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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.

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Solutions will need to be varied depending on local practice and on availability of cardiologists - eg in centres with a cardiologist all can have echo before discharge, others may need very early referral (next 24 hrs) etc

Agree that all should be assessed by
neonatologist / paediatrician first as there may be other causes, non cardiac of low sao2.

### 3. Overall conclusion

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

- the information requirements of parents and health professionals,
- training needs for midwives and others involved in newborn screening using pulse oximetry,
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<td></td>
<td>I think we can move beyond pilots. Training required is minimal. Data requirements are already in place on NIPE smart system.</td>
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<td><em>Newborn screening: Pulse oximetry</em>&lt;br&gt;Studies involving routine pulse oximetry in the newborn population agree on a cut-off of &lt;95% in either hand or foot on two consecutive occasions to define a positive screen. Some studies have also used a as an additional measure. The overall sensitivity of pulse oximetry does not vary significantly</td>
<td>This should be clarified to “either left hand or either foot” since right hand is pre-ductal, the cut off of 95% does not apply- it only applies to post ductal (left hand or left or right foot). We use either foot only (to avoid confusion as to which is the left and right hand….!)</td>
</tr>
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<td>Section 5 / page 18</td>
<td>Newborn screening</td>
<td>The data confirms the usefulness of this screening method for early suspicion and diagnosis of heart disease. The methods / technique can be further standardised after this being adopted as a standard practice.</td>
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☒ Yes  ☐ No

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<td>Page-15-20</td>
<td>Newborn screening</td>
<td>Pulse oximetry is a useful sign for early detection of heart disease and the pathways for referral can and should be developed to reduce long term morbidity and occasional mortality of these high risk newborns. The management of pathways is an administrative and management issue that needs to be assessed separately from the validity of the pulse oximetry test.</td>
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### 3. Overall conclusion

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

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<td>Pages 15-20</td>
<td>The pilot phase is not the requirement in my opinion. The implementation of policy and changes to the practice guided by audit would be the right way forward to minimise the avoidable morbidity among at risk children.</td>
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<td>need to establish how urgent cardiac echo is in asymptomatic babies with slightly low saturations</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Symptomatic babies (ie those with some respiratory distress) should be managed within existing pathways for babies with some respiratory distress</td>
<td></td>
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<td></td>
<td>Agree that managed introduction would permit systematic evaluation and improvement in pathways using pdsa cycles and small tests of change</td>
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<td>There is a time (and hence resource) cost and this must be assessed carefully. We include it at time of NIPE, but would be interesting to see if use more or less resource by doing with NIPE or at some other time</td>
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<td>16</td>
<td>Timing of oximetry</td>
<td>Early discharge before 12 hours is now common and may impact on the reliability of pre discharge oximetry</td>
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<td></td>
<td>Community based oximetry after discharge has not been studied if requires to be after 24 hours</td>
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<tr>
<td></td>
<td></td>
<td>Type of oximeter and probe used should be standardised</td>
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<td></td>
<td></td>
<td>Is there a risk that infants with lung disease and CHD who are hypoxic may be missed if their low saturation is attributed to a respiratory cause – should they have echo routinely?</td>
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3. Overall conclusion

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<td>Page 17</td>
<td>Reference to access for echocardiography</td>
<td>Training in echocardiography, equipment, telemedicine may all need to be enhanced with access from DGH and CMUs need to be considered as part of the screening plans in view of the urgency of action when a diagnosis of critical outflow obstruction is made.</td>
</tr>
<tr>
<td></td>
<td>Screening echo and reliable oximetry</td>
<td>Time for these tests added to routine examination especially when exam may be by midwives who have limited paediatric training has to be considered, the studies referred to have all been carried out by paediatric or cardiology staff who are likely to have been confident to discuss differential diagnosis etc with parents.</td>
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<td>18</td>
<td>Sensitivity and specificity of oximetry</td>
<td>False positive rate is relatively high and needs to be fully explained to parents including the need to remain in hospital for repeat testing and further assessment for a well baby who is in transition circulation and this impacts on discharge plans.</td>
</tr>
<tr>
<td></td>
<td>Benefit to parents</td>
<td>Early detection of life threatening CHD is increasingly valid as what were untreatable conditions are now amenable to early surgical intervention with optimistic outcomes. This has made the greatest case for adding oximetry to the routine examination of the newborn and feedback from bereaved parents emphasises the importance of giving the baby the best chance of survival by avoiding the rapid deterioration that follows ductus closure in the first 24 hours in babies with duct dependent lesions.</td>
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For parents whose baby is found to have an imoperable heart defect even this tragic news allows time for adjustment to the outcome and the knowledge that the baby’s death is inevitable and unavoidable rather than sudden and unexpected.

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<td>32</td>
<td>false positives are more likely within the first 24 hours</td>
<td>This review is undermined by the use of this term “false positive”. It is clear to those of us in practice that the majority of babies who are detected as “failing” the test to the extent where admission is required are not well – by definition a hypoxic newborn baby is unwell. The review falls into the trap of assuming that where no congenital heart disease is found, the test has failed by producing a “false positive”.</td>
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| 24                           | False positive results are also of concern to parents and may raise anxiety. Overall false positive rates for pulse oximetry appear to be around 1-1.5% 36 39, however higher false positive rates were reported in some studies | Again, review and methodology undermined by concept of “false positive”. While our false positive rate is below that you quote, I do not accept that any anxiety associated with “failing” the test is unwarranted. This could only be shown if, in a trial, some babies were left desaturated and to observe how many of them got more ill/ died. Obviously not ethical. In PULSEOX, some women whose babies did not have CHD, but who were desaturated were worried. But not without reason – these babies were not yet well. |
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| 20 | Pulse oximetry should be avoided in the first few hours after birth to avoid high false positive rates related to delayed transition from fetal to newborn circulation. | This statement is not supported by the data cited, and is too important to be left to the vagaries of one paper. It is simply not anything like our experience. We screen at 3-4 hours, and have nothing like the rate of abnormality cited. Less than 1%. We believe early screen is both practical (early discharge) safe and reasonable. |
| 19 | Non-cardiac conditions leading to low oxygen saturation, such as respiratory or infective illness, may be found in infants with low oxygen saturations (false positive screening results). The benefits and costs of further investigation and early diagnosis of such conditions requires further investigation before these diagnoses can be considered a benefit of screening. | Only a screening review would say this last statement! The “false positives” should be seen as diagnostically helpful – sick babies get detected. Some of them very sick. This is a benefit to early screening. Diagnosing ill babies could only be neutral or (as we believe) a major benefit. |
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.

☐ No

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<tr>
<td>28</td>
<td>. Additional facilities would be required for investigation and diagnosis after a presumed positive screen result on pulse oximetry, particularly if initial investigations did not identify a cardiac cause for low oxygen saturation.</td>
<td>This is at odds with our experience. We see nowhere near 2% “false positives” and no additional diagnostic facilities are needed to diagnose babies either as having cardiac disease, or for other causes of desaturation – this is bread and butter neonatology.</td>
</tr>
<tr>
<td>21</td>
<td>A presumed positive result on pulse oximetry screening should prompt referral for an expert cardiological opinion, and further investigations such as detailed echocardiography, to confirm or exclude a CHD diagnosis</td>
<td>This is wrong. Babies screening positive on pulse oximetry are usually assessed first by a neonatologist. Many have respiratory disorders, and do not need cardiology assessment. Few if any screen positive babies travel to our cardiac centre for diagnosis who do not have a clear diagnosis of congenital heart disease (albeit type may be unspecified in some cases). In most protocols, not all babies get an echo. See, for eg, Richmond paper.</td>
</tr>
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</table>

3. Overall conclusion

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

p. the information requirements of parents and health professionals,  
q. training needs for midwives and others involved in newborn screening using pulse oximetry,
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.

☐ No

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<td>27</td>
<td>The existing evidence strongly suggests that pulse oximetry in conjunction with clinical examination is more cost-effective than clinical examination alone.</td>
<td>Lets just get on with it then</td>
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4. Any other comments

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☐ No

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| Page 16                      | a) Pulse oximetry is clinically useful and will increase the number of congenital heart defects detected in the newborn period. | a) Pulse oximetry as a screening tool to pick up the condition 'Newborn babies with cardiac lesions undetectable antenatally but only detectable by pulse ox at birth' In the UK study this was 10 babies from a group of 20020 babies (See table 6 flow diagram on this HTA report [http://www.hta.ac.uk/fullmono/mon1602.pdf](http://www.hta.ac.uk/fullmono/mon1602.pdf)) This is an incidence of 0.5 per 1000 Similarly, Prudhoe’s work from the north this year archives [http://fn.bmj.com/content/98/4/F346.abstract](http://fn.bmj.com/content/98/4/F346.abstract) also shows pulse ox aided diagnosis in 10/31946 babies = incidence 0.3 per 1000 but missed 20 babies (0.6 per 1000) The critical issue apart from obvious training needs etc is what threshold of
b) Pulse oximetry is very good for identifying babies with obstructed pulmonary circulation, incidence justifies screening. The collateral benefits of screening (picking up respiratory problems etc) appear to argue more strongly for its case. See more below.

b) Our Trust was a participant of the UK Pulse Ox trial (see references 3, 39), and has since continued monitoring babies after birth, using the same strategy. In a 12 month audit conducted in 2012, 35 neonates who tested positive on pulse oximetry screening (i.e. failed to achieve desired pulse oximetry readings) after birth were reviewed on the neonatal unit (approximate births at Trust = 4500/year). 10 of these were associated with cardiac abnormalities, of which 2 (5.7%) had a complex cardiac lesion undetected in the antenatal period (TAPVD + PDA and TGA + AVSD + PDA) [6 had PPHN (1 with vein of Galen aneurysm), 1 had a PDA and 1 a VSD].

This tool was useful in promoting significant early interventions in 3 (Complex cardiac and vein of Galen Malformation) and contributed to implementing preventative strategies (such as oxygen therapy to reduce pulmonary hypertension) in at least a further 5.

It was however dependent on appropriate interpretation of the positive pulse oximetry screen, appropriate management of the clinical picture, and having the infrastructure to undertake echocardiography where clinically indicated.

c) and also good for detecting other (non cardiac) reasons for cyanosis

c) Of the 35 that were reviewed on the NNU for positive pulse oximetry screen, 10 were septic with elevated blood markers, 9 required respiratory support for pulmonary reasons, 1 was hypoglycaemic and 5 were considered normal. This means that pulse oximetry was an effective tool in identifying the unwell baby early in 20 additional cases in our Trust (20/35 = 57%; ~0.4% of total births), which serves a relatively less economically empowered population. We have not seen an increase in the number of unnecessary admissions to the NNU from these ‘false positives’, however the early detection of the unwell baby
potentially averted serious morbidity. More than its role in picking up the critical cardiac abnormality early, pulse oximetry is a very useful screening tool in identifying the early-unwell-baby in our Trust.

| Page 16 Paragraph 3 | Heterogeneity in site and timing of the test, devices and thresholds, number of repeat tests… | The optimal timing adopted by our unit is 24 hours of age however this is not practical, given the current length of stay in hospital for babies not generally exceeding 12 hours. Subjecting this to further studies will not be cost effective or yield striking benefit. Defining the window period for pulse oximetry screening within the first 12 hours (if needed) should be by expert consensus opinion.

   False call outs due to operator error (untrained HCAs performing test on baby, cold peripheries etc) are an issue, and will need adequate and intensive training of midwifery team if this is to be implemented nationally.

   There are no concerns with using right hand and either foot from our unit as we believe this optimises the interpretation of the test result. |

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<th>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.</th>
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<td>X Yes</td>
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<tr>
<td>No</td>
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<tr>
<td>No concerns regarding practical application of the test. If implementing de novo, this will require a period of training for all midwives/HCAs/neonatal teams who will be performing/interpreting the screening</td>
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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  
- [x] No

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<tr>
<td>Page 18 Paragraph 1</td>
<td>Current management pathways for screen positive as adopted by the UK pulse oximetry study (references 3 and 39) are adequate. It would be very difficult to provide exact management pathways for all babies with a false positive for cardiac lesion, but true positive for non-cardiac reasons. There has been no issue with acceptability of the pulse oximetry screening at our Trust. As part of the UK pulse oximetry trial (references 3, 39) and subsequently, we have now undertaken pulse oximetry screening in over 8000 deliveries at our hospital. Parents have accepted this as a screening tool and there have been no complaints regarding the false positives. In the least interventive scenario, a false positive screen results in an additional senior review and period of observation of baby on the unit, which parents have not objected to. In many ways this is reassuring to the parents.</td>
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3. Overall conclusion
The review recommends the use of pilots to explore the issues relating to testing, referral and, in addition to explore:

s. the information requirements of parents and health professionals,
t. training needs for midwives and others involved in newborn screening using pulse oximetry,
u. 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

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<td>Pilots for testing and referral</td>
<td>Not necessary; use based on consensus expert opinion and available literature</td>
<td></td>
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<tr>
<td>Explore information requirements of parents and health professionals</td>
<td>Adequate information and publications on the utility of pulse oximetry as a tool for some cardiac lesions Parent concerns have not emerged in our Trust</td>
<td></td>
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<tr>
<td>Explore training needs for midwives and others</td>
<td>Absolute must. This will fail at the outset without adequate training and clear pathways of triage between post natal ward, transitional care and the neonatal unit</td>
<td></td>
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<tr>
<td>Explore data and systems requirements for audit, quality assurance and monitoring of longer term outcomes</td>
<td>This can be done partly through Neonatal data capture systems such as Badger and SEND Audit, quality assurance and outcomes monitoring important.</td>
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4. Any other comments

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- [ ] Yes  
- [ ] No

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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

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<td>16-19</td>
<td>Review of the publications to date</td>
<td>The review is comprehensive, it identified 17 studies. It does highlight the limitations of oximetry as a screening tool regarding its poor performance in detecting some left heart obstructive malformation such as coarctation of the aorta. Despite heterogeneity between studies, sensitivity of the test did not change significantly when the screening was done within 24 hours of birth.39 There was no significant difference in detection rate when measurement was done in the foot only. There was not enough data to demonstrate whether pre and post ductal saturation difference aided the detection of duct dependent left heart obstruction (interruption of the aortic arch/ coarctation). In the UK largest study from single institution over 10 year period, routine pulse</td>
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oximetry aided the detection of 10 major malformations (5 critical and 5 serious) yet 15 babies with serious cardiac malformations were unrecognised before discharge from hospital. Prodhoe et al 31

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:

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<td>15-16,19</td>
<td>Applicability of the test</td>
<td>The test is simple, easy to perform, and it is not time consuming. The current oximetry devices are robust, they provide a more precise measurement. It is practical in my view to limit the test on one limb. There was no significant difference in detection rate when measurement was done in the foot only compared with that done on hand and foot simultaneously. Regarding whether the test is likely to result in more FP rate if performed within 24 hours, this is an issue which require further discussion and evaluation as the excess in FP is likely to represent –in some cases- the post natal circulatory adaptation. (table 6)</td>
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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   partly agree

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<td>Pages 19, 20, 21, 30, 32,</td>
<td>Criteria, 5, 6, 16, 17</td>
<td>I do agree with the first part of the statement but disagree that false positive limits the evaluation of the overall benefit. The review refers to an overall FP rate of less than 2%, and that such is attributable – in part to non-cardiac conditions. It also emphasized that FP rate was higher in those who implemented the screening on babies at less than 24 hours of age. However, this should be seen as an added advantage to the test in identification of babies who are ill for other pathologies. The FP rates in the 2 large UK studies are low and the impact on other service was not all demanding. Experience can be learnt from such centres to help address the some of the uncertainties relating to the referral pathways.</td>
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3. Overall conclusion

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

v. the information requirements of parents and health professionals,

w. training needs for midwives and others involved in newborn screening using pulse oximetry,

x. 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.
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<td>Page 27-30</td>
<td>Criteria 18-21</td>
<td>I partly agree with the above statement. As mentioned above, the experience from the centres who undergo the test can be used to help address some of the issues listed above. Examples would be training needs, data recording and audit. As far as the information requirements of parents and health professionals are concerned the work by Ewer tackled some of these issues and this work has been published.</td>
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<td>We have used oximetry as a screening test since 1999. We have the largest experience in this area and have supported clinicians both in the UK and abroad in the implementation of the test (Meberg, Norway). The test is simple to administer, it is easy to use and to train midwives and other health professionals, there will be a short period of high FP rate shortly after implementation. After nearly 14 years our FP rate is very low (less than 1%), and the impact upon finding a FP case due to non cardiac condition on other services is negligible. I am aware that the presence of clinician with cardiac/echo expertise on-site has</td>
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made our experience easily manageable but the utilization of the available technologies such as video echo link is likely to offer a great benefit, also the collaborative work with paediatric cardiologist in the regional cardiac centre. One word of caution is the exaggeration of the impact of dealing with “no-cardiac” FP.

In practice, the majority with FP cases can be assessed by neonatologist on site through clinical examination and other cot-side testing without the need to doing an urgent echo referral to the cardiac centre.

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- 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.
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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

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<td>Since implementation of pulseoximetry screening at our hospital I have personally seen a reduction in the number of severe morbidity and mortality from early sepsis (eg group B strep) which is almost certainly attributable to this screening tool. We have also picked up congenital heart disease which would otherwise have gone unnoticed at point of discharge from the hospital. This would have improved quality of care for the baby without doubt. In essence I would wholeheartedly recommend pulse ox screening should be rolled out nationally as a bench mark standard of care for newborn maternity units.</td>
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☐ Yes ☐ No

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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

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3. Overall conclusion

37
The review recommends the use of pilots to explore the issues relating to testing, referral and, in addition to explore:

y. the information requirements of parents and health professionals,
z. training needs for midwives and others involved in newborn screening using pulse oximetry,
aa. 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

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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. This will not only enhance the detection rate for critical congenital conditions but also other serious conditions (respiratory conditions like pneumonia, infection) in otherwise well looking children who are likely to present later with serious illness.

Now questions are being asked by various stake holders including parents, staff and public why pulse oximetry is not being routinely done despite such a good evidence in this vulnerable group of patients.

I am very convinced that there is enough evidence from current research studies pulse oximetry screening fulfills the criteria of universal screening. I strongly feel that routine pulse oximetry screening should be introduced as part of universal screening in the UK.

Best wishes,
Yogen

Dr Yogen Singh | Consultant Neonatologist and Paediatrician with Expertise in Cardiology
Cambridge University Hospitals NHS Foundation Trust

Paediatric Cardiology Secretary: [Redacted]
Neonatal Secretary: [Redacted]
Direct Tel: [Redacted] | Pager: [Redacted] | www.cuh.org.uk
Response to NSC consultation document on Pulse Oximetry Screening for congenital heart defects.

Dr Andrew Ewer. Reader in Neonatal Paediatrics, University of Birmingham and Consultant Neonatologist, Birmingham Women’s Hospital

Declaration of interest

- I was Chief investigator for the PulseOx study.
- I have performed two systematic reviews of the evidence for pulse oximetry screening and I am currently preparing a Cochrane review.
- I have lead a routine pulse oximetry screening service at Birmingham Women’s Hospital (BWH) since February 2009 (following end of recruitment to PulseOx study) and have advised on the initiation of screening services in other hospitals across the UK.
- I have advised the Secretary’s Advisory Committee on Heritable Disorders in Newborn and Children (SACHDNC) on the implementation of universal screening in the USA.
- I have recently analysed almost 4 years of local screening data from BWH and submitted this for publication (submitted manuscript attached).
- I have no connection, financial or otherwise, with any pulse oximeter companies

I found the response form rather limiting and the questions were mainly focused on the review and whether there was agreement with conclusions of the review. Mostly, a simple yes or no was an inadequate response. I have collated my response in 2 sections. The first is my overall response and considerations of the major issues and the second is response based on the questions within the response form.

Overall response

The main conclusions of the report with respect to pulse oximetry screening are as follows:

- ‘Pulse oximetry screening is clinically effective and cost effective screening modality for detecting critical or life-threatening CHDs, thus meriting implementation as part of the newborn screening programme’ (page 32 para 2)
- ‘There remains sufficient uncertainty about its use in a routine screening context to support a pilot or staged introduction…’ (page 32 para 2)

The main uncertainties identified by the report are i) screening protocols and ii) referral pathways. An additional uncertainty is the acceptability to parents

Screening protocols

The main concerns relate to i) timing of screening and ii) site of measurement. The published research studies can be categorised in these respects into:

i) those screening before and after 24 hours of age and

ii) those using one or two site measurement (post-ductal only or pre and post-ductal). UK national surveys\(^1,2\) indicate that, in units that employ screening, there is a variation of practice in both respects although the majority screen before 24 hours.
I have previously summarised these issues, based on the available evidence, in published reviews. Three extracts from published reviews are included below, which summarise the evidence as I see it.


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From Arch Dis Child Aug 9 [Epub ahead of print].

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Referral pathways

The concerns regarding referral pathways for test positive babies would benefit from consideration by clinicians involved with the care of these babies (neonatologists, paediatricians, neonatal nurses and midwives). Approximately 20% of UK maternity units are now routinely screening all babies and this number is steadily increasing. I have received, and continue to receive, communications from individual Units from across the UK, regarding the logistics of setting up local screening services. I have personally corresponded with clinicians from all units currently employing screening and the responses are universally positive. Test positive babies are absorbed into the existing clinical service and existing referral pathways for hypoxic infants are employed.

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.

It is my view that babies with low oxygen saturations are a common clinical finding (outside of screening) and pathways for evaluation and assessment of these babies exist within most neonatal units and, if they do not, a working group of clinicians should be able to devise an acceptable pathway. Babies with a non-cardiac diagnosis would not require an echocardiogram unless unexplained hypoxaemia persisted.

The NSC report states that referral pathways exist for newborn clinical examination and recommend that a similar pathway should be developed for pulse oximetry screening. Reviewing the current NIPE pathway for examination of the newborn heart (NIPE 2008), the guidance for a positive screen consists of the following:
‘Pulse oximetry and expert opinion within 24 hours of examination. Assessment will depend on the specific heart condition suspected.’

The pathway does not define what constitutes an abnormal examination result, what pulse oximetry measurements are acceptable, what constitutes an expert opinion [paediatrician or cardiologist?] or what assessment should be considered. Essentially the pathway allows clinical freedom to make the right decision based on the clinical circumstances i.e. not all babies with a murmur will necessarily be seen by a paediatric cardiologist. Perhaps a pulse oximetry pathway could be developed along similar lines allowing a degree of clinical freedom?

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.

Our experience at Birmingham Women’s Hospital over a 40 month period has just been submitted for publication. Over 40 months, we have screened over 25 000 babies, 208 (0.8%) were test positive. We detected 17 CHD (9 critical), 148 other significant diagnosis (pneumonia, EOS, PPHN etc.) and only 48 (21%) were ‘healthy’ (mild TTN, transitional circulation). We performed 61 echos as a result of PO screening and 48% were abnormal). Our pick up rate for CCHD using all 3 screens was 93% (26/28).8

In the UK, at least 20% of all maternity units are currently screening with 70% of non-screening units considering its introduction.2

Given the lack of clinical equipoise in the majority of UK clinicians and the huge number of asymptomatic patients screened both in studies and as a routine, it is highly unlikely that further pilot studies in the UK will add anything additional in terms of protocol refinement. In addition they will be expensive and delay a potentially life-saving test. At the moment screening protocols are heterogeneous. In my opinion, a better option would be to set up a working group of all interested parties working in conjunction with the NSC, RCPCH, BAPM, RCM etc. but particularly involving clinicians (neonatal, cardiology etc.) to assess the evidence and current UK practice and develop a protocol which is best suited for the UK. The evidence and experience is available to achieve this in a relatively short time period. Clearly, for a universal screening programme all issues of screening including training, referral pathways, data recording and management would have to be standardized and so a staged introduction (perhaps starting with those units that are already screening) would be a possible approach.

Acceptability to parents

The review document raises a number of concerns regarding parental acceptability of pulse oximetry screening and the issue of increased anxiety in parents, particularly those whose babies are subsequently found to be false positive. In my opinion, the review does not adequately describe the data on acceptability which was produced as a result of the pulseOx study (see comments below).

I think there is clear and unequivocal evidence of i) the acceptability of screening and ii) a lack of increased anxiety in mothers of false positives. This has been rigorously evaluated using robust methodology8,10 and it would incur considerable expense attempting to repeat
this. Our experience subsequent to the study (over 4 years) and the experience of other screening units is universally positive both from a staff and parents perspective.

References

6. Proposed pathway for managing hypoxaemia (attached)
8. Singh A, Rasiah SV, Ewer AK. The impact of routine pre-discharge pulse oximetry screening in a Regional Neonatal unit (submitted for publication)

Response Form

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?

This question is slightly confusing as there are 2 separate conclusions

i) ‘Pulse oximetry is clinically useful and will increase the number of CHD detected in the newborn period.’

ii) ‘The optimal approach to screening ... cannot be clearly defined on the basis of available studies.'

I agree wholeheartedly with the first conclusion but not with the second.

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Following publication of the Lancet systematic review of pulse oximetry screening in 2012 (ref 39) which included almost 230 000 babies screened, a large screening study in China involving over 121 000 babies has been undertaken (unpublished data). This brings the total number of asymptomatic babies screened using pulse oximetry to over 350 000. 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:

i) 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

ii) 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.

iii) 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.

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.

Please see comments above. I would make the following observations

**Page 17 table 4.**
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 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.

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.

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. Consideration should be given to why this should apply to positive pulse oximetry screens. Paediatricians are familiar with the assessment of babies with low oxygen saturations and are trained to 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.

3. Overall conclusion

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

bb. the information requirements of parents and health professionals,
cc. training needs for midwives and others involved in newborn screening using pulse oximetry,
dd. 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.

Page 28 section 20.
Parental information is important and available for those units and countries that 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 protocol by the suggested working group would be more appropriate in my opinion. This would give the opportunity to evaluate aspects of screening such as training, data collection and care pathways.

Page 28 section 19.
‘Additional facilities…’

This is important and these issues will need to be addressed however it can be seen that 20% of UK units have already implemented screening with no additional funding or staffing.

4. Any other comments

4a. If you have any other comments on the document please put them in the table below

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 an echocardiogram (Singh et al unpublished data).

4b. Are you aware of any publications that should have been considered in the review?

These references have been published or submitted after the review but the first three provide further analysis of existing data and the latter describes how pulse oximetry screening works in practice in a UK setting and the impact of screening on clinical services.

Singh AS, Rasiah SV, Ewer AK. The impact of routine pre-discharge pulse oximetry screening in a Regional Neonatal unit (submitted for publication).
Dear Mr. Marshall

I am writing in response to the UK National Screening Committee’s consultation on their policy on Congenital Heart Disease screening in newborns. I have been looking after children for 21 years, 14 of them as a cardiologist, and over this period, have increasingly realised the importance of an early screening programme for identifying neonates with significant cardiac defects. While there is no single assessment that can cover all bases, the use of pre & post-ductal saturations by Pulse Oximetry as proposed can pick up a significant number of these children along with other conditions that can potentially be life-threatening.

I would urge you to recommend that incorporation of the Pulse Oximetry screening is introduced across the UK as a routine check during neonatal assessments (baby checks).

Kind regards

Ashish

Dr. Ashish Chikermane
Consultant Paediatric Cardiologist & Clinical Lead - Cardiac Services

Dear Panel

I write as the neonatal lead for County Durham and Darlington NHS Foundation Trust, which incorporates University Hospital North Durham and Darlington Memorial Hospital. The Trust has used saturation monitoring as part of the neonatal check for a few years now.

It is a fast, easy assessment.

The benefits are not only in the detection of cardiac disease, but we have also detected a number of congenital pneumonias and neonatal sepsis using this tool, which would otherwise have gone undetected.

For us the benefits of using this tool are clear, and any tool that improves the detection of the ill baby, whatever the cause, is clearly beneficial.

I am happy to be asked any further details and would be happy to put my name to these comments.

Kind regards

Mehdi Garbash
Dear Mr Marshall,

I would like to express my views on behalf of the entire Paediatric Cardiology Department at Birmingham Children’s Hospital (including all my colleagues).

We have been the Cardiac centre supporting this research activity (Pulse Ox trial) undertaken by Dr. Ewer.

We have been able to diagnose critical congenital cardiac conditions where babies would have been discharged home and then collapsed leading major morbidity. We think that this is a simple, non-invasive test that would assist in diagnosing major cardiac conditions in neonates prior to discharge.

We have not seen any major unnecessary increase in our workload in terms performing Echocardiograms in neonates with false positive tests.

As a Cardiac team we would strongly support that Pulse oximetry would be included as a part of neonatal screening, as this will improve the early diagnosis of congenital cardiac conditions before they become life threatening emergencies.

Regards

Tarak

Dr. Tarak Desai
Consultant Paediatric and Fetal Cardiologist
Birmingham Children's Hospital NHS Foundation Trust
Tel:  
Fax:  

At CDDFT we went through these discussions 5 years ago and introduced the policy. We have 6000 deliveries per annum in two hospitals. We pick up a couple of cases a year and false positives pick up other such children that would be missed eg PPHN. We have to seek regional cardiology help and an initial concern was swamping them. This has not happened.

We would not consider stopping this system that has benefitted our population.

John Furness
Cons Paed
NB Dr [Redacted] Neonatal Lead appointed since we started saturation screening has told me that he has replied to similar effect
The literature review is reasonable, however after using this technique in the James Cook University Hospital in Middlesbrough for more than 15 years now and suggesting it for the Sunderland article I feel there are a number of issues.

1. This will only ever increase case acquisition and is not proper screening.
2. However, for individuals it can make a great difference.
3. Focusing merely on the heart disease is missing the point
   a. Some heart defects will be found, on the whole with earlier detection in well babies, the outcome is improved.
   b. More problems from infection and other issues will be detected than heart defects
      i. This is a common and consistent finding across the studies
      ii. This has not been addressed in the review which is a major loss and fault.
   c. All studies have identified a group of babies who are at present being sent home with low saturations from hospitals who are not doing this.
      i. How can we be happy with this?
      ii. Having detected this issue how can we ignore it?
      iii. All places will need a system to deal with positives.
4. At our unit we have not had a pure Persistent Pulmonary Hypertension of the Newborn in the time we have been doing this. I cannot know the reason but if babies are mildly cyanosed with high right sided pressures we put them into oxygen to reduce the pulmonary resistance and monitor them. These babies are few but we have seen no pure PPHN.
5. This is a relatively cheap non-invasive test. We feel it is also useful for parents whose babies become poorly later as they and we know that their saturations and heart rate were normal at discharge. This stops a lot of needless heartache and attempted litigation.

Yours sincerely

Jonathan Wyllie
Individual patient responses not submitted through the Children's Heart Federation

1.
I have campaigned to have the Pulse Oximetry Screening test introduced for every newborn. My own baby (now 1yr old) was born with an undiagnosed heart defect. She was found to have a heart murmur at 7 weeks old by her GP who misdiagnosed it as an "innocent" murmur and told me to take her back to the GP at her 1 year checkup. My daughter was let down by the GP and with the help of my health visitor and demanding a referral to a paediatrician who saw her at 12 weeks old my daughter's life was saved. The cardiologist her saw her at 12 weeks old told me that she would not have lasted another month and that I had saved her life, knowing that she was suffering. My daughter's heart condition was missed both in the womb and at the newborn checks. Although detected at 7 weeks of age, it was mis-diagnosed which would have then led to her death. My daughter's health had deteriorated and she had spent 3 months declining all which may have been prevented by the Pulse Oximetry Screening Test. The test takes so little time and is so readily available in our hospitals - but it could save so many babies lives and reduce their suffering. Surgery would be instigated earlier giving better quality of life. Pulse Oximetry Screening MUST be part of every newborn's hospital checks within 72 hours of birth.

2.
Not sure if this is the right way to contact you, but after listening to Woman's Hour this morning I wish to register my view that if the test for neo-natal heart defects is cheap, easy, available and used on adults then why not on babies?

Caroline Taylor

3.
Hi, my daughter XXXXXXXXX was born XXXXXXXXX at 22:22. We didn't discover she had a problem with her heart until 17 hours later. By which time her saturation levels dropped to a dangerous 38% She was critically ill. It took doctors 5 hours to stabilise her to ensure she could make the journey across London with the retrieval team in a blue light ambulance. We then discovered she has a very serious and rare chd-Pulmonary Atresia. She has had 3 catheter ops at 5 days, 18 days and 5 months. We were told she may have brain damage/learning difficulties due to the reduction of oxygenated blood. I am pleased to say she is doing well and quickly showed no signs if brain damage but each milestone in her development has been 'wait and see'. The shock and experience of that day still haunts me. We couldn't have changed the outcome of course but a simple check which is so easy to do after birth would have prevented her becoming so critically ill and risk to her physical/mental development could've been prevented.

I thank god that the paediatrician picked up her murmur on discharge as if we'd been sent home she probably wouldn't be here today. Please allow every child to have the proximity test. The sooner a problem is picked up the better.
I welcome the policy to try and improve detection rates in newborns. The use of pulse oximetry will assist in the detection of those heart defects which lead to low oxygen levels through the body. It will also help in detection of some non-cardiac conditions. However, the test must be used alongside proper physical examination by qualified medical personnel. Under no circumstances must it be used instead of a proper physical examination. It also must not be used to exclude the possibility of cardiac conditions if a normal reading is given. There are some cardiac conditions which do not produce low oxygen saturation levels. Proper physical examinations include other checks such as pulses which are extremely important to the detection of some conditions.

It is important that the screening committee together with medical personnel and NHS chiefs understand that even with the pulse oximetry testing there will still be a significant number of defects that will be undetected. These children will be the children who will be at risk of developing serious health problems later in life. The only way to have an extremely high detection rate is to also have monitoring or examinations later in childhood or teenage years. Some conditions will not produce any symptoms for some time. Like some inherited and acquired heart conditions together with the arrhythmia problems these only stand a chance of detection if further checks are introduced in year 6 (i.e. pulse and blood pressure) at schools or sports physicals introduced in secondary schools.

kind regards
S Saverton

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Dear Mr Marshall,

I am writing in response to the UK National Screening Committee’s consultation on their policy on Congenital Heart Disease screening in my daughter was born with tetralogy of fallots. Congenital heart defects are a leading cause of childhood mortality. Unfortunately it is estimated that around a third of children with congenital heart defects leave hospital without being diagnosed, leaving many babies undiagnosed for weeks, months or even years; often waiting until they are seriously ill before it is recognised. Pulse Oximetry screening can help to save babies lives, as well as avoiding needless long-term damage to a child and distress to their families.

With children in the UK still dying from undiagnosed heart defects, I would urge you to recommend that universal Pulse Oximetry screening is introduced across the UK as soon as possible; to give children with heart conditions the best chance for life-saving treatment.

Yours sincerely