SUMMARY
The Impact of Implementing a Universal Newborn Screening for Critical Congenital Heart Disease (PDX-003-11)

Sponsor
MEDNAX Center for Research, Education and Quality

Steering Committee
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Study type – Prospective Descriptive Study
Multicenter study - Number of sites – 30-40
Study enrollment goal - 6000
Site enrollment goal – 200

Purpose
The purpose of this study is to evaluate the impact of implementing a universal pulse oximeter screening as a way to detect critical congenital heart disease in otherwise well-appearing newborns.

Background
Congenital heart disease (CHD) is the most common fatal birth defect in the first year of life, affecting about 1 in 125 live births. Critical congenital heart disease (CCHD), which affects about 25% of those with CHD (e.g., 2 to 3/1000), includes those conditions that require intervention in the days or weeks after birth and for which early detection is associated with decreased morbidity and mortality. The benefits of early diagnosis include: stabilization during the pre-symptomatic or early symptomatic period; rapid initiation of prostaglandins for ductal-depending defects; and transfer to specialized facilities for further care, including surgical interventions. There are also potential financial benefits from decreased ICU and hospitalization time and decreased morbidity and follow up care requirements.

In the United States, between 100 and 200 newborns annually are found to have undetected CCHD at autopsy. Current screening practices for detection of CCHD involve prenatal ultrasound and postnatal physical examination. Prenatal ultrasound can only identify about 50% of cases of CCHD. Furthermore, not all women receive a prenatal ultrasound, and there is variation in both the methods used and the quality of the evaluation. The postnatal physical exam lacks accuracy for the detection of CCHD, because of the changes in the physiology in the newborn period. During cardiac transition from fetal to normal newborn physiology, cardiac shunts are changing. The patent ductus arteriosus and the foramen ovale are closing and pulmonary vascular resistance is falling. All these changes make it difficult to identify newborns with abnormally formed hearts and patients with CCHD are frequently discharged as “normal”.

Pulse oximetry has been evaluated for more than a decade as an adjunct for the identification of CCHD. In 2010, the United States Secretary of Health and Human Services (HHS) Advisory Committee on Heritable Disorders in Newborns and Children
(SACHDNC) evaluated the evidence supporting the addition of screening for CCHD, including hypoplastic left heart syndrome, pulmonary atresia, tetralogy of Fallot, total anomalous pulmonary venous return, transposition of the great arteries, tricuspid atresia, and truncus arteriosus available at: 

To provide further guidance, a draft implementation plan was developed, which was subsequently endorsed in August 2011 by the American Academy of Pediatrics, the American College of Cardiology, and the American Heart Association available at: 

The implementation plan included a consensus algorithm for screening. The consensus algorithm was based on published and unpublished data from multiple sources including large screening programs in Sweden and England. The algorithm was developed to minimize the number of false positives. Three key factors emerged in the process: screening after 24 hours of life decreases false positives associated with the transition period, repeat screening for those with borderline results decreased the false positive rate while not missing true positive cases, and screening both upper and lower extremities as explained in the algorithm increases the detection of non-cyanotic lesions (such as HLHS and coarctation of the aorta). The available data are only generalizable to full-term neonates. High-quality data is not available for neonates screened at high altitude (e.g., Denver, CO), who may normally have lower blood-oxygen levels. The implementation plan also recognized the challenge in obtaining echocardiograms for those with a positive screen in rural settings that may not have inpatient pediatric cardiology and echocardiography support. The expert panel highlighted the need to obtain prospective data in diverse populations and diverse regions to refine the algorithm and develop tracking tools and other systems to assure safe and effective (including cost) screening.

It is of an urgent matter to collect this prospective data on pulse oximetry screening for CCHD. Adoption of screening is moving quickly, and Pediatrix Medical Group is uniquely positioned to inform policy makers on the “real-world” implementation of screening. On August 31, 2011, New Jersey began screening all newborns following a legislative requirement. Unfortunately, data monitoring systems for this program are still being developed. Other states are developing similar legislative mandates including Maryland, Indiana, New York, Pennsylvania, Tennessee, and Minnesota. In September of 2011 the Secretary of the Department of Health and Human Services (HHS) endorsed the recommendations to begin screening for CCHD in all states. The recommendation is available at 

**Study Population**

This project will include full-term and late preterm newborns who do not require supplemental oxygen at the time of screening and have no other symptoms of possible CCHD. Parents must also agree to follow-up contact when their child reaches approximately one month and two months of age. Follow-up will be conducted on all enrolled subjects. If the neonate has a positive screen or is found to be a false-negative, these subjects will be followed until the neonate reaches approximately one year of age.
Neonates who are unable to tolerate room air, require NICU admission, or whose parents will not agree to follow-up will be excluded from the study.

Inclusion Criteria
1. Documentation of informed consent and authorization to release personal health information. Informed consent will be obtained from the parent or legal guardian by the Principal Investigator and/or designated research staff. Parent(s) must provide contact information in order to obtain the follow-up data on their child.
2. Full term and late preterm newborns (EGA 35-44 weeks)
3. On room air
4. Neonates known to have a congenital heart defect at the time of the screening, e.g., antenatal diagnosis or diagnosis within the first 24 hours after birth
5. Parents agree to follow-up contact post discharge

Exclusion Criteria
1. On supplemental oxygen
2. Admitted to the NICU
3. Parents do not agree to follow-up
4. Greater than 30 days of age

Outcome Measures
1. True positive rate. The numbers of subjects per 1000 screened subjects who have a positive pulse oximetry screening test and who in follow-up evaluation are found to have CCHD
2. False positive rate. The numbers of subjects per 1000 screened subjects who have a positive pulse oximetry screening test and who in follow-up evaluation are found to have normal hearts. Characteristics of these neonates will be described and the determination will be made if changes in the clinical screening algorithm could reduce the false positive rate.
3. True negative rate. The numbers of subjects per 1000 screened subjects who have a negative pulse oximetry screening test and who in follow-up evaluation are found to have normal hearts.
4. False negative rate. The numbers of subjects per 1000 screened subjects who have a negative pulse oximetry screening test and who in follow-up evaluation are found to have heart defects. Characteristics of these neonates will be described and the determination will be made if changes in the clinical screening algorithm could reduce the false negative rate.
5. The impact of altitude on the false positive/negative rates.
6. The impact of different monitors on the false positive/negative rates.
7. The median estimated cost of screening per patient.

Follow-up
Follow-up will be completed on all enrolled subjects. Follow-up will be coordinated by the MEDNAX Center for Research, Education and Quality research staff in conjunction with the site investigator and study coordinator. Follow-up will be completed primarily through phone calls to the parents when the neonate reaches approximately one month of age and again at approximately two months of age. Subjects that are screened positive will be followed to approximately one year of age.
References


