Screening for congenital heart disease
Consultation responses from national organisations

Professional organisations

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Organisation		**Royal College of Paediatrcis and Child Health**	
Name	Comments provided on behalf of the following: • Dr Anjum Gandhi (Consultant Paediatrician, on behalf of Paediatricians with Expertise in Cardiology Special Interest Group) • Dr Julia Thomson (Paediatric Consultant) • Dr Gopi Menon (Consultant Neonatologist, on behalf of the British Association of Perinatal Medicine) • Dr Andy Ewer (University of Birmingham and Birmingham Women's Hospital on behalf of the British Association of Perinatal Medicine) • Dr Sundeep Harigopal (Consultant Neonatologist on behalf of the British Association of Perinatal Medicine)	**Email Address**	[redacted]
1. Optimal test procedures for oxygen saturation measurement and newborn clinical examination			

1a. The review concludes that pulse oximetry is clinically useful and will increase the number of congenital heart defects detected in the newborn period. However, it also concludes that the optimal approach to screening (for example its timing, positioning of oximeter probes eg hand or foot or both, number of times the test should be repeated) cannot be clearly defined on the basis of the available studies. Do you agree with this conclusion? Please click either yes or no check boxes below.

☒ Yes ☐ No

Please let us know the reasons for your response in the table below:

Section and / or page number	Text to which comments relate	Comment *Please use a new row for each comment and add extra rows as required.*
		We Agree that pulse oximetry is likely to be useful and feel that it can be introduced with proper training and support.
		The review appropriately concludes that adding pulse oximetry to clinical examination as part of newborn screening for CHD increases the detection of serious CHD and is likely to be cost-effective and acceptable. CHD, a series of structural abnormalities with different presentations and outcomes, of necessity requires a pragmatic approach to screening. Whilst pulse oximetry is not specific to one particular group of these, it effectively utilises the fact that the newborn in the first few days is at a critical stage of development and is undergoing a major transition in anatomy and physiology, particularly in the respiratory and cardiovascular systems. It is clear that pulse oximetry adds significantly to the effectiveness of clinical examination in CHD detection. A phased introduction would be appropriate with attention to the issues raised in the review which would be important to the stringent application of this as a screening test. However, we would suggest that there should be a very focussed and time-limited approach to answering outstanding questions in order to avoid any delay in wider clinical implementation.
		This question is slightly misleading as there are 2 separate conclusions:

		• Pulse oximetry is clinically useful and will increase the number of CHD detected in the newborn period • The optimal approach to screening … cannot be clearly defined on the basis of available studies We agree wholeheartedly with the first conclusion but not with the second. Following publication of the Lancet systematic review of pulse oximetry screening in 2012 (ref 39) which included almost 230 000 babies screened, 2 further studies have been undertaken; one in Poland (ref 126) and one in China (unpublished data). The Polish study screened almost 52 000 babies and the Chinese study screened almost 121 000. This brings the total number of asymptomatic babies screened using pulse oximetry to over 400 000. Despite heterogeneous methodologies the data from these studies demonstrate the ability of this screening method to detect critical CHD that may otherwise be missed. The data also very clearly demonstrate the following: • The false positive rate is higher if babies are screened before 24 hours compared with after 24 hours, although false positive rate is consistently <1% whatever the timing of screening • There is no statistically significant difference in sensitivity between pre and post ductal screening (hand and foot) and post ductal screening (foot only) but individual cases will be missed by post ductal screening which would be identified by pre and post ductal. When these individual cases are scaled up to national populations they may become significant. • The number of time the test is repeated is likely to reduce false positives but increases the time taken to do the test and may delay diagnosis. These observations are summarized in Ref 83.
		There is paucity of data on screening in specific important cardiac anomalies. In spite of an apparently impressive total of over 250000 babies screened from all published studied, the number of CHD cases are very small even taking into account the possibility of a cardiac anomaly being raised for other reasons. Prudoe S et al showed that there were only 50

		cases of coarctation/aortic arch interruption, 49 cases of transposition, 28 cases of Fallot's tetralogy, 22 cases of hypoplastic left heart, and correspondingly smaller numbers of rarer conditions. As a consequence, the 95% CIs on published potential oximetry (PO) screening success by cardiac diagnosis are very wide. They stated "The number of published cases subjected to oximetry screening is too small to estimate the effectiveness of screening specific cardiac anomalies with precision." *(Prudhoe S, Abu-Harb M, Richmond S, Wren C. Neonatal screening for critical cardiovascular anomalies using pulse oximetry.Arch Dis Child Fetal Neonatal Ed. 2013 Jul;98(4):F346-50.)* The NSC draft quotes "CHDs with short presymtomatic interval can be considered life threatening and benefit form newborn screening. Conditions include – HLH, IAA, TGA, TAPVC, PA" So let us examine these conditions. According to the Pulse Ox study *(Pulse oximetry screening for congenital heart defects in newborn infants (PulseOx): a test accuracy study. Lancet 2011;378(9793):785-94).* 12/24 critical conditions were was antenatally diagnosed, HLH – 5 cases – all detected antenatally, 3 abnormal exam, I missed on PO TGA- 7 cases, 2 antenatal diagnosis, off the 5 remaining 3 had abnormal examination, 1 missed by PO, **1 detected purely by PO** TAPVC – 1 case, not detected AN, abnormal examination, PO positive PA- 3 cases, all 3 detected antenatally LHO – 6 cases, 1 antenatal diagnosis, 5 abnormal exam, 3 missed by PO ***Therefore, if you take into account antenatal diagnosis and abnormal examination,***

		only one extra baby with 'critical' CHD (case 13-TGA), and one extra baby with 'serious' CHD (case 29- Tricuspid atresia) was found as a result of pulse oximetry measurements, out of the ~ 20,000 babies tested. (Table 2) Prudhoe et al showed out of 29925 cases, 27 were critical cases, - 5 were detected by PO and 5 missed by PO. So 5 of the ~30000 cases were detected by PO. In a unit delivering 5000 babies that would mean detecting l.5 critical cases very 2 years or 3 cases every 4 year. If one were to include serious cases as well the detected rate would be 3 cases (critical & serious) every 2 years. Detecting every single case is important and therefore any test to aid in doing this should be carefully considered however the implications of late detection and the burden on the existing resources need to be considered. <u>Relationship between timing of diagnosis and outcome</u> One of the reasons to consider any form of screening would be if early diagnosis influenced outcome. Brown et al concluded that "Multiple analyses showed no relationship between route to recognition (antenatal, diagnosis before discharge and diagnosis after discharge) of CHD and the outcome measures (ventilation time and mortality)." However they found a statistically significant difference antenatal diagnosis and diagnosis after discharge for death [OR 0.33 (0.11 to 0.94)]. There was no difference between diagnosis before discharge and diagnosis after discharge for ventilation time [OR 1.37 (0.98 to 1.90)] and death [OR 1.54 (0.59 to 4.03)]. *(Brown KL, Ridout DA, Hoskote A, Verhulst L, Ricci M, Bull C. Delayed diagnosis of congenital heart disease worsens preoperative condition and outcome of surgery in neonates. Heart 2006;92(9):1298-302.)* <u>Sensitivity and Specificity</u> Ewer et al report specificity is 99.1% and sensitivity is 58.3% for detection of critical CHD.

		This takes both clinical exam and PO into account. Therefore it is difficult to access the additional benefit of PO to the clinical exam in detecting Critical CHD. According to Wennerholm (page 17 of the draft paper) Clinical exam + PO showed sensitivity of 83.8%, and Specificity 98-99% and pure clinical exam was sensitivity 62% but specificity of 98%.

1b. Has the review satisfactorily summarised the literature relating to the practical application of the test? Please click either yes or no check boxes below.

☐ Yes ☒ No

Please let us know the reasons for your response in the table below:

Section and / or page number	Text to which comments relate	Comment *Please use a new row for each comment and add extra rows as required.*
Page 17 table 4		Following publication of the Lancet systematic review of pulse oximetry screening in 2012, the reported screening sensitivities and specificities for Pulse oximetry and Clinical examination are incorrect. The figures are for pulse oximetry screening only (see ref 36). Clinical examination increased these sensitivities and overall 92% of CCHDs were identified if all 3 screening methods were used.
Page 18. Para 5	**Newborn screening**	'Subsequent meta-analyses… around 60-80% for pulse oximetry combined with clinical examination'. The meta-analysis (ref 39) reported sensitivity of 76.5% (95% CI 67·7–83·5) for pulse oximetry alone. Clinical examination in addition will increase the sensitivity further but this was not included in the Lancet meta-analysis.
Page 19. Para 3		'The benefits and costs of further investigation and early diagnosis of such conditions… before these…can be considered a benefit of screening.' Data are available on the routine impact of screening in a UK setting in this respect and have been reviewed by the authors (Singh et al Unpublished data).
Page 20	**Newborn screening: pulse oximetry**	'It is possible…coarctation of the aorta…pre and post ductal screening… further investigation in a larger population.' Pulse oximetry screening identifies some but not all babies with aortic obstruction (incl. coarctation). This has been described in a number of reviews. It is unlikely that further studies will produce dramatically different results given the

		large number of babies already screened.
Page 20. Section 7. Paras 2 and 3 and Page 24 section 14		'Focus groups undertaken for the PulseOx study suggested that parents and professionals would be supportive of…pulse oximetry…'. 'The acceptability of false positive and false negative screening…may require further examination.' These statements do not represent the data described in refs 3 and 81. Focus groups were used for the health professionals only. The acceptability to parents and anxiety induced by testing in a low risk population was rigorously evaluated using recognised psychological questionnaires. Over 800 mothers returned the questionnaires including 119 mothers of false positive babies. Acceptability was high and the mothers of false positive babies were no more anxious than those of true negatives. Further evaluation of this is unlikely to produce different results and will create additional delays and expense.
Page 26 para 5.		'…Fallot's tetralogy is not a major or critical CHD…' This is incorrect. Some cases of Fallot's may fulfil the criteria for critical CHD i.e. surgery within 28 days and almost all would be classified as serious. So the estimate is appropriate.
Page 28 section 21.		'There may be pressure to change the timing…' This is conjecture. There is no evidence for this. The vast majority (>99%) of patients will be true negative and hospital discharge will not be delayed.
Page 30 final para		'There are no randomised trials… and many are of moderate or low quality.' A randomised trial is not feasible in this clinical context and so it is unlikely that there ever will be one. The vast majority of recent trials are of relatively high quality. This statement should be justified indicating which studies are deemed to be of low quality.
Page 31 para 1		'There are no randomised trials… and many are of moderate or low quality.' A randomised trial is not feasible in this clinical context and so it is unlikely that there ever will be one. The vast majority of recent trials are of relatively high quality. This statement should be justified indicating which studies are deemed to be of low quality. There remains therefore some uncertainty…used routinely in a low risk population…' The vast majority of studies have been in asymptomatic 'low risk' population. 20% of UK units are using it routinely in these patients. At Birmingham Women's Hospital alone we have screened over 25 000 babies outside of a research study over a 4 year period (ref);

2. Pathways for referral for further investigations after a screen positive result (including cardiac and non-cardiac causes)		
The review concluded that further information is needed on the management pathways for newborns with screen positive results and on the outcomes for newborns with non-cardiac conditions. This limits the evaluation of the overall benefit and acceptability of adding pulse oximetry to current practice. Do you agree with this conclusion? Please click either yes or no check boxes below. ☒ Yes ☐ No **Please let us know the reasons for your response in the table below:**		
Section and / or page number	Text to which comments relate	Comment *Please use a new row for each comment and add extra rows as required.*
		The paediatricians with expertise in cardiology special interest group (PECSIG) calculates that one PEC is needed per 3000 deliveries to cover the demand for cardiology. There is nowhere near this number of appropriately qualified people in UK hospitals at the moment. You cannot have a pathway that ends with an echo by an untrained person. The only formal accreditation that is available to general paediatricians and adult echo techs is a challenging European certificate which requires a much higher level of knowledge than most non-cardiologists will ever need. An alternative national UK competency system is probably needed before this can be rolled out. Outcomes for newborns with non-cardiac conditions is not such a problem actually; we are used to dealing with PPHN, sepsis, polycythaemia already and picking those babies up early would be a bonus.
		We agree with this conclusion up to a point. It is important once a suspect screening result is obtained that further assessment is undertaken without undue delay. Access to neonatal echocardiography is the most important factor which needs to be optimised around the country. There are an increasing number of neonatologists and paediatricians with an expertise in echocardiography. The PECSIG group (Paediatricians with Expertise in Cardiology Special Interest Group) is developing standards for training in this. We do not believe that the non-cardiac false positives will be a big problem. Having

		persistently low oxygen saturations puts a baby in a high risk category in that transition to neonatal life has not gone smoothly. Many of these babies have potentially serious illnesses which need to be excluded, and paediatricians would want to know about this group and observe them for a period. Further analysis of this group through data collected during and after implementation would be important, and I think only then will the optimum approach to ruling out serious pathology whilst minimising emotional stress to the family be worked out.
Page 21	**Newborn Screening**	'A presumed positive result at Newborn examination should prompt referral for expert cardiological opinion, and further investigations such as detailed echocardiography…'. The NIPE standard for clinical examination of the newborn heart (NIPE 2008) states '…Pulse oximetry and expert opinion within 24 hours…' with no specific mention of acceptable limits for pulse oximetry and no definition of expert opinion. Most babies who have a murmur or other abnormalities detected on newborn examination will not see a paediatric cardiologist but will be assessed by a paediatrician who will make a judgement based on their clinical assessment, as to whether further cardiological advice is needed. There is no written pathway for echocardiography of babies with murmurs. The same should apply to positive pulse oximetry screens. Paediatricians are familiar with the assessment of babies with low oxygen saturations and can make a judgement about need for echocardiography in the same way that they do with murmurs (i.e. based of clinical examination, judgement and if necessary additional information such as blood tests and x-rays).
Page 21	**Final para**	'A policy for investigation after a positive screen result on pulse oximetry has not …been established and evaluated…'. With 20% of UK units currently screening a consensus pathway based on clinical experience and common sense could rapidly be established by the working group mentioned in the previous section. At the very least, a policy statement such as that for clinical examination – i.e. 'expert opinion within x hours' would not be unreasonable.
		One of the main issues with this review is that is has been written by non-clinicians and the available data has not been reviewed by neonatologists.
		It is important to consider the following: • The false positive rate of PO screening for detecting CCHD is relatively low (consistently <1%), which compares very favourably with other newborn screening methodologies such as

		hearing screening and clinical examination (murmur). • The information that is presented as a result of a positive screen - low oxygen saturations - is clinically relevant and important. • Paediatricians involved with care of the newborn assess babies with low oxygen saturations every day (mostly outside of a screening programme). • Most (if not all) paediatricians would not send home a baby who has oxygen saturations which are not in the normal range. • Paediatricians assess babies with heart murmurs every day and make a clinical judgment regarding their care based on their findings and refer for cardiological assessment when appropriate. One of the major concerns for the NSC is the potential influx of healthy babies to neonatal units as a result of a positive test. The consistent view of those units who currently screen is that this situation does not occur. The majority of test positive babies have a diagnosis which requires clinical intervention. These include potentially life-threatening conditions such as pneumonia, early-onset sepsis and PPHN. Screening identifies these babies early before they become unwell.

3. Overall conclusion

The review recommends the use of pilots to explore the issues relating to testing, referral and, in addition to explore:

a. the information requirements of parents and health professionals,
b. training needs for midwives and others involved in newborn screening using pulse oximetry,
c. data and systems requirements for audit, quality assurance and monitoring of longer term outcomes.

Such pilots may also provide information on the resource implications arising from pulse oximetry screening. Does this recommendation accurately reflect the state of the current knowledge about pulse oximetry screening? Please click either yes or no check boxes below.

☒ Yes ☐ No

Please let us know the reasons for your response in the table below:

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		While we feel that there is enough evidence to introduce routine pulse oximetry as part of neonatal screening, we are however are concerned about the increase in time needed per baby check. Presumably equipment needs to be replaced or at least cleaned between babies as well. Other juniors who have come from a hospital where they already screen all newborns with pulse oximetry comment that the small amount of extra time feels worth it when you pick up a baby with life-threatening CHD.
		We agree that these issues are all important. We think a phased implementation is appropriate, with work done during each stage informing the development of the methodology for implementation. During this process, specific projects can be undertaken to answer outstanding questions and develop parent information, training, and data systems. Some of the questions (for example about false positives) will only be answerable once a fairly large population has been subject to screening, and data collected and analysed. We would suggest that the question should be how rather than whether to introduce pulse oximetry screening throughout the country.
Page 28 section 20		Parental information is important and available for those units and countries who are already screening. It would be interesting to compare with the information provided by NIPE for parents relating to physical examination of the heart which does not mention false negatives or further investigations in any detail.
Page 32. Para 2		The review actually suggests a 'pilot or a staged introduction (such as that carried out in the initial implementation of the MCADD screening programme by the NSC). As previously stated further pilots would be unlikely to identify any additional major issues which would not have been identified in the units currently screening. Therefore a staged introduction following a consensus agreement of screening by the suggested working group would be more appropriate in my opinion.
Page 28 section 19		Additional facilities…' This is important and these issues will need to be addressed however as 20% of UK units have already implemented screening with no additional funding or staffing, it is likely to be achievable with relatively modest funding.
		It is important for both clinical staff and parents to recognise that it is a screening test and not by drawn it into a false sense of reassurance if the saturations are within normal limits. This information needs to percolate through to all levels.

		A pilot project would help help set up system of referrals and pathways assess the burden on transport services and regional cardiac services.
4. Any other comments		
4a. If you have any other comments on the document please put them in the table below:		
Section and / or page number	Text to which comments relate	Comment *Please use a new row for each comment and add extra rows as required.*
		The main uncertainties identified by the report are i) screening protocols and ii) referral pathways. An additional uncertainty is the acceptability to parents. The 2 most common life-threatening CHDs are coarctation of the aorta and critical aortic stenosis, neither of which are particularly likely to be picked up with oxygen saturation monitoring in the early stages. We have concerns about the practicalities of doing the screening in units with high birth rates but the same number of SHOs on the rota as the less intense units, the false positives, about length of stay issues on the postnatal wards and about the end of the pathway in hospitals where there is not a PEC or paediatric trained echo technician. The cost of training up/employing these staff does not seem to have been taken into account. Pulse oximetry screening is already happening at an ever increasing number of hospitals. It may be that practice will overtake the NSC's deliberations anyway and, if that is the case, it may make more sense to roll screening out fairly soon with a national guideline rather than end up with a lot of different local guidelines.
		This is an excellent opportunity to introduce a relatively easy to use, pragmatic test to help detect conditions which are a major contributor to neonatal and perinatal mortality, making use of the major test of transition that newborn babies are undergoing in the first few days of life. Whilst it is thus somewhat different from other tests recommended for national screening, it will help identify a group of babies at high risk of deterioration and death, enabling paediatricians to focus their observation and care on this group and support parents whilst doing this.

Page 26 para 1		‘cost of adding pulse oximetry …was £24 900’ This correct but the cost estimate assumed all babies who tested positive would undergo echocardiography. In practice this is not necessary and approximately 1 in 5 babies are likely to need and echocardiogram (Singh et al unpublished data).
		According to the Pule Ox study if 100000 babies underwent PO, 973 cases would be PO positive needing ECHO. 130 cases would be true positives for CHD. 843 cases would have abnormal PO but not have critical or serious CHD. So for Neonatal Networks with a birth rate of between 30,000 – 40000 per year this would mean 253 to 337 cases needing ECHO assessment per year. (This is excluding critical and serious cases). This will need to be factored in, especially in Networks where they rely on the region cardiac unit for ECHO and transport services. If you were to exclude cases of ‘other illness’ (non cardiac) then for a Neonatal Network with 30000-40000 births, you would have 184-245 normal cases who underwent ECHO assessment to detect 10-14 cases of critical CHD. PO screening for critical congenital heart disease alone has not been proven to be of benefit beyond doubt, especially for those who practice ‘targeted pulse oximetry’ (i.e. saturations measured in the presence of a murmur, weak femoral pulses, poor perfusion, any signs of unwellness) Clearly there does seem to be benefit in detecting occult diseases such as mild PPHN. However, these babies will need intervention such as oxygen (therefore admission) to the neonatal unit. This needs to be made clear if the screening program is rolled out. This will have a major impact on both transport and neonatal services (increased admissions for example oxygen delivery in other ‘well’ baby). A pilot project to assess the impact on all services (transport, cardiac and neonatal), setting local echocardiography facilities, video links etc. would be the way forward. This would also help establish clear referral pathways for example what happens to a baby with saturations

		of, for example 93% with a normal ECHO. Do they go home or need admission for oxygen?

4b. Are you aware of any publications that should have been considered in the review? Please click either yes or no check boxes below.

☒ Yes ☐ No

If yes, please let us know what these are below. *Please use a new row for each publication and add extra rows as required.*

Publication title	Publication author	Publication date and publisher
Pulse oximetry screening for critical congenital heart defects	Ewer AK	**2013**
Pulse oximetry screening for critical congenital heart defects: a UK national survey	Singh A, Ewer AK. ARTICLE REMOVED FOR COPYRIGHT PROTECTION	**2013**
Review of pulse oximetry screening for critical congenital heart defects	Ewer AK. ARTICLE REMOVED FOR COPYRIGHT PROTECTION	**2013**
How to develop a business case to establish a neonatal pulse oximetry programme for screening of congenital heart defects	Ewer AK ARTICLE REMOVED FOR COPYRIGHT PROTECTION	**2012**
Neonatal pulse oximetry screening: a	Kang SL, Tobin S, Kelsall W	**2011**

national survey	ARTICLE REMOVED FOR COPYRIGHT PROTECTION	
Proposed pathway for managing hypoxaemia	ARTICLE REMOVED FOR COPYRIGHT PROTECTION	
Newborn and Infant Physical Examination Standards and competencies	ARTICLE REMOVED FOR COPYRIGHT PROTECTION	**2008** http://nipe.screening.nhs.uk)
Pulse oximetry as a screening test for congenital heart defects in newborn infants: an evaluation of acceptability to mothers	Powell R, Pattison HM, Bhoyar A, Furmston AT, Middleton LJ, Daniels JP, Ewer AK. ARTICLE REMOVED FOR COPYRIGHT PROTECTION	**2013**
Pulse oximetry as a screening test for congenital heart defects in newborn infants: a test accuracy study with evaluation of acceptability and cost-effectiveness	Ewer AK, Furmston AT, Middleton LJ, Deeks JJ, Daniels JP, Pattison HM, Powell R, Roberts TE, Barton P, Auguste P, Bhoyar A, Thangaratinam S, Tonks AM, Satodia P, Deshpande S, Kumararatne B, Sivakumar S, Mupanemunda R, Khan KS ARTICLE REMOVED FOR COPYRIGHT PROTECTION	**2012**

Statement on Pulse Oximetry Screening for Congenital Heart Defects on behalf of Paediatricians with Expertise in Cardiology Special Interest Group (PECSIG)

Yogen Singh[1], Anjum Gandhi[2]
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[2] *Consultant Paediatrician with Expertise in Cardiology at Heart of England NHS Foundation Trust*

Dr Yogen Singh is an executive member of Paediatrician with Expertise in Cardiology Special Interest Group (PECSIG) and Dr Anjum Gandhi is the Chair Person for PECSIG. This statement is written on behalf of PECSIG.

Congenital heart defects (CHD) is a leading cause of infant death accounting for up to 40% of all deaths from congenital defects and 3-7.5% of infant deaths in the developed world (Lloyd 2003). Overall incidence of CHD is around 7-8/1000 while the incidence of critical CHD varies between 1.2-1.7 per 1000 live birth (Lowell 2012).

For some babies, the consequence of going home with an undiagnosed CHD will be fatal. Others will be admitted to hospital as an emergency following an acute collapse, their outcome having been significantly compromised by late diagnosis both in terms of success of cardiac surgery and long term morbidity related to the consequences of brain injury from ischemia.

The current screening tools to detect CHD in asymptomatic infants, antenatal ultrasound screening and routine examination of the newborn, have been in-effective. Newborn examination misses critical or serious CHD as hypoxemia and/or cyanosis is difficult to detect in newborn as transitional newborn circulation masks important clinical findings. Majority of the critical CHD presents with hypoxemia in the newborn period hence the usefulness of pulse oximetry.

Non-availability of an effective screening tool to detect CHD in well infants has been a great hazard to patient safety. Now research studies in over 230,000 babies have shown pulse oximetry screening to be a simple, non-invasive, feasible, highly specific, and cost effective test called pulse oximetry which could reduce this risk significantly. Current evidence (Ewer 2012, Granelli 2009) suggests that pulse oximetry will also identify other infants who need specialist neonatal care before they become critically unwell improving outcomes.

High quality studies have been published in well renowned journals such as the Lancet and include randomised controlled trials, systemic reviews and meta-analysis. All the studies have consistently showed it to be a simple, highly specific, cost-effective and acceptable method to detect critical CHD in asymptomatic infants.

Table showing results from recent pulse oximetry screening studies

Study	Population size	Oxygen saturation type and mean age at screening	Sensitivity	Specificity	False positivity
de-Wahl Granelli (2009)	39,000	Pre and post ductal sats; Mean postnatal age 38 hours	62%	99.8%	0.17%
Merberg (2009)	50,008	Postductal at 5 hours; repeated with 2-3 hours if abnormal	72%	99.3%	0.6%
Ewer (PulseOx; 2011)	20,000	Pre and post ductal sats; Mean postnatal age 12 hours	75%	99.1%	0.8%
Thangaratinam; Systemic review and meta-analysis (2012)	230,000	Variable	76.5%	99.9%	0.14% (0.05% if done < 24h)
Turska Kmiec (2012)	52,993	Postductal sats only; Mean postnatal age 7 hours	78.9%	99.9%	0.026%

The authors from the systematic review and meta-analysis (Thangaratinam 2012) concluded that pulse oximetry met the criteria for universal screening and in view of the number of babies who had now been studied; it was unlikely that any further research would demonstrate substantially different findings. They also concluded that pulse oximetry is well tolerated, simple and feasible; it is highly specific and sufficiently sensitive to qualify for screening. It is acceptable to parents and clinical staff and cost-effective in the current clinical setting and is endorsed by an increasing number of professional, national and international institutions.

There has been significant progress towards implementation of pulse oximetry screening in developed countries. In 2005, the Swiss Society of Neonatology and the Swiss Society of Paediatric Cardiology recommended that all neonates in Switzerland should undergo first day pulse oximetry screening and in 2010, this was also recommended by the Polish Ministry for Health.

In 2011, the US Secretary's Advisory Committee in Heritable Disorders in Newborns and Children convened a workgroup which recommended a standard protocol for routine screening. The subsequent statement by this group was endorsed by a number of professional bodies, including the American Academy of Paediatrics, American Heart Association and the US Health and Human Services Secretary. States across the USA are currently currently considering implementation of this recommendation and, to date, four states are currently screening all neonates, with the majority of the other states making progress towards this goal.

Triple screening (antenatal ultrasound screening, routine examination of newborn and pulse oximetry screening) to detect critical CHD will detect up to 92% cases. Pulse oximetry screening has limitations in detecting a group of critical CHD with normal postductal oxygen level for example in infants with a coarctation of the aorta, who are less likely to be detected in the immediate neonatal period.

A recent editorial in the Lancet (2012) described the technique as 'a new milestone in the history of congenital heart disease' and stated '…the question now is not "should pulse oximetry screening be introduced" but "why should screening not be introduced more widely". Now similar questions are being asked by the parents, public, staff and other stake holders.

We strongly feel that pulse oximetry screening should be made universal screening in the UK. It has got limitations in detecting a select group of congenital heart defects but it could help in detecting up to 92% cases of critical congenital heart defects before their clinical deterioration. This will also help in identifying a significant number of cases with infection (sepsis), respiratory infections and other serious conditions earlier and will in minimising the collapsed the children in postnatal ward. It could help in minimising children collapsing at home or emergency department, and hence will decrease morbidity and mortality in this vulnerable group of patients.

Response to pulse oximetry consultation

This paper represents Tiny Tickers' formal response to the UK National Screening Committee's consultation: *Heart disease screening in newborns using pulse oximetry – an evidence review*.

Introduction

Tiny Tickers is a national charity with the aims of improving prenatal detection rates of congenital heart defects, and the early treatment and care of babies born with CHD and their families. We are the only national charity with such a focus on the area of prenatal detection of CHD.

We have a proud history of providing training to sonographers throughout the United Kingdom, and commissioning research papers relevant to the subject. Many of the charity's supporters are parents of babies with CHD – representing the range of experiences from those who benefited from prenatal detection; those with children whose condition wasn't detected prenatally; and, sadly, those for whom the baby's condition wasn't detected until after he or she had passed away.

Given Tiny Tickers' charitable objectives and experience in this subject, this consultation regarding pulse oximetry is highly relevant to our organisation and beneficiaries.

Summary of Tiny Tickers' stance on pulse oximetry

In principle, Tiny Tickers is in favour of the introduction of pulse oximetry tests for all newborns prior to their discharge from hospital.

Tiny Tickers sees pulse oximetry as a 'safety net' for instances where prenatal detection has been missed or has not been possible. Tiny Tickers stresses that in no way should pulse oximetry be considered as a replacement for prenatal detection efforts, and that improvements should continue to be made by all relevant health organisations to ensure prenatal detection rates increase.

Tiny Tickers supports the introduction of pulse oximetry testing as part of an integrated screening pathway that includes but is not limited to: a fetal abnormality scan; a newborn clinical examination; and pulse oximetry testing.

Therefore, Tiny Tickers supports the review's recommendations to use pilot studies to further explore issues relating to testing, referral, information requirements, training and data systems – and hopes that these pilot studies resolve outstanding issues and lead to a recommendation to implement pulse oximetry nationally.

Linking Tiny Tickers' view to the consultation's study

We thought it useful to highlight how Tiny Tickers' view concurs with the *Screening for Congenital Heart Defects* paper by Dr Knowles and Ms Hunter – the report behind the consultation.

The report cites studies suggesting up to 15% of CHDs may remain undiagnosed at death – a stark reminder of the urgent need to increase detection rates.

We agree with the report's assertion that "early detection in the fetal or newborn period is essential to provide anticipatory care at delivery or soon after birth to prevent death before definitive management can be initiated, or the morbidity consequent of cardiovascular collapse".

We concur with the study's finding that cardiovascular collapse "can have significant long-term effects as a consequence of significant mutli-organ insults, including hypoxic-ischaemic brain injury", and recognise the vital role of fetal or newborn detection in preventing babies suffering such collapses.
We agree also with the report's statement: "Poor clinical status at the time of intervention increases interventional mortality and has an adverse effect on outcome".

In other words – if a life-threatening CHD is undetected and the baby suffers cardiovascular collapse, they are more likely to die or, if they survive, are more likely to have a worse quality of life. Early detection is, clearly, vital.

The report makes a similar stark warning: "If life-threatening CHDs are not detected sufficiently early then cardiovascular collapse, neurological sequelae or death remain potential outcomes".

Therefore, Tiny Tickers supports any measuring that increases the likelihood of CHD being detected, at any stage in the patient's life – including pulse oximetry at the newborn stage.

However, we recognise the clear benefits of prenatal detection over postnatal detection, and we would urge that pulse oximetry is seen as a back-up to improved prenatal detection rather than as an alternative.

With that in mind, we are pleased that the report recognises the importance of prenatal detection, stating: "Antenatal screening offers women and their partners an opportunity for information and counselling that may help them better prepare for the birth of their child, the option of delivery in a setting that will permit rapid access to specialist surgical or medical care, or the possibility of considering pregnancy termination or palliative care in the newborn period."

The study also states the clinical benefits of prenatal detection in specific conditions: "Prenatal diagnosis can allow a choice of birth place in order to optimise postnatal management. In utero transport to a specialist cardiac centre for delivery has been shown to improve survival of infants with left ventricular outflow tract obstruction."
Also (referencing a French study into TGA): "Infants with a prenatal diagnosis experienced reduced mortality and improved neurocognitive outcomes in the longer-term compared with those diagnosed after birth."

We note that the study reports that models suggest newborn screening will remain clinically effective and cost-effective until antenatal detection rates are above 85-90%. Given they are currently around 35% (although a lack of national data makes this as uncertain figure and we know there are significant variations between regions and individual hospitals), we stress again that significant improvements should be made to antenatal detection.

The fact that pulse oximetry will not identify defects only associated with murmurs or delayed absent pulses is another reason why it should be considered as part of a pathway of screening, rather than as a standalone test.

Conclusion

Tiny Tickers is supportive of pulse oximetry testing as part of an integrated screening pathway that also includes prenatal screening and the newborn clinical examination. The introduction of pulse oximetry must complement, rather than detract from, efforts to improve prenatal detection rates. We agree with the recommendations of the report.

Response from the British Heart Foundation
December 2013

The British Heart Foundation (BHF) is the nation's leading heart charity. We are working to achieve our mission of a world in which no-one dies prematurely of heart disease. In the fight for every heartbeat we fund ground breaking medical research, provide support and care to people living with heart disease and advocate for change.

Congenital heart defects are one of the leading causes of infant mortality in the developed world.[1] In the UK around 1 in every 180 babies are born with congenital heart defects that means on average 12 babies a day are born with congenital heart defects.[2] Thanks to medical advances the death rate of those who have died from congenital heart defects has decreased by 83 per cent since 1979.[3] Research estimates that of babies born today with congenital heart defects up to a third of cases are undiagnosed when discharged from hospital.[4]

We know that early diagnosis leads to better outcome, particularly in cases where surgery is required.[5] Early diagnosis and early surgical intervention, if necessary, also helps to reduce the psychological impact of late diagnosis. Late diagnosis can also compromise the success of later intervention therefore it is imperative that everything is done to identify and diagnose congenital heart defects as soon as possible.

On this basis the BHF supports the addition of pulse oximetry to the existing newborn congenital heart defect screening across the UK as it is a quick, cheap, easy and effective treatment to screen babies for congenital heart defects. We agree with the UK National Screening Committee (UK NSC) review of evidence that found pulse oximetry to be clinically useful and would increase the number of defects detected in the newborn period.

Congenital heart defects are abnormalities in the structure of the heart and major vessels which are present at birth. There are many forms of congenital heart defects, many of which do not require surgery. However more complex conditions can require medication or surgery.

The current screening strategy to detect congenital heart defects includes an antenatal ultrasound and physical examination, both of which have low detection rates. Some children with congenital heart defects may have lower levels of oxygen in their blood which is not always obvious to either healthcare professionals and parents. The pulse 2 oximetry test is designed to pick this up by using a sensor to shine a red light through a baby's skin which can measure the level of oxygen in the blood. A number of studies carried out across Europe have shown pulse oximetry to be a specific and sensitive test with a low rate of false positive results. [6,7,8] It has also been shown that when added adjunct to existing screening that the detection rate prior to discharge increased to over 90%.[9]

The BHF supports the introduction of pulse oximetry as research shows it is cost effective and quick and easy to administer. This should put no large demands on current capacity of resources available in postnatal wards. In 2012 a Health Technology Assessment into pulse oximetry conducted a cost-effectiveness analysis and found that the test takes an average just 6.9 minutes to conduct and costs on average £6.24 per test. Although the inclusion of the test would double the costs of existing tests, pulse oximetry would pick up an additional 30 diagnoses per 100,000 live births.[10] As these are cases that otherwise would have gone undetected, leading to costly late treatment and poor reduced quality of life for the child, the review concluded that pulse oximetry is a cost effective treatment option.

Currently around 20 per cent of hospitals across the UK have already added pulse oximetry to their routine newborn screening.[11] These hospitals have implemented the test with no additional support, demonstrating how easy universal roll out could be. For example in the USA, following endorsement from the Secretary for Health and Human Services, pulse oximetry was added in 2011 to the screening process. Currently 26 states have signed up to the screening, with most remaining states working towards implementation.[12] The Royal College of Physicians of Ireland have also recommended the universal use of pulse oximetry.

Like any test there is a chance that pulse oximetry testing will return a false positive, however this likelihood is low. In the UK in 2012 a study was conducted, to determine the acceptability of pulse oximetry and into the possible distress that the initial result of a false positive could have on parents. It was found that parents who had a false positive result were no more anxious than those with a true negative and deemed the test to be valuable. Similarly, clinical staff were found to respond positively to the addition of this test to screening.

Research suggests that conducting a pulse oximetry test within the first 24 hours of life is more likely to return a false positive. If pulse oximetry is added to the current screening process, early discharge times for non-complicated births must be taken into consideration. Consideration of how this test will be administered in home delivery settings is also required. The BHF are also supportive of the Children Heart Federation's petition for the adoption of pulse oximetry across the UK and have encouraged campaigners to sign their petition and respond to this consultation in favour of pulse oximetry.

For more information related to this response, please contact Amy Smullen, Policy Researcher

[redacted]

1 Ewer AK, Furmston AT, Middleton LJ, et al. (2012) 'Pulse oximetry as a screening test for congenital heart defects in newborn infants: a test accuracy study with evaluation of acceptability and cost-effectiveness.' *Health Technology Assessment*

2 British Heart Foundation (2013) *'Children and Young People Statistics 2013.'*

3 British Heart Foundation (2013) *'Children and Young People Statistics 2013.'*

4 Ewer AK, Furmston AT, Middleton LJ, et al. (2012) 'Pulse oximetry as a screening test for congenital heart defects in newborn infants: a test accuracy study with evaluation of acceptability and cost-effectiveness.' *Health Technology Assessment*

5 Brown, KL et al. (2006) 'Delayed diagnosis of congenital heart disease worsens preoperative condition and outcome of surgery in neonates.' *Heart* Sep:92(9)

6 De-Wahl Granelli A, Wennergren M, Sandberg K, et al. (2009) 'Impact of pulse oximetry screening on the detection of duct dependent congenital heart disease: a Swedish prospective screening study in 39 821 newborns.' *British Medical Journal* 338:a3037.

7 Riede FT, Worner C, Dahnert I, et al. (2010) 'Effectiveness of neonatal pulse oximetry screening for detection of critical congenital heart disease in daily clinical routine: results from a prospective multicenter study.' *European Journal of Paediatrics* 169.

8 Thangaratinam S, Brown K, Zamora J, et al.(2012) 'Pulse oximetry screening for critical congenital heart defects (CCHD) in asymptomatic newborns: a systematic review and meta-analysis.' *Lancet* 379:2459–2464.

9 Ewer, KA (2013) 'Review of pulse oximetry screening for critical congenital heart defects in newborn infants.' *Current Opinion Cardiology* 28(2).

10 Ewer AK, Furmston AT, Middleton LJ, et al. (2012) *'Pulse oximetry as a screening test for congenital heart defects in newborn infants: a test accuracy study with evaluation of acceptability and cost-effectiveness.' Health Technology Assessment*

11 Ewer, AK et al. (2013) 'Pulse oximetry screening for congenital heart defects.' *The Lancet* 382(9895)

12 ibid

13 Ewer AK, Furmston AT, Middleton LJ, et al. (2012) 'Pulse oximetry as a screening test for congenital heart defects in newborn infants: a test accuracy study with evaluation of acceptability and cost-effectiveness.' *Health Technology Assessment*

Heartline Families

NOTE: THIS RESPONSE IS ALSO INCLUDED AS PART OF THE CHFED RESPONSES AT HEARTLINE FAMILIES' REQUEST (RESPONSE NO.90)

Heartline Families is a Charitable Incorporated Organisation supporting children with heart disorders and their families, whatever the condition, wherever it is treated throughout UK and Ireland.

Please excuse this brief contribution to the consultation – I have read the documentation, and as a member of Children's Heart Federation would wish to associate Heartline Families with that response.

I would like to add that should additional pilots be run, this should be concurrently with universal adoption of PO screening – delay will be measured in mortality and morbidity, not in clarity of data.

There is little about the cost to families of late diagnosis of heart disease in children, whether critical or significant. The emotional cost to parents is very high. There is a degree of preparedness for a diagnosis soon after birth when tests are being carried out. Those whose children have 'failed to thrive' because of an undiagnosed heart condition (and where a diagnosis is left to a perceptive HV or GP who can overcome an assumption of an incompetent or overanxious mother) have their confidence in their abilities to protect and nurture their child undermined. If the financial cost of providing additional screening and diagnostic services are to be reckoned, I suggest the cost of anti-anxiety drugs and counselling to relieve the stresses these families encounter should also be calculated.

Kind Regards
Hazel Greig-Midlane
Chair of Board of Trustees
[redacted]
Web: www.heartline.org.uk

Tel: [redacted]

Down's Heart Group

Response to the Consultation on the UK NSC policy on Congenital Heart Disease screening in newborns

About us

Down's Heart Group is a UK national charity that has been providing support and information to parents, carers and professionals in relation to heart conditions associated with Down's Syndrome since 1988.

Comments

Down's Heart Group is strongly in favour of the implementation of Pulse Oximetry screening as an additional test to detect Congenital Heart Disease (CHD) in newborns in the UK as soon as possible. Currently screening for congenital heart defects relies on antenatal ultrasonography and postnatal clinical examination and despite the high incidence of CHD in babies with Down's Syndrome and the cardiac surveillance guidelines[i] issued by Down Syndrome Medical Interest Group, babies are still discharged from hospital before a CHD is diagnosed. Due to the propensity for babies with Down's Syndrome to develop pulmonary hypertension at an earlier age than their peer group[ii], this may comprise outcomes for these children.

Given the evidence from the NIHR Health Technology Assessment which demonstrates that Pulse Oximetry testing significantly increases the detection of Congenital Heart Disease in newborns, Down's Heart Group believes implementation of a UK wide screening programme is an important addition to the current tests for babies diagnosed with or even suspected of having Down's Syndrome and urges the UK National Screening Committee to recommend that Pulse Oximetry screening is introduced for newborns across all four countries in the UK, without delay.

Yours sincerely

Penny Green (Mrs)
Director

[1] Basic medical surveillance essentials for people with Down's Syndrome - Cardiac disease: congenital and acquired (revised 2007) http://www.dsmig.org.uk/library/articles/guideline-cardiac-5.pdf

[2] Cua CL, Blankenship A, North AL, Hayes J, Nelin LD. Increased incidence of idiopathic persistent pulmonary hypertension in Down syndrome neonates. Pediatr Cardiol. 2007 Jul-Aug;28(4):250-4. Epub 2007 May 5. PubMed PMID: 17486396.

December 13, 2013

To: UK National Screening Committee

R. Martin, MD, FAAP, FACC, FAHA
Senior Vice President, Center for Heart, Lung and Kidney Disease
C. Richard Beyda Distinguished Professor of Cardiology
Professor of Pediatrics, George Washington University School of Medicine and Health Sciences
Medical Director, Global Services

On behalf of the Children's National Health System's Congenital Heart Disease Screening Program, we write in strong support of routine newborn screening for critical congenital heart disease (CCHD) using pulse oximetry. In combination with the existing detection methods such as fetal ultrasound and newborn assessment, the addition of pulse screening provides the current optimal approach to early detection, early intervention and improved long term outcomes for babies born with CCHD.

In September 2011, Secretary Kathleen Sebelius endorsed the addition of pulse oximetry screening for CCHD to the recommended uniform screening panel for all newborns in the United States. In 2013 alone, over 20 states have passed legislation and currently 33 states states mandate screening of the infants in their states. At Children's National, we have successfully worked with hospitals, state departments of health and foreign countries to implement CCHD screening programs in their nurseries. In the United Arab Emirates, within the first two years of screening, over 50,000 infants were screened, 21 of whom were found to have CCHD.

Numerous studies, state experiences and outcomes reports on pulse oximetry screening for CCHD have been published in 2013 since the conclusion of the Committee's literature review, with additional study results published every month. In August 2013, New Jersey was the first state to report on outcomes; within the first nine months 73,320 newborns were screened and three infants were identified with previously unsuspected CCHD. Also in August, the Centers for Disease Control and Prevention (CDC) released the first U.S. study examining costs and health outcomes, concluding pulse oximetry screening can be cost-effective.

We believe pulse oximetry screening for CCHD meets the criteria established for implementation at the national level. It is an effective, quick, painless and low-cost test that is essential to ensure that all infants in the United Kingdom have the best opportunity for early detection and that the outcomes of infants born with CCHD will be improved.
Thank you for your attention to this urgent issue.
Sincerely,

Gerard R. Martin, MD, FAAC, FAAP, FAHA
Lisa A. Hom, RN Esq.
Lindsay Attaway
www.childrensnational.org/pulseox

cc: John Marshall, Evidence Lead, UK National Screening Committee
[redacted]Birmingham Women's Hospital, University of Birmingham.

[redacted] **Ph: ([redacted] Fax: [redacted] [redacted]**

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Little Hearts Matter
Half a heart...not half a life

12th December 2013

John Marshall

Dear Mr Marshall

Little Hearts Matters Response to the Consultation on the Need for O2 Saturation Tests to be included as part of the New-born and Infant Screening Programme

am writing in response to the above rather than submitting your proposed consultation questionnaire because the documents and questions posed seem to be bias towards the need for a further O2 Saturation study even though the evidence presented by professional research teams makes it clear that the case for improved detection, of both cardiac and respiratory problems, has been proved. A position confirmed further by the fact that O2 Saturation monitoring has already been adopted by 1 in every 5 maternity units.

As a national charity that offers specialist support and information services to children, and their families, diagnosed as having a single ventricle circulation we have a very relevant interest in the swift provision of this logical and non- invasive test. Most single ventricle conditions are incompatible with life in the first few days after birth, it is therefore hugely beneficial if a swift and accurate diagnosis is made prior to a newborn baby's discharge from hospital or their subsequent collapse at home.

understand that there are some concerns that false negatives are expensive and distressing for parents. There are two important responses to this concern.

- Having been involved in the West Midland study it is clear that parents, rather than being unnecessarily distressed by further testing, were very confident that all avenues had been explored professionally and that they were taking a healthy child home.
- The experience and professionalism of Neonatologists and Paediatricians to follow through any signs of a potential cardiac problem in a responsible way would not lead to every child being offered the full gambit of cardiac testing. Research protocols always remove all variations in response.

On behalf of the thousands of patients and families who are members of Little Hearts Matter I urge NIPE to consider using the funds that would be designated to conducting a further, and unnecessary, study to fund the simple detection equipment needed to improve the survival of children with complex heart conditions.

Yours sincerely

Suzie Hutchinson RGN; RSCN,
Chief Executive

The Information Standard
Certified member

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