

## 5-14-14 Addendum to the 4-28-14 Nomination of Unrecognized Critical Congenital Heart Disease

Since the nomination of unrecognized critical congenital heart disease (CCHD) to the Wisconsin Newborn Screening Panel, data collected through the Wisconsin SHINE Project has been further analyzed and a new report was published in the Lancet [1] on the use of pulse oximetry screening in more than 120,000 babies in China. These updates should be included in the evaluation of pulse oximetry screening for CCHD.

### **CRITERION 6: Clinical Validation**

#### **SHINE Data**

Since the nomination was first authored, the SHINE data has been further analyzed and data entry errors corrected. In the original nomination the false positive rate was reported at 0.082% but after further evaluation the false positive rate is 0.063%. The positive predictive value for CCHD remains 23% with 46% of infants who failed the screening having an important disease process other than CCHD. An additional infant with a coarctation who passed their oximetry screening was identified in the cohort, raising the number of false negatives to seven. A summary of these results is included below.

### **Pulse Oximetry Screening for CCHD** Preliminary Data 1-1-13 to 1-31-14



#### **3 True Positives**

HLHS  
Ebstein's  
Interrupted Aortic Arch

**Reporting  
Rate  
81.9%**

	<b>CCHD</b>	<b>No CCHD</b>	
<b>Fail</b>	<b>3</b>	<b>10</b>	<b>13</b>
<b>Pass</b>	<b>7</b>	<b>15873</b>	<b>15880</b>
	<b>10</b>	<b>15883</b>	<b>15893</b>

#### **10 False Positives**

6 Other Diseases Requiring Care  
Non CCHD Heart Disease 3  
AV Canal  
Pulmonary Hypertension  
Mitral Regurgitation  
Infection 3  
2 Incidental Heart Disease  
2 Healthy Newborns

#### **7 False Negatives**

Tetralogy of Fallot (2)  
Coarctation (2)  
Coarctation with VSD (1)  
TAPVR (1)  
Single Ventricle (1)

Failure Rate **1:1,230**  
False Positive Rate **0.063%**  
CCHD Sensitivity **30.00%**  
CCHD Specificity **99.94%**  
CCHD Negative Predictive Value **99.96%**  
CCHD Positive Predictive Value **23.08%**  
Any Disease Positive Predictive Value **69.23%**

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### Chinese Data

A large study by Zhao[1], published electronically on 4-23-14, was not incorporated in the original nominating document. This study evaluated the use of pulse oximetry screening in 122,738 Chinese infants. The case definitions were based on a British study by Ewer[2] and used the designations critical heart defects (needing intervention before 28 days), serious (needing intervention before 1 year), significant (persisting beyond 6 months but not requiring intervention in the first year), and non-significant. These designations differ than those customarily used in the United States.

Of the 179 infants with critical heart defects, 22 were detected prenatally (12%) and 11 (6%) were symptomatic before screening. Of the 146 asymptomatic babies with critical defects not detected prenatally, 122 failed oximetry screening, 14 passed oximetry screening but were identified on physical examination, and 10 were discharged prior to diagnosis. 23 of the asymptomatic newborns with critical cardiac malformations would have been discharged inappropriately had pulse oximetry not been used. Through the use of pulse oximetry the rate of missed critical heart defects decreased from 18.4% to 5.6%.

The false positive rate in the Zhao study of 0.3% was higher than the 0.063% in the SHINE project. The positive predictive value was 23% for critical cardiac defects and 36% when serious defects were included. However Zhao's study only assessed the presence or absence of cardiac defects and did not assess the identification of other causes for hypoxia such as infection or pulmonary disease.

1. Zhao, Q.M., et al., *Pulse oximetry with clinical assessment to screen for congenital heart disease in neonates in China: a prospective study*. Lancet, 2014.
2. Ewer, A.K., et al., *Pulse oximetry screening for congenital heart defects in newborn infants (PulseOx): a test accuracy study*. Lancet, 2011. **378**(9793): p. 785-94.

The above Addendum was received May 14, 2014 by the Department of Health Services and considered as part of the nomination process.