five cases of classic galactosemia had treatment started within seven days of life.

BIOTINIDASE DEFICIENCY

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

MS/MS DISORDERS

Seven of the eight diet-treated PKU cases were treated in the first week of life. The remaining case had treatment initiated at 18 days of life. One case of MSUD was treated in the first week. Of the two TYR I cases identified, one was treated in the first seven days and the other on the tenth day of life.

For organic acid disorders, seven of the eight cases with known start dates had treatment initiated in the first week of life. The remaining MMA case had treatment initiated on the eighth day of life.

Of the 16 infants with fatty acid oxidation disorders, all were treated within the first week of life.

Table 16: Time to Treatment of Amino Acid Disorders, Organic Acid, Fatty Acid Oxidation, and Endocrine Disorders, Michigan, 2014

Disorder		Total	Treatment Time (days from birth)			Treatment Time Range (days)
			N			
		N	1-7	8-14	>14	
Galactosemia	Classic (GG)	5	5			2-5
	Duarte (DG)	2		2		9-11
Biotinidase Deficiency	Partial	21	4	9	8	3-41
	Profound	2	2			5-6
Amino Acid Disorders	PKU-Diet treated	8	7	1		4-8
	MSUD	1	1			6
	TYR I	2	1	1		4-10
	<i>Total</i>	<i>11</i>	<i>9</i>	<i>2</i>		<i>4-10</i>
Organic Acid Disorders	3MCC	1	1			3
	GAI	1	1			5
	MMA ¹	4	2	1		3-8
	IBG	3	3			3-6
	<i>Total</i>	<i>9</i>	<i>7</i>	<i>1</i>		
Fatty Acid Oxidation Disorders	SCAD	5	5			3-5
	MCAD	9	9			3-5
	VLCAD	1	1			4
	CPT II	1	1			5
	<i>Total</i>	<i>16</i>	<i>16</i>			<i>3-5</i>
Endocrine Disorders	CH					
	Borderline	32	2	3	27	4-113
	Strong	52	27	13	12	4-49
	CAH					
	Salt-wasting	11	10	1		1-8
Non salt-wasting	0					
<i>Total</i>		<i>161</i>	<i>81</i>	<i>30</i>	<i>47</i>	<i>1-113</i>

Notes: Disorders that do not require treatment are excluded from the table.

¹Missing treatment start date on one infant.

ENDOCRINE DISORDERS-CAH AND CH

The salt-wasting form of CAH is life-threatening in the first few weeks of life. Ten of the eleven salt-wasting cases of CAH were treated within the first week of life. The remaining case of salt-wasting CAH had treatment started on the eighth day 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 52 CH cases with a strong positive screen, 40 (77%) were treated by the 14th day of life.

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 46 cases having a penicillin start date reported, 93% were treated with penicillin within the first four months, 4% began treatment between four and five months of life, 0% began treatment between five and six months, and 2% began treatment beyond six months of age.

Table 17: Time to Penicillin Initiation for Sickle Cell Disorders, Michigan, 2014

Disorder	Penicillin Prophylaxis Initiation Time			
	< 120 days	120-149 days	150-179 days	≥ 180 days
Sickle Cell Disorders*	43 (93.5%)	2 (4.3%)	0 (0%)	1 (2.2%)

*6 cases missing penicillin initiation date.

VI. Conclusions

NBS is a critical public health program protecting the lives of our State's newest residents. The NBS Laboratory screened 112,513 infants born in 2014, and the NBS Follow-up Program tracked approximately 5,800 strong and borderline positive, isolated elevation, unsatisfactory, early, and transfused specimens; newborns with strong positive screening results were immediately referred to the appropriate medical management coordinating center for evaluation. A total of 259 newborns were identified with a disorder by NBS in 2014, as well as 2,961 carriers. Since NBS began in Michigan in 1965, 5,711 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.