Michigan Department of
Community Health

MICHIGAN NEWBORN SCREENING PROGRAM

Annual Report 2010

Michigan Department of Community Health
MDCH
Rick Snyder, Governor
Olga Dazzo, Director

Public Health
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Acknowledgements

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Executive Summary

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

Since the program began in 1965 with screening for phenylketonuria, 49 additional disorders have been added to the screening panel. Through 2010, millions of infants have been screened with 4,691 diagnosed with diseases included in the NBS panel.

Of the 112,986 infants screened in 2010, 112,680 were Michigan residents and 280 (0.2%) were diagnosed with a disease. Overall, one infant out of 402 screened was diagnosed with disorders included in the NBS panel.

Developments occurring in 2010:

- The findings from different studies and analyses related to NBS were presented at the following meetings:
    - ◊ Newborn Screening and Genetic Testing Symposium (Orlando, FL)
    - ◊ Genetic Alliance National Conference (Bethesda, MD)
    - ◊ National Conference on Blood Disorders in Public Health (Atlanta, GA)
    - ◊ National Birth Defects Prevention Network Conference (National Harbor, MD)
    - ◊ Michigan Epidemiology Conference (East Lansing, MI)
    - ◊ International Public Health Learning Collaborative on Hemoglobinopathies (Atlanta, GA)
    - ◊ National Conference on Genomics and Public Health (Bethesda, MD)
    - ◊ National Maternal and Child Health Epidemiology Conference (San Antonio, TX)

- "Newborn Screening Follow-up Within the Lifespan Context: Michigan's Experience" was published in the American Journal of Preventive Medicine.

- A member of the NBS laboratory staff was a co-author of "Newborn Screening by Tandem Mass Spectrometry; Proposed Guideline", a document released by the Clinical and Laboratory Standards Institute.

- A new NICU protocol went into effect in July 2010. The NICU protocol revision was based on reviewing data on the detection of additional cases of congenital hypothyroidism and 5 years of experience with detection of disorders in transfused newborns or those on total parenteral nutrition by tandem mass spectrometry. According to the new protocol, two newborn screens are requested from all newborns in the NICU, regardless of birth weight. The first screen should be collected between 24-36 hours of life, and the second screen should be collected at 30 days of life or at discharge, whichever comes first.

- In February 2010, the Division of Genomics, Perinatal Health, and Chronic Disease Epidemiology, where the NBS Follow-up Program is housed, received one of six cooperative agreements to implement a hemoglobinopathies registry and surveillance system. To learn more about this cooperative agreement, click here or select the link from the NBS Follow-up website (www.michigan.gov/newbornscreening).

- As part of the cooperative agreement, a module was developed to allow long-term follow-up of individuals identified with sickle cell disease through NBS. This module is located on the Michigan Care Improvement Registry (MCIR), a web-based application used to record immunizations. Information collected through a health status assessment form in the module will allow for continued assessment of health outcomes of those with sickle cell disease.

- New laboratory equipment was introduced for hemoglobinopathy testing.

- The NBS Follow-up Program website (www.michigan.gov/newbornscreening) was re-designed in April 2010 to be more user-friendly.

- The NBS/BioTrust Education Initiative was launched in June 2010 and is on-going. More than 650 nursing CEUs have been issued to date.

- The BioTrust for Health consent process was implemented statewide on October 1, 2010. Parental consent allows for residual dried blood spots to be stored and made available for use in research. For more information on the BioTrust for Health, visit www.michigan.gov/biotrust.

- Quarterly reports sent to birthing units were revised to include indicators related to the BioTrust for Health consent process. As of the 4th quarter of 2010, birthing units are informed how many consent forms overall and how many non-blank consent forms they are returning. The goal is to have a returned consent form, regardless of parental response, for every screened newborn.

- The NBS Follow-up Program held the second Family Recognition Day on May 1, 2010. Approximately 130 people attended the event at Impression 5 Science Center in Lansing.

- In October 2010, the Quality Assurance Advisory Committee voted to add severe combined immunodeficiency (SCID) to the NBS panel. The NBS laboratory will begin screening for SCID on October 1, 2011.

- The Primary Immunodeficiency Disorders Quality Improvement Committee was founded in 2010 to assist in developing screening, follow-up, and medical management algorithms for primary immunodeficiency disorders, to oversee the implementation of screening for primary immunodeficiency disorders, and to make recommendations for improvements.

Listing of Figures & Tables

Figures

Tables

Acronym Key

Acronym	Name
ACMG	American College of Medical Genetics
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
PPV	Positive Predictive Value
QA	Quality Assurance
QAAC	Quality Assurance Advisory Committee
SCDAA	Sickle Cell Disease Association of America
U of M	University of Michigan

I. Introduction

The Newborn Screening (NBS) Annual Report provides an overview of Michigan's NBS Program, target outcomes, screening performance metrics related to disorders included in the NBS panel, and quality assurance information. This report also includes a chapter providing in-depth information on the Healthy People 2020 objectives related to NBS (Chapter IV). This chapter contains a description of each Healthy People 2020 objective related to NBS and how Michigan is, or plans to, track those objectives. 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 outcomes
- A detailed account of Healthy People 2020 NBS-related objectives
- Quality assurance information
- Future directions for NBS in Michigan

What is Newborn Screening?

NBS is the process of early identification of health conditions followed by their subsequent timely 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, mental retardation, 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. 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

[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.

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.

The introduction of tandem mass spectrometry (MS/MS) in 2003 enabled the state laboratory to efficiently screen for a large number of disorders detectable from a single blood spot. The first disorder 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]

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 730,000 infants have been screened for the disorders through 2010, and no cases have been detected. Screening for Citrullinemia Type II began in 2004, meaning approximately 855,000 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, including algorithms, can be found in the NBS Procedure Manual available on the NBS website.

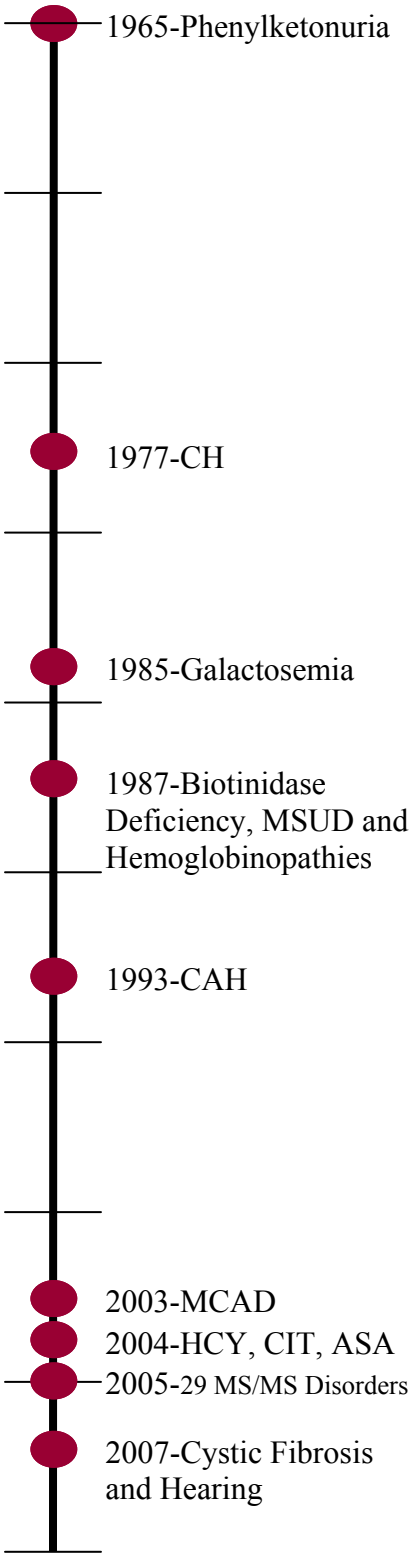

Figure 1. Addition of Disorders to the NBS Panel, Michigan, 1965-2010

[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, 2010

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	**Endocrine Disorders**
20. Glutaric acidemia Type II	46. Congenital adrenal hyperplasia
21. Long-chain L-3-hydroxyl acyl-CoA dehydrogenase deficiency	47. Congenital hypothyroidism
22. Medium/short-chain L-3-hydroxyl acyl-CoA dehydrogenase deficiency	**Other Disorders**
23. Medium-chain acyl-CoA dehydrogenase deficiency	48. Biotinidase deficiency
24. Medium-chain ketoacyl-CoA thiolase deficiency	49. Galactosemia
25. Short-chain acyl-CoA dehydrogenase deficiency	50. Cystic fibrosis
26. Trifunctional protein deficiency	51. Hearing
27. Very long-chain acyl-CoA dehydrogenase deficiency	

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, #15/#17, #21/#26, #29/#36, #41/#37-39, #25/#35.

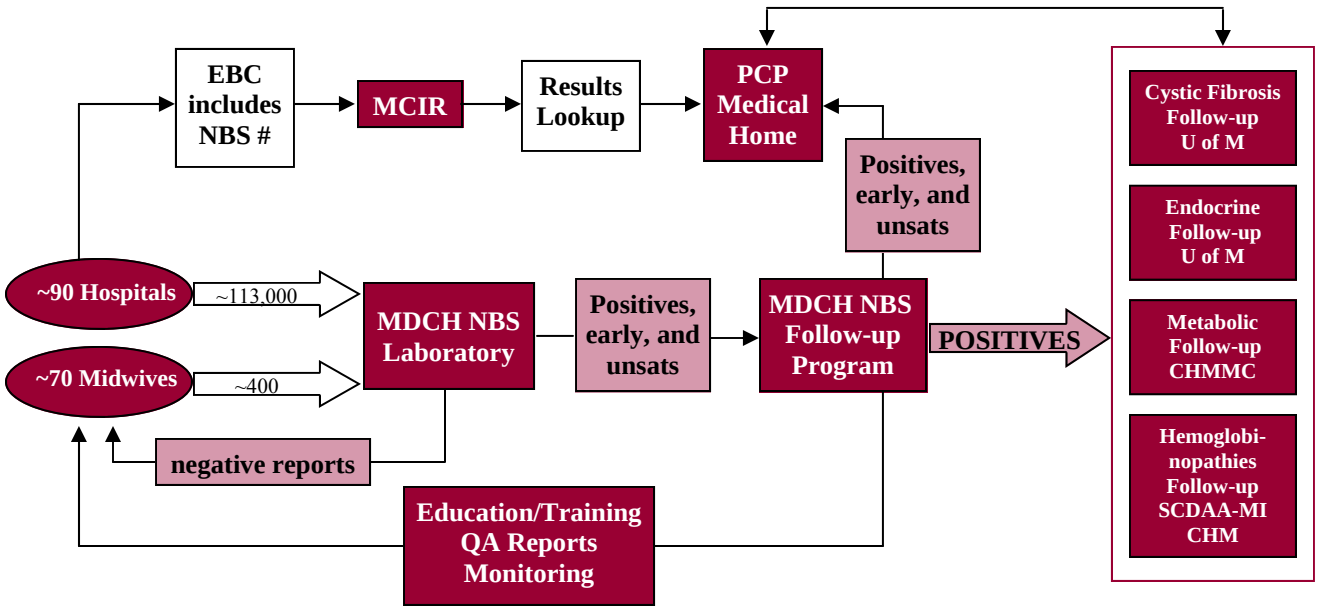

Figure 2. Overview of the Michigan Newborn Screening Program

HOSPITALS

In 2010, Michigan had 89 hospitals with newborn nurseries. Each hospital has a designated NBS coordinator who helps facilitate the screening process. Hospital coordinators receive a quarterly quality assurance report that includes information on hospital-specific performance indicators compared to the state overall. Hospitals receive 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 67 midwives registered with the NBS Program. Midwives also receive quarterly quality assurance reports and 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 four medical management centers. More detailed descriptions of each entity are included in previous reports available on the NBS website (www.michigan.gov/newbornscreening) or by clicking here.

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 2010 (n=113,446) 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 both Michigan residents and for out-of-state residents screened in Michigan. This report focuses on cases and screening results among Michigan residents. Our reason for focusing on Michigan residents is because 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 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) time from birth to treatment, by disorder.

III. Screening Results

DEMOGRAPHIC CHARACTERISTICS OF SCREENED NEWBORNS

This section describes the population of screened newborns born in 2010 in terms of race, birth weight, gestational age, and birth place (hospital regular nursery, NICU, 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 99.6% of the live births occurring in Michigan in 2010, as determined by the linkage of NBS records to preliminary live births records received from the Vital Records & Health Data Development Section and follow-up of unmatched records (Figure 3). Of the 113,446 live births that occurred in 2010, 514 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 112,932 remaining live births, the linkage algorithm successfully matched newborn screens for 112,002 infants (99.2%). The 930 unmatched records were sent to NBS Follow-up Program technicians for further investigation. This more in-depth follow-up revealed that 484 (52.0%) 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, 446 infants (0.4%) born in the state were not screened. Infants may not have been screened due to parental refusal of screening (n=58), transfer out of state (n=19), infant expired (n=12), or missed screened (n=357). 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 2010, 44 infants born in hospitals are known to have been missed by NBS, and hospitals were contacted. Of the 44, 25 have been screened to date and the remaining 19 are pending. Of the 313 missed home births, 11 were screened after being contacted by the NBS Follow-up Program.

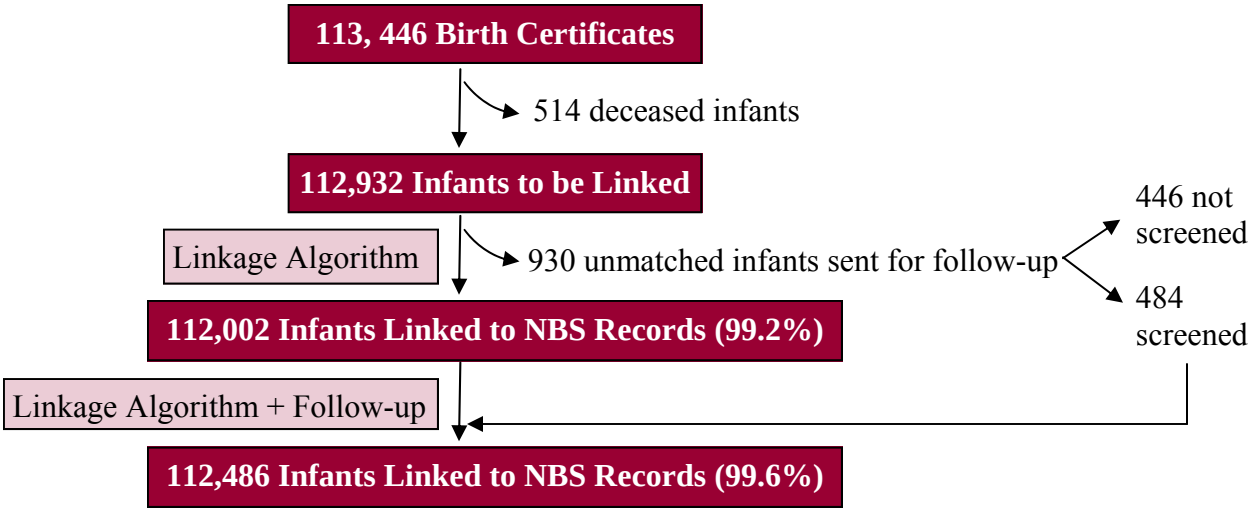

Figure 3. Newborn Screening and Live Births Records Linkage, Michigan, 2010

In total, newborn screens were received for 112,986 infants born in 2010. Of those, 306 (0.3% of screens) belonged to out-of-state residents. Tables 3 and 4 report the demographic and perinatal characteristics by race of in-state and out-of-state residents screened in 2010, respectively. This report details the screening results for in-state residents only. 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, 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, 2010, Excluding Out-of-State Residents, N=112,680

Race	Column Total		Nursery Type						Low Birth Weight (g)		Gestational Age (wks)	
			Regular Hospital		NICU		Non-Hospital		<2500		<37	
	N	%	N	%	N	%	N	%	N	%	N	%
White	71,076	69.6	63,552	89.4	6,887	9.7	637	0.9	4,689	6.7	6,115	8.9
Black	20,282	19.9	16,746	82.6	3,526	17.4	10	0.1	2,697	13.5	2,746	14.2
American Indian	443	0.4	396	89.4	45	10.2	2	0.4	35	8.0	44	10.2
Asian/Pac Islander	2,375	2.3	2,165	91.2	208	8.8	2	0.1	192	8.2	184	7.9
Middle Eastern	2,684	2.6	2,446	91.1	234	8.7	4	0.2	200	7.5	213	8.1
Multi-Racial	5,275	5.2	4,710	89.3	541	10.3	24	0.4	401	7.7	468	9.1
Column Total:	*102,135*	*100*	*90,015*	*88.1*	*11,441*	*11.2*	*679*	*0.7*	*8,214*	*8.2*	*9,770*	*9.9*

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 10,545 infants did not have race recorded on the newborn screening card. An additional 1,347 and 3,139 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.

Table 4: Demographics of Infants Screened by Race, Michigan, 2010, Out-of-State Residents, N=306

Race	Column Total		Nursery Type						Low Birth Weight (g)		Gestational Age (wks)	
			Regular Hospital		NICU		Non-Hospital		<2500		<37	
	N	%	N	%	N	%	N	%	N	%	N	%
White	219	79.1	187	85.4	30	13.7	2	0.9	17	8.0	21	9.9
Black	33	11.9	24	72.7	9	27.3	0	-	8	24.2	5	15.2
American Indian	0	-	0	-	0	-	0	-	0	-	0	-
Asian/Pac Islander	9	3.3	6	66.7	3	33.3	0	-	2	22.2	4	44.4
Middle Eastern	9	3.3	8	88.9	1	11.1	0	-	0	-	0	-
Multi-Racial	7	2.5	6	85.7	1	14.3	0	-	0	-	0	-
Column Total:	*277*	*100*	*231*	*83.4*	*44*	*15.9*	*2*	0.7	*27*	*10.0*	*30*	*11.2*

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 29 infants did not have race recorded on the newborn screening card. An additional 6 and 10 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 screened for in 2010. The total number of cases detected both in and through 2010 is presented along with screening performance metrics. The disorders are organized into four categories: metabolic, endocrine, cystic fibrosis, and hemoglobinopathies, corresponding to the four medical management programs responsible for diagnosis and treatment.

CUMULATIVE DETECTION RATE

Table 5 reports the cumulative detection rate of disorders identified via NBS by classification both in and through 2010. 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 5: Disorders Identified in Newborns via Newborn Screening, Michigan Newborn Residents, 1965-2010

Type of Disorder Classification (Year Screening Began)	Cases in 2010 (N)	Cases Through 2010 (N)	Cumulative Detection Rate
Galactosemia (1985)	11	170	1:20,480
Biotinidase Deficiencies (1987)	13	196	1:16,357
Amino Acid Disorders (1965)	14	653	1:9,863
Organic Acid Disorders (2005)	16	43	1:16,897
Fatty Acid Oxidation Disorders (2003)	24	114	1:8,659
Congenital Hypothyroidism (1977)	101	1,720	1:1,864
Congenital Adrenal Hyperplasia (1993)	5	116	1:20,098
Hemoglobinopathies (1987)	61	1,565	1:2,048
Cystic Fibrosis (October 2007)	35	114	1:3,319
Total	280	4,691	-

Notes: Denominators, 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 2007-2010.

As indicated in Table 5 and Figure 4, CH and hemoglobinopathies were the most prevalent disorders in 2010, while CAH and galactosemia were the least prevalent. CF accounted for 13% of cases detected in 2010 and 2% of cases detected cumulatively. The cumulative percentage of CF cases is low compared to the 2010 percentage because screening began recently (October 2007) relative to the other disorders. Disorders detected by MS/MS (amino acid, organic acid, and fatty acid oxidation disorders) accounted for 19% of cases in 2010 and 17% cumulatively. However, PKU, the first disorder screened in Michigan, is now screened by MS/MS, meaning the overall proportion of cases detected by MS/MS is an overestimate because it includes cases detected prior to 2003 when MS/MS screening was initiated. The cumulative detection rate for fatty acid oxidation disorders is an underestimate because MCAD screening began in 2003, while other conditions were not screened until 2005. This means that births included in the denominator from 2003-2005 were not eligible for being diagnosed with fatty acid oxidation disorders other than MCAD leading to an artificially low cumulative detection rate. The MS/MS detection rate does not include thirteen cases of formiminoglutamic acid disorder (FIGLU) detected because the disorder is not included in the NBS panel. Galactosemia, including Duarte compound heterozygotes, accounted for 4% of all disorders detected in 2010 and 4% cumulatively. Biotinidase deficiency, including partial biotinidase deficiency, accounted for 5% of all cases detected in 2010 and 4% of all cases detected cumulatively. CAH accounted for 2% all of cases in 2010 and 3% of all cases detected cumulatively.

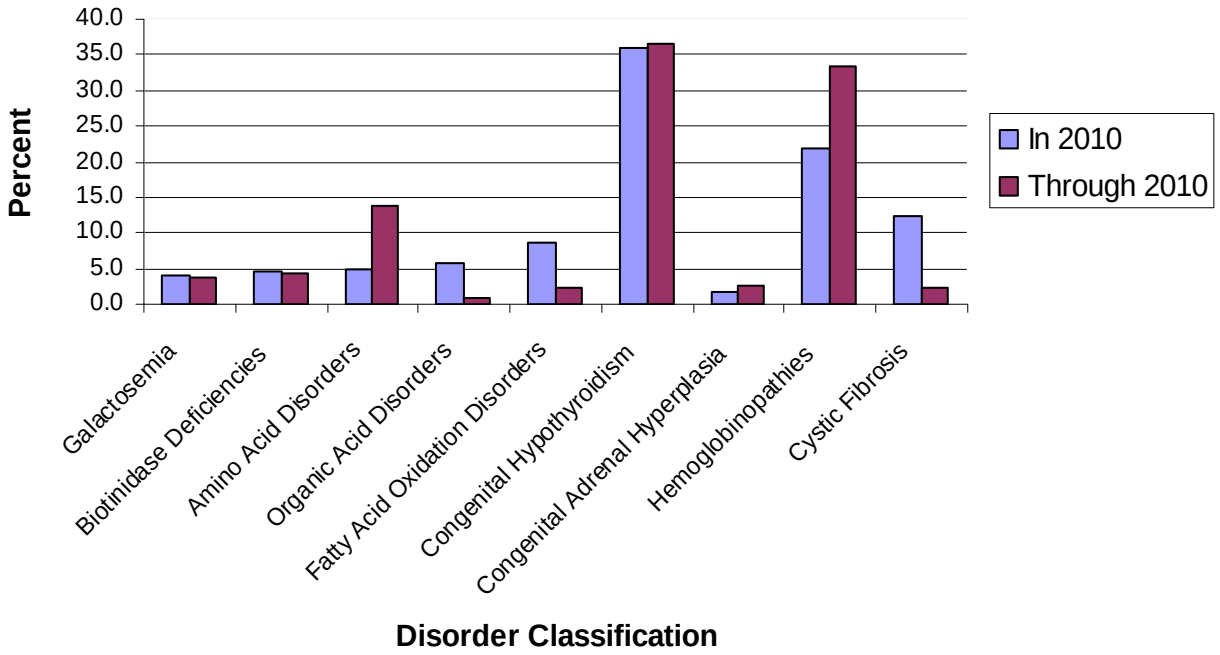

Figure 4. Percent Distribution of Disorders Identified in Newborns via Newborn Screening, Michigan Residents, in 2010 and through 2010

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 6 reports screening performance metrics for all disorders in 2010. Performance metrics for individual MS/MS disorders are provided in separate tables (see Tables 8-10).

GALACTOSEMIA, BIOTINIDASE DEFICIENCY & CYSTIC FIBROSIS

The galactosemia detection rate (including Duarte D/G variants) was 1:10,244 in 2010. The FPR and PPV were 0.01% and 41%, respectively. Although the purpose of galactosemia screening is to detect classic galactosemia only, no cases of classic galactosemia were detected in 2010; all 11 detected cases were Duarte D/G variants.

The biotinidase deficiency detection rate (including partial biotinidase deficiency) was 1:8,668; the FPR and PPV were 0.2% and 6%, respectively.

Thirty-five cases of cystic fibrosis (CF) were detected in 2010 (detection rate-1:3,219); the associated FPR and PPV were 0.3% and 11%, respectively. Additionally, two cases of CFTR-related metabolic syndrome were also detected. Chapter IV of the 2008 Annual Report provides more detailed information about CF screening in Michigan.

ENDOCRINE DISORDERS-CH AND CAH

The CH screening FPR is 1%, and the PPV is 8%. The overall detection rate for CH was 1:1,116. Chapter IV of the 2007 Annual Report provides more detailed information about CH screening in Michigan.

The CAH screening FPR is 0.1%, and the PPV is 4%. The overall detection rate for CAH was 1:22,536. A new assay for CAH was implemented in August 2009. This new assay resulted in a dramatic improvement in screening performance metrics. Compared to the performance metrics for CAH in 2009, the FPR decreased from 0.5% to 0.1%, a 4-fold difference; the PPV increased from 0.3% to 4%, an 11-fold difference.

HEMOGLOBINOPATHIES

Additional hemoglobinopathy screening outcome information is reported in Table 7. Hemoglobinopathy 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 7, hemoglobinopathies are quite common among African Americans, who accounted for 97% of the cases in 2010. While the overall incidence of hemoglobinopathies is approximately one case per 1,847 screened, the incidence in African Americans is one in 344 screened in Michigan.

Table 6: Screening Results and Performance Metrics, Michigan, 2010

Disorder Type	Total N	Total + N (% NICU)	Confirmed + N	Positive Detection Rate	FPR %	PPV %
Galactosemia	112,680	27 (14.8)			0.01	40.74
Classic (GG)			0	-		
Duarte (DG)			11	1:10,244		
Total			*11*	*1:10,244*		
Biotinidase Deficiency		224 (33.9)			0.19	5.80
Profound			1	1:112,680		
Partial			12	1:9,390		
Total			*13*	*1:8,668*		
Cystic Fibrosis		312 (13.1)	35	1:3,219	0.25	11.22
Congenital Hypothyroidism		1,250 (27.5)	101	1:1,116	1.02	8.08
Congenital Adrenal Hyperplasias		140 (90.7)			0.12	3.57
Salt wasting			4	1:28,170		
Non-Salt wasting			1	1:112,680		
Total			*5*	*1:22,536*		
Hemoglobinopathies		86 (16.3)	61	1:1,847	0.02	70.9
Amino Acid*		92 (9.8)	14	1:8,049	0.07	15.22
Organic Acid*		91 (16.5)	16	1:7,043	0.07	17.58
Fatty Acid Oxidation*		77 (20.8)	24	1:4,695	0.05	31.17
*MS/MS Disorders Total***		*238 (13.0)*	*54*	*1:2,087*	*0.16*	*22.69*

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). A total of 13 cases are still pending.
**Detected by MS/MS*
***SCAD and IBG are screened using the same analyte. Thus, the 21 infants with elevated levels of that analyte 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.*

Table 7: Hemoglobinopathy Screening Performance Metrics, Michigan, 2010

Disorder	Newborns (N)	Confirmed + (N)		Positive Detection Rate	
		Total	Among Blacks	Total	Among Blacks
Sickle Cell Anemia	112,680	33	32	1:3,415	1:634
SC Disease		23	22	1:4,899	1:922
Sickle β thalassemia		5	5	1:22,536	1:4,056
Total		*61*	*59*	*1:1,847*	*1:344*

Notes: Out of the number of Michigan resident infants screened, total N=112,680, among Blacks N=20,282

MS/MS DISORDERS

The overall FPR for MS/MS disorders is 0.2%. The PPV is 23%, and the detection rate is 1:2,087.

SCREENING PERFORMANCE METRICS-INDIVIDUAL MS/MS DISORDERS

AMINO ACID DISORDERS

Fourteen newborns were identified with amino acid disorders (Table 8) by MS/MS. Phenylketonuria (PKU) was the most frequent amino acid disorder identified, found in one of every 11,268 newborns screened. As indicated in the table, PKU screening had the highest PPV (59%) among amino acid disorders. Chapter IV of the 2009 Annual Report provides more detailed information about PKU screening in Michigan. Three cases of hypermethioninemia and one case of argininemia were confirmed in 2010.

ORGANIC ACID DISORDERS

Sixteen newborns were identified with organic acid disorders (Table 9) by MS/MS. Five infants were diagnosed with 3-Methylcrotonyl-CoA carboxylase deficiency (3MCC); four were diagnosed with methylmalonic acidemia (MMA); five were diagnosed with isobutyryl-CoA dehydrogenase deficiency; one was diagnosed with propionic acidemia (PA); one was diagnosed with glutaric acidemia type I. Of note, in 2010 two maternal cases of 3MCC and three maternal cases of Vitamin B12 Deficiency were detected following their infant's positive screens for 3MCC and PA/MMA, respectively.

FATTY ACID OXIDATION DISORDERS

Twenty-four children were identified with fatty acid oxidation disorders (Table 10); eleven medium-chain acyl-CoA dehydrogenase deficiency (MCAD), ten short-chain acyl-CoA dehydrogenase deficiency, one very long-chain acyl-CoA dehydrogenase deficiency, one carnitine palmitoyl transferase II deficiency, and one glutaric acidemia type II (GAII). Of the disorders detected, GAII and MCAD had the highest PPV (100% and 92%, respectively).

Table 8: Amino Acid Disorders Detected by Tandem Mass Spectrometry, Screening Performance Indicators, Michigan, 2010

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Phenylketonuria	112,680	17			0.006	58.8
Classic (PKU)			4	1:28,170		
Mild			2	1:56,340		
Benign Hyperphenyl-alaninemia (H-PHE)			3	1:37,560		
Biopterin Cofactor Defects (BIOPT)			1	1:112,680		
Total			*10*	*1:11,268*		
Argininemia (ARG)		8	1	1:112,680	0.006	12.5
Citrullinemia (CIT)/CIT II/ASA		11	0	-	0.010	-
Tyrosinemia (TYR I)		41	0	-	0.036	-
Homocystinuria (HCY)/ Hypermethioninemia (MET)		6	3	1: 37,560	0.003	50.0
Maple Syrup Disease (MSUD)		9	0	-	0.008	-

Table 9: Organic Acid Disorders Detected by Tandem Mass Spectrometry, Screening Performance Indicators, Michigan, 2010

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Isovaleric Acidemia (IVA)/2-Methylbutyryl-CoA Dehydrogenase Deficiency (2MBG)	112,680	2	0	-	0.002	-
3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC)		14	5	1:22,536	0.008	35.7
Glutaric Acidemia Type I (GA I)		14	1	1:112,680	0.012	7.1
Propionic Acidemia (PA)/ Methylmalonic Acidemia (MMA)		31	5	1:22,536	0.023	16.1
3-OH 3-Methyl Glutaric Aciduria (HMG)/3-Methylglutaconic Aciduria (3MGA)		8	0	-	0.007	-
Isobutyryl-CoA Dehydrogenase Deficiency (IBG)		22	5	1:22,536	0.015	22.73

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 10: Fatty Acid Oxidation Disorders Detected by Tandem Mass Spectrometry, Screening Performance Indicators, Michigan, 2010

Disorder	Newborns N	Total + N	Confirmed + (N)	Positive Detection Rate	FPR (%)	PPV (%)
Carnitine Uptake Defect-(CUD)	112,680	26	0	-	0.023	-
Short-Chain Acyl-CoA Dehydrogenase deficiency (SCAD)		22	10	1:11,268	0.011	45.5
Carnitine Palmitoyltrans-ferase I Deficiency (CPT I)		1	0	-	0.001	-
Carnitine/Acylcarnitine Translocase Deficiency-(CACT)/Carnitine Palmi-toyltransferase II Defi-ciency (CPT II)		6	1	1:112,680	0.004	16.7
Glutaric Acidemia Type II (GA II)		1	1	1:112,680	0.0	100.0
Medium-Chain Acyl-CoA Dehydrogenase Defi-ciency (MCAD)		12	11	1:10,244	0.001	91.7
Very Long-Chain Acyl-CoA Dehydrogenase Defi-ciency (VLCAD)		8	1	1:112,680	0.006	12.5
Medium/Short-chain L-3-hydroxy Acyl-CoA Dehy-drogenase Deficiency (M/SCHAD)		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 11 because their performance metrics have been previously reported. Disorders not detected in 2010 and detected disorders with no borderline positive screens are also excluded from Table 11, as there would be no change in screening performance.

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 11, the FPRs and PPVs among strong positive screens are significantly improved relative to the overall screening performance metrics among all positive screens. Maternal cases and carriers identified through NBS are not included in Table 11.

Table 11: Screening Performance Metrics (FPR and PPV) among Strong Positive Screens compared to All Positive Screens, Michigan, 2010

Disorder Type	Among All +		Among Strong +	
	FPR	PPV	FPR	PPV
	%	%	%	%
Galactosemia	0.01	40.74	0.001	75.00
Biotinidase Deficiency	0.19	5.80	0.0	100.0
Congenital Hypothyroidism (CH)	1.02	8.08	0.146	30.80
Congenital Adrenal Hyperplasia (CAH)	0.12	3.57	0.020	17.86
Phenylketonuria (PKU)*	0.01	58.82	0.0	100.0
Homocystinuria (HCY)/ Hypermethion-inemia (MET)*	0.003	50.00	0.002	60.00
Propionic Acidemia (PA) / Methylmalonic Acidemia (MMA)*	0.02	16.13	0.005	40.00
Isobutyryl-CoA Dehydrogenase Defi-ciency (IBG)*	0.02	22.73	0.014	23.81
3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC)*	0.01	35.71	0.002	71.43
Carnitine/Acylcarnitine Translocase De-ficiency- (CACT)/Carnitine Palmitoyl-transferase II Deficiency (CPT II)*	0.004	16.67	0.0	100.0
Short-Chain Acyl-CoA Dehydrogenase deficiency (SCAD)*	0.01	45.45	0.010	47.62
Very Long-Chain Acyl-CoA Dehydro-genase Deficiency (VLCAD)*	0.01	12.50	0.005	14.29

**MS/MS Disorders*

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 galactosemia is reduced 16-fold, and the PPV is increased nearly 2-fold among strong positive screens relative to all positive screens. Both strong positives for biotinidase deficiency were confirmed with disease, resulting in a 17-fold increase in PPV for strong positives compared to all positives.

The FPR for CH is reduced nearly 7-fold for strong positive screens, and the PPV is increased approximately 4-fold. The FPR and PPV for CAH are decreased and increased by 6-fold and 5-fold, respectively, among strong positives.

Among MS/MS disorders, all eight strong positives for PKU and the one strong positive for CPTII confirmed with disease, meaning the PPV among strong positives was 100% and the FPR was 0%. The FPR and PPV decreased and increased 4-fold and 3-fold, respectively, for PA/MMA and 4-fold and 2-fold, respectively, for 3MCC. Since nearly all positive screens for IBG, SCAD, and VLCAD were strong positives, the FPR and PPV improved only slightly among strong 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 2010, a total of 3,124 infants were identified as carriers of a disease included in the NBS panel, following an abnormal screen (Table 12). The majority of these infants (n=2,856) had sickle cell trait. Over 250 infants (n=258) were cystic fibrosis carriers, two infants were citrullinemia carriers, five were galactosemia carriers, thre were VLCAD carriers, and one was identified as a biotinidase carrier.

Table 12: Carriers Identified from Newborn Screening, Michigan, 2010

Disorder	N
Biotinidase	1
Citrullinemia	2
Cystic fibrosis	258
Galactosemia	5
Sickle Cell Trait	2,856
VLCAD	3

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

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 2010, five maternal disorders were identified following an infant's positive NBS (Table 13). Two infants with a strong positive screen for 3MCC were confirmed normal, but the disorder was identified in the mothers. Three mothers were confirmed with Vitamin B12 deficiency following their infant's positive screen for PA/MMA.

Table 13: Maternal Disorders Identified from Newborn Screening, Michigan, 2010

Maternal Disorder	N
3-Methylcrotonyl-CoA carboxylase deficiency (3MCC)	2
Vitamin B12 deficiency	3

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

IV. Healthy People 2020 NBS-related Objectives

Healthy People provides science-based, 10-year national objectives for improving the health of all Americans.[1] For the past 30 years, Healthy People has produced a framework for public health prevention priorities and actions. Healthy People has established benchmarks and monitored progress over time to: 1) encourage collaborations across sectors; 2) guide people toward making informed health decisions; and 3) measure the impact of prevention activities.

In December 2010, the U.S. Department of Health and Human Services released Healthy People 2020 (HP 2020), which contains new 10-year goals and objectives. HP 2020 is the end product of an iterative process involving a variety of review groups including federal, state, and local government staff, public health and prevention experts, and the general public. Based on this review process, several new areas of health were included in HP 2020. These areas are diverse and include topics such as adolescent health, genomics, and blood disorders and blood safety.

Several objectives included in HP 2020 are directly related to the NBS process or to populations identified through NBS. Table 14 lists the objectives for NBS overall, as well as whether Michigan can measure those objectives and which data sources will be used to measure each objective. Table 15 lists the same information for objectives related to those with hemoglobinopathies.

Table 14. Healthy People 2020 Objectives related to Newborn Screening, Data Sources used for each Objective, and Baseline Michigan Data

Number	Title	Is MI able to measure?	Data source(s)	Baseline
MICH-32.1	Increase the number of States and the District of Columbia that verify through linkage with vital records that all newborns are screened shortly after birth for conditions mandated by their State-sponsored screening program	Yes	Newborn screening records linked to live births records	Michigan has routinely conducted this linkage since 2007. In 2010, the linkage and subsequent follow-up identified that 99.6% of live births in Michigan were screened.
MICH-32.2	Increase the proportion of screen-positive children who receive follow-up testing within the recommended time period	Yes	NBS databases	In 2010, 89.4%* of children received follow-up testing within 7 days of birth.
MICH-32.3	(Developmental) Increase the proportion of children with a diagnosed condition identified through NBS who have an annual assessment of services needed and received	Yes	NBS databases	To be determined

**Includes infants who had strong positive initial screens for any of the MS/MS disorders or galactosemia, confirmed with a disorder requiring treatment, and were born in Michigan.*

1. http://www.healthypeople.gov/2020/about/default.aspx. Accessed June 16, 2011.

Table 15. Healthy People 2020 Objectives related to Hemoglobinopathies, Data Sources used for each Objective, and Baseline Michigan Data

Number	Title	Is MI able to measure?	Data source(s)	Baseline
BDBS-1	Vaccinations of persons with hemoglobinopathies	Yes	Michigan Care Improvement Registry	Of those aged 19-35 months and born 2004-2008, approximately 66% of children with SCD completed the 4:3:1:3:3:1:4 series.
BDBS-2	Patient and family referral for hemoglobinopathies	No	To be determined	To be determined
BDBS-3	Hemoglobinopathies care in a medical home	Yes	Health Status Assessment	Of those born 2005-2010, approximately 33 (35%) have a primary care physician, 2 of which have a hematologist for primary care.
BDBS-4	Screening for complications of hemoglobinopathies	Yes	Health Status Assessment	Of those born 2005-2010, approximately 14% had Transcranial Doppler screening in the past 12 months. Of those screened, 17% had abnormal results.
BDBS-5	Disease-modifying therapies for hemoglobinopathies	Yes	Health Status Assessment	Of those born 2005-2010, approximately 11% are currently on hydroxyurea therapy. Of those not on hydroxyurea, 70% have discussed it with a health professional in the past year.
BDBS-6	Penicillin prophylaxis for SCD	Yes	Health Status Assessment, NBS Follow-up database	Of those born in 2010 and diagnosed with SCD, 46 out of 50 with a known penicillin initiation date (92%) began treatment before 4 months of age.
BDBS-7	Hospitalizations for SCD	Yes	Health Status Assessment, Michigan Inpatient Database	Children with born 2005-2010 were admitted to the hospital an average of 1.6 times during the previous year. In 2007, there was an estimated 4,570 hospital stays during which sickle cell disease was noted as a diagnosis.
BDBS-8	High school completion among those with hemoglobinopathies	No	To be determined	To be determined
BDBS-9	Community-based organization campaigns for hemoglobinopathies	Yes	SCDAA, NBS Follow-up database	To be determined
BDBS-10	Awareness of hemoglobinopathy carrier status	Yes	SCDAA, NBS Follow-up database	To be determined

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 16 reports specimen characteristics by nursery type. Although 10.9% of infants were admitted to the NICU, 41% and 28% of strong and borderline positive screens were received from infants in the NICU, respectively. Isolated elevations of one or more amino acids and/or acyl-carnitines were also more prevalent among specimens received from infants in the NICU; these elevations are commonly associated with infants receiving total parenteral nutrition or transfusions or low birth weight or preterm infants. While the overall number of unsatisfactory specimens was greatest among hospital nurseries, the proportion of unsatisfactory specimens was greatest among non-hospital samples (4.4%). 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 5,000 specimens required follow-up in 2010.

Table 16: Specimen Characteristics by Nursery Type, Michigan, 2010

Indicator	Type of Birth					
	Regular Nursery		NICU		Non-Hospital	
	N	%	N	%	N	%
Strong Positive Specimens	224	0.22	158	1.29	4	0.99
Borderline Positive Specimens	1,058	1.06	422	3.44	11	1.56
All Positive Specimens*	1,623	1.63	643	5.24	17	2.40
Isolated elevations of amino acids and acyl-carnitines	12	0.01	545	4.44	0	-
Unsatisfactory Specimens	1,534	1.54	517	4.22	31	4.38
Late (>6 days) Specimens	63	0.06	36	0.29	55	7.85
Early (<1 day) Specimens	365	0.37	883	7.20	2	0.28
Transfused Specimens	0	-	126	1.03	0	-
Specimens Missing Demographics **	10,954	10.99	969	7.90	69	9.76
Total Births Screened	99,708	88.5	12,265	10.9	707	0.6

**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 2010, the quarterly reports include five indicators. Table 17 lists the indicators and the performance goal for each indicator.

Table 17: Indicators and Performance Goals for Newborn Screening, Michigan, 2010

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

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

Table 18 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 just under 3% of screens being collected more than 36 hours after birth. Of note, nearly 60% 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 and had over 97% of specimens received in the state laboratory within four days of collection. Non-hospital births were close to, but did not meet, the goal. None of nursery types met the goal for unsatisfactory specimens for 2010. However, this may have been caused card defects due to a specific printing of NBS cards and not related to blood collection practices. The issue with the card defects was resolved during 2010 and should not affect the measure for 2011. Both NICUs and non-hospital births met the batching goal, while regular nurseries did not. For recording of the NBS card number on birth certificates, neither regular nurseries or non-hospital births met the goal. However, birth certificates coming from regular nurseries were approximately 10 times more likely to have the NBS kit number recorded than certificates coming from non-hospital births.

During the fourth quarter of 2010, two indicators related to the Michigan BioTrust for Health were added to the quarterly reports. These indicators include: 1) percent of specimens with a returned BioTrust for Health consent form and 2) percent of forms completed appropriately based on parent decision to consent or decline. Statistics for these measures will be included in next year's annual report.

Table 18: Measures for Newborn Screening, by Nursery Type, Michigan, 2010

Measure	Nursery Type	N	%	Met Goal?
Late Screens	Regular	2,859	2.9	No
	NICU	797	6.5	No
	Non-hospital	417	59.5	No
Courier Time	Regular	96,825	97.7	Yes
	NICU	11,874	97.4	Yes
	Non-hospital	585	85.9	No
Unsatisfactory Screens	Regular	1,460	1.5	No
	NICU	426	3.5	No
	Non-hospital	25	3.5	No
Batching	Regular	735	3.5	No
	NICU	106	1.7	Yes
	Non-hospital	1	0.2	Yes
NBS Card Number	Regular	92,213	89.7	No
	NICU*	NA		
	Non-hospital	89	8.7	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 19 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 20). As indicated in Table 19, time to treatment ranged from one to 125 days after birth 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 AND BIOTINIDASE DEFICIENCY

Seven of the 11 cases of Duarte galactosemia were treated within 14 days of life. The sole case of profound biotinidase deficiency was treated on the eighth day of life. Three cases of partial biotinidase deficiency were treated by the first week of life; the remaining nine cases were treated beyond the first week of life.

MS/MS DISORDERS

Fifty-four newborns were confirmed with disorders detected by MS/MS (three newborns with hyperphenylalaninemia and three newborns with MET did not require treatment).

Six of the seven cases of PKU were treated within the first week of life; the remaining case was treated on the ninth day of life. One case of ARG was treated beyond two weeks of age, but the child was treated within five days of the positive screen being received by the state laboratory.

Fourteen of the 16 cases of organic acid disorders had treatment started before eight days of life. The remaining two cases (both MMA) were treated on the ninth and eleventh day of life, respectively. All infants identified with GA I (n=1), 3MCC (n=5), and IBG (n=5) had treatment initiated within the first week of life.

Of the 23 infants with fatty acid oxidation disorders and a treatment start date, all were treated within the first week of life.

ENDOCRINE DISORDERS-CAH AND CH

The salt-wasting form of CAH is life-threatening in the first few weeks of life. Four of the five CAH cases detected were salt-wasting. All four salt-wasting cases of CAH were treated within the first two weeks of life (Days 1, 6, 8 and 13). 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 CH cases with a strong positive screen, 48 (66%) were treated by the 14th day of life.

Table 19: Time to Treatment of Amino Acid Disorders, Organic Acid, Fatty Acid Oxidation, and Endocrine Disorders, Michigan, 2010

Disorder		Total	Treatment Time (days from birth)			
			N			
		N	1-7	8-14	>14	Treatment Time Range (days)
Galactosemia	Duarte (DG)	11	2	5	4	3-95
Biotinidase Deficiency	Partial	12	3	2	7	6-58
	Profound	1		1		8
Amino Acid Disorders	ARG	1			1	22
	PKU					
	Classic	4	3	1		5-9
	Mild	2	2			7
	Hyperphenylalaninemia*	3				
	BIOPT	1	1			2
	MET*	3				
	Total	*14*	*6*	*1*	*1*	*2-22*
Organic Acid Disorders	PA/MMA	5	3	2		4-11
	GA I	1	1			6
	3MCC	5	5			1-6
	IBG	5	5			2-6
	Total	*16*	*14*	*2*		*2-11*
Fatty Acid Oxidation Disorders	SCAD	10	10			3-7
	MCAD	11	11			1-6
	VLCAD	1	1			6
	GAII[1]	1				
	CPTII	1	1			7
	Total	*24*	*22*	*1*		*1-7*
Endocrine Disorders	CH					
	Borderline	28		1	27	12-125
	Strong	73	24	24	25	5-65
	CAH					
	Salt-wasting	4	2	2		1-13
	Non salt-wasting	1	1			4

[1]Baby expired before treatment began.
*Disorder does not require treatment.

HEMOGLOBINOPATHIES

Table 20 reports the time to treatment among newborns with hemoglobinopathies. The target is to initiate penicillin prophylaxis by four months of life. Of the 49 cases having a penicillin start date reported, 92% 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 2% began treatment beyond six months of age.

Table 20: Time to Penicillin Initiation for Sickle Cell Disorders, Michigan, 2010

Disorder	Penicillin Prophylaxis Initiation Time			
	< 120 days	**120-149 days**	**150-179 days**	**≥ 180 days**
Sickle Cell Disorders*	45 (91.8%)	3 (6.1%)	1 (2.0%)	1 (2.0%)

*11 cases missing penicillin initiation date

VI. Conclusions

NBS is a critical public health program protecting the lives of our State's newest residents. In 2010, the NBS Laboratory screened 112,986 infants, and the NBS Follow-up Program tracked approximately 5,000 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 280 newborns were identified with a disorder by NBS in 2010. Since NBS began in Michigan in 1965, 4,691 newborns have been diagnosed and treated.

Future plans include continuing to develop innovative methods for using administrative databases to promote long-term follow-up by monitoring the health outcomes and healthcare utilization of those with disorders diagnosed via NBS. In conclusion, we are continuing to both expand and refine the NBS Program in order to better protect the health of infants born in Michigan.