## Editorial

# Newborn Screening for Critical Congenital Heart Disease: Essential Public Health Roles for Birth Defects Monitoring Programs

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Newborn screening for critical congenital heart defects, added in September 2011 to the Recommended Uniform Screening Panel in the United States, is a new public health priority and has particular relevance for state birth defects surveillance programs. In this commentary, we review the background to potential involvement by birth defects programs with screening, and detail key questions that these programs can evaluate: (1) health outcomes after newborn screening among affected children; (2) missed primary targets of screening (i.e., affected children who were not screened or had false-negative screens); (3) burden and screening accuracy for secondary targets; (4) the role of altitude, sociodemographic characteristics, and other special circumstances; (5) the contribution of prenatal and clinical diagnoses before newborn screening; and (6) costs and service utilization. To address these issues, monitoring programs will need to pay particular attention to: (1) data sources and quality; (2) timeliness; (3) long-term follow-up for comprehensive outcomes; (4) reporting standards; and (5) state and national program coordination. Although some aspects of involvement with these screening programs will require new partnerships and paradigm shifts in birth defects program operations, the visibility of these screening programs among stakeholders will also provide birth defects programs with new opportunities to demonstrate their usefulness. *Birth Defects Research (Part A) 94:965–969, 2012.* © 2012 Wiley Periodicals, Inc.

In this special issue of *Birth Defects Research (Part A)*, the introduction to the 2012 National Birth Defects Prevention Network (NBDPN) surveillance report (Mai et al., 2012) highlights newly compiled U.S. data for seven types of critical congenital heart disease (CCHD): dextrotransposition of the great arteries, hypoplastic left heart syndrome, pulmonary atresia (with intact ventricular septum), tetralogy of Fallot, total anomalous pulmonary venous return, tricuspid atresia, and truncus arteriosus. Congenital heart defects in general, and newborn screening programs for CCHDs specifically, have become new public health priorities in the United States. State programs and national birth defects systems, assuming that they are adequately supported and enhanced, are uniquely positioned to play a key role in the implementation and ongoing evaluation of CCHD newborn screening. In this editorial, we outline avenues for birth defects programs to become effectively and integrally involved with this new public health focus. We believe that the potential benefits of such integration – in terms of improved quality of public health services and reduced costs – are considerable for both CCHD screening and birth defects surveillance.

## ACCELERATING HISTORICAL DEVELOPMENTS, BRIEFLY CONSIDERED

The seven types of CCHD highlighted in this year's NBDPN surveillance report were considered by a U.S. advisory committee as primary targets for pulse oximetry screening (Kemper et al., 2011). These seven CCHDs, which usually present in newborns with hypoxemia that might be missed clinically but identified by pulse oximetry, were designated previously by a working group led by the American Heart Association and the American Academy of Pediatrics (Mahle et al., 2009). The advisory committee's recommendation to include this type of

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screening in the Recommended Uniform Screening Panel was adopted by the U.S. Secretary of Health and Human Services in September 2011, and has been further endorsed by the American Academy of Pediatrics (Mahle et al., 2012). For effective screening implementation, the Health and Human Services Secretary reiterated the need for: new research data; evaluation as implementation occurs; and cost-effectiveness analyses (http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/recommendations/correspondence/cyanoticheartsecre09212011.pdf). Of note, several state legislatures are considering or have already passed legislative initiatives to mandate or move toward implementation of universal CCHD screening. Such implementation is occurring piecemeal and concurrently in many locations *before* the availability of population-based evaluation data from vanguard states. With the accelerating pace of discussions and implementation of CCHD screening, birth defects programs should emerge as crucial, widely available public health resources that can be put to work quickly and efficiently as part of ongoing monitoring and evaluation of screening.

## BIRTH DEFECTS PROGRAM CAPACITIES

What capacities are necessary for birth defects programs to be effectively involved in screening evaluations? Are such capacities already present in some states? If not, how can these capacities be achieved quickly? What role can population-based birth defects surveillance have in addressing gaps in knowledge that might impede fully successful implementation of universal CCHD screening? To begin addressing these questions, NBDPN investigators conducted surveys in 2010 and 2011, the results of which were compiled recently (Centers for Disease Control and Prevention, 2012). Of respondents from all 50 states and the District of Columbia, 43 reported having a birth defects surveillance program. Among these 43 programs, the majority reported being able to collect information that could be used to evaluate outcomes of interest, such as survival, links to support services, and even data to assess screening accuracy. Indeed, population-based data gathered before 2010 in state health departments already helped to evaluate the sensitivity and specificity of pulse oximetry screening, and provided early indications about the potential benefits of early identification to prevent delayed diagnoses and deaths from CCHD not recognized in newborn nurseries (Kuehl et al., 1999; Koppel et al., 2003; Aamir et al., 2007; Chang et al., 2008; Ng and Hokanson, 2010). Since then, more comprehensive analyses from other countries have addressed accuracy issues (de-Wahl Granelli et al., 2009; Riede et al., 2010; Ewer et al., 2012; Thangaratinam et al., 2012). However, there remains a need for ''real world'' data from widespread implementation across diverse populations. To gather such data, birth defects monitoring programs will need to further strengthen public health activities, even beyond those suggested in previous editorials (Correa and Kirby, 2010).

## ADDRESSING THE IMPORTANT QUESTIONS

In considering the role of birth defects surveillance programs in CCHD screening, it is helpful to return to two key concepts. First, newborn screening is not a test, but a comprehensive process, and this process ideally also involves follow-up assessment of a wide range of outcomes (Pass et al., 2000). Birth defects programs, if appropriately enhanced and integrated into the screening process, are well positioned to provide much of this information efficiently. Second, screening activities are by their nature long-term and ongoing. Thus, the related evaluations and monitoring of outcomes need to be ongoing and timely, and the information thus generated needs to be fed back quickly to the screening activities for systematic program improvement. These characteristics – ongoing, systematic, timely monitoring of birth defects linked to public health activities – are the core elements of birth defects surveillance (Hall et al., 2012). Whereas one-time studies are important for generating initial data, ongoing birth defects surveillance is and will continue to be an indispensable component of CCHD screening programs.

More specifically, Table 1 outlines some of the many lingering questions related to the evidence of benefits of CCHD screening, which can be addressed by evaluations through birth defects surveillance programs. For example, programs could provide new and continuously updated population-based data to quantify the burden, outcomes, and screening accuracy of pulse oximetry for the seven primary CCHDs and other heart defects identified through screening (defined here as cardiac ''secondary targets''). Some secondary targets have been reported in limited numbers or not at all in pilot studies (de-Wahl Granelli et al., 2009; Riede et al., 2010), particularly major defects obstructing the left ventricular outflow tract, such as critical aortic stenosis, coarctation of the aorta, and interrupted aortic arch.

Most notably, only statewide surveillance programs would systematically ascertain primary targets that might have been overlooked through current protocols, either by not being screened or by passing a pulse oximetry screen (false negatives). The frequency of missed cases and the related determinants are of critical importance not only in the initial implementation of screening but also as part of continuing quality improvement of the system, and every effort should be taken to minimize missed cases. Such events might occur due to local complications with implementation procedures, oximetry thresholds that might be inappropriate in special circumstances such as high altitudes, or other implementation realities that are inevitable with any widespread point-of-care screening program. The relative impact of these factors might vary in different areas or states; for this reason, surveillance programs ideally would be in place wherever screening occurs. Other data categories detailed in Table 1 of particular interest to surveillance programs include prenatal and clinical diagnoses before newborn screening; outcomes after screening such as hospitalizations, surgical interventions, or deaths; and cost-effectiveness analyses.

## IMPROVING BIRTH DEFECTS MONITORING

Table 2 highlights particular issues for birth defects programs concerned with CCHD screening evaluations. Briefly, there needs to be a relentless focus on quality, including standards on the accuracy of diagnoses compiled in surveillance data (Bedard et al., 2012), timeliness of ascertainment and reporting, and longitudinal outcomes beyond the newborn period. State-based programs

Table 1
Critical Congenital Heart Disease Newborn Screening: Questions for Birth Defects Programs Conducting Population-Based Surveillance

| Evaluation question | Comment |
|---|---|
| Health outcomes after screening | • Currently mortality is fairly easy to ascertain directly or through record linkage (e.g., vital records, National Death Index).<br>• Other key outcomes such as morbidity and disability need to be assessed. While historically challenging to assess for many surveillance programs, these outcomes could be addressed by improved integration of data sources and additional record abstraction. |
| Missed cases (rates of false negative screens and unscreened but affected) | • Evaluating frequencies and reasons for missed cases is crucial. Surveillance programs must have the ability to follow the cohort of all children with CCHDs longitudinally, well beyond the newborn period.<br>• Missed case information could be used to revise screening algorithms for improved screening results. |
| Burden and accuracy for secondary screening targets | • Noncardiac conditions such as pulmonary defects and diseases and some cardiac 'secondary targets' (heart defects that present with hypoxemia only in some instances) will be identified by CCHD screening.<br>• Many BD programs currently perform population-based ascertainment of many types of congenital heart defects (beyond CCHDs), and are thus positioned to help assess the usefulness of CCHD screening beyond the primary targets. |
| Role of altitude, sociodemographic characteristics, and other special circumstances | • BD programs represent diverse geographic regions of the United States and many ascertain cases statewide, and therefore are positioned to provide population-based data about screening accuracy rates in a variety of geographic settings.<br>• Modified screening algorithms for high altitudes can be evaluated by BD programs population-wide.<br>• Prenatal (fetal echocardiography) and pulse oximetry screening rates and outcomes can be stratified by demographic characteristics such as rural/urban residence, race/ethnicity, maternal age, or place of delivery. |
| Impact of prenatal and clinical diagnoses before NBS | • Prenatal diagnosis is possible for many CCHDs and genetic disorders frequently associated with CCHDs, but uptake and sensitivity vary by specific CCHD, genetic disorder, and population.<br>• Because screening is specifically useful for newborns with CCHDs that were not identified by fetal echocardiography, programs need to find or improve ways to collect prenatal diagnostic information.<br>• Some affected newborns will present with signs and symptoms in the pre-screening period immediately after birth or have neonatal echocardiograms before screening due to prenatal genetic diagnoses, so ideally programs should also collect accurate information about the timing and methods of diagnosis for these types of CCHDs.<br>• Population-based, pre-screening diagnostic data will be important metrics for evaluating the impact of NBS. |
| Costs and service utilization | • CEAs to date on NBS for CCHD have been conducted in specific geographic areas of the world and specific birth cohorts, and do not completely reflect population-based ascertainment of parameter (data) inputs.<br>• BD programs could provide robust, up-to-date information so that new CEAs could include population-based clinical data (e.g., prenatal diagnosis, specific treatments, medical complications, and mortality) and health services data (e.g., location/type of birthing center, transfers, transports, hospitalizations, and rehabilitation services). |

CCHD, critical congenital heart disease; BD, birth defects; NBS, newborn screening; CEAs, cost-effective analyses.

inevitably differ as they are shaped by local regulations, available resources, local expertise, and other factors (Mai et al., 2007). Nevertheless, common standards and effective coordination can and ought to emerge. A key role can be played by organizations such as NBDPN, which have effectively supported the development of multistate surveillance.

An example is the aforementioned compilation of multistate CCHD data, which required consensus coding standards for ascertaining such data across programs. Further multistate standardization with high-quality surveillance procedures will allow for better sharing of compatible data. Showing the immediate importance of their data for a real-time program should allow birth defects programs to increase their visibility, and perhaps even their resources, while enhancing their value for public health.

## PERSPECTIVES ON THE ROAD AHEAD

Efforts to implement CCHD screening programs are well underway. As is appropriate with CCHD screening, much of the initial emphasis will be on the practicalities of point-of-care screening: the ability to conduct accurate and timely screening at the bedside before discharge from the nursery. These activities will include organizing screening, communication, and follow-up protocols; educating parents; and training providers. Because of their ties to local stakeholders and their expertise in congenital defects, birth defects programs can facilitate these efforts.

In addition to these important activities during implementation, birth defects surveillance programs have an even greater role to play in ensuring the core public health functions of assessment, such as epidemiologic studies of CCHDs, and assurance, such as evaluations of

Table 2
Program Issues for Birth Defects Monitoring Related to Critical Congenital Heart Disease Newborn Screening

| Issue | Needs |
|---|---|
| Data sources and quality | • To address the complexity of CCHDs, key data sources are likely to include medical records with echocardiography results and follow-up information, from specialty clinics and referral hospitals.<br>• Accurate case review and classification require specialized clinical expertise. |
| Timeliness | • Timely, systematic feedback is a major task for surveillance programs, because of their role in evaluating and improving NBS services.<br>• BD programs should consider ways to streamline notification and processing of records related to CCHDs. |
| Long-term follow-up for comprehensive outcomes | • BD programs need to incorporate follow-up well beyond the neonatal period.<br>• Enhancements in data sources, data quality, and expert review will likely be necessary to assess many outcomes, including morbidity, disability, health service utilization, and costs. |
| Standardization of reporting | • Standardized case definitions and diagnostic codes and associated variables will allow for appropriate comparisons within and between programs (states) and over time.<br>• To maximize the use of data from programs with varying abilities and resources, it is important to define sets of variables (e.g., core, expanded, and optional), with explicit definitions and quality indicators. |
| State and national program coordination | • In some states, there will be a need to develop closer interactions between NBS and BD programs for comprehensive evaluations to address the points above.<br>• Interstate data exchange agreements can be critical in some localities when birth and postnatal referral patterns cross state lines.<br>• Nationally, pooling of standardized data would be necessary to improve evaluations, particularly for rarer outcomes and to assess diverse demographic issues.<br>• Technical assistance to some BD programs would need to be expanded to include broader sets of outcomes, cost-effectiveness analyses, and other new activities. |

CCHD, critical congenital heart disease; BD, birth defects; NBS, newborn screening.

prevention effectiveness (Khoury, 1996). Specifically for newborn screening programs, evaluation needs include long-term follow-up activities, particularly for continuous quality improvement (e.g., refining screening algorithms, screening procedures, and follow-up) and new knowledge discovery (Kemper et al., 2008). To conduct these activities well, monitoring programs will need to reach high standards of timeliness, flexibility, quality, and acceptability (German et al., 2001). In some cases, programs will need to shift resources and priorities. Such a shift might be challenging in the short run, but ultimately could provide considerable rewards: efficient integration of public health resources (e.g., screening and surveillance) within state health departments, less additional state burdens in implementing screening (by enhancing existing surveillance rather than creating a new system), and higher quality birth defects surveillance. From a systems perspective, these integrated methods should translate into better value (quality/cost) for the investments that CCHD screening will likely require from the public health system, the health care sector, and medical professionals. From a health perspective, for individuals with CCHDs and their families, this approach should lead to realistic but useful evaluations of this promising new phase of newborn screening.

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