Updated Strategies for Pulse Oximetry Screening for Critical Congenital Heart Disease

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Seven years after its addition to the US Recommended Uniform Screening Panel, newborn screening for critical congenital heart disease (CCHD) using pulse oximetry became mandatory in the United States. Although CCHD newborn screening reduces morbidity and mortality, there remain important opportunities to improve. An expert panel convened for a 1-day meeting in September 2018, including subject matter experts and representatives from stakeholder organizations. Presentations on CCHD outcomes, variations in approach to screening, and data and quality improvement helped identify improvement opportunities. The expert panel concluded that sufficient evidence exists to recommend modifying the current American Academy of Pediatrics algorithm by (1) requiring an oxygen saturation of at least 95% in both (formerly either) the upper and lower extremities to pass and (2) requiring only 1 repeat screen instead of 2 for cases that neither pass nor fail initially. The panel underscored the importance of improving public health reporting by further specifying the targets of screening and criteria for reporting outcomes (false-negative and false-positive cases). The panel also highlighted the need to ensure sufficient public health funding for CCHD newborn screening and opportunities for education and global implementation. Newborn screening for CCHD using pulse oximetry has led to significant improvements in child health outcomes. However, further important work is required to understand and improve the effectiveness and efficiency of screening.

Seven years after the addition of newborn screening for critical congenital heart disease (CCHD) to the Recommended Uniform Screening Panel (RUSP), it became required in the United States.1

This public health milestone was the culmination of 23 years of work, with the first reports of the use of pulse oximetry screening (POS) to detect CCHD in newborns being published in 1995.2,3

In 2009, a scientific statement from the American Academy of Pediatrics (AAP) and American Heart Association (AHA) reviewed the available evidence and concluded that POS may improve CCHD detection, but evidence from larger population-based studies was required before recommending the addition of POS to routine newborn screening.4 European studies and a meta-analysis of the literature provided the evidence that was missing at the time of the scientific statement.5-8 In 2010, the US Department of Health and Human Services (HHS) Secretary’s Advisory Committee on Heritable Diseases in Newborns and Children examined

abstract

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention, the Health Resources and Services Administration, the National Institutes of Health, the Food and Drug Administration, or the US Department of Health and Human Services.

Dr Martin conceptualized and drafted the initial manuscript; Drs Burns, Ewer, Kemper, and Oster and Ms Gaviglio, Ms Hom, Ms Saarinen, and Ms Sontag contributed important intellectual content; and all authors reviewed and revised the manuscript, approved the final manuscript as submitted, and agree to be accountable for all aspects of the work.

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newly available evidence and recommended to the Secretary of HHS that POS for CCHD be added to the RUSP.9

A workgroup of experts and stakeholders in CCHD POS met in January 2011 to discuss strategies for implementation (Supplemental Information).10 The workgroup recommendations received endorsement from medical societies, and the US Secretary of HHS officially added CCHD to the RUSP later in 2011.11,12 A second stakeholder meeting took place in February 2012.13

With federal recommendations in place, state advocacy efforts advanced rapidly. In 2011, Indiana, Maryland, and New Jersey were the first states to pass legislation mandating CCHD newborn screening. Public acceptance increased dramatically after media reports of infants who were identified by this screen had successful outcomes. By the end of 2015, >80% of states were screening for CCHD, and by July 2018, CCHD screening was adopted in all states.

After this important landmark, a third stakeholder meeting was organized to review current challenges and successes, identify future opportunities to improve CCHD newborn screening, and recommend changes to the published screening algorithm.

METHODS

An expert panel convened for a 1-day meeting in September 2018 in Washington, District of Columbia (Table 1). Focused discussions on data and quality-improvement opportunities, algorithm variations (and how they might influence outcomes), and global implications and opportunities took place as well as several formal presentations on current successes and challenges of screening. The group evaluated 5 potential modifications of the current AAP-recommended algorithm.

<table>
<thead>
<tr>
<th>TABLE 1 Workgroup Attendees</th>
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</thead>
<tbody>
<tr>
<td>Clinicians</td>
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<tr>
<td>Pediatricians</td>
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<tr>
<td>Pediatric cardiologists</td>
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<tr>
<td>Neonotologists</td>
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<tr>
<td>Nurses</td>
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<tr>
<td>Representatives from</td>
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<tr>
<td>American College of Cardiology Foundation AHA</td>
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<tr>
<td>American College of Medical Genetics and Genomics</td>
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<tr>
<td>American Board of Pediatrics</td>
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<tr>
<td>International Society for Neonatal Screening March of Dimes</td>
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<td>Association of Maternal and Child Health Programs</td>
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<tr>
<td>National Association of Neonatal Nurse Practitioners</td>
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<td>NewSTEPs (Association of Public Health Laboratories)</td>
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<td>Centers for Disease Control and Prevention US Food and Drug Administration US HHS</td>
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<td>National Institutes of Health</td>
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<tr>
<td>National Library of Medicine</td>
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<tr>
<td>State public health officials</td>
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<tr>
<td>CCHD parent advocates</td>
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</tbody>
</table>

CCHD NEWBORN SCREENING IN THE UNITED STATES

Although prenatal ultrasound and physical examination including cardiac auscultation remain important, POS for CCHD has been a valuable addition to newborn screening. Since the 2009 AAP-AHA Scientific Statement, numerous studies from outside the United States have shown improvements in the detection of newborns before discharge from the hospital.5-8,14-17 Although a few early adopter states published their experiences,18,19 no such large population-based study in the United States has been performed. However, a recent study has shown the association of state implementation of POS policies with a significant reduction in early infant cardiac deaths.20 States with legislation mandating screening achieved a 33% reduction in early cardiac deaths due to CCHD compared with states with no policy or a nonmandatory policy. This reduction in mortality resulted in ∼120 lives saved (95% confidence interval: 38–181) per year and an additional 21% reduction in other or unspecified CHD deaths in states, which is equivalent to another 117 lives saved (95% confidence interval: 38–185) per year. There is no evidence that hospitals are facing a significant increased clinical burden from POS despite earlier concerns of delayed discharges and possible unnecessary echocardiograms after failed screening. In the United States, the percentage of POS test-positive newborns who require further diagnostic testing has been low. From 2012 to 2015, demonstration projects in 10 US states showed that there were only 645 of 708,318 (0.09%) newborns testing positive, with only 58 of these newborns (9%) having a CCHD diagnosis.21 Similarly, investigators in the United Kingdom have shown a low rate of failed POS, albeit a bit higher than that in the United States, possibly because screening was performed before 24 hours of age. Singh et al22 found failing results in 208 of 25,859 newborns (0.8%) when testing was performed before 24 hours of age. Congenital heart disease (CHD) was found in 17 of 208 failed screen cases (8%), and no newborns had collapse during their hospitalization. Echocardiography was performed in only 61 of 208 (29%) failed POS newborns, and 29 of 61 (48%) newborns undergoing echocardiography had abnormal scan results. Other significant clinical conditions were found in 148 newborns who failed the POS. Thus, only 43 of 208 (21%) failed screen results represented false-positive screen results.

MODIFYING THE CCHD SCREENING ALGORITHM

Participants in the January 2011 stakeholder meeting recommended a protocol for use in the United States that was influenced by European protocols5,8 and intended to limit the number of false-positive results.10
This was the approach endorsed by the AAP. Most states implemented the protocol recommended by the AAP, with a few states such as New Jersey, Minnesota, and Tennessee using variations of the protocol (Table 2). The stakeholders considered 5 modifications to the current AAP algorithm.

i. Screen Using Only Lower Extremity (Postductal Saturations of Either Foot)

The original proof-of-concept studies used only postductal saturations in the screening algorithm, arguing that this would be quicker and simpler and capture most cases of CCHD. A modification of this algorithm using a higher oxygen saturation threshold (<97%) has also been recommended in Tennessee. The advantage of this strategy is that there would presumably be less time and cost involved if only 1 extremity needed to be screened. However, the concern is that it will miss conditions with reversed differential cyanosis, in which the postductal oxygen saturations are higher than preductal oxygen saturations (eg, d-transposition of the great arteries with high pulmonary vascular resistance, d-transposition of the great arteries with interrupted aortic arch, and supracardiac total anomalous pulmonary venous drainage). In addition, some CCHDs, such as coarctation of the aorta, may not be hypoxic, and postductal saturations may be normal.

In 2005, de Wahl Granelli et al evaluated cases of CCHD and the pre- and postductal saturations. The screening strategy with the highest sensitivity was if both the lower and upper extremity saturations were <95% or there was a difference of >3% between the upper and lower extremities. However, this study included only 66 CCHD cases with a mean age of 3 days, and the majority of newborns were on prostaglandin infusions. In an attempt to further increase the sensitivity, Ewer et al proposed a further modification to this algorithm (either pre- or postductal saturation of <95% or a difference of >2%). Three major (>20,000 patients screened) studies have used pre- and postductal saturations, and 2 meta-analyses have shown no difference in sensitivity between postductal-only and pre- and postductal saturation algorithms. However, there is a preponderance of postductal studies, which may bias the meta-analysis, and only 2 pre-post studies reported raw saturation data for all CCHDs within the cohort. Applying the postductal-only algorithm to patients with CCHD who were identified in these studies would have missed 4 CCHD case patients (detected because of a difference of 4 or more between the extremities).

Extrapolating these figures results in an estimated incidence of CCHD cases missed by using a postductal-only algorithm of 7 per 100,000 newborns screened.

**Outcome: The Expert Panel Was in Favor of Maintaining the Recommendation for 2-Extremity (Pre- and Postductal) Screening.**

The current AAP recommendation, based on the de Wahl Granelli algorithm, recommends that both pre- and postductal saturations must be <95% or have a difference of >3% to lead to a retest or fail. New Jersey modified it such that either a pre- or postductal saturation of <95%, regardless of the difference between the 2, results in a retest or fail. Adopting both saturation measurements of >94% as a pass avoids the perverse situation in which an infant could pass with (potentially abnormal) saturations of 92% (hypothetical scenario: first screen, 98% preductal oxygen saturation and 94% postductal oxygen saturation [result, retest]; second screen, 97% preductal oxygen saturation and 93% postductal oxygen saturation [result, retest]; third screen, 95% preductal oxygen saturation and 92% postductal oxygen saturation [result, pass]). Furthermore, given that the New Jersey modification would capture at least all newborns who would fail under the AAP algorithm, the sensitivity of the modified algorithm would be expected to be the same as or higher than that of the AAP algorithm. There is insufficient evidence to identify how many additional newborns with CCHD may be missed by screening using the AAP algorithm. With regard to a potentially higher false-positive rate with the New Jersey algorithm, this concern has not born out in practice. The New Jersey experience from 2012 to 2015 had a false-positive rate of 0.06%, a value that is consistent with that of other states. Moreover, it has been shown that the initial AAP

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**TABLE 2 Variations in Algorithms in Use for POS for CCHD**

<table>
<thead>
<tr>
<th>Algorithm</th>
<th>Extremity Screened</th>
<th>POS for Pass, %</th>
<th>Difference Between Arm and Leg for Pass, %</th>
<th>Rescreens, n</th>
<th>Screen Age, h</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAP</td>
<td>RH, foot</td>
<td>95 in either</td>
<td>≤3</td>
<td>2</td>
<td>&gt;24</td>
</tr>
<tr>
<td>New Jersey</td>
<td>RH, foot</td>
<td>95 in both</td>
<td>≤3</td>
<td>2</td>
<td>&gt;24</td>
</tr>
<tr>
<td>Tennessee</td>
<td>Foot (AAP if test fail)</td>
<td>97</td>
<td>≤3 on rescreen</td>
<td>2</td>
<td>&gt;24</td>
</tr>
<tr>
<td>de Wahl Granelli</td>
<td>RH, foot</td>
<td>95 in either</td>
<td>≤3</td>
<td>2</td>
<td>&lt;24</td>
</tr>
<tr>
<td>Ewer</td>
<td>RH, foot</td>
<td>95 in both</td>
<td>≤2</td>
<td>1</td>
<td>6–24</td>
</tr>
<tr>
<td>Poland</td>
<td>Foot</td>
<td>95</td>
<td>—</td>
<td>1</td>
<td>&lt;24</td>
</tr>
<tr>
<td>Germany</td>
<td>Foot</td>
<td>96</td>
<td>—</td>
<td>1</td>
<td>&gt;24</td>
</tr>
</tbody>
</table>

RH: right hand; —, not applicable.
algorithm can be confusing and prone to misinterpretation due to human error.\textsuperscript{27} Simplifying the algorithm such that a saturation of 95\% is needed for both the right hand and a lower extremity in order to pass may help improve the quality of screening.

**Outcome:** The Expert Panel Was in Favor of Changing the Recommended Algorithm Such That a Saturation of <95\% in Either the Right Hand or a Lower Extremity Is a Retest or Fail.

### iii. Eliminate Second Retest

The AAP algorithm includes up to 2 retests if oxygen saturations do not meet passing criteria but remain at \( \geq 90\% \). Clinical assessment of the newborn is not required until after the second retest.

Diller et al.\textsuperscript{28} modeled the removal of the second retest in \( >77,000 \) infants showing no change in sensitivity and only a modest increase in the false-positive rate. Studies using the Ewer algorithm show that up to 80\% of test-positive newborns have a significant cardiac or noncardiac condition requiring urgent attention.\textsuperscript{8,22} The second rescreen, therefore, reduces the number of test-positive results by a modest amount but potentially delays the treatment of a serious clinical condition by 1 to 2 hours. Such delays may have detrimental effects on the patients and result in worse outcomes.

**Outcome:** The Expert Panel Was in Favor of Eliminating the Second Retest.

### iv. Change the Pre- and Postductal Differential Saturation to 2\%\

The additional difference in the cutoff criteria for a positive test result between the de Wahl Granelli\textsuperscript{5} and the Ewer\textsuperscript{8} algorithms is the differential between the pre- and postductal saturations. de Wahl Granelli used >3\%, and Ewer used >2\%. This marginal difference means that the Ewer algorithm will identify all newborns picked up by the de Wahl Granelli algorithm plus some additional case patients.

Most of these additional cases will ultimately be false-positives, but in principle, these more conservative cut-offs have the potential to identify more newborns with CCHD who are frequently missed by POS, namely those with aortic arch obstruction. Most of these newborns will have saturations in the normal range of 95\% to 100\%, and it is feasible that small changes in the algorithm may identify more affected newborns. Unfortunately, there is a significant lack of data to corroborate this because there are only data from 2 published studies.\textsuperscript{5,8} Application of the de Wahl Granelli algorithm to the Ewer cohort shows that the former would miss 1 CCHD case (hypoplastic left heart syndrome), 1 serious CHD (truncus arteriosus), and 1 case of Ebstein anomaly.\textsuperscript{8} From a population screening perspective, these additional findings need to be balanced against the increased false-positive rate.

**Outcome:** The Expert Panel Was in Favor of Not Changing the Pre- and Postductal Differential Saturation to 2\%.

### v. Earlier Screening, Within the First 24 hours of Life

There has been debate about the best time to perform CCHD screening. Although the CCHD screening false-positive rate is higher if screening occurs within the first 24 hours of life compared with later screening (0.47\%–0.5\% vs 0.05\%–0.11\%),\textsuperscript{29} some hospitals and countries routinely discharge healthy appearing newborns by 24 hours.

Two additional considerations related to timing include (1) many newborns with CCHD present within the first 24 hours as the ductus arteriosus is closing, some with relatively mild symptoms at first and others with rapid cardiovascular collapse or even death,\textsuperscript{29} and (2) newborns with serious noncardiac conditions, such as sepsis, pneumonia, and persistent pulmonary hypertension, also usually present in the first 24 hours. The former consideration is demonstrated in 2 studies,\textsuperscript{5,6} which performed screening after 24 hours. Half of CCHD case patients were never screened because they presented before screening was set to take place. In de Wahl Granelli’s study,\textsuperscript{7} 10\% of case patients presented with acute cardiovascular collapse with acidosis in the hospital before diagnosis. Because the aim of CCHD screening is to prevent such events, this information should be taken into account when assessing the appropriate timing of the screen.\textsuperscript{29}

In the United Kingdom, where early screening is more common, it takes \( \sim 2873 \) screens to detect 1 CCHD compared with 12 212 screens in the United States.\textsuperscript{22,29} Balance this with the difference in false-positive rates (United Kingdom 0.8\% versus United States 0.08\%). In the United Kingdom, 79\% of those with false-positive results had a noncritical CHD condition that required treatment, making the true false-positive rate closer to 0.17\%. It is not specified, but it is likely that many patients with CCHDs presented before screening, including in the prenatal period via ultrasound. Diller et al.\textsuperscript{28} screened >77 000 newborns, but only 1 case of CCHD was detected via pulse oximetry (out of an estimated prevalence of 77–154 cases) and only 10 cases of non-CCHD illness.\textsuperscript{28} In comparison, during a 2-year period, Washington state screened 179 488 newborns and diagnosed 22 cases of CCHD by POS compared with 33 case patients who became symptomatic before screening (R. Abouk, PhD, unpublished data, 2018).\textsuperscript{30}

**Outcome:** The Expert Panel Was in Favor of Not Changing the Time of Screening but Acknowledged That Earlier Screening Is Acceptable.
IMPROVING PUBLIC HEALTH CCHD REPORTING

To better assess the effectiveness and gaps of CCHD newborn screening, the expert panel recognized that support and infrastructure for public health reporting of CCHD screening results and outcomes need to be improved. Public health reporting of POS requires data sharing between hospitals and birthing centers, surgical and intervention centers, and state public health agencies. There is variation between states in the public reporting of CCHD screening on the basis of legislative authority to collect pertinent data and available resources. Some states require reporting of the saturations in all newborns who are screened, others report saturations and outcomes of only the failed screens, some only report the number of newborns screened in aggregate, and still others have no requirement for reporting at all. Two issues that lead to poor reporting are that (1) each state has different regulations with respect to data collection authority, and (2) the funding of public health agencies for data collection and analysis is lacking. Participants in each of the 3 previous stakeholder meetings have commented on the importance of public health reporting, including a recommended minimal data set. In addition, information regarding the dates of diagnostic echocardiography and subsequent interventions (such as surgery or cardiac catheterization) are worthwhile to collect.

Public health programs specify the targets of newborn screening so the accuracy of the screening test can be assessed. For the US RUSP, CCHD is listed as a condition. There can be inconsistency as to what is deemed critical. Previous clinical studies have used the age at intervention (with critical cases being defined as requiring intervention within the first year of life) to classify a case as critical. Such a definition may either under or overcount CCHD by discounting cases with defects that require intervention shortly after 1 month or including cases that were stable for most of the infant’s first year of life. Furthermore, from a public health standpoint, it may be challenging to track the interventions received and for what reason they were received. Some have proposed using a diagnosis-based definition, but some conditions such as critical pulmonic stenosis and critical aortic stenosis lack a specific code that differentiates them from milder valve diseases that may never need an intervention. Given the complexity of CCHD and the variation in care, any single definition is likely to be either too encompassing or not encompassing enough. In an effort to provide some clarity on this issue, in 2016 the AAP Expert Panel created a uniform list of target conditions, including 12 core conditions plus an option to include other rare critical heart disease conditions not otherwise specified. A diagnosis of any of these core conditions, regardless of severity, is considered a true-positive result.

The complexity of the definitions has important ramifications for the overall reported sensitivity and specificity of this important public health screening program. Although the policy of POS has been demonstrated to save lives, it is still expected that some newborns with CCHD will be missed by POS given the inherent limitations of this test and the variability in the clinical presentations of CHDs in the newborn. That is, a negative screening result does not rule out the possibility of CCHD. When considering the total group of CCHD that had an intervention in the first 28 days of life, a Cochrane Review found moderate sensitivity 76.3% (confidence interval 69.5–82.0). When examining individual lesions, the range of sensitivity was much broader (33%–100%). There are various reasons why a child with a CCHD may not be detected via POS. Anatomic conditions with isolated outflow tract obstruction, such as pulmonic stenosis, aortic stenosis, or coarctation of the aorta, may have milder obstruction at the time of POS and discharge from the newborn nursery or lack a communication for right to left shunting and have normal POS results. This accounts for their lower level of sensitivity with POS and why, from a public health perspective, some have recommended that left-sided outflow tract obstruction defects should not be included. Similarly, some of the conditions with complete mixing of systemic and pulmonary venous blood may have low pulmonary vascular resistance or lack significant pulmonary valve stenosis, and thus have high pulmonary blood flow with resultant high oxygen saturations that may result in a passing POS. This explains why some infants with a single ventricle, total anomalous pulmonary venous drainage, truncus arteriosus, and hypoplastic left heart syndrome are not identified by POS and can be listed as having a false-negative result. Lastly, for tetralogy of Fallot and Ebstein anomaly of tricuspid valve, the severity of the valvar component of the condition may influence POS results. In cases of CCHD not being identified by POS but presenting later in life, newborn screening programs should (1) verify that screening was performed properly and (2) collaborate with birth defects monitoring programs as necessary to collect information such as age at diagnosis and eventual intervention or outcome. Such data may be helpful in identifying opportunities for improvement in the CCHD screening protocol.

A model has been created for estimating the different rates of detection for each particular CCHD condition (Table 3). However, given the rarity of some of the particular CCHD conditions, public health programs evaluating CCHD screening...
in their state should not focus on the performance for any single defect because there may be notable differences in sensitivity and the number of detected cases from state to state. Rather, public health programs should focus on protocol adherence and appropriate data collection, ensuring that the CCHD screening is being conducted and interpreted as recommended, and entering all cases (detected and not) into NewSTEPs for national tracking purposes.35

On the other hand, some newborns without a CCHD fail POS. Many of these children with a false-positive screening result may have a significant disease other than CCHD that otherwise may not have been detected in a timely fashion. The AAP Expert Panel listed such secondary conditions that are important for health care providers to consider in any newborn who fails POS.31 Although such cases are considered false-positives with regard to CCHD screening, detecting and treating such cases can have important ramifications for improving overall public health and should be tracked to better assess the impact of POS as a public health tool.

### Education for Health Care Providers and Parents

The expert panel identified a need for continued education and training of clinicians and parents regarding CCHD newborn screening. Specific topics needing further work included (1) education regarding the limitations of screening, (2) the ability of POS to detect other important health conditions, and (3) continued training and reiteration of the recommended algorithm, especially as changes are being proposed.

### Global CCHD Screening Efforts

Gains are being made in the global spread of CCHD screening (Fig 1).

#### TABLE 3 Expected Sensitivity of Pulse Oximetry for Detection of CCHD Screening Targets

<table>
<thead>
<tr>
<th></th>
<th>High (&gt;80%)</th>
<th>Medium (60%-80%)</th>
<th>Low (&lt;60%)</th>
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</thead>
<tbody>
<tr>
<td>Critical pulmonary stenosis</td>
<td>Critical aortic stenosis</td>
<td>Coarctation of the aorta</td>
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<tr>
<td>d-transposition of the great arteries</td>
<td>Double-outlet right ventricle</td>
<td>Ebstein anomaly</td>
<td></td>
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<tr>
<td>Hypoplastic left heart syndrome</td>
<td>Tricuspid atresia</td>
<td>Interrupted aortic arch</td>
<td></td>
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<tr>
<td>Pulmonary atresia</td>
<td>Single ventricle</td>
<td>Tetralogy of Fallot</td>
<td></td>
</tr>
<tr>
<td>Single ventricle</td>
<td>Total anomalous pulmonary venous drainage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Truncus arteriosus</td>
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#### FIGURE 1

Map of CCHD screening activity (updated February 2019).
North America and Europe have had the greatest activity in POS for CCHD.32,35–37 Impressive activity in South and Central America is occurring, with more countries having national recommendations, guidelines (such as those from the Sociedad Iberoamericana de Neonatologia), or pilot projects.38 Implementation is underway in Australia; Asia has made progress in select regions.16,39 Africa is further behind in implementation, as is newborn screening and access to specialized medical intervention in general. The global spread may be impacted by the problem of availability of corrective surgery for infants in some regions. Globally, more may be gained from the detection of secondary conditions such as pneumonia and neonatal sepsis, which are more easily treated.

The workgroup felt that advocacy and research for global POS for CCHD is an opportunity for the AAP, American College of Cardiology Foundation, and AHA, each of which have a growing international membership.

**DISCUSSION**

The addition of POS for CCHD has been a success in the United States, with a recent study showing that the enactment of legislation or regulation mandating POS is associated with lower mortality in infants with CCHD.20 The workgroup identified opportunities to improve POS for CCHD.

1. The current algorithm could be improved and simplified by requiring an oxygen saturation of at least 95% in both the upper and lower extremities and requiring only 1 repeat screen instead of 2 for cases that neither pass nor fail initially (Fig 2). There was agreement to continue to recommend 2 extremity measurements.

2. Efforts should be made to improve reporting at the state level through the creation of new legislation that requires and funds reporting and analysis and/or by improving clarity on the results of testing. Reporting will allow for better documentation of the impact of POS and provide data for quality improvement at hospitals and/or birthing centers.

3. Both providers and parents will benefit from a better understanding of CCHD screening, identifying education as an
important ongoing opportunity for the AAP, American College of Cardiology, and AHA.

4. International efforts to implement POS for CCHD presents opportunity for the AAP, American College of Cardiology, and AHA. The numbers of countries with a recommendation and the numbers of countries implementing POS are increasing.

IMPLICATIONS OF ALGORITHM CHANGES

The most important outcome of this stakeholder meeting is the new recommended algorithm for use in the United States (Fig 2). The new algorithm has 2 key differences: (1) requiring 95% or greater in both the right hand and foot to be considered passing and (2) having only 1 retest instead of 2. These changes are expected to simplify the algorithm interpretation and screening process, and they may increase the overall sensitivity of POS. However, these changes may also slightly increase the false-positive rate. Any infant who would have failed the initial algorithm will also fail with these changes, and a few additional children may also fail. Some of these additional failed test results may represent a true-positive result with CCHD, and others may be false-positive results.

Yet, it is important to recognize that a false-positive result from screening with pulse oximetry does not mean that the test is not useful. Rather, it has been well demonstrated that many children who have a false-positive result from screening still have significant previously unrecognized clinical disease even if that disease is not CCHD. It is because of this experience that, in 2016, experts recommended the following workup for failed screens:

Additional evaluation and testing of the infant should be prioritized according to the conditions most relevant for each case, and such evaluation should not be delayed while awaiting an echocardiogram. Depending on the resources of the birthing location where the newborn is tested, transfer to another center where adequate resources exist to complete the evaluation might be required. The child should not be discharged without resolving the cause of desaturation or at least before excluding potentially life-threatening conditions. If a cause other than CCHD is identified and appropriately treated with resolution of hypoxemia, an echocardiogram might not be necessary.

STEPS FOR IMPLEMENTATION OF THE NEW ALGORITHM

In the United States, newborn screening is a public health program administered separately by each state. As such, the algorithm used for CCHD screening in any particular birthing location is state dependent. Before implementing changes, clinicians should consult relevant state regulations.

ABBREVIATIONS

AAP: American Academy of Pediatrics
AHA: American Heart Association
CCHD: critical congenital heart disease
CHD: congenital heart disease
HHS: US Department of Health and Human Services
POS: pulse oximetry screening
RUSP: Recommended Uniform Screening Panel

REFERENCES


4. Mahle WT, Newburger JW, Matherne GP, et al; American Heart Association Congenital Heart Defects Committee of the Council on Cardiovascular Disease in the Young, Council on Cardiovascular Nursing, and Interdisciplinary Council on Quality of Care and Outcomes Research; American Academy of Pediatrics Section on Cardiology And Cardiac Surgery; Committee On Fetus And Newborn. Role of pulse oximetry in examining newborns for congenital heart disease: a scientific statement from the AHA and AAP. Pediatrics. 2009; 124(2):823–836


34. Ailes EC, Gilboa SM, Honein MA, Oster ME. Estimated number of infants.
detected and missed by critical congenital heart defect screening. Pediatrics. 2015;135(6):1000–1008


