Michigan Department of
Community Health

MICHIGAN NEWBORN SCREENING PROGRAM

Annual Report 2012

Michigan Department of Community Health

MDCH

Rick Snyder, Governor
James K. Haveman, Director

Public Health
FOR MICHIGAN
FOR YOU

Acknowledgements

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Governor **Rick Snyder**

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Director **James K. Haveman**

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Deputy Director **Melanie Brim**

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Director **Corinne Miller**, **PhD, DDS**

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Director **Sandip Shah, PhD**

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Authors

Mary Kleyn, MSc
Newborn Screening Epidemiologist, Maternal and Child Health Epidemiology Unit, Division of Lifecourse Epidemiology and Genomics

William Young, PhD
Manager, Newborn Screening Follow-up Program, Division of Lifecourse Epidemiology and Genomics

Karen Andruszewski, BS
Quality Assurance Coordinator, Newborn Screening Follow-up Program, Division of Lifecourse Epidemiology and Genomics

Harry Hawkins, BS
Manager, Newborn Screening Laboratory, Chemistry and Toxicology Division, Bureau of Laboratories

Table of Contents

Executive Summary

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

Since the program began in 1965 with screening for phenylketonuria, over 50 disorders have been added to the screening panel. Through 2012, over 6.6 million infants have been screened with over 5,100 diagnosed with diseases included in the NBS panel.

Of the 111,509 infants screened in 2012, the vast majority were Michigan residents and 274 (0.2%) were diagnosed with a disease. Overall, one infant out of 407 screened was diagnosed with one of the disorders included in the NBS panel (see Table 1 for list of disorders).

Developments occurring in 2012:

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:
  - ◊ National Conference on Blood Disorders in Public Health (Atlanta, GA)
  - ◊ Michigan Epidemiology Conference (East Lansing, MI)
- "Michigan BioTrust for Health: Public Support for Using Residual Dried Blood Spot Samples for Health Research" was published in *Public Health Genomics* 2012;15:146-55.
- "Screening for Congenital Hypothyroidism in Newborns Transferred to Neonatal Intensive Care" was published in *Archives of Disease in Childhood. Fetal and Neonatal Edition* 2013;98:F310-5.
- "Performance Metrics after Changes in Screening Protocol for Congenital Hypothyroidism" was published in *Pediatrics* 2012;130:e1252-60.

MDCH continued to provide educational outreach and training:

- The NBS Follow-up Program held four regional trainings for birthing hospital staff and attendants across the state. The trainings included presentations on NBS laboratory processes, pulse oximetry screening for critical congenital heart defects, and the diagnosis and treatment of severe combined immunodeficiency.
- NBS Follow-up Program staff successfully applied for a Baby's First Test Challenge Award aimed at "Improving Newborn Screening Rates within the Michigan Homebirth Community."

New capacity was added for NBS:

- The Health Resources and Services Administration awarded Michigan a grant to develop pulse oximetry screening for critical congenital heart disease (CCHD). The goals of the grant are to:
    - Increase the number of Michigan newborns screened for CCHD using a validated screening protocol prior to hospital discharge
    - Develop state infrastructure for collection of CCHD screening data through electronic health information exchange to enable effective public health follow -up, quality assurance and evaluation
- Hemoglobin H disease was added to the NBS panel.

The MDCH NBS Laboratory activities include:

- Continued work on the Severe Combined Immunodeficiency Disorder (SCID) grant, including:
    - A validation of a new and improved version of the SCID assay that was implemented on September 1, 2012. Laboratory staff continued to fine tune the cutoffs for SCID in 2012.
    - Training Ohio laboratory personnel on the Michigan SCID method as they prepared to add SCID to their test panel.
    - Offering support to other labs by sharing the plasmid calibrator and Michigan's method.

MDCH received other grant work related to NBS:

- The Centers for Disease Control and Prevention awarded MDCH, in collaboration with several Michigan hospitals, a grant for the "Michigan Transfusion Exposure & Risk Monitoring System". The project aims to establish better monitoring and identification of gaps in services for hemoglobinopathy patients receiving transfusions.

Educational outreach about the BioTrust for Health continued:

- MDCH staff presented information on the BioTrust for Health at 9 community events and 21 events for health professionals and had 18 social media posts.

Listing of Figures & Tables

Figures

Tables

Acronym Key

Acronym	Name
ACMG	American College of Medical Genetics
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
MDCH	Michigan Department of Community Health
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]

In sum, 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.

[1]All of these appendices can be found in previous annual reports, which are available at www.michigan.gov/newbornscreening.
[2]For more information on the history of PKU and PKU-related NBS Program evaluations conducted in Michigan, see Chapter IV of the 2009 NBS Annual Report.

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

In 2005, a pilot project was initiated to expand the screening panel to 48 disorders by including the 29 additional MS/MS disorders recommended by the American College of Medical Genetics (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.

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. Screening for all of these un-detected disorders, except for Citrullinemia Type II and Tyrosinemia Type II and III, began in 2005, so approximately 950,000 infants have been screened for the disorders through 2012, and no cases have been detected. Screening for Citrullinemia Type II began in 2004, meaning nearly 1.1 million infants have been screened, and no cases have been identified. 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 "Information for Hospitals and Health Professionals" link on the NBS website (www.michigan.gov/newbornscreening).

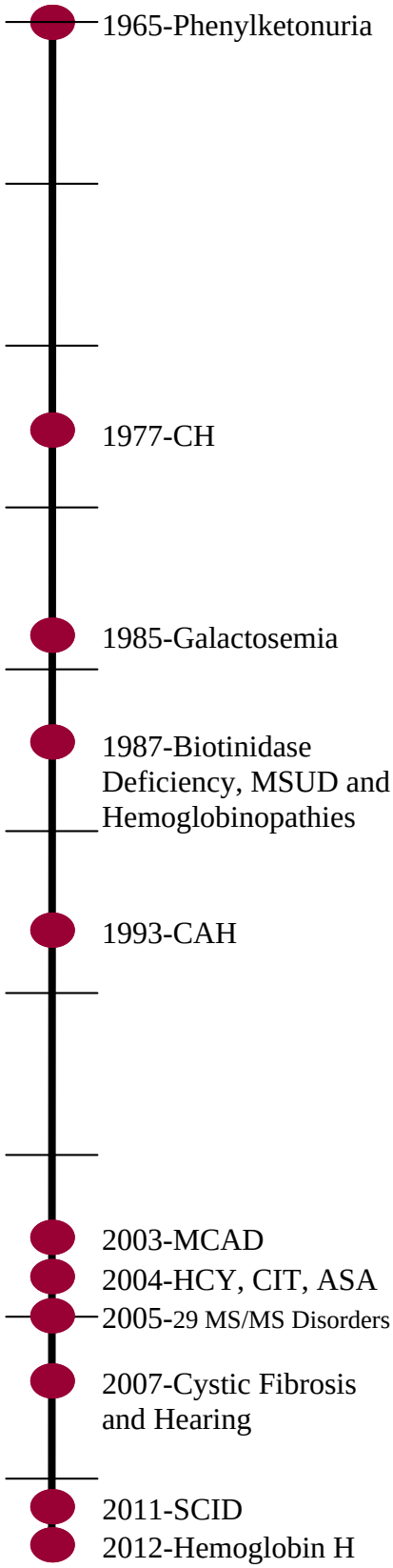

Figure 1. Addition of Disorders to the NBS Panel, Michigan, 1965-2012

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

Table 1. Disorders included in the Newborn Screening Panel, Michigan, 2012

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.

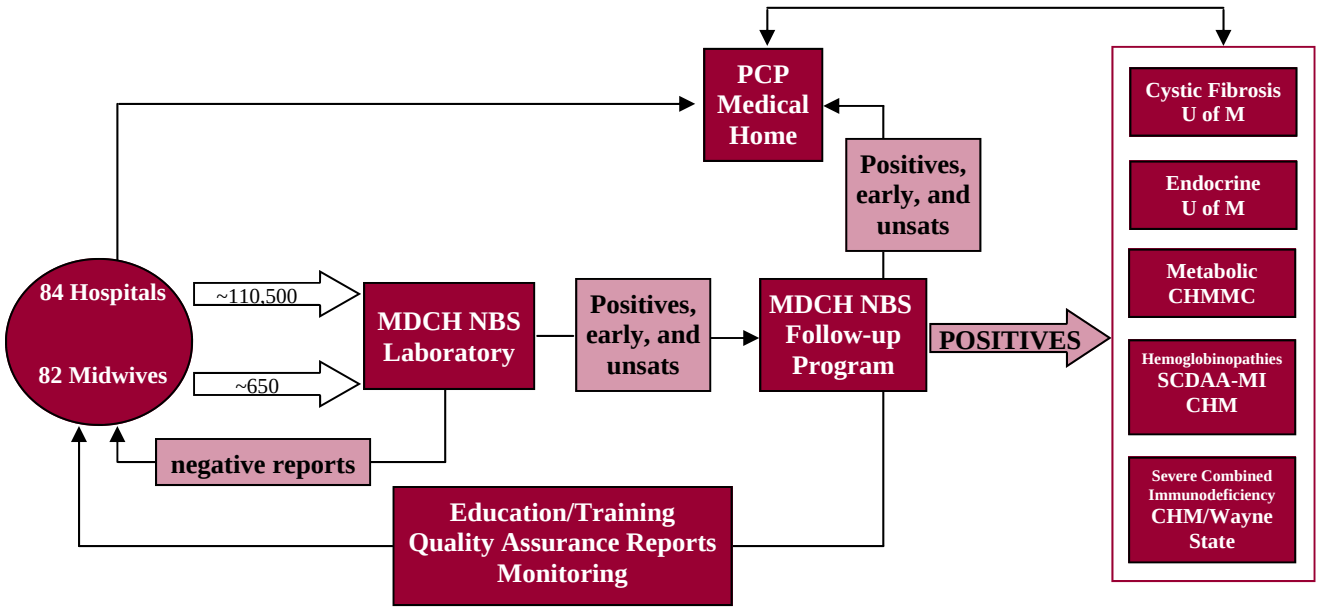

Figure 2. Overview of the Michigan Newborn Screening Program, 2012

Abbreviations: MDCH-Michigan Department of Community Health; NBS-Newborn Screening; PCP-Primary Care Provider; U of M-University of Michigan; CHMMC-Children's Hospital of Michigan Metabolic Clinic; SCDAA-MI-Sickle Cell Disease Association of America-Michigan Chapter; CHM-Children's Hospital of Michigan

HOSPITALS

In 2012, 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 Follow-up Program Coordinator or Nurse Consultant to evaluate the screening process and make recommendations for improvement.

MIDWIVES AND HOME BIRTH ATTENDANTS

There are 82 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 COMMUNITY HEALTH

The MDCH NBS Program includes the NBS Laboratory, the Follow-up Program, and five medical management 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 MDCH to determine the total number of live births statewide eligible for screening. The number of live births in 2012 (n=112,199) is a preliminary estimate as the final files have not been released yet.

TOTAL NUMBER OF NEWBORNS DIAGNOSED BY NEWBORN SCREENING

We used the MDCH laboratory information system (PerkinElmer Life Sciences, Inc.) to identify positive cases. We also used data collected at the medical management 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 medical management centers. QA indicators included 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, f) number of screened births with BioTrust consent form returned, and g) number of non-blank BioTrust consent forms returned out of all returned forms. 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 newborns born in 2012 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 2012, as determined by the linkage of NBS records to preliminary live births records received from the Vital Records & Health Data Development Section and follow-up of unmatched records (Figure 3). Of the 112,199 live births that occurred in 2012, 426 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 111,773 remaining live births, the linkage algorithm successfully matched newborn screens for 110,703 infants (99.0%). The 1,070 unmatched records were sent to NBS Follow-up Program technicians for further investigation. This more in-depth follow-up revealed that 548 (51.2%) 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, 522 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=163), transfer out of state (n=17), infant expired (n=13), or missed screened (n=329). For all infants who were missed, the NBS Follow-up technicians either contact the nurse coordinator for hospital births or send a parental notification letter for home births. In 2012, 40 infants born in hospitals are known to have been missed by NBS, and hospitals were contacted. Of the 40, 14 have been screened to date and the remaining 26 are pending.

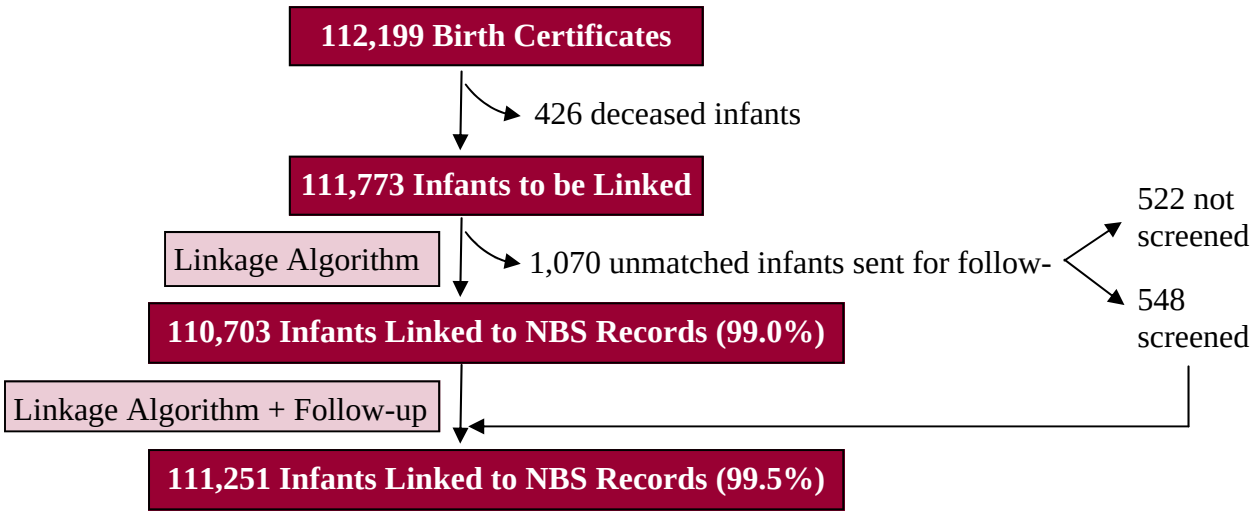

Figure 3. Newborn Screening and Live Births Records Linkage, Michigan, 2012

In total, newborn screening samples were received from 111,509 infants born in 2012. Of those, 325 (0.3% 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 2012. 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 10% 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, 2012, Excluding Out-of-State Residents, N=111,184

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	71,107	64.0	63,526	89.3	6,849	9.6	732	1.0	4,582	6.6	5,886	8.5
Black	20,045	18.0	16,438	82.0	3,592	17.9	15	0.1	2,682	13.6	2,629	13.7
American Indian	442	0.4	397	89.8	43	9.7	2	0.5	26	6.0	41	9.7
Asian/Pac Islander	2,495	2.2	2,280	91.4	210	8.4	5	0.2	215	8.7	208	8.6
Middle Eastern	3,362	3.0	3,092	92.0	267	7.9	3	0.1	257	7.7	251	7.7
Multi-Racial	5,601	5.0	4,936	88.1	626	11.2	39	0.7	484	8.7	562	10.3
Missing	8,132	7.3	7,332	90.2	767	9.4	33	0.4	621	7.9	703	10.3
Column Total:	111,184	100	98,001	88.1	12,354	11.1	829	0.8	8,867	8.1	10,280	9.6

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 1,901 and 3,874 newborns were missing birth weight and gestational age on the card, respectively. Non-hospital nurseries include 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 2012. The total numbers of cases detected both in and through 2012 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 programs responsible for diagnosis and treatment.

CUMULATIVE DETECTION RATE

Table 4 reports the cumulative detection rate of disorders identified via NBS by classification both in and through 2012. 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, 1965-2012

Type of Disorder Classification (Year Screening Began)	Cases in 2012 (N)	Cases Through 2012 (N)	Cumulative Detection Rate
Galactosemia (1985)	2	172	1:21,541
Biotinidase Deficiencies (1987)	17	224	1:15,310
Amino Acid Disorders (1965)	19	686	1:9,714
Organic Acid Disorders (2005)	5	54	1:17,591
Fatty Acid Oxidation Disorders (2003)	33	172	1:7,038
Congenital Hypothyroidism (1977)	78	1,876	1:1,828
Congenital Adrenal Hyperplasia (1993)	8	132	1:19,354
Sickle Cell Disease (1987)	51	1,677	1:2,045
Hemoglobin H Disease (2012)	3	3	1:37,061
Cystic Fibrosis (October 2007)	33	160	1:3,76
Primary Immunodeficiencies (October 2011)	25	25	1:8,934
Total	274	5,181	-

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 2012, while Hemoglobin H Disease and galactosemia were the least prevalent. CF accounted for 12% of cases detected in 2012 and 3% of cases detected cumulatively. The cumulative percentage of CF cases is low compared to the 2012 percentage because screening began recently (October 2007) relative to the other disorders. Similarly, primary immunodeficiencies (PID) accounted for 9% of cases and 0.5% 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 21% of cases in 2012 and 18% cumulatively. However, PKU, the first disorder screened in Michigan, is now screened by MS/MS, meaning the overall proportion of cases detected by MS/MS is an overestimate because it includes cases detected prior to 2003 when MS/MS screening was initiated. The cumulative detection rate for fatty acid oxidation disorders is an underestimate because MCAD screening began in 2003, while other conditions were not screened until 2005. This means that births included in the denominator from 2003-2005 were not eligible for being diagnosed with fatty acid oxidation disorders other than MCAD leading to an artificially low cumulative detection rate. The MS/MS detection rate does not include cases of formiminoglutamic acid disorder (FIGLU) detected because the disorder is not included in the NBS panel. Galactosemia, including Duarte compound heterozygotes, accounted for 1% of all disorders detected in 2012 and 3% cumulatively. Biotinidase deficiency, including partial biotinidase deficiency, accounted for 6% of all cases detected in 2012 and 4% of all cases detected cumulatively. CAH accounted for 3% all of cases in 2012 and 3% of all cases detected cumulatively.

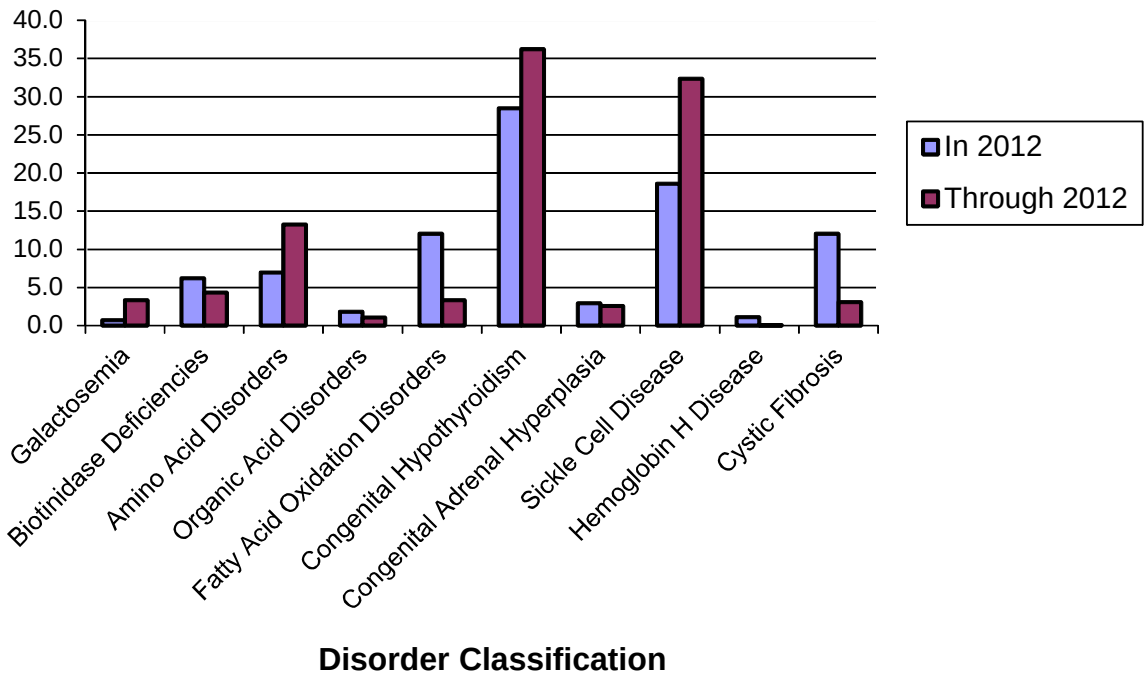

Figure 4. Percent Distribution of Disorders Identified in Newborns via Newborn Screening, Michigan Residents, in 2012 and through 2012

SCREENING PERFORMANCE METRICS

Screening performance metric targets are available in previous reports. Screening performance metrics include the detection rate, false positive rate, and positive predictive value. Table 5 reports screening performance metrics for all disorders in 2012. 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 no cases of classic galactosemia were detected in 2012, resulting in a FPR of 0.003%.

The biotinidase deficiency detection rate (including partial biotinidase deficiency) was 1:6,540; the FPR and PPV were 0.03% and 33.3%, respectively. Of the 17 cases detected, 13 were partial and 4 were profound. The number of positive biotinidase screens decreased from 167 in 2011 to 51 in 2012 and confirmed cases increased from 11 to 17. These changes are most likely due to the switch in August 2011 from a qualitative colorimetric assay to a quantitative fluorometric assay.

Thirty-three cases of cystic fibrosis (CF) were detected in 2012 (detection rate-1:3,369); the associated FPR and PPV were 0.3% and 10.2%, respectively. Additionally, five cases of CFTR-related metabolic syndrome were also 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 0.6%, and the PPV was 10.2%. The overall detection rate for CH was 1:1,425. Chapter IV of the 2007 Annual Report provides more detailed information describing CH screening in Michigan.

The CAH screening FPR was 0.09%, and the PPV was 7.3%. The overall detection rate for CAH was 1:13,898. All eight cases detected were salt-wasting.

HEMOGLOBINOPATHIES

Hemoglobinopathies include sickle cell disease (SCD) and Hemoglobin H disease. The Hemoglobin H disease FPR was 0.02% and the PPV was 10.0%. The overall detection rate for Hemoglobin H disease was 1:37,061.

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 92% of the cases in 2012. While the overall incidence of SCD is approximately one case per 2,180 screened, the incidence in African Americans is one in 426 screened in Michigan.

Table 5: Screening Results and Performance Metrics, Michigan, 2012

Disorder Type	Total N	Total + N (% NICU)	Confirmed + N	Positive Detection Rate	FPR %	PPV %
Galactosemia	111,184	5 (0)			0.003	40.00
Classic (GG)			0	-		
Duarte (DG)			2	1:55,592		
Total			*2*	1:55,592		
Biotinidase Deficiency		51 (5.9)			0.03	33.33
Profound			4	1:27,796		
Partial			13	1:8,553		
Total			*17*	*1:6,540*		
Cystic Fibrosis		324 (13.3)	33	1:3,369	0.26	10.19
Congenital Hypothyroidism		768 (32.8)	78	1:1,425	0.62	10.16
Congenital Adrenal Hyperplasias		109 (86.2)			0.09	7.34
Salt wasting			8	1:13,898		
Non-Salt wasting			0	-		
Total			*8*	*1:13,898*		
Sickle Cell Disease		61 (19.7)	51	1:2,180	0.01	83.61
Hemoglobin H Disease		30 (36.7)	3	1:37,061	0.02	10.00
Primary Immunodeficiencies		337 (61.7)			0.28	7.42
SCID			3	1:37,061		
Syndromes with T-cell Impairment			14	1:7,942		
Non-preterm Secondary T-cell Lymphopenias			8	1:13,898		
Total			*25*	*1:4,447*		
Amino Acid		56 (12.5)	19	1:5,852	0.03	33.93
Organic Acid		38 (15.8)	5	1:22,237	0.03	13.16
Fatty Acid Oxidation		98 (27.6)	33	1:3,369	0.06	33.67
*MS/MS Disorders Total***		*172 (19.2)*	*57*	*1:1,951*	*0.10*	*33.14*

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 20 infants with elevated levels are included in the 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, 25 cases of primary immunodeficiencies (PID) were identified, resulting in FPR of 0.3% and PPV of 7.4%. Of the 25 cases, three were considered SCID (two Leaky SCID/Omenn; one variant SCID), fourteen had syndromes with t-cell impairment, and eight 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 33%, and the detection rate was 1:1,951.

SCREENING PERFORMANCE METRICS-INDIVIDUAL MS/MS DISORDERS

AMINO ACID DISORDERS

Nineteen newborns were identified with amino acid disorders (Table 7) by MS/MS. Phenylketonuria (PKU) was the most frequent amino acid disorder identified, found in one of every 8,553 newborns screened. As indicated in the table, PKU screening had the highest PPV (65%) among amino acid disorders. Chapter IV of the 2009 Annual Report provides more detailed information about PKU screening in Michigan. One case of citrullinemia type I, one case of argininosuccinic acidemia, two cases of hypermethioninemia, and two cases of homocystinuria were also detected in 2012. Two of the diet-treated PKU cases are still pending and were considered mild PKU.

ORGANIC ACID DISORDERS

Five newborns were identified with organic acid disorders (Table 8) by MS/MS. Two infants were diagnosed with 2-Methylbutyryl-CoA dehydrogenase deficiency (2MBG); one was diagnosed with isovaleric acidemia (IVA); one was diagnosed with Glutaric acidemia type I; and one was diagnosed with isobutyryl-CoA dehydrogenase deficiency. The disorders 2MBG and IVA are screened using the same analyte, and their pooled PPV is 75%, the highest of the organic acid disorders. Of note, in 2012, one known and one probable maternal case of 3-methylcrotonyl-CoA carboxylase deficiency (3MCC) were found following their infant's positive screens. A 3MCC carrier was also identified following a positive screen.

FATTY ACID OXIDATION DISORDERS

Thirty-three children were identified with fatty acid oxidation disorders (Table 9); ten medium-chain acyl-CoA dehydrogenase deficiency (MCAD), seventeen short-chain acyl-CoA dehydrogenase deficiency (SCAD), three very long-chain acyl-CoA dehydrogenase deficiency, one carnitine uptake defect, one long-chain L-3-hydroxy acyl-CoA dehydrogenase deficiency, and one carnitine palmitoyltransferase I deficiency. Of the disorders detected, MCAD and SCAD had the highest PPV (91% and 85%, respectively). One MCAD carrier was detected following a positive screen.

Table 6: Hemoglobinopathy Screening Performance Metrics, Michigan, 2012

Disorder	Newborns (N)	Confirmed + (N)		Positive Detection Rate	
		Total	Among Blacks	Total	Among Blacks
Sickle Cell Anemia	111,184	31	28	1:3,587	1:716
SC Disease		18	17	1:6,177	1:1,179
Sickle β thalassemia		1	1	1:111,184	1:20,045
SE Disease		1	1	1:111,184	1:20,045
Total		*51*	*47*	*1:2,180*	*1:426*

Notes: Out of the number of Michigan resident infants screened, total N=111,184, among Blacks N=20,045

Table 7: Amino Acid Disorders Detected by Tandem Mass Spectrometry, Screening Performance Metrics, Michigan, 2012

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Phenylketonuria	111,184	20			0.006	65.0
Classic (PKU)			3	1:37,061		
Mild			3	1:37,061		
Benign Hyperphenyl-alaninemia (H-PHE)			7	1:15,883		
Biopterin Cofactor Defects (BIOPT)			0	-		
Total			*13*	*1:8,553*		
Argininemia (ARG)		4	0	-	0.004	-
Citrullinemia (CIT)/CIT II/ASA		6	2	1:55,592	0.004	33.3
Tyrosinemia I (TYR I)		1	0	-	0.001	-
Tyrosinemia II-III (TYR II-III)		14	0	-	0.013	-
Homocystinuria (HCY)/ Hypermethioninemia (MET)		11	4	1:27,796	0.006	36.4

Notes: Two cases of diet-treated PKU are still pending classification and were considered mild PKU in this table.

Table 8: Organic Acid Disorders Detected by Tandem Mass Spectrometry, Screening Performance Metrics, Michigan, 2012

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Isovaleric Acidemia (IVA)/2-Methylbutyryl-CoA Dehydrogenase Deficiency (2MBG)	111,184	4	3	1:37,061	0.001	75.0
3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC)		7	0	-	0.006	-
Glutaric Acidemia Type I (GA I)		3	1	1:111,184	0.002	33.3
Propionic Acidemia (PA)/ Methylmalonic Acidemia (MMA)		4	0	-	0.004	-
Isobutyryl-CoA Dehydrogenase Deficiency (IBG)		20	1	1:111,184	0.017	5.0

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). 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, 2012

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Carnitine Uptake Defect (CUD)	111,184	49	1	1:111,184	0.043	2.0
Short-Chain Acyl-CoA Dehydrogenase deficiency (SCAD)		20	17	1:6,540	0.003	85.0
Carnitine/Acylcarnitine Translocase Deficiency-(CACT)/Carnitine Palmitoyltransferase II Deficiency (CPT II)		2	0	-	0.002	-
Glutaric Acidemia Type II (GA II)		2	0	-	0.002	-
Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD)		11	10	1:11,118	0.001	90.9
Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)		4	3	1:37,061	0.001	75.0
Long-chain L-3-hydroxy Acyl-CoA Dehydrogenase Deficiency (LCHAD)		2	1	1:111,184	0.001	50.0
Carnitine Palmitoyltransferase I Deficiency (CPT I)		5	1	1:111,184	0.004	20.0
Medium/Short-chain L-3-hydroxy Acyl-CoA Dehydrogenase Deficiency (M/SCHAD)		2	0	-	0.002	-
Dienoyl-CoA reductase deficiency (DERED)		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 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. Disorders not detected in 2012 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, 2012

Disorder Type	Among All +		Among Strong +	
	FPR	PPV	FPR	PPV
	%	%	%	%
Biotinidase Deficiency	0.03	33.33	0.002	81.82
Congenital Hypothyroidism (CH)	0.62	10.16	0.122	23.60
Congenital Adrenal Hyperplasia (CAH)	0.09	7.34	0.027	18.92
Phenylketonuria (PKU)	0.006	65.00	0.001	90.91
Homocystinuria (HCY)/ Hypermethio-ninemia (MET)	0.006	36.36	0.004	44.44
Very Long-Chain Acyl-CoA Dehydro-genase Deficiency (VLCAD)	0.001	75.00	0.0	100.0
Isovaleric Acidemia (IVA)/2-Methylbutyryl-CoA Dehydrogenase De-ficiency (2MBG)	0.001	75.00	0.0	100.0
Cystic Fibrosis (CF)	0.26	10.19	0.001	95.00
Primary Immunodeficiency	0.28	7.41	0.134	13.37

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 biotinidase is reduced 17-fold, and the PPV is increased approximately 2.5-fold among strong positive screens relative to all positive screens.

The FPR for CH is reduced nearly 5-fold for strong positive screens, and the PPV is increased approximately 2-fold. The FPR and PPV for CAH are each decreased and increased by 3-fold

among strong positives.

Among MS/MS disorders, all three strong positives for VLCAD and the one strong positive for IVA were confirmed with disease, meaning the PPV among strong positives was 100% and the FPR was 0%.

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 291-fold and the PPV increased from 10% to 95% when excluding children with a heterozygote DNA mutation.

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

In sum, 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 AND MATERNAL 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 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 2012, a total of 2,900 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=2,622) had sickle cell trait. Over 270 infants (n=272) were cystic fibrosis carriers, four were identified as sickle cell trait with Barts, one was identified as a MCAD carrier and one was identified as a 3MCC carrier.

Table 11: Carriers Identified from Newborn Screening, Michigan, 2012

Disorder	N
3-Methylcrotonyl-CoA carboxylase deficiency (3MCC)	1
Cystic fibrosis	272
Medium-chain acyl-CoA dehydrogenase deficiency (MCAD)	1
Sickle Cell Trait	2,622
Sickle Cell Trait with Barts	4

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.

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 2012, two maternal disorders were identified following an infant's positive NBS (Table 12). Two infants with a strong positive screen for 3MCC were confirmed normal, but the disorder was identified in the mothers. One mother had been previously diagnosed in 2008 following the birth of an infant.

Table 12: Maternal Disorders Identified from Newborn Screening, Michigan, 2012

Maternal Disorder	N
3-Methylcrotonyl-CoA carboxylase deficiency (3MCC)	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.

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, 58% and 33% 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 (7%). Early and transfused specimens were more common among infants from the NICU, while late specimens, those collected after six days of life, were most common among non-hospital deliveries. The NBS Follow-up Program tracks all strong and borderline positive, isolated elevation, unsatisfactory, early, and transfused specimens; approximately 5,300 specimens required follow-up in 2012.

Table 13: Specimen Characteristics by Nursery Type, Michigan, 2012

Indicator	Type of Birth					
	Regular Nursery		NICU/SCN		Non-Hospital	
	N	%	N	%	N	%
Strong Positive Specimens	196	0.20	274	2.22	4	0.48
Borderline Positive Specimens	642	0.66	318	2.57	7	0.84
All Positive Specimens*	1,183	1.21	658	5.33	15	1.81
Isolated elevations of amino acids and acyl-carnitines	9	0.01	369	2.99	1	0.12
Unsatisfactory Specimens	2,357	2.41	565	4.57	57	6.88
Late (>6 days) Specimens	58	0.06	30	0.24	63	7.61
Early (<1 day) Specimens	266	0.27	786	6.37	5	0.60
Transfused Specimens	7	0.00	114	1.05	1	0.13
Specimens Missing Demographics **	1,696	1.73	222	1.80	35	4.22
Total Births Screened	98,001	88.1	12,354	11.1	829	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 2012, the quarterly reports included seven indicators. Table 14 lists the indicators and the performance goal for each indicator.

Table 14: Indicators and Performance Goals for Newborn Screening, Michigan, 2012

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 4 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 95% of specimens have a returned BioTrust for Health consent form
Non-blank BioTrust for Health Consent Forms	At least 90% of returned BioTrust for Health consent forms are not blank

*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, none of the three nursery types met the goal, but regular nurseries were closest to meeting the goal with approximately 2.2% of screens being collected more than 36 hours after birth. Of note, nearly 56% 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 97% of specimens received in the state laboratory within four days of collection. Non-hospital births did not meet the goal. None of the nursery types met the goal for unsatisfactory specimens for 2012, 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. Additionally, birth certificates coming from regular nurseries were approximately 9 times more likely to have the NBS kit number recorded than certificates coming from non-hospital births. Although none of the nursery types met either BioTrust for Health measure, regular nurseries were the closest; 93% of regular nursery births had a BioTrust for Health consent form returned and 86% of those returned forms had parental response recorded.

Table 15: Measures for Newborn Screening, by Nursery Type, Michigan, 2012

Measure	Nursery Type	N	%	Met Goal?
Late Screens (<2%)	Regular	2,109	2.2	No
	NICU/SCN	541	4.4	No
	Non-hospital	460	55.6	No
Courier Time (>90%)	Regular	96,429	98.7	Yes
	NICU/SCN	11,954	97.2	Yes
	Non-hospital	587	71.6	No
Unsatisfactory Screens (<1%)	Regular	2,357	2.4	No
	NICU/SCN	565	4.6	No
	Non-hospital	57	6.9	No
Batching (<2%)	Regular	349	1.6	Yes
	NICU/SCN	73	1.1	Yes
	Non-hospital	2	0.3	Yes
NBS Card Number (>95%)	Regular	97,238	95.6	Yes
	NICU/SCN*	NA		
	Non-hospital	114	9.1	No
Returned BioTrust for Health Consent Forms (>95%)	Regular	91,048	92.9	No
	NICU/SCN	10,017	81.1	No
	Non-hospital	742	89.5	No
Non-blank BioTrust for Health Consent Forms (>90%)	Regular	78,389	86.1	No
	NICU/SCN	7,467	74.5	No
	Non-hospital	503	67.8	No

*Recording of NBS card number is not a performance measure for NICUs since the birth hospital is asked to draw the NBS card 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

target for other disorders varies.

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 0 to 378 days of life among all disorders. Limiting factors in the screening and diagnostic process for some disorders such as partial biotinidase deficiency and CH affect the ability to meet treatment targets. These 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

One Duarte galactosemia case had treatment initiated on the fourth day of life and one was missing the treatment start date.

BIOTINIDASE DEFICIENCY

Three of the four profound biotinidase deficiency cases were treated in the first week of life. Of the partial biotinidase cases, six had treatment initiated in the first week of life and six had treatment initiated in the second week. Another case had treatment initiated on day 378 following re-classification after a quality improvement study.

MS/MS DISORDERS

The majority of PKU cases were hyperphenylalaninemia which does not require treatment. All six diet-treated PKU cases were treated in the first week of life. One cases of CIT was treated in the first week of life, while the ASA case had treatment initiated on the 28th day. The two HCY cases had treatment initiated in the first week of life.

Both the GAI and IBG cases identified had treatment initiated on the fourth day of life. Both cases of 2MBG had treatment initiated within two weeks of birth. The IVA case had treatment initiated on day 41.

Of the 30 infants with fatty acid oxidation disorders and a treatment start date, 27 were treated within the first week of life. The remaining CUD case was treated on day 9 and two VLCAD cases began treatment on day 16. One SCAD case was missing the date treatment began. One LCHAD case expired before treatment began.

Table 16: Time to Treatment of Amino Acid Disorders, Organic Acid, Fatty Acid Oxidation, and Endocrine Disorders, Michigan, 2012

Disorder		Total	Treatment Time (days from birth) N			Treatment Time Range (days)
		N	1-7	8-14	>14	
Galactosemia	Classic (GG)	0				
	Duarte (DG)[1]	2	1			4
Biotinidase Deficiency	Partial	13	6	6	1	3-378
	Profound	4	3		1	4-27
Amino Acid Disorders	PKU					
	Classic	3	3			5-6
	Mild	3	3			5
	CIT/ASA	2	1		1	6-28
	HCY	2	2			4-5
	Total	*10*	*9*		*1*	*4-28*
Organic Acid Disorders	IVA/2MBG	3	1	1	1	5-41
	GAI	1	1			4
	IBG	1	1			4
	Total	*5*	*3*	*1*	*1*	*4-41*
Fatty Acid Oxidation Disorders	SCAD[2]	16	15			3-6
	MCAD	10	10			0-5
	VLCAD	3	1		2	0-16
	LCHAD[3]	1				
	CUD	1		1		9
	CPTI	1	1			6
	Total	*32*	*27*	*1*	*2*	*0-16*
Endocrine Disorders	CH					
	Borderline	26	1	7	18	5-107
	Strong	52	30	11	11	3-107
	CAH					
	Salt-wasting	8	4	3	1	3-17
	Non salt-wasting	0				

Notes: Disorders that do not require treatment are excluded from the table.
[1]Missing treatment start date on 1 case.
[2]Missing treatment start date on 1 case.
[3]Baby expired.

ENDOCRINE DISORDERS-CAH AND CH

The salt-wasting form of CAH is life-threatening in the first few weeks of life. Seven of the eight salt-wasting cases of CAH were treated within the first two weeks of life. One case of salt-wasting CAH had treatment started on the 17th 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, 30 (79%) 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 43 cases having a penicillin start date reported, 88% were treated with penicillin within the first four months, 5% began treatment between four and five months of life, 0% began treatment between five and six months, and 7% began treatment beyond six months of age.

Table 17: Time to Penicillin Initiation for Sickle Cell Disorders, Michigan, 2012

Disorder	Penicillin Prophylaxis Initiation Time			
	< 120 days	**120-149 days**	**150-179 days**	**≥ 180 days**
Sickle Cell Disorders*	38 (88.4%)	2 (4.7%)	0 (0%)	3 (7.0%)

*3 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 111,509 infants born in 2012, and the NBS Follow-up Program tracked approximately 5,300 strong and borderline positive, isolated elevation, unsatisfactory, early, and transfused specimens; newborns with strong positive screening results were immediately referred to the appropriate medical management center for evaluation. A total of 274 newborns were identified with a disorder by NBS in 2012. Since NBS began in Michigan in 1965, 5,181 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.