Michigan Department of
Community Health

MICHIGAN NEWBORN SCREENING PROGRAM

Annual Report 2013

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Michigan Department of Community Health

MDCH

Rick Snyder, Governor
Nick Lyon, Director

Public Health

FOR MICHIGAN FOR YOU

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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 2013, nearly 6.8 million infants have been screened with over 5,400 diagnosed with diseases included in the NBS panel.

Of the 112,062 infants screened in 2013, the vast majority were Michigan residents and 271 (0.2%) were diagnosed with a disease. Overall, one infant out of 412 screened was diagnosed with one of the disorders included in the NBS panel (see Table 1 for list of disorders).

Developments occurring in 2013:

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:

    ◊ Newborn Screening and Genetic Testing Symposium (Atlanta, GA)
    ◊ North American Cystic Fibrosis Conference (Salt Lake City, UT)
    ◊ National Birth Defects Prevention Network Annual Meeting (Atlanta, GA)
    ◊ Healthy Mothers, Healthy Babies Conference (Bay City, MI)

- "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.

- "Transient Hypothyroidism at 3-Year Follow-Up among Cases of Congenital Hypothyroidism Detected by Newborn Screening" was published in *Journal of Pediatrics* 2013;162:177-82.

- "Evaluation of Genetic Counseling among Cystic Fibrosis Carriers, Michigan Newborn Screening" was published in *Pediatric Pulmonology* 2013;48:123-9.

- "From Newborn Screening to Population Health Research: Implementation of the Michigan BioTrust for Health" was published in *Public Health Reports* 2013;128:377-84.

- The NBS Nurse Educator presented at five regional Children's Special Health Care Services trainings.

The Michigan Department of Community Health (MDCH) continued to provide educational outreach and training:

- NBS Follow-up Program staff worked on a project, "Improving Newborn Screening Rates within the Michigan Homebirth Community," funded by a Baby's First Test Challenge Award.

New capacity was added for NBS:

- The NBS Program continued work on developing pulse oximetry screening for critical congenital heart disease (CCHD), funded by the Health Resources and Services Administration.

- The Quality Assurance Advisory Committee voted to add CCHD to the screening panel, with mandated reporting beginning April 1, 2014. The committee also voted to add Pompe Disease to the panel. Screening is not currently scheduled to begin before October, 2016.

Outreach and evaluation of the BioTrust for Health consent process continued:

- The 2013 BioTrust Annual Report was released and is available on the website (www.michigan.gov/biotrust).

- A revised BioTrust parental consent form began circulation in 2013 following a study to assess whether the on-going BioTrust consent process was logistically feasible with minimal burden on hospital staff and to identify areas for improvement. Hospital NBS Coordinators were sent an email invitation to participate in an on-line survey and were asked to distribute to relevant staff. Surveys were completed by 146 staff from 32 birthing hospitals. A majority of respondents indicated the process could be improved by revision to the BioTrust consent form, specifically adding a clear check box for both the parent decline and consent decision with a parent signature collected on all forms. This study demonstrated continued surveillance and collaboration with birthing hospital staff is necessary to maintain high performance standards in administering the BioTrust consent process.

Listing of Figures & Tables

Figures

Tables

Acronym Key

Acronym	Name
ACMG	American College of Medical Genetics and Genomics
CCHD	Critical Congenital Heart Disease
CDC	Centers for Disease Control and Prevention
CHM	Children's Hospital of Michigan
CHMMC	Children's Hospital of Michigan Metabolic Clinic
EBC	Electronic Birth Certificate
FIGLU	Formiminoglutamic acid disorder
FPR	False Positive Rate
HPLC	High Performance Liquid Chromatography
HRSA	Health Resources and Services Administration
MCIR	Michigan Care Improvement Registry
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]

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.

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[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 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.

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 nearly 1.1 million infants have been screened for the disorders through 2013, and no cases have been detected. Screening for Citrullinemia Type II began in 2004, meaning approximately 1.2 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).

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[1]More information about the newborn hearing screening program can be found at www.michigan.gov/ehdi.
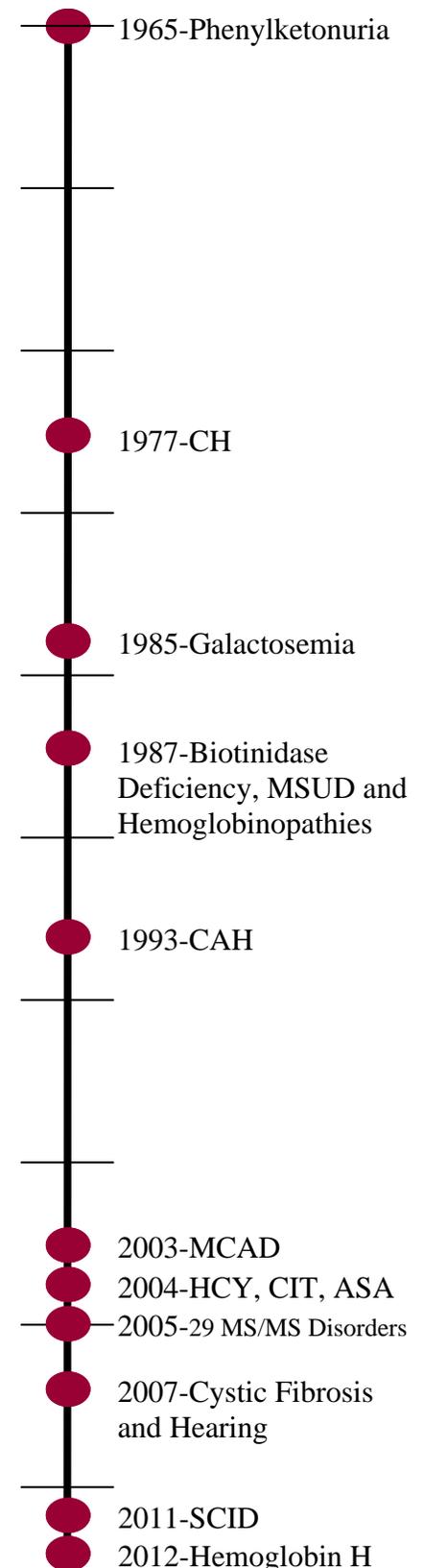
Figure 1. Addition of Disorders to the NBS Panel, Michigan, 1965-2013

1965-Phenylketonuria
1977-CH
1985-Galactosemia
1987-Biotinidase Deficiency, MSUD and Hemoglobinopathies
1993-CAH
2003-MCAD
2004-HCY, CIT, ASA
2005-29 MS/MS Disorders
2007-Cystic Fibrosis and Hearing
2011-SCID
2012-Hemoglobin H

Table 1. Disorders included in the Newborn Screening Panel, Michigan, 2013

Amino Acid Disorders

1. Argininemia

2. Argininosuccinic acidemia

3. Citrullinemia

4. Citrullinemia Type II

5. Homocystinuria

6. Hypermethioninemia

7. Maple syrup urine disease

8. Phenylketonuria

9. Benign hyperphenylalaninemia defect

10. Biopterin cofactor biosynthesis defect

11. Biopterin cofactor regeneration defect

12. Tyrosinemia Type I

13. Tyrosinemia Type II

14. Tyrosinemia Type III

Fatty Acid Oxidation Disorders

15. Carnitine acylcarnitine translocase deficiency

16. Carnitine palmitoyltransferase I deficiency

17. Carnitine palmitoyltransferase II deficiency

18. Carnitine uptake defect

19. Dienoyl-CoA reductase deficiency

20. Glutaric acidemia Type II

21. Long-chain L-3-hydroxyl acyl-CoA dehydrogenase deficiency

22. Medium/short-chain L-3-hydroxyl acyl-CoA dehydrogenase deficiency

23. Medium-chain acyl-CoA dehydrogenase deficiency

24. Medium-chain ketoacyl-CoA thiolase deficiency

25. Short-chain acyl-CoA dehydrogenase deficiency

26. Trifunctional protein deficiency

27. Very long-chain acyl-CoA dehydrogenase deficiency

Organic Acid Disorders

28. 2-Methyl-3-hydroxy butyric aciduria

29. 2-Methylbutyryl-CoA dehydrogenase deficiency

30. 3-Hydroxy 3-methylglutaric aciduria

31. 3-Methylcrotonyl-CoA carboxylase deficiency

32. 3-Methylglutaconic aciduria

33. Beta-ketothiolase deficiency

34. Glutaric acidemia Type I

35. Isobutyryl-CoA dehydrogenase deficiency

36. Isovaleric acidemia

37. Methylmalonic acidemia (Cbl A, B)

38. Methylmalonic acidemia (Cbl C, D)

39. Methylmalonic acidemia (mutase deficiency)

40. Multiple carboxylase deficiency

41. Propionic acidemia

Hemoglobinopathies

42. S/Beta thalassemia

43. S/C disease

44. Sickle cell anemia

45. Variant hemoglobinopathies

46. Hemoglobin H disease

Endocrine Disorders

47. Congenital adrenal hyperplasia

48. Congenital hypothyroidism

Other Disorders

49. Biotinidase deficiency

50. Galactosemia

51. Cystic fibrosis

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.
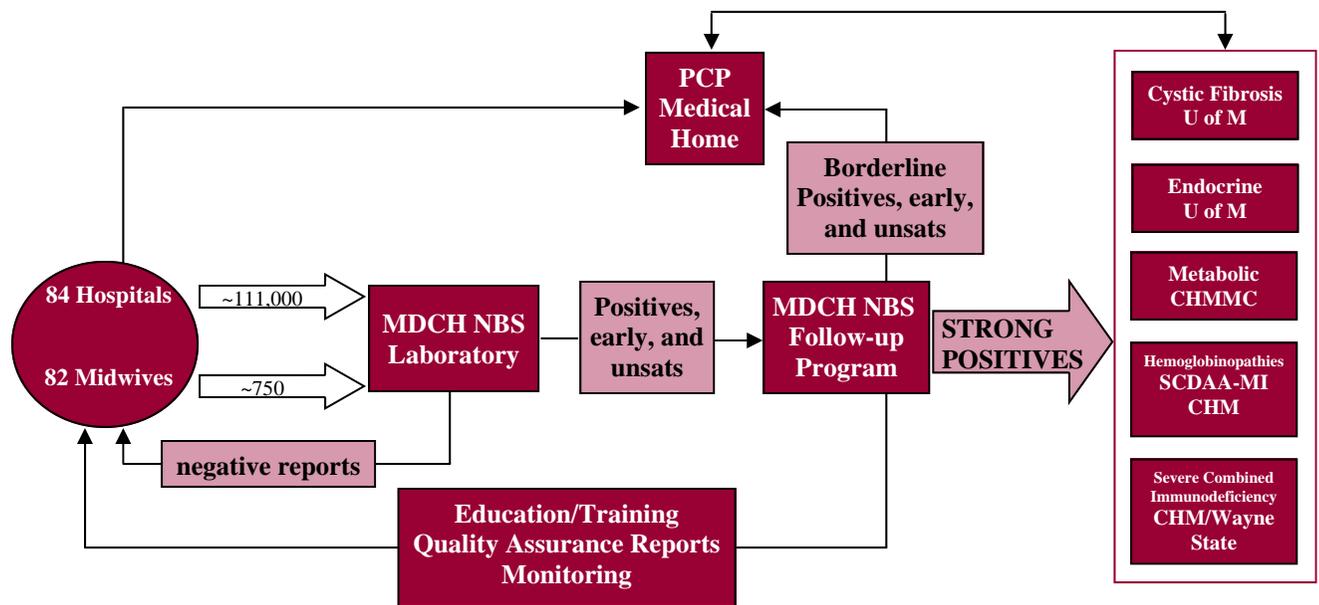
Figure 2. Overview of the Michigan Newborn Screening Program, 2013

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 2013, 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 2013 (n=112,818) 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 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 newborns born in 2013 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 2013, 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 112,818 live births that occurred in 2013, 430 were listed as deceased on the birth certificate. Many of these infants are not screened due to their short life spans, so they are excluded from the linkage calculations. Of the 112,388 remaining live births, the linkage algorithm successfully matched newborn screens for 111,432 infants (99.1%). The 956 unmatched records were sent to NBS Follow-up Program technicians for further investigation. This more in-depth follow-up revealed that 419 (43.8%) 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, 537 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=204), transfer out of state (n=34), infant expired (n=16), or some other reason for not being screened (n=283). For all infants who are missed, the NBS Follow-up technicians either contact the nurse coordinator for hospital births or send a parental notification letter for home births. In 2013, 48 infants born in hospitals are known to have been missed by NBS, and hospitals were contacted. Of the 48, 28 have been screened to date and the remaining 20 are pending.
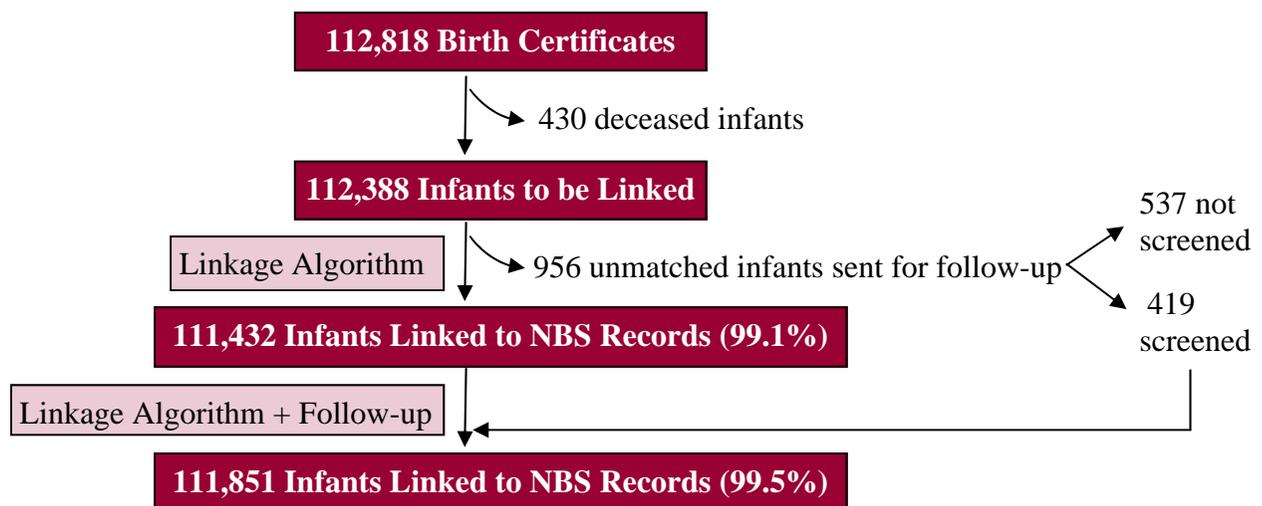

Figure 3. Newborn Screening and Live Births Records Linkage, Michigan, 2013

In total, NBS samples were received from 112,062 infants born in 2013. Of those, 341 (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 2013. 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, 2013, Excluding Out-of-State Residents, N=111,721

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	71,064	63.6	63,447	89.3	6,941	9.8	676	0.9	4,613	6.6	5,778	8.3
Black	20,432	18.3	16,985	83.1	3,434	16.8	13	0.1	2,563	12.7	2,515	12.7
American Indian	485	0.4	436	89.9	46	9.5	3	0.6	29	6.1	32	6.8
Asian/Pac Islander	2,524	2.3	2,286	90.6	235	9.3	3	0.1	201	8.1	174	7.0
Middle Eastern	3,727	3.3	3,419	91.7	306	8.2	2	0.1	278	7.6	263	7.3
Multi-Racial	6,040	5.4	5,369	88.9	638	10.6	33	0.6	456	7.7	565	9.6
Missing	7,449	6.7	6,805	91.4	626	8.4	18	0.2	522	7.3	620	8.8
Column Total:	111,721	100	98,747	88.4	12,226	10.9	748	0.7	8,662	7.9	9,947	9.2

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 1,935 and 3,116 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 2013. The total numbers of cases detected both in and through 2013 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 2013. 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, 1965-2013

Type of Disorder Classification (Year Screening Began)	Cases in 2013 (N)	Cases Through 2013 (N)	Cumulative Detection Rate
Galactosemia (1985)	9	181	1:21,087
Biotinidase Deficiencies (1987)	21	245	1:14,453
Amino Acid Disorders (1965)	16	702	1:9,652
Organic Acid Disorders (2005)	6	60	1:17,694
Fatty Acid Oxidation Disorders (2003)	20	192	1:6,886
Congenital Hypothyroidism (1977)	90	1,966	1:1,801
Congenital Adrenal Hyperplasia (1993)	5	137	1:19,463
Sickle Cell Disease (1987)	56	1,733	1:2,043
Hemoglobin H Disease (2012)	1	4	1:55,726
Cystic Fibrosis (October 2007)	32	192	1:3,716
Primary Immunodeficiencies (October 2011)	15	40	1:8,377
Total	271	5,452	-

Notes: Denominators for the cumulative detection rates, the number of live births eligible to have been screened, are cal-culated from the year screening began onward; thus, if screening commenced other than at the start of the year the de-nominator will be slightly larger than the true denominator. The CF detection rate denominator includes births from Oc-tober 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 2013, while Hemoglobin H Disease, CAH, and organic acid disorders were the least prevalent. Cystic fibrosis (CF) accounted for 12% of cases detected in 2013 and 4% of cases detected cumulatively. The cumulative percentage of CF cases is low compared to the 2013 percentage because screening began recently (October 2007) relative to the other disorders. Similarly, primary immunodeficiencies (PID) accounted for 6% of cases and 0.7% 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 16% of cases in 2013 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 3% of all disorders detected in 2013 and 3% cumulatively. Biotinidase deficiency, including partial biotinidase deficiency, accounted for 8% of all cases detected in 2013 and 5% of all cases detected cumulatively. CAH accounted for 2% all of cases in 2013 and 3% of all cases detected cumulatively.
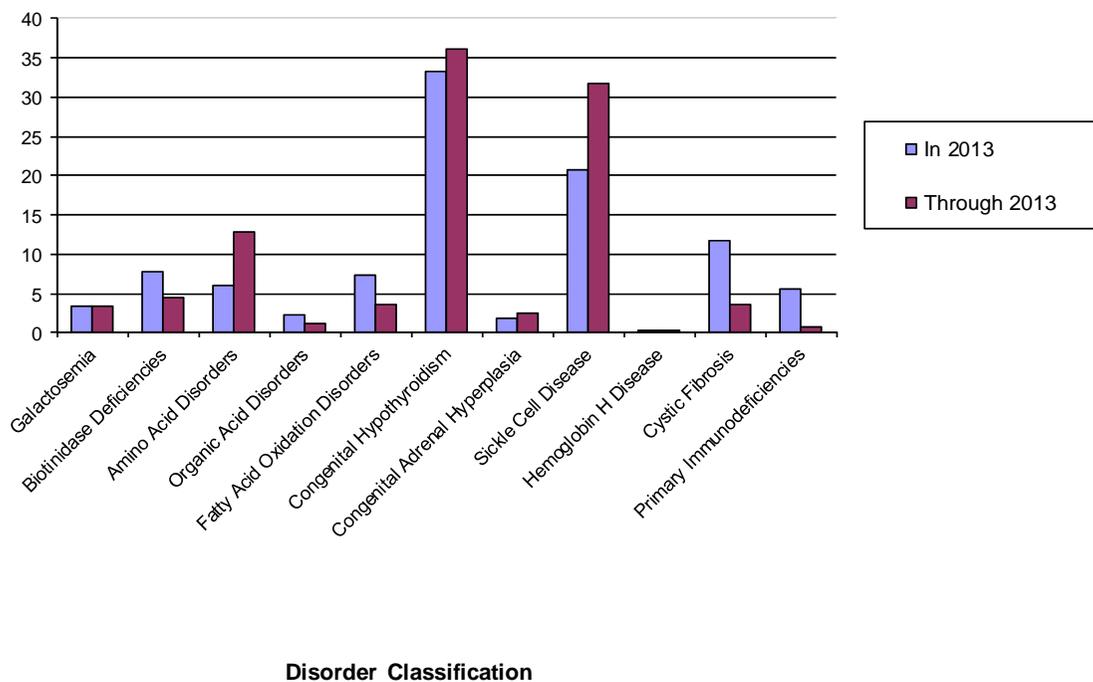

Disorder Classification

Figure 4. Percent Distribution of Disorders Identified in Newborns via Newborn Screening, Michigan Residents, in 2013 and through 2013

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 2013. Performance metrics for individual MS/MS disorders are provided in separate tables (see Tables 7-9).

GALACTOSEMIA, BIOTINIDASE DEFICIENCY & CYSTIC FIBROSIS

Seven cases of Duarte D/G variant and 2 cases of classic galactosemia were detected in 2013, resulting in a FPR of 0.005% and PPV of 60%.

The biotinidase deficiency detection rate (including partial biotinidase deficiency) was 1:5,320; the FPR and PPV were 0.07% and 22%, respectively. Of the 21 cases detected, all were partial and none were profound. One carrier was detected and 8 newborns with homozygous D444H were also identified.

Thirty-two cases of CF were detected in 2013 (detection rate-1:3,491); the associated FPR and PPV were 0.3% and 9.4%, respectively. Additionally, 10 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 0.8%, and the PPV was 9.0%. The overall detection rate for CH was 1:1,241. Chapter IV of the 2007 Annual Report provides more detailed information describing CH screening in Michigan.

The CAH screening FPR was 0.11%, and the PPV was 3.9%. The overall detection rate for CAH was 1:22,344. Three of the cases detected were salt-wasting and the remaining two were non-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 1.9%. One case was identified in 2013, resulting in a detection rate for Hemoglobin H disease of 1:111,721.

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 87.5% of the cases in 2013. While the overall incidence of SCD is approximately one case per 1,995 screened, the incidence in African Americans is one in 417 screened in Michigan.

Table 5: Screening Results and Performance Metrics, Michigan, 2013

Disorder Type	Total N	Total + N (% NICU)	Confirmed + N	Positive Detection Rate	FPR %	PPV %
Galactosemia						
Classic (GG)		15 (0)	2	1:55,861	0.005	60.00
Duarte (DG)			7	1:15,960		
Total			*9*	1:12,413		
Biotinidase Deficiency						
Profound		94 (12.8)	0	-	0.07	22.34
Partial			21	1:5,320		
Total			*21*	*1:5,320*		
Cystic Fibrosis		340 (15.9)	32	1:3,491	0.28	9.41
Congenital Hypothyroidism		997 (30.8)	90	1:1,241	0.81	9.03
Congenital Adrenal Hyperplasias						
Salt wasting		127 (96.9)	3	1:37,240	0.11	3.94
Non-Salt wasting			2	1:55,861		
Total	111,721		*5*	*1:22,344*		
Sickle Cell Disease		74 (17.6)	56	1:1,195	0.02	75.68
Hemoglobin H Disease		53 (37.7)	1	1:111,721	0.05	1.89
Primary Immunodeficiencies						
SCID		77 (79.2)	0	-	0.06	19.48
Syndromes with T-cell Impairment			2	1:55,861		
Non-preterm Secondary T-cell Lymphopenias			13	1:8,594		
Total			*15*	*1:7,448*		
Amino Acid		45 (11.1)	16	1:6,983	0.03	35.56
Organic Acid		22 (18.2)	6	1:18,620	0.01	27.27
Fatty Acid Oxidation		86 (12.8)	20	1:5,586	0.06	23.26
*MS/MS Disorders Total**		*153 (13.1)*	*42*	*1:2,660*	*0.10*	*27.45*

Notes: Maternal cases and carriers identified following an abnormal newborn screen are not included as confirmed cases in the screening performance indicators (i.e., considered false positives).
**SCAD and IBG are screened using the same analyte. The infants with elevated levels are included in 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, 15 cases of primary immunodeficiencies (PID) were identified, resulting in FPR of 0.06% and PPV of 19%. Of the 15 cases, 2 had syndromes with t-cell impairment and 13 had non -preterm secondary T-cell lymphopenias. No classic SCID cases were detected in 2013. 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 1:2,660.

SCREENING PERFORMANCE METRICS-INDIVIDUAL MS/MS DISORDERS

AMINO ACID DISORDERS

Sixteen newborns were identified with amino acid disorders (Table 7) by MS/MS. Phenylketonu-ria (PKU) was the most frequent amino acid disorder identified, found in one of every 15,960 newborns screened (seven newborns total). As indicated in the table, argininosuccinic acidemia (ASA) screening had the highest PPV (100%) among amino acid disorders (six confirmed out of six positive screens). Chapter IV of the 2009 Annual Report provides more detailed information about PKU screening in Michigan. One citrullinemia (CIT) case was detected and an additional four CIT carriers were identified. One case of hypermethioninemia was also identified.

ORGANIC ACID DISORDERS

Six newborns were identified with organic acid disorders (Table 8) by MS/MS. One infant was diagnosed with 2-Methylbutyryl-CoA dehydrogenase deficiency (2MBG); one was diagnosed with multiple carboxylase deficiency (MCD); and four were diagnosed with methylmalonic acidemia (MMA). The MCD case was the first detected in Michigan's NBS Program. MCD had a PPV of 100%. Of note, in 2013, one maternal case of 3-methylcrotonyl-CoA carboxylase deficiency (3MCC) resulted in an infant's positive screen. That mother had been previously identified through NBS in 2011.

FATTY ACID OXIDATION DISORDERS

Twenty children were identified with fatty acid oxidation disorders (Table 9); six medium-chain acyl-CoA dehydrogenase deficiency, eight short-chain acyl-CoA dehydrogenase deficiency, four very long-chain acyl-CoA dehydrogenase deficiency (VLCAD), one carnitine uptake defect, and one carnitine palmitoyltransferase I deficiency. Of the disorders detected, VLCAD had the highest PPV (80%). One maternal case of carnitine uptake defect and two carriers were found following an infant's positive screen.

Table 6: Hemoglobinopathy Screening Performance Metrics, Michigan, 2013

Disorder	Newborns (N)	Confirmed + (N)		Positive Detection Rate	
		Total	Among Blacks	Total	Among Blacks
Sickle Cell Anemia	111,721	34	29	1:3,286	1:705
SC Disease		14	13	1:7,980	1:1,572
Sickle β thalassemia		8	7	1:13,965	1:2,919
SE Disease		0	0	-	-
Total		*56*	*49*	*1:1,995*	*1:417*

Notes: Out of the number of Michigan resident infants screened, total N=111,721, among Blacks N=20,432

Table 7: Amino Acid Disorders Detected by Tandem Mass Spectrometry, Screening Performance Metrics, Michigan, 2013

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Phenylketonuria	111,721	15			0.007	46.7
Diet-treated (PKU)			4	1:27,930		
Benign Hyperphenyl-alaninemia (H-PHE)			2	1:55,861		
Biopterin Cofactor Defects (BIOPT)			1	1:111,721		
Total			*7*	*1:15,960*		
Argininemia (ARG)		2	0	-	0.002	-
Citrullinemia (CIT)/CIT II		9	1	1:111,721	0.007	11.1
Argininosuccinic Acidemia (ASA)		6	6	1:18,620	0.000	100.0
Tyrosinemia I (TYR I)		1	0	-	0.001	-
Tyrosinemia II-III (TYR II-III)		5	0	-	0.005	-
Homocystinuria (HCY)/ Hypermethioninemia (MET)		5	1	1:111,721	0.004	20.0
Maple Syrup Urine Disease (MSUD)		2	1	1:111,721	0.001	50.0

Table 8: Organic Acid Disorders Detected by Tandem Mass Spectrometry, Screening Performance Metrics, Michigan, 2013

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Isovaleric Acidemia (IVA)/2-Methylbutyryl-CoA Dehydrogenase Deficiency (2MBG)	111,721	3	1	1:111,721	0.002	33.3
3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC)		3	0	-	0.003	-
Glutaric Acidemia Type I (GA I)		4	0	-	0.004	-
Propionic Acidemia (PA)/ Methylmalonic Acidemia (MMA)		11	4	1:27,930	0.006	36.4
Multiple Carboxylase Deficiency (MCD)		1	1	1:111,721	0.0	100.0

Notes: Maternal cases and carriers identified following an abnormal newborn screen are not included as confirmed cases in the screening performance indicators (i.e., considered false positives). 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, 2013

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Carnitine Uptake Defect (CUD)		49	1	1:111,721	0.043	2.0
Short-Chain Acyl-CoA Dehydrogenase deficiency (SCAD)		16	8	1:13,965	0.007	50.0
Carnitine/Acylcarnitine Translocase Deficiency-(CACT)/Carnitine Pal-mitoyltransferase II Deficiency (CPT II)		1	0	-	0.001	-
Glutaric Acidemia Type II (GA II)	111,721	2	0	-	0.002	-
Medium-chain Acyl-CoA Dehydrogenase Deficiency (MCAD)		10	6	1:18,620	0.004	60.0
Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)		5	4	1:27,930	0.001	80.0
Long-chain L-3-hydroxy Acyl-CoA Dehydrogenase Deficiency (LCHAD)		1	0	-	0.001	-
Carnitine Palmitoyltransferase I Deficiency (CPT I)		2	1	1:111,721	0.001	50.0

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 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 2013 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, 2013

Disorder Type	Among All +		Among Strong +	
	FPR	**PPV**	**FPR**	**PPV**
	%	**%**	**%**	**%**
Congenital Hypothyroidism (CH)	0.81	9.03	0.140	29.73
Congenital Adrenal Hyperplasia (CAH)	0.11	3.94	0.022	16.67
Phenylketonuria (PKU)	0.007	46.67	0.001	85.71
Maple Syrup Urine Disease (MSUD)	0.001	50.00	0.000	100.00
Cystic Fibrosis (CF)	0.28	9.41	0.006	78.79
Primary Immunodeficiency	0.06	19.48	0.027	25.00

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

The FPR for CH is reduced nearly 6-fold for strong positive screens, and the PPV is increased approximately 3-fold. The FPR and PPV for CAH are each decreased and increased by 5-fold and 4-fold among strong positives, respectively.

Among MS/MS disorders, the one strong positive for MSUD confirmed with disease, meaning the PPV among strong positives was 100% and the FPR was 0%. For PKU, the FPR decreased 8-fold and the PPV doubled among strong positives compared to all positives.

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 44-fold and the PPV increased from 9% to 79% when excluding children with a heterozygote DNA mutation.

For PID, the FPR decreased 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 2013, a total of 3,057 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=2,772) had sickle cell trait. Over 270 infants (n=277) were cystic fibrosis carriers, 4 were identified as CIT carriers, 2 were identified as CUD carriers, 1 was identified sickle cell trait with Barts, and 1 was identified as a biotinidase carrier. Overall, nearly 3% of the screened infants born in 2013 had sickle cell trait.

Table 11: Carriers Identified from Newborn Screening, Michigan, 2013

Disorder	N
Biotinidase	1
Cystic fibrosis	277
Carnitine uptake defect (CUD)	2
Citrullinemia (CIT)	4
Sickle Cell Trait	2,772
Sickle Cell Trait with Barts	1

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

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 2013, two maternal disorders were identified following an infant's positive NBS (Table 12). One mother was identified with 3MCC (previously detected in 2011) and another mother was identified with CUD.

Table 12: Maternal Disorders Identified from Newborn Screening, Michigan, 2013

Maternal Disorder	N
3-Methylcrotonyl-CoA carboxylase deficiency (3MCC)	1
Carnitine uptake defect (CUD)	1

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, 49% and 31% 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 (9%). 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 5,400 specimens required follow-up in 2013.

Table 13: Specimen Characteristics by Nursery Type, Michigan, 2013

Indicator	Type of Birth					
	Regular Nursery		NICU/SCN		Non-Hospital	
	N	%	N	%	N	%
Strong Positive Specimens	196	0.20	190	1.55	0	0.0
Borderline Positive Specimens	745	0.75	335	2.74	7	0.94
All Positive Specimens*	1,321	1.34	611	5.00	8	1.07
Isolated elevations of amino acids and acyl-carnitines	5	0.01	370	3.03	2	0.27
Unsatisfactory Specimens	2,098	2.12	519	4.25	59	7.89
Late (>6 days) Specimens	65	0.07	40	0.33	63	8.42
Early (<1 day) Specimens	248	0.25	795	6.50	5	0.67
Transfused Specimens	3	0.00	117	1.06	0	0.00
Specimens Missing Demographics **	1,716	1.74	209	1.71	23	3.07
Total Births Screened	98,747	88.4	12,226	10.9	748	0.7

*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 2013, 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, 2013

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 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 1.9% of screens being collected more than 36 hours after birth. Of note, over 59% 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 2013, 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 the BioTrust for Health measure, regular nurseries were the closest; 82% of regular nursery births had a BioTrust for Health consent form returned that was appropriately completed compared to approximately 60% of NICU/SCN and non-hospital births.

Table 15: Measures for Newborn Screening, by Nursery Type, Michigan, 2013

Measure (Goal)	Nursery Type	N	%	Met Goal?
Late Screens (<2%)	Regular	1,902	1.9	Yes
	NICU/SCN	448	3.7	No
	Non-hospital	443	59.2	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	2,098	2.1	No
	NICU/SCN	519	4.3	No
	Non-hospital	59	7.9	No
Batching (<2%)	Regular	281	1.2	Yes
	NICU/SCN	46	0.7	Yes
	Non-hospital	1	0.1	Yes
NBS Card Number (>95%)	Regular	99,213	96.4	Yes
	NICU/SCN*	NA		
	Non-hospital	141	11.3	No
Returned BioTrust for Health Consent Forms Completed Appropriately (>90%)	Regular	80,756	81.8	No
	NICU/SCN	7,285	59.6	No
	Non-hospital	467	62.4	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 1 to 128 days of life among all disorders. Certain disorders often require one or more retests before being referred for confirmatory diagnosis. For that reason, CH is presented separately by initial screening result (strong or borderline) in the table.

GALACTOSEMIA

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

BIOTINIDASE DEFICIENCY

Of the 21 partial biotinidase cases identified, all had treatment started within 19 days of life, and 16 had treatment initiated within two weeks of life.

MS/MS DISORDERS

Three of the four diet-treated PKU cases were treated in the first week of life. The remaining case had treatment initiated at 43 days of life following a re-classification from non-diet-treated PKU to diet-treated PKU. One case of MSUD was treated in the first week, while four of the six ASA cases had treatment initiated within the first week. One newborn with CIT expired before treatment began.

The 2MBG case had treatment initiated on day 16 of life. The MCD case had treatment initiated on the first day of life, and the three surviving MMA cases had treatment initiated between three and five days of life.

Of the 20 infants with fatty acid oxidation disorders and a treatment start date, 19 were treated within the first week of life. The remaining CUD case was treated on day 13.

Table 16: Time to Treatment of Amino Acid Disorders, Organic Acid, Fatty Acid Oxidation, and Endocrine Disorders, Michigan, 2013

Disorder		Total	Treatment Time (days from birth) N			Treatment Time Range (days)
		N	1-7	8-14	>14	
Galactosemia	Classic (GG)	2	2			3-4
	Duarte (DG)	7	1	2	4	5-59
Biotinidase Deficiency	Partial	21	2	14	5	4-19
	Profound	0				
Amino Acid Disorders	PKU-Diet treated	4	3		1	4-43
	MSUD	1	1			6
	CIT/ASA[1]	7	4		2	4-16
	Total	*12*	*8*		*3*	*4-43*
Organic Acid Disorders	IVA/2MBG	1			1	16
	MCD	1	1			1
	MMA[1]	4	3			3-5
	Total	*6*	*4*		*1*	*3-16*
Fatty Acid Oxidation Disorders	SCAD	8	8			4-6
	MCAD	6	6			3-5
	VLCAD	4	4			4-5
	CUD	1		1		13
	CPTI	1	1			1
	Total	*20*	*19*	*1*		*1-13*
Endocrine Disorders	CH					
	Borderline	23		3	20	9-111
	Strong	66	29	19	18	1-128
	CAH					
	Salt-wasting	4	3		1	3-37
	Non salt-wasting	1	1			7
Total		*162*	*69*	*39*	*52*	*1-128*

Notes: Disorders that do not require treatment are excluded from the table.
[1]One baby expired.

ENDOCRINE DISORDERS-CAH AND CH

The salt-wasting form of CAH is life-threatening in the first few weeks of life. Three of the four 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 37th day of life after re-classification from non-salt-wasting CAH.

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 66 CH cases with a strong positive screen, 48 (73%) 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 52 cases having a penicillin start date reported, 78% were treated with penicillin within the first four months, 6% began treatment between four and five months of life, 2% began treatment between five and six months, and 15% began treatment beyond six months of age.

Table 17: Time to Penicillin Initiation for Sickle Cell Disorders, Michigan, 2013

Disorder	Penicillin Prophylaxis Initiation Time			
	< 120 days	120-149 days	150-179 days	≥ 180 days
Sickle Cell Disorders*	42 (77.8%)	3 (5.6%)	1 (1.9%)	8 (14.8%)

*2 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 111,721 infants born in 2013, and the NBS Follow-up Program tracked approximately 5,400 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 271 newborns were identified with a disorder by NBS in 2013, as well as 3,057 carriers. Since NBS began in Michigan in 1965, 5,452 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.