Genetics inMedicine | ORIGINAL RESEARCH ARTICLE

Developing a public health-tracking system for follow-up of newborn screening metabolic conditions: a four-state pilot project structure and initial findings

Cynthia F. Hinton, PhD, MPH[1], Cara T. Mai, MPH[1], Sarah K. Nabukera, MD, DrPH[2], Lorenzo D. Botto, MD[3], Lisa Feuchtbaum, DrPH, MPH[4], Paul A. Romitti, PhD, MS[5], Ying Wang, PhD, MPH[6], Kimberly Noble Piper, RN, BS[7] and Richard S. Olney, MD, MPH[1]

Purpose: The aim of this study was to describe the methods, cases, and initial results of a pilot project using existing public health data collection programs (birth defect surveillance or newborn screening) to conduct long-term follow-up of children with metabolic disorders.

Methods: California, Iowa, New York, and Utah expanded birth defect surveillance or newborn screening programs to collect long-term follow-up data on 19 metabolic disorders. Data elements to monitor health status and services delivered were identified, and record abstraction and data linkages were conducted. Children were followed up through to the age of 3 years.

Results: A total of 261 metabolic cases were diagnosed in 1,343,696 live births (19.4 cases/100,000; 95% confidence interval = 17.1–21.8). Four deaths were identified. Children with fatty acid oxidation disorders had a higher percentage of health service encounters compared with children with other disorders of at least one health service encounter (hospitalization, emergency room, metabolic clinic, genetic service provider, or social worker) except for hospitalizations; children with organic acid disorders had a higher percentage of at least one hospitalization during their third year of life than children with other disorders.

Conclusion: Existing public health data programs can be leveraged to conduct population-based newborn screening long-term follow-up. This approach is flexible according to state needs and resources. These data will enable the states in assessing health burden, assuring access to services, and supporting policy development.

Genet Med advance online publication 5 December 2013

Key Words: long-term follow-up; newborn screening metabolic disorders; public health surveillance

INTRODUCTION

Newborn screening (NBS) long-term follow-up (LTFU) begins on confirmed diagnosis of a disorder[1] and may continue throughout life. With the expansion of the recommended uniform screening panel in all the US states,[2] it has become increasingly important to develop the means to understand the long-term health outcomes and resource use in newborns detected through public health NBS. Additionally, national activities such as the charter of the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) in 2003 and passage of the Newborn Screening Saves Lives Act (NBSSLA 2008) have increased interest nationally to better understand the long-term outcomes. The SACHDNC has also issued policy statements on the importance of LTFU.[3,4]

The components of LTFU include care coordination through a medical home, evidence-based practice, continuous quality improvement, and new knowledge discovery to maximize optimal outcomes for affected children.[3] However, population-based, LTFU data for such children are challenging to capture due to the following reasons: (i) lack of programs in place to systematically capture and assess outcomes and (ii) lack of standards for data elements, sources, and case definitions.[5,6] Nationally, efforts are beginning to explore the means to capture LTFU data. The Maternal and Child Health Bureau of the Health Resources and Services Administration funded a national network of regional genetics and NBS collaboratives[7] that produced several projects aimed at strengthening LTFU.[8–10] The National Institute of Child Health and Human Development funded the Newborn Screening Translation Research Network to develop data capacity among clinical centers to support outcomes research.[11]

Recently, the Centers for Disease Control and Prevention (CDC) funded a pilot project to enhance the collection and quality of population-based data for children with a confirmed metabolic NBS disorder via existing birth defect surveillance and NBS programs. The purpose of the project is to demonstrate the feasibility of expanding existing population-based, public health data collection programs (birth defect

At the time of this study, S.K.N. was working with the University of Iowa.
[1]Centers for Disease Control and Prevention, Atlanta, Georgia, USA; [2]Social and Scientific Systems, Silver Spring, Maryland, USA; [3]Division of Medical Genetics, Department of Pediatrics, University of Utah, Salt Lake City, Utah, USA; [4]Genetic Disease Screening Program, California Department of Public Health, Sacramento, California, USA; [5]University of Iowa, Iowa City, Iowa, USA; [6]New York State Department of Health, Albany, New York, USA; [7]Iowa Department of Public Health, Des Moines, Iowa, USA. Correspondence: Cynthia F. Hinton (chinton@cdc.gov)

Submitted 10 July 2013; accepted 3 October 2013; advance online publication 5 December 2013. doi:10.1038/gim.2013.177

surveillance or NBS) to conduct LTFU of children with 1 of the 19 metabolic disorders through to the age of 3 years. Such high-quality, collaborative data collection programs are needed to conduct surveillance, maintain assurance of care, identify areas for quality improvement, and better understand the epidemiology of recently added NBS disorders. Existing efforts to collaboratively collect and disseminate birth defect surveillance data have largely focused on structural malformations and chromosomal disorders.[12] The addition of case finding and LTFU for confirmed NBS disorders would utilize existing standardized data elements (such as demographic information) to provide centralized, uniform reporting of such disorders by demographic and clinical characteristics. This article presents an overview of the project methodology, case inclusion, and initial descriptive results.

MATERIALS AND METHODS

Four states, California, Iowa, New York, and Utah, received a CDC grant to participate in this pilot project. Iowa and Utah expanded their state-wide, ongoing, active birth defect surveillance programs to include LTFU data on confirmed metabolic disorders; New York strengthened the existing linkages among administrative and clinical program databases (New York City births were not included)[13]; and California enhanced its state-wide NBS reporting program to better collect LTFU data.[14] To carry out LTFU, each state had legal authority to access the data needed, as well as established relationships and demonstration of cooperation with appropriate partners (e.g., birth defect surveillance and NBS programs, vital records, and appropriate health-care providers), to facilitate access to both short- and long-term outcome data.

Birth cohorts

Each state was required to monitor a minimum of 100,000 live births for a 3-year follow-up period. State and CDC investigators developed a data set with variables for demographics, health-care service encounters, and major clinical outcomes. Cases were live-born infants with a confirmed metabolic disorder identified by the respective state's NBS program. The birth cohorts for each state are summarized in Table 1. The goal was to follow up each child through to the third birthday, with data collection completed for each year of follow-up. Attrition could result from the following: (i) death, (ii) moving out of the catchment area, (iii) treatment deemed unnecessary by the provider, (iv) parental refusal of follow-up, or (v) lost to follow-up.

Table 1 State birth cohorts

State	Cohort years	Live births
California	2006[a]–2007	808,429
Iowa	2005–2007	120,815
New York[b]	2006–2007	250,280
Utah	2006–2008	164,172
Total		1,343,696

[a]2006 data are for August to December. [b]Excluding New York City.

Case definition

This project relied on each state to use its defined case definition for the 19 selected metabolic disorders for case inclusion (Table 2). Case definitions for very-long-chain acyl-CoA dehydrogenase deficiency (VLCADD) and 3-methylcrotonyl-CoA carboxylase deficiency were known to differ somewhat across states; project medical geneticists developed a surveillance case definition for each disorder (see **Supplementary Table S1** online) and reviewed all cases of very-long-chain acyl-CoA dehydrogenase deficiency and 3-methylcrotonyl-CoA carboxylase deficiency in the cohort to standardize the final case inclusion.

Data collection

Standardized data elements were developed to capture information about health status and use of services. Specific data domains included diagnosis, treatments (e.g., medical diet and medications), encounters with specific service providers (e.g., medical geneticist, metabolic dietitian, genetic counselor, and social worker), growth, development, hospitalizations, comorbidities, and mortalities. A data dictionary, modeled based on the National Birth Defects Prevention Network data set,[15] was

Table 2 Population-based prevalence of the 19 metabolic disorders from four states (California, Iowa, New York, and Utah)

Type	Disorder	Cases	Percentage of cases	Rate/100,000 live births (95% CI)
Organic acid	3MCC	42	16.1	3.1 (2.2–4.1)
	MUT	15	5.7	1.1 (0.6–1.7)
	GA1	11	4.2	0.8 (0.3–1.3)
	IVA	4	1.5	0.3 (0.0–0.6)
	MMA, cblA and cblB forms	4	1.5	0.3 (0.0–0.6)
	PROP	2	0.8	0.2 (0.0–0.4)
Fatty acid	MCADD	80	30.7	6.0 (4.7–7.3)
	VLCADD	19	7.3	1.4 (0.8–2.0)
	CUD	12	4.6	0.9 (0.4–1.4)
	LCHADD	1	0.4	0.1 (0.0–0.2)
Amino acid	PKU	58	22.2	4.3 (3.2–5.4)
	MSUD	7	2.1	0.5 (0.1–0.9)
	ASA	4	1.5	0.3 (0.0–0.6)
	CIT	2	0.8	0.2 (0.0–0.4)
Total[a]		261	100.0	19.4 (17.1–21.8)

3MCC, 3-methylcrotonyl-CoA carboxylase deficiency; ASA, argininosuccinic acuduria; BKT, β-ketothiolase deficiency; CUD, carnitine uptake defect; CI, confidence interval; CIT, citrullinemia; GA1, glutaric acidemia type 1; HCY, homocystinuria; HMG, hydroxymethylglutaryl lyase deficiency; IVA, isovaleric acidemia; LCHADD, long-chain hydroxyacyl-CoA dehydrogenase deficiency; MSUD, maple syrup urine disease; MCADD, medium-chain acyl-CoA dehydrogenase deficiency; MCD, multiple-CoA carboxylase deficiency; MMA, methylmalonic aciduria; MUT, methylmalonyl-CoA mutase deficiency; PKU, phenylketonuria; PROP, propionic acidemia; TFP, trifunctional protein deficiency; VLCADD, very-long-chain acyl-CoA dehydrogenase deficiency.

[a]There were no cases of HMG, BKT, MCD, TFP, or HCY.

created (see **Supplementary Table S2** online). Resources used to develop the data elements included the American College of Medical Genetics and Genomics' ACTion Sheets, the Regional Genetics and NBS Collaboratives,[8,10,16,17] and the existing data dictionaries used by the participating states' surveillance and NBS programs.

Key staff, including principal investigators and data managers, from the four participating sites and CDC met via biweekly conference calls over the first year to develop the data elements. A data source hierarchy was established for each element in consultation with medical record abstractors. A mid-year data collection trial was undertaken to assess the process and the feasibility of merging data from each state. Data elements were refined accordingly, and by the end of the first year, the data dictionary had 121 elements, plus additional text fields for further annotation of the data. Of these elements, 40 (33%) overlapped with the National Birth Defects Prevention Network recommended data elements for birth defect surveillance and included demographics, diagnostic tests, and mortality.

Follow-up data were collected using different strategies. Metabolic clinics in California are contractually obligated to submit annual data to the Genetic Disease Screening Program in the California Department of Public Health. Iowa, New York, and Utah had trained abstractors to collect clinical and administrative data. Each state submitted anonymized, individual-level data for each year of follow-up. Data were transferred to CDC via a secured file transfer protocol. Subsequent data transmission occurred semiannually, and the data elements continued to be refined over the course of the project. All data analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC).

RESULTS

The state NBS programs identified 261 infants with one of the 19 eligible metabolic disorders among 1,343,696 live births (**Table 2**) for an overall prevalence of 19.4/100,000 live births (95% confidence interval = 17.1–21.8). Descriptive epidemiology of the infants and mothers are provided in **Table 3**. Approximately 60% of the infants were non-Hispanic white and 26% were Hispanic. A majority of mothers had health insurance, with 52% covered by private insurance and 38% covered by Medicaid or other public insurance. Cases were primarily located in metropolitan counties, with 49% located in a metro county of 1 million or greater population. A majority of the mothers (62%) were between 23 and 34 years of age. Three disorders accounted for 69% of all cases: medium-chain acyl-CoA dehydrogenase deficiency (6.0/100,000 live births), phenylketonuria (PKU; 4.3/100,000 live births), and 3-methylcrotonyl-CoA carboxylase deficiency (3.1/100,000 live births) (**Table 2**).

Health-care service encounters over the 3-year follow-up period are summarized in **Table 4**. Changes in denominators reflect children who died or moved out of the catchment area the previous year. During the first year, 38% of children had at least one hospitalization and 27% had at least one emergency room visit. At the year 3 of follow-up, a drop was observed in both hospitalization (12%) and emergency room visits (14%).

Table 3 Case contribution by state and case demographic information

Characteristic	*N*	Percentage
Confirmed metabolic cases by state		
California	132	51
Iowa	21	8
New York (excluding New York city)	57	22
Utah	51	19
Infant sex		
Male	147	56
Female	114	44
Maternal race/ethnicity		
White/non-Hispanic	155	59
Black/non-Hispanic	10	4
Hispanic	69	26
Asian/Pacific Islander	22	8
Other/unknown	5	2
Insurance		
Private	136	52
Medicaid/public	98	38
Self-pay	7	3
Other	6	2
Unknown	14	5
Rural–urban continuum		
Large urban (metro area ≥1 million population)	129	49
Small urban (metro area <1 million population)	112	43
Large rural (nonmetro area with urban population ≥20,000)	9	3
Small rural (non-metro area with urban population <20,000)	11	4
Mother's education		
<HS	58	22
HS/GED	60	23
Some college/associate's degree	60	23
College/postcollege degree	77	30
Unknown	6	2
Maternal age (years)		
≤23	59	23
24–34	162	62
≥35	40	15
Gravidity		
1	96	37
2	73	28
≥3	89	34
Unknown	3	1

GED, general education degree; HS, high school.

Table 4 Number of infants or children who had at least one health service encounter by disorder type and year of follow-up

		Disorder type			
		Organic acid	Fatty acid	Amino acid	Total[a]
Encounter type	**Year of follow-up**	***N* (%)**	***N* (%)**	***N* (%)**	***N* (%)**
≥1 Hospitalization for the year	Year 1	34 (34)	42 (42)	23 (23)	99/261 (38)
	Year 2	15 (36)	20 (48)	7 (17)	42/248 (17)
	Year 3*	14 (50)	11 (39)	3 (11)	28/224 (12)
≥1 ER visit for the year	Year 1	23 (32)	32 (45)	16 (23)	71/261 (27)
	Year 2	18 (32)	24 (43)	14 (25)	56/248 (23)
	Year 3	12 (35)	12 (35)	10 (29)	34/224 (15)
≥1 Metabolic clinic visit for the year	Year 1	66 (29)	98 (43)	66 (29)	230/261 (88)
	Year 2	48 (25)	82 (43)	61 (32)	191/248 (77)
	Year 3	39 (24)	66 (41)	58 (36)	163/224 (74)
≥1 Visit with a metabolic geneticist for the year	Year 1	73 (28)	104 (42)	68 (28)	245/261 (94)
	Year 2	56 (22)	83 (32)	64 (25)	203/248 (82)
	Year 3	51 (28)	75 (41)	57 (31)	183/224 (82)
≥1 Visit with a metabolic dietitian for the year	Year 1*	52 (25)	85 (42)	68 (33)	205/261 (78)
	Year 2*	33 (42)	76 (45)	59 (35)	168/248 (68)
	Year 3	31 (22)	62 (43)	50 (35)	143/224 (64)
≥1 Visit with a genetic counselor for the year	Year 1	39 (30)	58 (44)	35 (26)	132/261 (51)
	Year 2	14 (23)	30 (50)	16 (27)	60/248 (24)
	Year 3	12 (28)	17 (40)	14 (33)	43/224 (19)
≥1 Visit with a social worker for the year	Year 1	29 (30)	39 (41)	27 (28)	95/261 (36)
	Year 2	30 (35)	31 (36)	24 (28)	85/248 (34)
	Year 3	15 (28)	22 (41)	17 (32)	54/224 (24)

The denominator excludes cases who died or moved out of catchment area. The denominator for each percent is the number of cases for the disorder.

ER, emergency room.

[a]Due to rounding, numbers may not add up to 100. *$P < 0.05$.

Overall, 88% received care at a metabolic clinic at least once during their first year of life, 77% had at least one metabolic clinic visit during their second year, and 74% during their third year. During the first year of follow-up, 94% of children saw a metabolic geneticist at least once, 78% saw a metabolic dietitian, 51% saw a genetic counselor, and 36% saw a social worker. Compared with year 1, the percentage of encounters with each type of provider decreased during year 2 and further decreased during year 3.

Compared with children with amino acid or organic acid disorders, a higher percentage of children with fatty acid oxidation disorders had at least one encounter with each type of health service (Table 4) during the 3-year follow-up except for one health service: hospitalization. More children with organic acid disorders had at least one hospitalization during their third year of life compared with children with the other two groups of disorders. Hospitalizations for year 3 and dietitian visits for years 1 and 2 were differed significantly ($P < 0.05$)

There were four deaths identified before the age of 3 years (1 in 65 or 1.7% overall). Of these, two had VLCADD, one had methylmalonic aciduria, and one had glutaric acidemia type 1. The condition-specific mortality by the age of 3 years was 10.5% for VLCADD (2 deaths/19 affected), 25% for methylmalonic aciduria (1 death/4 affected), and 9% for glutaric acidemia type 1 (1 death/11 affected). Two deaths associated with VLCADD occurred at 4 days and 10 weeks of age, the death associated with methylmalonic aciduria occurred at 16 days of age, and the death associated with glutaric acidemia type 1 occurred at 21 months of age. The births of these four children were covered under public insurance. Among the four mothers of each deceased infant or child, three had less than high school education or high school graduation or general education degree. Each mother was a resident of a large urban area. There were no mortalities attributed to amino acid disorders.

DISCUSSION

With the expansion of disorders in the Secretary of Health and Human Services' Recommended Uniform Screening Panel,[18] health-care providers and public health programs are increasingly confronted with difficult questions on how best to monitor, follow up, and evaluate the success of NBS. From a public health perspective, critical gaps in knowledge remain, including

the population-wide impact of NBS conditions, comorbidities, and mortality and the associated use of services, disparities, and outcomes. Studies originating from metabolic clinics are helpful, particularly in establishing clinical guidelines, but limited in their ability to follow up an entire population, including those families who drop out of the clinical follow-up.

A population-based question requires a population-based solution and ideally one that is standard based, sustainable, and practical, focusing on key public health questions. State public health programs could benefit from considering the feasible methods to conduct and evaluate LTFU for affected children, especially by leveraging existing birth defects surveillance or NBS programs to conduct LTFU of affected children using standardized data elements. This pilot project not only improved the state-level data but also provided pooled data that permitted a better understanding of rare disorders that might otherwise require many years for a single state to gather enough cases to better understand the long-term outcomes of these children.

The guiding principle behind the data elements used was to capture enough information but not to become a burdensome activity for state programs to assess both access to specialty-care follow-up services and health outcomes of children with metabolic disorders detected through mandated NBS. Overall, the data elements will help public health programs to conduct core public health functions of assessment (prevalence, mortality, and morbidities), assurance (access to services and bridging gaps), and support policy development best practices (programmatic and clinical). Data on specific clinical visits, treatments, or laboratory values were not as detailed as those that might be captured through other NBS LTFU projects[8,11] or through focused clinical investigations. The data set is flexible and can be tailored to accommodate state needs and resources. At a minimum, a LTFU data set would include the diagnosis, providers (specialty or general pediatrician), and annual indicators of vital and follow-up status. A state might use the opportunity to verify treatment in a medical home, which could also be of benefit for children detected through NBS who might not be followed up in a specialty clinic.

Prevalence estimates for the most common disorders reported in this pilot project were comparable to other published US data. The estimate for 3-methylcrotonyl-CoA carboxylase deficiency (3.1/100,000 live births) was comparable with 2006 data from a four-state study of expanded NBS (2.4)[19] and from the National Newborn Screening Information System national database (2.3).[20] Likewise, the estimates for medium-chain acyl-CoA dehydrogenase deficiency (6.0/100,000 live births) and for PKU (4.3/100,000 live births) were compared, respectively, with those for medium-chain acyl-CoA dehydrogenase deficiency (5.8[19] and 5.3[20]) and PKU (5.2[19] (which included cases of clinically significant hyperphenylalaninemia) and 4.2[20]) from each of these previously mentioned data sources. Rates of common metabolic disorders (e.g., PKU) vary by race and ethnicity; therefore, some variation among states can be expected, given differences in population composition.[21] Furthermore, at the time of the data collection, there were no standard US-based surveillance case definitions; thus, case definitions might vary across states and regions.

Data for service encounters during the first 3 years of life showed that almost all children identified (94%) were seen by a metabolic geneticist at least once during their first year of life. This first-year visit is expected because most of these children would need to be seen for a diagnosis and treatment plan. By the third year, the number of children who saw a metabolic geneticist dropped to 82%. The second most commonly seen specialist was a metabolic nutritionist (78% in the first year and 64% in the third year). Such visits will vary based on the diagnosis (e.g., a child with PKU should have a service encounter with a dietitian, whereas a child with medium-chain acyl-CoA dehydrogenase deficiency might not). It is worth noting that there is no indication that 6% of the infants saw a metabolic geneticist at least once during their first year, an observation that would need to be confirmed through further study. There are no best practice guidelines by which to evaluate the types and frequency of service encounters over the 3-year pilot period. Moreover, for families of newborns identified through the respective state's dried blood spot screening, there are limited published reports about the numbers of encounters with genetic service providers.[22]

This public health surveillance approach has several strengths. First, existing public health programs were leveraged to identify and track children with metabolic disorders for 3 years. This permitted project activities to be included under public health surveillance laws or administrative rule, use established infrastructures and data elements, and minimize start-up costs. Second, our design was population based rather than clinical center based. Cases were identified through each state's NBS program rather than through a particular clinical-center catchment area, which permitted follow-up of a defined birth cohort to minimize selection bias. Third, each state used a multiple-source ascertainment that included vital records, NBS reports, and, in some instances, administrative databases, such as hospital discharge data. This multiple-source methodology can increase a program's sensitivity to monitor the long-term outcomes of children detected through NBS. The methodology also provides an opportunity to initiate or strengthen connections with other specialty providers, primary-care providers, and medical homes.

This project has several limitations. First, it was challenging to capture service encounters for other service providers beyond the genetic specialists, e.g., other medical geneticists (not metabolic), nursing encounters, and physical or occupational therapists. Possible reasons for this included data source limitations, need for such services in the first 3 years of life, or need for improved definitions of data elements. For example, the "nurse" term was generic so that it was challenging to capture such information uniformly. Second, the availability of certain outcome data was limited by the type of data sources. Although administrative databases yielded information on hospitalizations, emergency room visits, morbidities, and mortalities, they did not include

information on other variables, such as service encounters for other providers, treatments, and developmental outcomes. These data could only be obtained from a genetics clinic. During the course of the project, New York investigators added medical record abstraction to their methods in order to capture data from the genetics clinic data. Administrative data sources made it difficult to ascertain if hospitalizations or emergency room visits were due to the metabolic disorder or due to other factors. Because the service encounter outcomes data were obtained mostly from metabolic clinics, encounters or outcomes collected by primary-care providers or other providers would be missed in this model, without developing alternative sources and the ability to link data sets.[6] For instance, the family of a child with a mild metabolic disorder might decide to discontinue follow-up through the metabolic clinic and be managed by a primary-care provider. Due to the severity of many metabolic disorders, however, one would expect children to be managed by specialists at metabolic clinics.

Ideally, the need for LTFU spans from birth to adulthood, encompassing preconception and prenatal care for women. The length of time designated for LTFU is often determined by the rules and regulations of the state and by available resources. Long-term clinical studies are beyond the scope of typical public health surveillance, but the need to assure developmental outcomes and successful life transitions (entering school, adolescence, learning self-care, and transition to post-high school) remains a public health concern. The ability to link surveillance data with other public health systems could be tremendously useful to assure that children are receiving recommended well care (immunizations), appropriate early services (early intervention systems), and Medicaid claims (treatments and documenting health service utilization) and that they are assessing school progress (education). Incorporating informatics, such as HL7 and electronic health records, into existing birth defects surveillance can only help in improving states' abilities to conduct long-term follow-up of children detected through public health NBS. Leveraging existing resources becomes even more critical to LTFU success.

In summary, this project demonstrated the feasibility of expanding and enhancing state public health data collection programs to include LTFU for children detected by NBS. Public health surveillance in the 21st century will need to rely on multiple data sources to guide program planning, interventions, and family support.[23,24] It will also need to consider resource restraints and adapt to the changing landscape of NBS. For these reasons, an approach that leverages existing public health data collection programs may help decrease time to program implementation and operation costs. This public health surveillance approach is one of several regional and national efforts to contribute toward NBS LTFU data projects.[8–10,16,17,25] These projects collectively encourage collaboration among public health and clinical stakeholders to ensure optimal health and outcomes for persons with metabolic disorders.

SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at http://www.nature.com/gim

ACKNOWLEDGMENTS

This project was supported in part by the cooperative agreement no. DD08-810 from the National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (CDC). We acknowledge key individuals who contributed to the project: Christopher Johnson and Marilyn Sango-Jordan for newborn screening data and preparing the final data set in New York; Sunaina Dowray and Jennifer Carter for data coordination and management in California; Aliese Franck, Marcia L. Feldkamp, Amy E. Nance, and Miland Palmer for data abstraction and database preparation and support in Utah; Jan Vanderflugt, Florence Foo, and Carrie Fall for data abstraction in Iowa. In addition, we thank Coleen Boyle, Margaret Honein, Harry Hannon, and Carla Cuthbert from the CDC for their support of the project.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

DISCLOSURE

The authors declare no conflict of interest

REFERENCES

1. Pass KA, Lane PA, Fernhoff PM, et al. US newborn screening system guidelines II: follow-up of children, diagnosis, management, and evaluation. Statement of the Council of Regional Networks for Genetic Services (CORN). *J Pediatr* 2000;137(suppl 4):S1–S46.
2. Watson MS, Mann MY, Lloyd-Puryear MA, Rinaldo P, Howell RR; American College of Medical Genetics Newborn Screening Expert Group. Newborn screening: toward a uniform screening panel and system–executive summary. *Pediatrics* 2006;117(suppl 3):S296–S307.
3. Kemper AR, Boyle CA, Aceves J, et al. Long-term follow-up after diagnosis resulting from newborn screening: statement of the US Secretary of Health and Human Services' Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children. *Genet Med* 2008;10:259–261.
4. Hinton CF, Feuchtbaum L, Kus CA, et al. What questions should newborn screening long-term follow-up be able to answer? A statement of the US Secretary for Health and Human Services' Advisory Committee on Heritable Disorders in Newborns and Children. *Genet Med* 2011;13:861–865.
5. Hoff TP, Hoyt AMPH, Therrell BP, Ayoob MMPH. Exploring barriers to long-term follow-up in newborn screening programs. *Genet Med* 2006;8:563–570.
6. Hoff T, Ayoob M, Therrell BL. Long-term follow-up data collection and use in state newborn screening programs. *Arch Pediatr Adolesc Med* 2007;161:994–1000.
7. Puryear M, Weissman G, Watson M, Mann M, Strickland B, van Dyck PC. The regional genetic and newborn screening service collaboratives: the first two years. *Ment Retard Dev Disabil Res Rev* 2006;12:288–292.
8. Berry SA, Jurek AM, Anderson C, Bentler K; Region 4 Genetics Collaborative Priority 2 Workgroup. The inborn errors of metabolism information system: a project of the Region 4 Genetics Collaborative Priority 2 Workgroup. *Genet Med* 2010;12(suppl 12):S215–S219.
9. Sahai I, Eaton RB, Hale JE, Mulcahy EA, Comeau AM. Long-term follow-up to ensure quality care of individuals diagnosed with newborn screening conditions: early experience in New England. *Genet Med* 2010;12(suppl 12):S220–S227.
10. Singh RH, Hinman AR. Newborn dried bloodspot screening: long-term follow-up activities and information system requirements. *Genet Med* 2010;12(suppl 12):S261–S266.
11. Berry SA, Lloyd-Puryear MA, Watson MS. Long-term follow-up of newborn screening patients. *Genet Med* 2010;12(suppl 12):S267–S268.
12. Mai CT, Law DJ, Mason CA, McDowell BD, Meyer RE, Musa D; National Birth Defects Prevention Network. Collection, use, and protection of population-based birth defects surveillance data in the United States. *Birth Defects Res Part A Clin Mol Teratol* 2007;79:811–814.

13. Wang Y, Caggana M, Sango-Jordan M, Sun M, Druschel CM. Long-term follow-up of children with confirmed newborn screening disorders using record linkage. *Genet Med* 2011;13:881–886.
14. Feuchtbaum L, Dowray S, Lorey F. The context and approach for the California newborn screening short- and long-term follow-up data system: preliminary findings. *Genet Med* 2010;12(suppl 12):S242–S250.
15. National Birth Defects Prevention Network (NBDPN). *Guidelines for Conducting Birth Defects Surveillance.* In: Sever LE (ed). NBDPN: Atlanta, GA, 2004. http://www.nbdpn.org/bdsurveillance.html.
16. Kronn D, Mofidi S, Braverman N, Harris K; Diagnostics Guidelines Work Group. Diagnostic guidelines for newborns who screen positive in newborn screening. *Genet Med* 2010;12(suppl 12):S251–S255.
17. Wright EL, Van Hove JL, Thomas J; Mountain States Metabolic Consortium. Mountain States Genetics Regional Collaborative Center's Metabolic Newborn Screening Long-term Follow-up Study: a collaborative multi-site approach to newborn screening outcomes research. *Genet Med* 2010;12(suppl 12):S228–S241.
18. Secretary's Advisory Committee on Heritable Disorders in Newborns and Children. Recommended Uniform Screening Panel of the Secretary's Advisroy Committee on Heritable Disorders in Newborns and Children. http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/recommendedpanel/index.html. Accessed 11 February 2013.
19. CDC. Impact of expanded newborn screening–United States, 2006. *MMWR Morb Mortal Wkly Rep* 2008;57:1012–1015.
20. National Newborn Screening Information System. http://ww2.uthscsa.edu. Accessed 20 October 2009.
21. Feuchtbaum L, Carter J, Dowray S, Currier RJ, Lorey F. Birth prevalence of disorders detectable through newborn screening by race/ethnicity. *Genet Med* 2012;14:937–945.
22. Livingston J, Therrell BL Jr, Mann MY, et al. Tracking clinical genetic services for newborns identified through newborn dried bloodspot screening in the United States-lessons learned. *J Community Genet* 2011;2:191–200.
23. CDC. Public health surveillance in the United States: evolution and challenges. *MMWR* 2012;61(suppl):3–9.
24. CDC. Lexicon, definitions, and conceptual framework for public health surveillance. *MMWR* 2012;61(suppl):10–14.
25. Lloyd-Puryear MA, Brower A. Long-term follow-up in newborn screening: a systems approach for improving health outcomes. *Genet Med* 2010;12(suppl 12):S256–S260.