Curr Treat Options Peds (2015) 1:202–210
DOI 10.1007/s40746-015-0020-x

Neonatology (T Thorkelsson, Section Editor)

The Value of Pulse Oximetry as a Screening Tool for Congenital Heart Disease

Alf Meberg, MD, PhD

Address
The Neonatal Unit, Department of Pediatrics, Vestfold Hospital Trust,
3103 Tønsberg, Norway
Email: alfmeberg@yahoo.no

Published online: 31 July 2015

This article is part of the Topical Collection on *Neonatology*

Keywords Pulse oximetry · Screening · Newborn infants · Critical congenital heart defect

Opinion Statement

Universal pulse oximetry (POX) screening of apparently healthy newborn infants is useful for detection of critical congenital heart defects (CCHDs). First-day-of-life screening shortens time of the diagnostic process at the expense of a higher false positive rate than screening after 24 h of age. A substantial number of false positives, however, represent potentially severe extracardiac disorders. Early detection of such disorders is an added advantage. *POX-screening may thus not be looked upon only as a heart screening, however, also a screening for other disorders with true hypoxemia, most hidden pulmonary pathology*. Simple postductal screening (probe on foot) may be an alternative to combined pre- and postductal arterial oxygen saturation measurements (SpO_2) (probe on right hand and a foot). By combining POX-screening with routine clinical heart examination, a predischarge detection rate for CCHDs of 90 % is obtained. Moderate sensitivity for detecting obstructive lesions from the left heart, especially coarctation of the aorta, emphasizes the need for better screening methods for these conditions.

Introduction

Structural heart defect is the most common type of congenital malformations, occurring in about 10 per 1000 live-born infants [1]. Some of these are classified as critical because they untreated in a few days or weeks after birth will progress into a life-threatening circulatory collapse or severe cardiac failure. Without therapeutic intervention, the baby will die. Others use a more pragmatic definition, classifying as critical congenital heart defects (CCHDs), those causing death or requiring invasive intervention before 28 days, and apply the term major defects for those who die or require invasive intervention within 12 months of age [2•]. Table 1 lists the types of defects most often classified as critical. The prevalence of CCHDs is about 1–2 per 1000 live-born infants [3•, 4•, 5], accounting for 10–20 % of all heart defects, and thus represents an important pre- and early postnatal diagnostic and therapeutic challenge.

Table 1. Main specific critical congenital heart defects

Ductus dependent systemic circulation
Hypoplastic left heart syndrome
Critical aortic stenosis
Coarctation of the aorta
Interrupted aortic arch
Ductus dependent pulmonary circulation
Pulmonary atresia (with intact septum)
Tricuspid atresia
Miscellanous
Double outlet right ventricle
d-Transposition of the great arteries
Ebstein anomaly
Tetralogy of Fallot
Total anomalous pulmonary venous return
Truncus arteriosus
Single ventricle

Some CCHDs are asymptomatic or have subtle symptoms during the first hours or days of life and may be missed in the clinical routine examination of newborns after birth [6–8]. Most CCHDs are dependent on an open ductus arteriosus, and the baby deteriorates rapidly when the ductus closes. When such infants are discharged with their condition undetected the risk for readmittance in a circulatory collapse is high [6, 9]. From England Wren et al. found that one third of infants with a potentially life threatening heart defect were discharged with the disorder undetected, and that 5 % of these died with the condition first recognized by autopsy [9]. Similar results have recently been published by Dawson et al. [8] and Fixler et al. [10]. Short stay in hospital after birth may be a risk factor for missing CCHDs. In infants in need of invasive therapeutic heart procedures before 2 months of age Mellander and Sunnegårdh found that cases of CCHDs discharged home with the defect overlooked increased to 26 % contemporary with a decreasing length of stay in hospital after birth [11]. For those with a ductus-dependent pulmonary circulation, who often present with a visible cyanosis, only 4 % were missed, while 30 % of those with a ductus-dependent systemic circulation, often with a subnormal arterial oxygen saturation (SpO_2) without visible cyanosis, were missed. Of non-ductus-dependent CCHDs 38 % were missed. In a Norwegian study, 82 % of the missed CCHDs were obstructive lesions from the left heart, most coarctation of the aorta and interrupted aortic arch [3•]. Similar findings have been reported by Dawson et al. [8] and by Wren et al., who in addition registered total anomalous pulmonary venous return often to be missed, as well as a minor part of other CCHDs [9]. Better strategies obviously are needed to detect CCHDs before progressing into a circulatory collapse.

Pre- and Postnatal Screening for Congenital Heart Defects

Routine clinical examination of newborn infants before discharge home from the nursery will detect most congenital heart defects (CHDs). However, as many as one fourth may be overlooked and left for post discharge detection, some of them critical defects [1]. A substantial percentage of infants with CCHDs will have a subnormal SpO_2 which may not show as visible cyanosis [11, 12]. The patient is "not as pink as you think" [13]. Such defects may be detected by pulse oximetry (POX). An important goal for POX-screening programs thus is to reduce the number of infants with CCHDs discharged undiagnosed. Peterson et al. estimated that 29.5 % of non-syndromic live-born infants with CCHDs received a diagnosis more than 3 days after birth and therefore might have benefited from routine POX-screening at birth hospitals [14]. On this background, universal POX-screening of apparently healthy newborn infants has been implemented in many hospitals during the last decade.

Prenatal ultrasound heart screening has the potential to detect CCHD in the fetus. In pregnancies referred to centers of excellence, the detection rate may be as high as 57–67 % [15–17]. However, such studies also include intrauterine deaths and terminated pregnancies of fetuses with CCHDs, often associated with syndromes or extracardiac malformations. Calculated this way, a high percentage of detection is obtained. In some tertiary-care birthing centers with a very effective prenatal echocardiography screening, nearly all CCHDs may be detected [18], leaving POX-screening more important in settings with a lower prenatal diagnosis rate. In large unselected populations of live-born infants, the prenatal detection rate of CCHDs vary considerably between regions and is found to be as low as about 30 % for whole countries [3•, 19•]. This leaves the vast majority of CCHDs in infants born alive to be detected after birth.

Accuracy of POX-Screening

In 2012, Thangaratinam et al. published a large metaanalysis of POX-screening including 13 high-quality studies in 229,421 infants [20••]. Table 2 shows

Table 2. Accuracy estimates in a metaanalysis including 13 studies of pulse oximetry for the detection of critical congenital heart defects in 229,421 newborn infants according to Thangaratinam et al. [20••]

	% (95 % CI)	
Sensitivity	76.5 (67.7–83.5)	
Specificity	99.9 (99.7–99.9)	
Likelihood ratio positive	549.2 (232.8–1195.6)	
Likelihood ratio negative	0.24 (0.17–0.33)	
False positive rate	0.14 (0.06–0.33)	
	Sensitivity % (95 % CI)	False positive rate % (95 %CI)
Test timing		
<24 h	84.8 (69.8–93.1)	0.5 (0.29–0.86)
≥24 h	77.5 (61.8–88.0)	0.05 (0.02–0.12)
Measurement site		
Foot and right hand	70.0 (54.9–81.7)	0.19 (0.04–0.89)
Foot only	80.2 (69.5–87.8)	0.12 (0.04–0.35)
Antenatal screen positive for CHD		
Excluded	76.7 (66.4–84.5)	0.08 (0.03–0.19)
Included	88.1 (62.6–97.0)	0.73 (0.50–1.05)

CI confidence interval, *CHD* congenital heart defect

the accuracy estimates in this metaanalysis. A sensitivity of 76.5 % for detection of CCHDs was found for all studies combined. Same sensitivity was found when screening was undertaken before 24 h after birth, as after. However, a significantly lower false positive rate was found when screening was undertaken later than 24 h. Sensitivity for detection was equal whether the probe was placed postductally on a foot or combined on right hand and a foot, paying attention to the difference in pre- and postductal SpO_2 in addition to subnormal values. The conclusions were that POX-screening was highly specific for detection of CCHDs and met criteria for universal screening.

Since the metaanalysis by Thangaratinam et al. was published, large studies from Poland (51,698 infants postductually screened first day of life) [21] and China (122,738 screened combined pre- and postductually 6–72 h of life) [22] have shown comparable results. Several smaller studies published recently have also added findings supporting the usefulness of POX-screening for detection of CCHDs [23, 24].

Sensitivity for detecting CCHDs varies between different types of heart defects and causes concern for false negative results. Obstructive lesions from the left heart, especially coarctation of the aorta, remains a challenge, with a sensitivity for detection of only 29–50 % [2•, 4•, 25]. Better methods for detecting such lesions are needed. Perfusion index, a measure for peripheral blood flow calculated from the pulse waveform curve, may be a promising parameter, and integrated in pulse oximeters [26].

When combining POX-screening with routine clinical examination before discharge, the sensitivity for detecting CCHDs increases and reaches about 90 %. Studies from Sweden and Norway have shown that only 8 and 12 % of infants with CCHDs respectively were discharged with the disorder undetected [3•, 4•]. Similar results have been reported by others [17, 22].

Sensitivity for detecting major CHDs (died or requiring invasive intervention before 12 months of age) is lower (49 %) than for CCHDs alone (75 %) (died or requiring invasive intervention before 28 days of age) according to a study of Ewer at al. from England [2•]. When antenatally detected defects were excluded, they found a lower sensitivity for POX-screening detecting major cases (29 %) as well as for CCHDs (58 %). This emphasizes that more antenatally detected CHDs have a low SpO_2 postnatally, and that this population of heart defects carries a high grade of severity. Meberg at al found that 74 % of antenatally detected CHDs would have failed the POX-screening, making this screening a security net when CCHDs are missed in the fetal ultrasound heart examination [27•].

For the total cohort of live-born infants with heart defects, the detection rate by POX-screening has been found as low as 6 % [27•, 28]. This demonstrates that most CHDs, which are of minor or moderate severity, have a normal SpO_2 because of left-to-right shunting through septal defects or a patent ductus, or valvar stenosis or leakage without shunting. Most of these defects will be detected by routine clinical examination before or after discharge from hospital after birth [1, 27•].

The Challenge of False Positives

Although reducing false positives may be important for minimizing futile use of resources and avoiding parental anxiety, a substantial number of such cases in fact represent potentially severe extracardiac conditions in need of early detection. Meberg et al. published data showing that 41 % of false positives in first-day-of-life POX-screening were disorders such as transient tachypnea, systemic infections (among them group B streptococcal septicemia), amniotic fluid aspiration, pulmonary hypertension, and pneumothorax [27•]. In addition, some non-critical CHDs were detected. Ewer at al published comparable results showing that 27 % of their false positives were conditions in need of urgent medical intervention [2•]. Similar findings have since been published by Zaho et al. [22], Singh, Rasiah, and Ewer [23] and Bhola, Kucklow, and Evans [24]. *POX-screening thus may be looked upon not only as a heart screening, however, also as a screening for extracardiac conditions with true hypoxemia, especially hidden pulmonary disorders*. This is an added advantage to the main goal of detecting CCHDs. As extracardiac hypoxemic conditions detected by POX-screening, especially first-day-of-life, may outnumber the cases of CCHDs detected [2•, 22–24, 27•], the importance of this "side effect" should be valued. As "true" false positives may be defined cases with a normal heart, however, with a prolonged phase of transitional circulation where an increased pulmonary vascular resistance causes right-to-left or bidirectional shunting of blood through an open ductus arteriosus [27•].

When to Screen?

Screening strategies have been divided between first-day-of-life screening and screening more that 24 h after birth (unless the infant is discharged before). The last alternative has been promoted in the USA with a screening protocol endorsed by the American College of Cardiology (ACC), the American Academy of Pediatrics (AAP), and the American Heart Association (AHA) (Fig. 1) [29•, 30]. The reason for this choice has primarily been to minimize false positives. In Europe, first-day-of-life screening has been recommended in the Nordic countries [19•], Switzerland [31], and Poland [21] among others. One argument for first-day-of-life screening has been that it makes a very early detection of CCHDs possible, shortening time to start further diagnostic procedures. Meberg et al. found by first-day-of life screening that median time for predischarge detection of CCHDs was only 6 h after birth [3•, 27•]. For hospitals not performing POX-screening, the corresponding time was 17 h ($p<0.001$) [3•]. A second argument for early screening has been the early detection of potentially severe extracardiac disorders, as mentioned above.

The higher false positive rate by first-day-of-life screening may cause extra use of "unnecessary" echocardiography, however, within acceptable limits [24, 32, 33]. Put into perspective a false positive rate of 0.5 %, as found in the metaanalysis of Thangaratinam et al. (Table 2) [20••], will generate need for less than one extra echocardiography per month in a hospital with 2000 deliveries a year. When hypoxemia obviously is caused by an extracardiac condition, the infant may not be referred for echocardiography, further reducing the consumption of extra resources. Based on careful clinical assessment and available evidence, Singh, Rasiah, and Ewer recognized that less than one third of babies failing the POX-screening would need an echocardiogram [23]. On the other hand, there should in general be a low threshold for undertaking echocardiography. Infants with a slightly subnormal SpO_2 should, although looking healthy, not be discharged without passing echocardiography, as CCHDs may be missed in such cases [3•].

Pre- or Combined Pre- and Postductal SpO_2 Measurements

There have been some discussion whether the POX-screening should be undertaken by postductal SpO_2 measurements only [27•] or as combined pre- and postductal registrations [19•, 29•]. Using the last strategy attention is paid not only to a subnormal SpO_2 but also to an SpO_2 difference of more than 3 %, even if saturation levels are within the normal range both pre- and postductally. Studies undertaking postductal measurements only use an SpO_2 of below 95 % as criterium for failing the test [21, 27•, 31]. Meberg et al. performed 1000 consecutive postductal registrations in apparently healthy newborn infants first day of life and found an SpO_2 of 95 % to represent two standard deviations below mean [27•]. SpO_2 below this level thus seems reasonable to use for identifying those who need retesting or immediate referral for echocardiography.

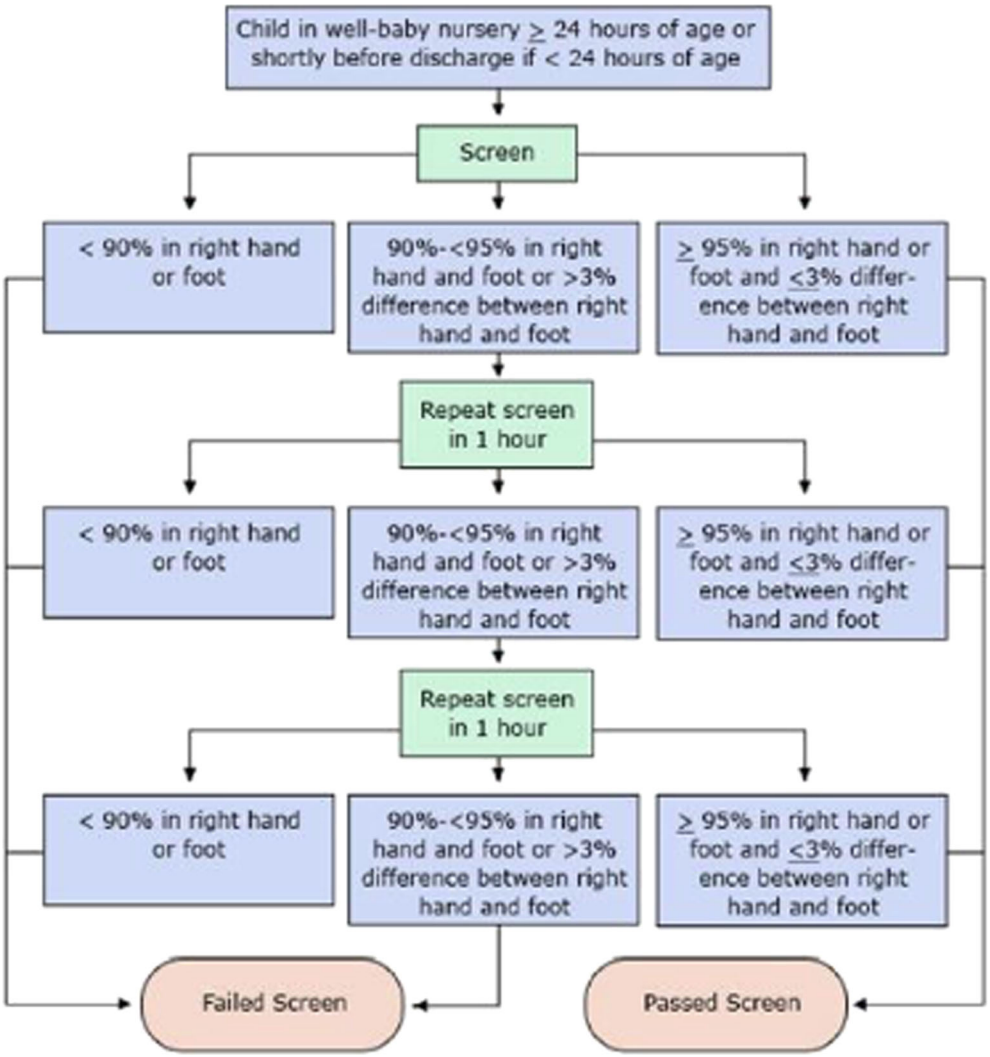

Fig. 1. Algorithm for screening for critical congenital heart defects. Screening protocol endorsed by the American College of Cardiology, the American Academy of Pediatrics, and the American Heart Association. Available at http://www.cdc.gov/ncbddd/heartdefects/hcp.html.

However, this study included infants born at sea level. At higher altitudes, SpO_2 is slightly lower, and algorithm cutoffs therefore may need adjustment in high-altitude nurseries [34].

For screening large populations of newborns, simplicity of testing and easy and reliable interpretation of the results are important. A simple algoritm for postductal screening is shown in Fig. 2 and the more sophisticated American algorithm for contemporary pre- and postductal measurements in Fig. 1. The last one is quite similar to an algorith recommended by a Nordic group [19•], except that the Nordic one recommends first-day-of-life screening and the American one screening later than 24 h of life as the main strategy [29•, 35•]. An advantage of combined pre- and postductal screening is that it may detect coarctation of the aorta with a lower postductal than preductal SpO_2. In some cases of transposition of the great arteries, the postductal SpO_2 may be normal while the preductal saturation may be subnormal [36]. Scientific evidence for the combined

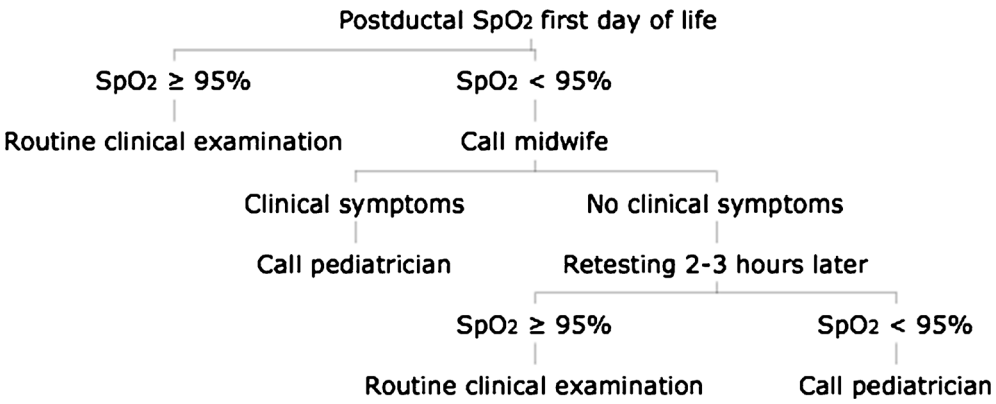

Fig. 2. Algorithm for postductal pulse oximetry screening according to Meberg et al. [27•].

screening being better than simple postductal screening is, however, weak. In their large metaanalysis, Thangaratinam et al. did not find any significant difference in sensitivity for detecting CCHDs whether the probe was placed on the foot alone or combined on foot and right hand (Table 2) [20••]. Neither did the false positive rates differ significantly.

Oster, Kuo, and Mahle evaluated the algorithm endorsed by AAP and AHA with combined pre- and postductal SpO_2 measurements and found the manual algorithm for interpretation of the results to be susceptible to human error [37•]. Sets of screening scenarios were answered correctly in only 81.6 % when manually interpreting the algorithm vs 98.3 % when using a computer-based tool ($p<0.001$). The authors recommended implementation of a computer-based tool to aid in the interpretation of the results to improve accuracy and quality. Interpretation of results from a postductal screening algorithm (Fig. 2) may, however, be more easy and makes this way of screening an alternative to the combined one, at least if a computer-based tool is not available.

POX-Screening of Different Populations

The relative risk for a late diagnosis of CCHDs has been shown to be higher in level I and II hospital nurseries than in level III nurseries, possibly related to more extensive use of pulse oximeters and other diagnostic tools in the higher level nurseries [8]. POX-screening has been found to be successfully implemented in screening for CCHDs in community hospitals [38, 39] and also for planned out-of-hospital births [40]. Acceptance of the value of POX-screening in out-of-hospital births is increasing among midwives [41]. In Holland, with a large number of home births, a protocol for POX-screening is to be implemented to increase safety [42]. In regions with a birth pattern decentralized to small and low-level units, and to out-of-hospital births, POX may be especially useful because of convenience in use and reliable results. Using the simplified algorithm with postductal measurements of SpO_2 could make the POX-screening in such settings even more easy (Fig. 2) [43]. This may also be relevant if a computer-based tool for interpretation of the results is not available. In neonatal intensive care units, predischarge POX-screening for CCHDs has also proven useful, however, with some higher rate of false positives compared with asymptomatic newborn infants [44].

Cost-Effectiveness

Pulse oximeters have been used extensively in routine clinical examinations and monitoring of many types of patients. Thus, the devices and their practical use have grown familiar for doctors as well as midwives, nurses, and other health care providers. The equipment is relatively cheap and the use simple and little time consuming. POX-screening thus may be integrated in daily routines with minimal increase in nursing workload and no need for extra staff [8, 38, 45, 46]. Physicians involved in newborn medicine deem it an effective tool [47]. Studies addressing cost-effectiveness of universal POX-screening of newborns for CCHDs suggest such programs to be cost-effective in light of currently accepted thresholds [38, 48, 49]. Lower screening costs may be obtained by applying reusable screening sensors [49].

Quo vadis POX-Screening?

Although it seems an obvious advantage to diagnose CCHDs before progressing into a circulatory collapse, the hard end-points of survival, physical, and mental functioning and quality of life are not yet documented to be improved as a result of universal POX-screening. POX-screening most probably is a right thing to do; however, it may not be clear that the actual benefits outweigh the downsides (overall costs of screening, delayed diagnosis of false negative screen results, costs of evaluation and anxiety in families with false positive screen results, and diagnosis of CCHDs where early diagnosis offers no added benefit over late detection), as stated in an editorial by Taylor [50]. Further research is needed to answer these questions.

Quality of the POX-screening may be improved by special training of the health care providors undertaking the screening [43, 51]. They should be able to interpret the results correctly, and rapidly alert the doctor when a baby fails the test. A computer-based system for interpretion of the screening result may increase correctness of the interpretation. If such systems are not available, simplification of the algorithm by using a postductal screening strategy may be an alternative. POX-screening programs should be implemented in nurseries of all levels. Screening should not be missed in babies with very short stay in hospital after birth and also be implemented for out-of hospital births as well as predischarge in special and intensive care neonatal units. Motion stable devices should be used [19•, 30, 35•]. Screening data should be registered in computerized databases so they can be retrieved for large populations for quality assurance and research purposes [2•, 19•, 35•].

Compliance with Ethics Guidelines

Conflict of Interest

Dr. Alf Meberg declares that he has no conflict of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- • Of importance,
- •• Of major importance

1. Meberg A. Congenital heart defects through 30 years. Open J Pediatr. 2012;2(3):219–27.
2.• Ewer AK, Middleton LJ, Furmston AT, Bhoyar A, Thangaratinam S, Deeks JJ, et al. Pulse oximetry screening for congenital heart defects in newborn infants (PulseOx): a test accuracy study. Lancet. 2011;378(9793):785–94.

Important population-based multicenter study from England.

3.• Meberg A, Andreassen A, Brunvand L, Markestad T, Moster D, Nietsch L, et al. Pulse oximetry screening as a complementary strategy to detect critical congenital heart defects. Acta Paediatr. 2009;98(4):682–6.

Population based multicenter study from Norway including data for the whole country comparing results of POX-screening with hospitals not screening.

4.• de-Wahl Granelli A, Wennergren M, Sandberg K, Mellander M, Bejlum C, Inganäs L, et al. Impact of pulse oximetry screening on the detection of duct dependent congenital heart disease: a Swedish prospective screening study in 39 821 newborns. BMJ. 2009;8:338–a3037. doi:10.1136/bmj.a3037.

Important population-based multicenter study from Sweden.

5. Liske MR, Greeley CS, Law DJ, Reich JD, Morrow WR, Baldwin HS, et al. Report of the Tennessee Task Force on screening newborn infants for

critical congenital heart disease. Pediatrics. 2006;118(4):e1250–6.
6. Abu-Harb M, Hey E, Wren C. Death in infancy from unrecognised congenital heart disease. Arch Dis Child. 1994;71(1):3–7.
7. Meberg A, Otterstad JE, Frøland G, Hals J, Sorland SJ. Early clinical screening of neonates for congenital heart defects: the cases we miss. Cardiol Young. 1999;9(2):169–74.
8. Dawson AL, Cassell CH, Riehle-Colarusso T, Grosse SD, Tanner JP, Kirby RS, et al. Factors associated with late detection of critical congenital heart disease in newborns. Pediatrics. 2013;132(3):e604–11.
9. Wren C, Reinhardt Z, Khawaja K. Twenty-year trends in diagnosis of life-threatening neonatal cardiovascular malformations. Arch Dis Child Fetal Neonatal Ed. 2008;93(1):F33–5.
10. Fixler DE, Xu P, Nembhard WN, Ethen MK, Canfield MA. Age at referral and mortality from critical congenital heart disease. Pediatrics. 2014;134(1):e98–105.
11. Mellander M, Sunnegårdh J. Failure to diagnose critical heart malformations in newborns before discharge—an increasing problem? Acta Paediatr. 2006;95(4):407–13.
12. O'Donnell CP, Kamlin CO, Davis PG, Carlin JB, Morley CJ. Clinical assessment of infant colour at delivery. Arch Dis Child Fetal Neonatal Ed. 2007;92(6):F465–7.
13. Pass KA. Not as pink as you think! Pediatrics. 2003;111(3):670–1.
14. Peterson C, Ailes E, Riehle-Colarusso T, Oster ME, Olney RS, Cassell CH, et al. Late detection of critical congenital heart disease among US infants: estimation of the potential impact of proposed universal screening using pulse oximetry. JAMA Pediatr. 2014;168(4):361–70.
15. Tegnander E, Williams W, Johansen OJ, Blaas HG, Eik-Nes SH. Prenatal detection of heart defects in a non-selected population of 30 149 fetuses—detection rates and outcome. Ultrasound Obstet Gynecol. 2006;27(3):252–65.
16. Moe Eggebø T, Heien C, Berget M, Lycke EC. Routine use of color Doppler in fetal heart scanning in a low-risk population. ISRN Obstet Gynecol. 2012;2012:496935. doi:10.5402/2012/496935.
17. Liberman RF, Getz KD, Lin AE, Higgins CA, Sekhavat S, Markenson GR, et al. Delayed diagnosis of critical congenital heart defects: trends and associated factors. Pediatrics. 2014;134(2):e373–81.
18. Johnson LC, Lieberman E, O'Leary E, Geggel RL. Prenatal and newborn screening for critical congenital heart disease: findings from a nursery. Pediatrics. 2014;134(5):916–22.
19.• De-Wahl Granelli A, Meberg A, Ojala T, Steensberg J, Oskarsson G, Melander M. Nordic pulse oximetry screening—implementation status and proposal for uniform guidelines. Acta Paediatr. 2014;103(11):1136–42.
Common guidelines proposed for pulse oximetry screening in the Nordic countries.
20.•• Thangaratinam S, Brown K, Zamora J, Khan KS, Ewer AK. Pulse oximetry screening for critical congenital heart defects in asymptomatic newborn babies: a systematic review and meta-analysis. Lancet. 2012;379(9835):2459–64.
Important metaanalysis of 13 high-quality studies on POX-screening.
21. Turska KA, Borszewska Kornacka MK, Blaz W, Kawalec W, Zuk M. Early screening for congenital heart defects in asymptomatic newborns in Mazovia province: experience of the POLKARD pulse oximetry programme 2006–2008 in Poland. Kardiol Pol. 2012;70:370–6.
22. Zhao QM, Ma XJ, Ge XL, Liu F, Yan WL, Wu L, et al. Pulse oximetry with clinical assessment to screen for congenital heart disease in neonates in China: a prospective study. Lancet. 2014;384(9945):747–54.
23. Singh A, Rasiah SV, Ewer AK. The impact of routine predischarge pulse oximetry screening in a regional neonatal unit. Arch Dis Child Fetal Neonatal Ed. 2014;99(4):F297–302.
24. Bhola K, Kluckow M, Evans N. Post-implementation review of pulse oximetry screening of well newborns in an Australian tertiary maternity hospital. J Paediatr Child Health. 2014;50(11):920–5.
25. Valmari P. Should pulse oximetry be used to screen for congenital heart disease? Arch Dis Child Fetal Neonatal Ed. 2007;92(3):219–24.
26. Granelli AW, Östman-Smith I. Noninvasive peripheral perfusion index as a possible tool for screening for critical left heart obstruction. Acta Paediatr. 2007;96(10):1455–9.
27.• Meberg A, Brügmann-Pieper S, Due Jr R, Eskedal L, Fagerli I, Farstad T, et al. First day of life pulse oximetry screening to detect congenital heart defects. J Pediatr. 2008;152(6):761–5.
Important population-based multicenter study from Norway, with data for detection also of extracardiac conditions with hypoxemia by POX-screening.
28. Meberg A. Critical heart defects—the diagnostic challenge. Acta Paediatr. 2008;97(11):1480–3.
29.• Mahle WT, Newburger JW, Matherne GP, Smith FC, Hoke TR, Koppel R, et al. Role of pulse oximetry in examining newborns for congenital heart disease: a scientific statement from the AHA and AAP. Pediatrics. 2009;124(2):823–36.
Guidelines for POX-screening in USA.
30. Mahle WT, Martin GR, Beekman 3rd RH, Morrow WR, Section on Cardiology and Cardiac Surgery Executive Committee. Endorsement of Health and Human Services recommendation for pulse oximetry screening for critical congenital heart disease. Pediatrics. 2012;129(1):190–2.
31. Kuelling B, Arlettaz M, Bauersfeld U, Balmer C. Pulse oximetry screening for congenital heart defects in Switzerland: most but not all maternity units screen their neonates. Swiss Med Wkly. 2009;139(47–48):699–704.

32. Hoffman JI. It is time for routine neonatal screening by pulse oximetry. Neonatology. 2011;99(1):1–9.
33. Ewer AK. Pulse oximetry screening: do we have enough evidence now? Lancet. 2014;384(9945):725–6.
34. Samuel TY1, Bromiker R, Mimouni FB, Picard E, Lahav S, Mandel D, et al. Newborn oxygen saturation at mild altitude versus sea level: implications for neonatal screening for critical congenital heart disease. Acta Paediatr. 2013;102(4):379–84.
35.• Kemper AR, Mahle WT, Martin GR, Cooley CW, Kumar P, Morrow R, et al. Strategies for implementing screening for critical congenital heart disease. Pediatrics. 2011;128:e1259–62.
Guidelines for POX-screening in the USA.
36. Yap SH, Anania N, Alboliras ET, Lilien LD. Reversed differential cyanosis in the newborn: a clinical finding in the supracardiac total anomalous pulmonary venous connection. Pediatr Cardiol. 2009;30(3):359–62.
37.• Oster ME, Kuo KW, Mahle WT. Quality improvement in screening for critical congenital heart disease. J Pediatr. 2014;164(1):67–71.
Important study on challenges in interpretation of results from combined pre- and postductal POX-screening.
38. Bradshaw EA, Martin GR. Screening for critical congenital heart disease: advancing detection in the newborn. Curr Opin Pediatr. 2012;24(5):603–8.
39. Pflugeisen BM, Amoroso PJ, Zook D, Welke KF, Reedy A, Park MV. Quality improvement measures in pulse-oximetry newborn heart screening: a time series analysis. Pediatrics. 2015;135(2):e531–9.
40. Lhost JJ, Goetz EM, Belling JD, van Roojen WM, Spicer G, Hokanson JS. Pulse oximetry screening for critical congenital heart disease in planned out-of-hospital births. J Pediatr. 2014;165(3):485–9.
41. Evers PD, Vernon MM, Schultz AH. Critical congenital heart disease screening practices among licensed midwives in Washington state. J Midwifery Womens Health. 2015;60(2):206–10.
42. Narayen IC, Blom NA, Verhart MS, Smit M, Posthumus F, van den Broek AJ, et al. Adapted protocol for pulse oximetry screening for congenital heart defects in a country with homebirths. Eur J Pediatr. 2015;174(1):129–32.
43. Kochilas LK, Lohr JL, Bruhn E, Borman-Shoap E, Gams BL, Pylipow M, et al. Implementation of critical congenital heart disease screening in Minnesota. Pediatrics. 2013;132(3):e587–94.
44. Manja V, Mathew B, Carrion V, Lakshminrusimha S. Critical congenital heart disease screening by pulse oximetry in a neonatal intensive care unit. J Perinatol. 2015;35(1):67–71.
45. Centers for Disease Control and Prevention (CDC). Rapid implementation of pulse oximetry newborn screening to detect critical congenital heart defects—New Jersey, 2011. MMWR Morb Mortal Wkly Rep. 2013;62(15):292–4.
46. Peterson C, Grosse SD, Oster ME, Olney RS, Cassell CH. Cost-effectiveness of routine screening for critical congenital heart disease in US newborns. Pediatrics. 2013;132(3):e595–603.
47. Studer MA, Smith AE, Lustik MB, Carr MR. Newborn pulse oximetry screening to detect critical congenital heart disease. J Pediatr. 2014;164(3):505–9. e1-2.
48. Roberts TE, Barton PM, Auguste PE, Middleton LJ, Furmston AT, Ewer AK. Pulse oximetry as a screening test for congenital heart defects in newborn infants: a cost-effectiveness analysis. Arch Dis Child. 2012;97(3):221–6.
49. Peterson C, Grosse SD, Glidewell J, Garg LF, Van Naarden BK, Knapp MM, et al. A public health economic assessment of hospitals' cost to screen newborns for critical congenital heart disease. Public Health Rep. 2014;129(1):86–93.
50. Taylor JA, Phillipi CA. Potential—and potential pitfalls—of screening newborns for critical congenital heart disease. JAMA Pediatr. 2014;168(4):311–2.
51. Ryan DJ, Mikula EB, Germana S, Silva SG, Derouin A. Screening for critical congenital heart disease in newborns using pulse oximetry: evaluation of nurses' knowledge and adherence. Adv Neonatal Care. 2014;14(2):119–28.