Title: Oxygen Saturation Screening in Newborns: a Clinical Effectiveness Review

Date: 19 March 2008

Context and policy issues:

An appreciable proportion of newborns are discharged home with serious congenital heart disease (CHD) that is not detected by routine neonatal physical examination. The current trend toward earlier postnatal discharge may increase the risk of undiagnosed CHD.

Congenital heart defects are an important cause of death and morbidity in early childhood. The prevalence of CHD is five to 10 in every 1,000 live births. CHD contributes to 3% of all infant mortality and 46% of deaths from congenital malformations. One in 10 infants with a congenital heart defect dies in the first year of life without being diagnosed before death. Early diagnosis followed by appropriate surgical correction can prevent progression to cardiac failure, cardiovascular collapse, neurological sequelae, and death.

Newborns currently undergo a routine physical examination, usually in the first 24 hours of life, which includes a careful assessment of the cardiovascular system. Physical signs of a congenital cardiac defect may manifest as visible cyanosis, a cardiac murmur, or diminished femoral pulses. However, it is estimated that routine neonatal exam fails to pick up over 50% of babies with undiagnosed congenital heart defects. Too often, serious defects are only recognized when the infant develops life-threatening symptoms of cardiovascular collapse.

Newborn screening programs have been developed for metabolic, hematologic and endocrine disorders, and more recently for hearing loss. Pulse oximetry has been suggested as a method to screen newborns for cardiac malformations, since many life-threatening defects are associated with cyanosis.

Pulse oximetry is a simple, inexpensive, non-invasive method to evaluate whether the blood is carrying sufficient oxygen. A probe is attached to the infant’s finger, toe, or the edge of the foot to measure the percentage of hemoglobin in the arterial blood that is saturated with oxygen. Values below 95% are considered to be abnormal. The patient’s pulse rate is also monitored with pulse oximetry.
Cyanotic heart disease and left-sided obstructive disease are two types of congenital heart defects that may be detected by screening with pulse oximetry. Left-sided obstructive disease includes coarctation of the aorta, interrupted aortic arch, hypoplastic left heart syndrome and critical aortic stenosis. These structural defects have been shown to be the main causes of death after discharge from hospital. The estimated incidence of critical cyanotic heart disease is eight to 10 per 10,000 live births and for critical left-sided obstructive disease it is six to seven per 10,000 births.

A review of the evidence on the effectiveness of oxygen saturation measurement to detect congenital cardiac defects would help decision makers determine if this testing should be used as a routine screening tool in all newborns.

Research question(s):

What is the evidence for the clinical effectiveness of routine oxygen saturation screening in newborns to detect cardiac anomalies?

Methods:

A limited literature search was conducted on key health technology assessment resources, including Pre-Medline, Medline, Embase, Biosis, CINAHL, Pubmed, the Cochrane Library (Issue 1, 2008), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international HTA agencies, and a focused Internet search. Results include articles published between 2003 and the February 2008, and are limited to English language publications only. Filters were applied to limit the retrieval to health technology assessments, systematic reviews, randomized controlled trial (RCT) studies and observational studies.

Summary of findings:

One health technology assessment, two systematic reviews and one observational study were identified that examined the use of oxygen saturation as a screening test for CHD. No randomized controlled trials (RCTs) were identified.

The Tennessee Task Force on Screening Newborn Infants for Critical Congenital Heart Disease also reviewed the same studies identified in the health technology assessment.

Health technology assessments

A health technology assessment (HTA) from the UK’s National Health Service (NHS) was published in 2005. The objective of the study was to review the performance, effects and costs of newborn screening strategies for congenital heart defects, including pulse oximetry, clinical examination and echocardiography. Another goal of the HTA was to explore the perspectives of parents and health professionals on the quality of life of children with congenital heart defects by using a self-administered anonymous questionnaire. Findings from focus groups of parents of children with congenital heart defects were also compared with a review of the medical literature. For the purposes of this report, a summary of the methods, results and conclusions will be limited to the performance of pulse oximetry to detect congenital heart defects.

Studies were included that had at least 20 patients who were assessed with pulse oximetry as a screening test in the first year of life. Two reviewers appraised the studies and a third reviewer resolved disagreement on eligibility. Two of three reviewers validated data extraction and appraisal.
Four studies were included that reported the use of pulse oximetry in asymptomatic newborns; data from these four studies are included in Appendix 1.

- In the first study (Richmond et al; 2002) all babies born over a two-year period in one hospital (excluding those admitted to the neonatal unit at birth) had oxygen saturation measured by pulse oximetry at a mean of 11.7 hours. The cut-off for a normal oxygen saturation was ≥ 95%. Congenital heart defects were found in 50 of 6,166 asymptomatic newborns (8.1 per 1,000) Twenty-six of these malformations were an isolated ventricular septal defect (VSD). Of the 24 newborns with other heart defects, a low pulse oximetry reading was the first indication of a problem in six babies; four other babies, first noticed for other reasons, also had low oxygen saturations. Of six babies diagnosed with coarctation of the aorta, only three were identified by pulse oximetry. Low oxygen saturation also drew attention to 13 other babies with non-cardiac illness. The study concluded that pulse oximetry in the first 24 hours of life can alert clinicians to the presence of critical congenital heart defects that might otherwise have been missed or delayed. It may also identify other serious illnesses that require treatment.

- The second, a case-control study, (Hoke et al; 2002) included 2,972 newborns admitted to well baby nurseries and 32 newborns with CHD. The utility of arm and leg oxygen saturation was assessed for the early detection of ductal-dependant left heart obstructive disease. An oxygen saturation < 92% in the leg or a saturation 7% lower in the leg than in the arm was defined as abnormal. Of the well babies, 57 had an abnormal pulse oximetry reading; of these, four babies were found to have congenital heart defects, including one case of coarctation of the aorta. A fifth baby was found to have pulmonary hypertension. Of the 32 newborns with congenital heart disease, 11/13 (85%) with left-heart obstructive disease had abnormal oxygen saturation as did 15/19 (79%) of babies with other congenital heart defects. An important limitation of the study was that not all newborns with abnormal oxygen saturations underwent echocardiography nor was clinical follow-up available for many of the children. The authors concluded that a large prospective study is needed to determine if pulse oximetry could serve as a suitable screening test for CHD.

- The third study (Reich et al; 2003) evaluated whether pulse oximetry can be used as a screening tool to detect CHD in asymptomatic newborns before discharge. All babies born during a one-year period (except those admitted to the neonatal unit or those who had an echocardiogram, or if parents refused consent) were assessed with a single pulse oximetry reading. Of 2,335 eligible newborns, those with an oxygen saturation ≤ 94% that persisted with a second reading were further assessed by echocardiogram. An echocardiogram was performed in 88 infants, which was abnormal in 43 babies, and 13 required management. Pulse oximetry screening failed to detect one child with total anomalous pulmonary venous return. Data from this group of babies were compared with a “control” group of babies born in the previous 12-month period at the same hospital. No statistically significant difference was shown between the two groups. In this study, pulse oximetry was nearly 100% specific for detecting cyanotic congenital heart disease; as a result, there was no increase in the number of echocardiograms generated. The number of patients was too small to calculate the sensitivity, which is a significant limitation of the study.

- The fourth study (Koppel et al; 2003) assessed the sensitivity, specificity, predictive value and accuracy of pulse oximetry screening of 11,281 asymptomatic newborns in two hospitals. Diagnostic echocardiogram was performed in infants with oxygen saturation ≤ 95% within the first 24 hours of life. Three babies with CHD were identified (but none had a
critical left-heart obstructive lesion). Two patients with negative screens were later readmitted: one with aortic coarctation and one with hypoplastic left pulmonary artery with aorto-pulmonary collaterals. No unnecessary echocardiograms were generated by the study. The sensitivity of the screening test was calculated to be 60%, with a specificity of 99.95%, a positive predictive value of 75% and a negative predictive value of 99.98%. However, when applied to left heart obstructive lesions (both of the missed cases), the sensitivity of pulse oximetry screening was 0%. The authors concluded that oximetry screening will increase the likelihood of identifying clinically occult critical congenital cardiovascular malformations.

The HTA applied data from these four studies to a decision analytic model. In a population of 100,000 live-born infants, the model predicted 121 infants with life-threatening congenital heart defects undiagnosed at screening, of whom 82 (68%) would be detected by pulse oximetry and 39 (32%) by clinical exam alone. Of these, 71 and 34, respectively, would receive a timely diagnosis. The model predicted 1,168 (1.3%) false-positive screening diagnoses per 100,000 infants with pulse oximetry and 46 (0.5%) with clinical exam. The authors of the HTA concluded that pulse oximetry is a promising alternative newborn screening test. The positive-predictive value of a low oxygen saturation appears to be high in three studies, however, the sample size is too small to define the detection rate overall. Cases of coarctation of the aorta and total anomalous pulmonary venous connection were missed. An unintended benefit of pulse oximetry screening is the early detection of hypoxia related to non-cardiac illness. Further evaluation is needed to obtain more precise estimates of pulse oximetry test performance and to inform optimal timing, diagnostic and management strategies.

In 2006, a Tennessee Task Force reviewed the same four studies described in the above HTA to determine if a statewide screening program should be initiated to detect critical congenital heart disease. The nearly unanimous consensus of the task force was that mandatory screening should not be implemented. This decision was based on the unclear false-positive rates of a screening program, the questionable reliability of current oximeter technology in asymptomatic babies and the inability to generate a reasonable cost/benefit estimate. They recommended a very large (~160,000 infants) prospective study to definitively determine the sensitivity and false-positive rate of pulse oximetry testing.

**Systematic Reviews and Meta-Analyses**

Two systematic reviews were identified. The first systematic review (2005) was authored by the same UK group that performed the health technology assessment described above. The objective of the review was to compare the effectiveness of clinical examination with either pulse oximetry or screening echocardiography to detect treatable but life-threatening congenital heart defects. The cost-effectiveness of the screening methods was compared using a decision-analytic model based on 100,000 live births, and future research priorities were assessed. A systematic literature search identified published and unpublished studies to provide data for the model. Further inclusion criteria were not identified. No information was provided about how studies were selected, nor how data extraction and appraisal were validated. Three additional studies, together with the four studies previously described, were identified. Data from the additional three studies are summarized in Appendix 1 and described here.
• In the first, a case-control study, (de Wahl Granelli et al; 2005) the objective was to determine optimal cut-off values for normal oxygen saturations, and estimate the probable screening performance of pulse oximetry readings in 200 asymptomatic infants compared with 66 infants with congenital heart disease. Pulse oximetry readings were taken in the right hand and one foot, using two different oximeters simultaneously. A cut-off value for oxygen saturation < 95% in both hand and foot or a difference of ± 3% between hand and foot gave a sensitivity of 98.5%, a specificity of 96.0%, a positive predictive value of 89.0% and a negative predictive value of 99.5%. A limitation of the study was that infants screened with pulse oximetry in the control group had a median age of 24 hours; 50% of infants with CHD develop signs and symptoms only after the second day of life. The authors concluded that the sensitivity (accuracy) of screening with pulse oximetry can be very high if a high-performance new-generation oximeter is used and if saturation values are compared from the right hand and one foot.

• Another study (Arlettaz et al; 2006) evaluated the effectiveness of pulse oximetry screening to detect structural CHD on the first day of life in all babies (n=3,663) born during a one-year period who were > 35 weeks gestation and had no respiratory distress. Also evaluated was whether pulse oximetry combined with clinical examination is superior to clinical exam alone to diagnose CHD. Oxygen saturation readings from one foot were considered normal with oxygen saturations > 95%. Twenty-four infants had repeated oxygen saturations < 95% and had an echocardiogram. Of these, 17 had CHD and five had pulmonary hypertension. One child had a myocardial tumour and one infant had a normal heart. No false negative cases were reported. Limitations of the study include small sample size and the inclusion of cases of CHD detected prenatally. The authors concluded that pulse oximetry should be added to clinical examination as a screening method for CHD. The results of this study led the Swiss Societies of Pediatric Cardiology and Neonatology to recommend general neonatal screening with pulse oximetry.

• Another study (Bakr et al: 2005) evaluated combined pulse oximetry and clinical examination as a screening method for CHD in all asymptomatic infants (excluding those admitted to the neonatal unit) born during a six-month period. Of 5,211 infants, five babies were identified with an oxygen saturation <94%, which was considered abnormal. One infant had total anomalous pulmonary venous return, one had pulmonary atresia, one had a large ventricular septal defect and another child had a truncus arteriosis. The fifth child had a normal heart. Three babies were later diagnosed with CHD that was not detected by pulse oximetry screening when being investigated for failure to thrive and respiratory symptoms. The sensitivity of the combined method of screening was 77%, whereas it was 30.8% for oximetry alone and 46% for clinical exam alone, Specificity was approximately 100% for all methods. The positive predictive value was 80% for pulse oximetry alone. Limitations of the study include the lack of follow-up for infants who moved out of the study region; cases of undiagnosed CHD could have been missed because postmortem exams are not routinely practiced; and antenatal diagnosis for CHD was not available at the study centre. The authors concluded that combining pulse oximetry with clinical exam can enhance the clinician’s ability to detect life-threatening CHD in a timely manner and should become a part of the discharge plan of every newborn.

The limitations of the systematic review by Griebisch et al. include the small sample size and the heterogeneity among studies. The review concluded that adding pulse oximetry to clinical examination is likely to detect twice as many life-threatening CHDs in affected infants before death or collapse occurs. This is likely to be cost-effective, however protocols are needed to specify how
oxygen saturation is to be measured and how positive screening results should be followed up before implementing this strategy in clinical practice. Larger studies are needed to more precisely estimate the detection rate of pulse oximetry and to estimate the risk of falsely reassuring parents that their child does not have a CHD when the defect is acyanotic.

A second systematic review conducted by Thangaratinam (2007) evaluated the accuracy of pulse oximetry to screen for CHD in asymptomatic newborns. Primary and review articles that evaluated the accuracy of pulse oximetry to detect CHD in asymptomatic newborns were identified by a systematic literature search and included in the review. Two reviewers independently extracted data on study characteristics, quality and results. A random effects bivariate model was used to perform a meta-analysis estimate of the sensitivity and specificity of pulse oximetry as a screening test. The seven previously described studies were included, plus one additional observational study.

- In this observational study (Rosati et al; 2005) the usefulness and consistency of pulse oximetry screening was verified for the early detection of critical cardiovascular malformations in 5,292 consecutive asymptomatic newborns. Symptomatic infants and those with a prenatal diagnosis of heart malformations were excluded. Echocardiography was performed on all infants with oxygen saturations ≤95%. Two true positives were found (one intracardiac total anomalous pulmonary venous return and one ductus-dependant aortic coarctation) and two false positive readings. There was one false negative result: an infant was re-admitted at 26 days of age for a non-ductus-dependant aortic coarctation. A pulse oximetry cut-off value of ≤95% showed a 66.7% sensitivity (95 CI: 99.9% to 100%), a 100% specificity (95% CI: 99.9% to 100%), a 50% positive predictive value and a 100% negative predictive value in identifying critical congenital cardiac malformations. A limitation of the study was that pulse oximetry was performed at a median age of 72 hours, reflecting a relatively longer length of stay for asymptomatic newborns compared to other international centres. The authors of the observational study concluded that pulse oximetry screening for CHD is a non-invasive and specific screening tool for early detection of CHD.

The eight studies analyzed in Thangaratinam’s systematic review included a total of 35,960 asymptomatic newborns. Three studies excluded newborns with an antenatal diagnosis of congenital heart disease. Pulse oximetry measured either functional or fractional oxygen saturation, with oxygen saturation below 95% considered to be abnormal in most studies. A meta-analysis estimate of the eight studies determined that pulse oximetry had a sensitivity of 63% (95% CI 39% to 83%) and a specificity of 99.8%. (95% CI 99% to 100%) The false positive rate was 0.2% (95% CI 0% to 1%) The limitations of the review include the generally poor quality of the included studies and a lack of blinding for the reference standard assessment in all the studies. There was significant heterogeneity among the studies, including the type of saturation chosen (functional versus fractional), method and time of testing and the inclusion or exclusion of infants diagnosed before birth as having congenital heart disease. The authors concluded that pulse oximetry is a highly specific screening tool with very low false-positive rates to detect CHD; however large studies are essential to assess the sensitivity with higher precision.

**Observational studies**

Data from the observational studies included in the health technology assessment and the two systematic reviews are included in Appendix 1. One additional observational study was found and is described here.
The aim of the study (Reich et al; 2007) was to assess whether routine pulse oximetry helped identify babies with critical CHD and to determine the reliability of a single pulse oximeter reading to routinely screen all newborns before hospital discharge. Pulse oximetry was performed on all asymptomatic newborns born during a two-year period (n=7,962). Babies were excluded for prematurity (gestational age < 36 weeks), specialist consultation, prior fetal echocardiogram, or hospitalization exceeding 72 hours. The probe was placed on the toe and a normal reading was defined as an oxygen saturation exceeding 94%. Pulse oximetry data were evaluated for reliability during two study phases. In the first phase, nursery personnel did not know that their data collection was being monitored. In the second phase, staff was made aware that its efforts were being monitored and additional training in pulse oximetry testing was provided. Newborns diagnosed with critical congenital heart disease were identified to assess whether the oximetry reading initiated their diagnosis. Of the 7,962 newborns tested, there were 12 postnatal diagnoses of critical congenital heart disease. No cases of congenital heart defects were identified initially by routine pulse oximetry. Eleven children were identified by physical exam findings. One child was sent home following normal pulse oximeter reading and normal physical exam, but was re-hospitalized at one week of age and had a successful surgical repair of tetralogy of Fallot. Pulse oximetry reliability improved between phases 1 and 2 (38% versus 60%; p<0.0001) when nursery staff became aware that their technique was being monitored and additional training was provided. Limitations of the study included significant differences noted in the readings between available commercial pulse oximeters, as well as substantial human factors that resulted in poor reliability of the measurements. The authors concluded that universal screening should not be instituted until a study demonstrates acceptable sensitivity and clinical value of the testing.

Future studies underway

A large multicentre prospective study is underway in the UK (start date July 2007) to enroll 20,000 women to assess the diagnostic accuracy and cost-effectiveness of routine pulse oximetry to screen for congestive heart disease in asymptomatic newborns born after 35 weeks gestation. The primary outcome is timely diagnosis of life-threatening congestive heart failure. Secondary outcome is significant congestive heart failure and non-cardiac serious illness. The report is anticipated to be published in early 2011.

Limitations

The two systematic reviews and one HTA identified observational studies only, which do not control for potential bias. No randomized controlled trials were identified.

A comparison of the observational studies is difficult because the study designs, methods and denominators were all different. The newborn’s age at the time of measurement, the method of measurement, the duration of probe placement and on which limb, the normal oxygen saturation cut-off value, the inclusion or exclusion of newborns diagnosed antenatally with congenital heart disease, and the type of cardiac malformation analyzed varied significantly across the studies. A limitation to the studies is the potential for verification bias since echocardiography was not performed in all children to verify the true number of patients with false-positive or false-negative results. This may have resulted in an overestimation of the sensitivity of pulse oximetry to detect CHD. Another important limitation in one of the studies was that not all newborns with abnormal screening tests underwent follow-up echocardiography, nor was clinical follow-up available for all of these children.

A further limitation is the variation in the type of oxygen saturation measured: one type of pulse oximeter measures functional oxygen saturation and another type displays fractional oxygen

Oxygen Saturation Screening in Newborns
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Functional oxygen saturation is thought to be about 1.6% to 2% higher at saturation levels used as cut-offs in pulse oximetry screening and could potentially increase the false-positive or false-negative rates.\(^7\) Five of the studies used functional oxygen saturation,\(^2,5,7,10,12\) two studies used fractional oxygen saturation,\(^9,14\) and two studies did not specify the type of measurement used.\(^8,15\)

Conclusions and implications for decision or policy making:

In summary, our limited literature search identified two systematic reviews, one HTA and one observational study (not included in the systematic reviews) that examined the use of pulse oximetry to screen for CHD in asymptomatic newborns.

The 2005 HTA used data from four observational studies that reported variable results to populate a decision-analytic model. All of the observational studies had methodological issues, such as small sample size and epidemiological bias; there was also significant heterogeneity among the studies. The model predicts that screening with pulse oximetry would detect 82 (68%) of 121 infants with life-threatening congenital heart defects that would not be detected by clinical exam alone. The authors concluded that pulse oximetry is a promising alternative newborn screening test, but that further evaluation is needed to define the precision of the testing and to inform diagnostic methods and management strategies.

The 2005 systematic review included three additional observational studies, as well as the four studies included in the HTA. Again, the observational studies had methodological issues, such as small sample size and epidemiological bias, and there was also significant heterogeneity among the studies. The authors concluded that adding pulse oximetry to clinical examination could result in the detection of twice as many life-threatening CHDs in affected infants, and would likely be cost-effective. However they cautioned that larger studies are needed to more precisely estimate the detection rate of pulse oximetry and protocols are needed to specify how oxygen saturation is to be measured and how positive screening results should be followed up before implementing this strategy in clinical practice.

The 2007 systematic review included the seven observational studies identified in the HTA and the 2005 systematic review, as well as one further observational study. A meta-analysis of the results reported for the 35,960 newborns included in the eight studies estimated that pulse oximetry had sensitivity (true positive) of 63% (95% CI 39% to 83%) and a specificity (true negative) of 99.8%. (95% CI 99% to 100%) The authors concluded that pulse oximetry is a highly specific screening tool with very low false-positive rates to detect CHD; however large studies are essential to assess the sensitivity with higher precision.

One further observational study was identified that was not reported in the reviews above.\(^8\) The authors of this study concluded that pulse oximetry was neither reliable nor an important diagnostic tool for 7,972 asymptomatic newborns that were cross-referenced against 12 confirmed cases of CHD. None of the newborns diagnosed with CHD was initially detected by pulse oximetry. Furthermore, important human factors, such as oximeter probe placement time, oximetry training and nursing degree, affected the reliability of the testing.

It should be emphasized that the nine observational studies included in Appendix 1 evaluated routine pulse oximetry using different objectives, different inclusion criteria, and different methodology. Consequently, they have shown a wide variety of findings. The sensitivity of a single pulse oximetry reading to detect critical CHD varied from 31% to 100% in eight of the nine studies. One study\(^8\) attributed the poor sensitivity of pulse oximetry to human factors. Less than one-half of
650 pulse oximetry readings were found to be reliable and even with additional training and quality control measures, reliability in a subsequent 800 readings was only 60%. The study authors suggested that this could explain the range of sensitivities reported in several screening studies. In clinical practice, the addition of pulse oximetry to newborn screening could potentially enhance the clinician’s ability to detect life-threatening cases of congenital heart disease in a timely manner. However, a screening test to prevent morbidity and mortality must be sensitive, reliable and reproducible before universal adoption is recommended. This has not been demonstrated to date.

A number of questions remain related to the use of pulse oximetry as a screening tool for CHD in asymptomatic newborns, including:

- What is the optimal age for newborn screening?
- What type of pulse oximetry testing should be used (fractional versus functional)?
- What is the optimal duration of probe placement?
- On which limb? (finger, toe, foot)
- What training is required of personnel doing the testing?
- What is the oxygen saturation level that would constitute a positive screening result?
- How should abnormal results be managed, particularly if cardiology consultation or pediatric echocardiography is not readily available?
- How are noncardiac causes of cyanosis to be diagnosed in an appropriate manner?
- What transport arrangements are acceptable when the infant is asymptomatic?
- What are the legal implications of a false negative test?

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Appendix 1: Data from studies assessing pulse oximetry to detect congenital heart disease in asymptomatic newborns.

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient population</th>
<th>Screening technique</th>
<th>Findings</th>
<th>General results</th>
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<tbody>
<tr>
<td>Richmond et al, 2002</td>
<td>Asymptomatic newborns (n=6,166)</td>
<td>Fractional O₂ sat measured over 2 minutes, after the age of 2 hours and before discharge, in one foot of all babies, with repeat testing in one to two hours if results were abnormal. Normal result defined as O₂ sat ≥ 95%.</td>
<td>Sensitivity 53% Specificity 99%</td>
<td>There were 10 true positives, 54 false positives, nine false negatives and 5,553 true negatives. Of the 54 false positives, 42 infants had O₂ sats &lt;95% but 30 had normal repeat O₂ sats plus exam and 12 had a normal echo. Only three of six cases of coarctation of the aorta were identified by oximetry test; low O₂ sat also drew attention to 12 infants with non-cardiac illness.</td>
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<td>Hoke et al, 2002</td>
<td>Well newborns (n=2,972) and newborns with suspected CHD (n=32)</td>
<td>Functional O₂ sat measured in both the arm and the leg at &lt; 6 hours of age, at 24 hours of age and/or at discharge. Abnormal result defined as O₂ sat in the leg &lt; 92% or a saturation 7% lower in the leg than in the arm.</td>
<td>Sensitivity 81% (to detect any CHD) Specificity 99%</td>
<td>An abnormal pulse oximetry test was found in 57 well newborns; of these, four infants were found to have congenital heart defects, including one case of coarctation of the aorta. A fifth child had pulmonary hypertension. Of the 32 newborns with CHD, 11/13 (85%) with left heart obstructive disease had abnormal O₂ sats as did 15/19 (79%) of those with other CHD.</td>
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<tr>
<td>Reich et al, 2003</td>
<td>Well newborns (n=2,335)</td>
<td>Functional O₂ sat measured close to discharge Normal result defined as O₂ sat &gt; 94%</td>
<td>Sensitivity - number of patients too small to calculate Specificity 99.9% PPV 33.3% NPV 100%</td>
<td>Low pulse oximetry readings led to the detection of one case of tetrology of Fallot and follow-up echocardiograms in three other patients revealed two with patent ductus arteriosus and one with right ventricular outflow tract obstruction. One false negative occurred in a child later diagnosed with total anomalous pulmonary venous return to the coronary sinus.</td>
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### Studies included in Griebsch’s 2005 systematic review (in addition to the four studies above)

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<tr>
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<tr>
<td>Koppel et al, 2003&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Asymptomatic newborns (n = 11,281)</td>
<td>Functional $\Omega_2$ sat was measured at &gt; 24 hours of age and before discharge (average length of stay 56.9 hours for vaginal delivery and 103.2 hours for cesarean)</td>
<td>Sensitivity 60% Specificity 99.5% PPV 75% NPV 99.98%</td>
<td>Three cases of congenital cardiovascular malformations were identified; two infants with a false-negative screen were re-admitted with coarctation and hypoplastic left heart syndrome; one infant had a false-positive screen.</td>
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<td>De-Wahl et al, 2005&lt;sup&gt;12&lt;/sup&gt;</td>
<td>Asymptomatic newborns (n = 200) and infants with critical CHD (n = 66)</td>
<td>Functional $\Omega_2$ sat measured in the right hand and one foot using a new generation pulse oximeter (NGoxi) and a conventional oximeter (CToxi)</td>
<td>Sensitivity 98.5% Specificity 96.0% PPV 89.0% NPV 99.5%</td>
<td>The CToxi pulse oximeter had a false positive rate of 41%. The NGoxi oximeter had a false-positive rate of 1%. A screening cutoff of &lt;95% gave false-negative results in 7 of 66 newborns with CHD. Detection of critical CHD was superior using saturation readings both from the right hand and one foot with a new-generation oximeter.</td>
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<td>Arlettaz et al, 2005&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Newborns &gt; 35 weeks gestation (n = 3,262)</td>
<td>Functional $\Omega_2$ sat measured with pulse oximetry between six and 12 hours of age on either the right or left foot.</td>
<td>Sensitivity 100% Specificity 99.7% PPV 63% NPV 100%</td>
<td>Twenty-four newborns had $\Omega_2$ sat &lt;95%; of these, 17 had CHD, five had pulmonary hypertension, one had a myocardial tumour and one infant had a normal heart. The false positive readings due to pulmonary hypertension were considered beneficial because they led to early diagnosis and treatment. The Swiss Societies of Pediatric Cardiology and Neonatology used the results of this study to recommend general screening by pulse oximetry.</td>
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<td>Bakr et al, 2005¹⁴</td>
<td>Asymptomatic newborns (n=5,211)</td>
<td>Fractional O₂ sat measured with pulse oximetry before discharge Normal result defined as a fractional O₂ sat ≥ 94%</td>
<td>Sensitivity 30.8% Specificity 99.9% PPV 80% NPV not reported</td>
<td>Five newborns had O₂ sat &lt; 94%; one of these was a false positive. When pulse oximetry was combined with clinical exam, sensitivity was 77%, positive predictive value was 66.7% and specificity was 100%.</td>
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<td>Additional study included in Thangaratinam’s 2007 systematic review (in addition to the seven studies above)</td>
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<tr>
<td>Rosati et al, 2005¹⁵</td>
<td>Asymptomatic newborns (n=5,292)</td>
<td>O₂ sat (unspecified type) measured for two minutes before discharge at a median age of 72 hours Normal result defined as an O₂ sat ≥ 95%</td>
<td>Sensitivity 66.7% (95% CI 11.6% to 94.5%) Specificity 100% (95% CI 99.9% to 100%) PPV 50% NPV 100%</td>
<td>There were two true positives, one false negative, two false positives and 5,288 true negatives.</td>
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<tr>
<td>Reich et al, 2007⁸</td>
<td>Asymptomatic newborns (n=7,962) Cross-referenced with confirmed cases of CHD (n=12)</td>
<td>O₂ sat (unspecified type) measured before discharge (median length of hospital stay unspecified) Normal result defined as O₂ sat ≥ 94%</td>
<td>NR</td>
<td>Twelve of the 7,962 newborns were diagnosed with CHD. None was initially identified by routine pulse oximetry.</td>
</tr>
</tbody>
</table>

O₂ sats – oxygen saturation
CHD – congestive heart disease
PPV – positive predictive value
NPV – negative predictive value
NR – not reported
References:


