How to develop a business case to establish a neonatal pulse oximetry programme for screening of congenital heart defects

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pulseOx
Should pulse oximetry screening be routine?

...and if so, how should we do it?
Overview

• Evidence

• Current practices

• Option appraisal of potential screening pathways
Congenital Heart Defects (CHD)

- Relatively common
- 6 – 10/1000 live births.

Critical CHD (CCHD)
~ 2-3/1000

1400-- 2100/yr in UK

Leading cause of infant death in developed countries
Critical CHDs (CCHDs)

• May only be recognised when babies develop life-threatening collapse.

• Collapse and acidosis significantly compromise surgical outcome and subsequent neurodevelopment.
Neonatal screening

Examination for CHD

- Up to 50% of babies with CHD may be missed by neonatal exam and up to a third of critical CHD

- Earlier discharge reduces time-window for signs and symptoms to develop

Antenatal screening

- Anomaly scan detection rates very variable
Proportion of babies requiring intervention for CHD within 1 year of life (major CHD excluding PDA and ASD) who were identified antenatally in UK

http://www.ccad.org.uk/congenital
Pulse oximetry
Pulse oximetry screening

Rationale

Clinically undetectable low oxygen levels (low saturations) present in the majority of critical CHD

Pulse oximetry may detect babies with CCHD early, before they collapse
Pulse oximetry screening

Early studies in mid 90s (abstract only)

First published studies in early 2000s

Richmond, UK (2002)
Koppel, USA (2003)
Pulse oximetry screening

8 studies 35 960 patients
Small numbers of patients, low prevalence of CCHD, methodological variations
More high quality studies (in larger study populations) needed to precisely define test accuracy
Included 2 further studies

‘Future studies in larger populations and across a broad range of newborn delivery systems are needed to determine whether this practice should become standard of care in the newborn assessment of the neonate’
Pulse oximetry screening for congenital heart defects in newborn infants (PulseOx): a test accuracy study

Andrew K Ewer, Lee J Middleton, Alexandra T Furmston, Abhay Bhoyar, Jane P Daniels, Shakila Thangaratinam, Jonathan J Deeks, Khalid S Khan, on behalf of the PulseOx Study Group
Methods

- Screened asymptomatic newborns >34 wks
- Pulse oximetry testing within 1st 24 hrs or prior to discharge
- Pre and post ductal saturations
- Test +ve - <95% in either or >2% difference
Results

• 20,055 babies screened

• 24 cases of CCHD

Sensitivity 75% (95% CI 53.29%-90.23%)
Specificity 99.16% (95% CI 99.02%-99.28%)

(54 cases of non-critical CHD [14] and non-cardiac serious illness [40])
Added value

• When combined with anomaly scan and newborn examination screening, 92% of CCHD were detected.

• In a cohort of 700,000 babies, PO could detect an additional 245 cases of CCHD.

Likely to be higher in areas where the AN detection rates are lower.
Pulse oximetry studies 2009 - 2012

- Granelli – Sweden, (BMJ 2009)
- Riede – Germany, (EJP 2010)
- Ewer – UK, (Lancet 2011)
- Turska–Kmieć – Poland, (Kardiologia Polska 2012)
Detection of significant non-cardiac disease an important additional finding in all studies (30-70% of false positives)

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<tr>
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<th>Sensitivity</th>
<th>Specificity</th>
<th>Added value</th>
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<tr>
<td>Granelli</td>
<td>62%</td>
<td>99.8%</td>
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<td>Riede</td>
<td>77.8%</td>
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<td>Ewer</td>
<td>75%</td>
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<td>Turska-Kmieć</td>
<td>78.9%</td>
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Pulse oximetry screening for critical congenital heart defects in asymptomatic newborn babies: a systematic review and meta-analysis

Shakila Thangaratinam, Kiritrea Brown, Javier Zamora, Khalid S Khan, Andrew KEwer

13 studies  229 421 patients (c.f. 8 studies, 36 000 pts)
(Did not include Polish study)

Overall sensitivity 76.5% (95% CI 67.7% - 83.5%)
Overall specificity 99.9% (99.7% -99.9%)
False positive rate 0.14% (0.06 - 0.33)
(FPR <24 hrs 0.5% FPR >24 hrs 0.05%)
A new milestone in the history of congenital heart disease

...surely the question now is not ‘should pulse oximetry screening be introduced?’ but ‘why should such screening not be introduced more widely?’
Further work

Pulse oximetry as a screening test for congenital heart defects in newborn infants: a test accuracy study with evaluation of acceptability and cost-effectiveness

AK Ewer, AT Furmston, LJ Middleton, JJ Deeks, JP Daniels, HM Pattison, R Powell, TE Roberts, P Barton, P Auguste, A Bhoyar, S Thangaratnam, AM Tonks, P Satodla, S Deshpande, B Kumararatne, S Silvakumar, R Mupanesunda and KS Khan

January 2012
10.3310/hta16020

Health Technology Assessment
NIHR HTA programme
www.hta.ac.uk
Further work

Pulse oximetry screening for congenital heart defects in newborn infants: an evaluation of acceptability to mothers

Rachael Powell,1 Helen M Pattison,1 Abhay Bhoyar,2 Alexandra T Furmston,3 Lee J Middleton,3 Jane P Daniels,3 Andrew K Ewer4,5

Pulse oximetry screening

• Is acceptable to parents and staff
• Anxiety not increased in parents of false positives
Further work

Pulse oximetry as a screening test for congenital heart defects in newborn infants: a cost-effectiveness analysis

T E Roberts,¹ P M Barton,¹ P E Auguste,¹ L J Middleton,² A T Furmston,² A K Ewer³,⁴

Arch Dis Child 2012;97:221–226. doi:10.1136/archdischild-2011-300564

• £24 000 per additional timely diagnosis
• Is cost-effective in an NHS setting
• ‘worst case’ scenario costing
Limitations

- Not a perfect test
- Will miss approximately 25% of CCHD
- Commonest defects missed – CoA, IAA

  Ewer – 43% (3/7)
  Turska–Kmieć – 33% (1/3)
  Granelli – 21% (3/14)
  Riede – 0% (0/2)
Strategies for Implementing Screening for Critical Congenital Heart Disease

CONCLUSIONS: The work-group members found sufficient evidence to begin screening for low blood oxygen saturation through the use of pulse-oximetry monitoring to detect CCHD in well-infant and intermediate care nurseries.
September 21, 2011

R. Rodney Howell, M.D.
Committee Chairperson
Secretary’s Advisory Committee on Heritable
Disorders in Newborns and Children
5600 Fishers Lane, Room 18A19
Rockville, MD 20857

Dear Dr. Howell:

'... I would like to commend the SACHDNC on your success in creating and implementing an external scientific evidence review process for rare conditions that incorporates systematic evidence-based and peer-reviewed recommendations. I am encouraged by the emerging evidence base for the utility of early diagnosis and detection of CCHD via measurement of blood oxygen saturation, as well as the momentum and commitment that is evidenced at the state and federal levels to support implementation and investigation of successful screening programs. While we collectively engage in the remaining work that needs to be completed, HHS will continue to encourage states, health care facilities, and individual clinicians to provide this screening and contribute to the knowledge base in this important area. ...

Sincerely,

Kathleen Sebelius

Kathleen Sebelius
• Switzerland – 85% of newborns screened although no central mandate

• Ireland – RCPI recommended screening in 2012
What’s happening in the UK?

- 2010 - only 15 of 224 units (7%) were screening
  (Kang et al Arch Dis Child 2011;96:312)

- 2012 Survey (Singh and Ewer, Lancet in press)

All units surveyed 204/204 (100%) responded

36/204 (18%) screening (8 about to start)

However – 71% of non-screening units are considering introduction
Screening protocols

36 units screening

- 18 post-ductal
- 18 pre- and post-ductal
- 17 ‘before discharge’
- 13 <24 hours
- 1 >24 hours
- 1 ‘within 48 hrs’
Option appraisal

Heterogeneity of screening algorithms

Which is most appropriate?
Screening considerations

Current situation

• No of deliveries, AN CCHD detection rate, length of postnatal stay, postnatal staffing, neonatal and echo services

• No of babies with CCHD and non cardiac illnesses collapsing or dying pre-diagnosis
Screening protocols

Cut-off parameters for a positive test

- Lower limit for an acceptable saturation value?

- Post ductal or pre- and post-ductal?

- If pre and post— one or both saturations <95%? Difference of >2% or >3%?

- Number of repeat tests?
Cut-off thresholds

• lower limit for a positive test varies between 92% - 96%
• numbers in the different subgroups too small to identify sensitivity differences*
• majority of studies used <95%.

*Thangaratinam et al Lancet 2012
Post-ductal or pre/post-ductal

• 60% of studies used post-ductal
• no difference in sensitivity, but almost twice no of subjects
• sensitivity estimates in sub-groups too imprecise to make any inference
• pre/post-testing will pick up babies with CCHD who would have been missed by post-ductal alone

*Thangaratinam et al Lancet 2012
Pre and post ductal difference

>3% (Granelli, Sweden)
FP rate 0.17%, sensitivity 62%

>2% (Ewer, UK)
FP rate 0.8%, sensitivity 75%

2 CHD (1 critical) identified by >2% alone
Early or late screening (<24 or >24hrs)

• Most babies have ‘normal’ sats within 2 hr

• FP lower if PO screening >24 hr
  0.05 vs 0.5
False positives

• High false positive rate
  - earlier screening
  - conservative threshold

Granelli* FP rate 0.17% vs 0.8% (sens 62% vs 75%)
  - screened later 38 vs 12 hrs

However in Granelli’s study…

28/57 CCHD presented before screening

‘Collapse’ in 11/57 (19%) [incl. 5 in hospital]
c.f. 1/26 (4%) in PulseOx [0]

*Granelli et al BMJ 2009;338:A3037
False positives

Need to consider trade off between false positive rate and timely diagnosis

Also…
Earlier diagnosis of respiratory/infective cases
Increasing discharges within 24 hours

False positives are babies with low oxygen levels
No baby should have unexplained persistent hypoxaemia
Number of repeat screens

- Most studies used 1 repeat screen
- Granelli study used 2 repeats
- $2^{\text{nd}}$ repeat likely to reduce FPs
Who should screen?

• Midwives?

• Health Care Assistants?

• Doctors/ANNPs/MWs at PN exam?

• ‘Screeners’?
Equipment

• Motion tolerant oximeters

• Reusable probes
Cost

- Staff costs
- Equipment costs
- Cost of investigating test positive infants
Staff costs

• HTA health economic analysis assumed midwives would perform test

• £4.68 - £6.24 per test (incl. equipment)

• HCAs or ‘screeners’ likely to be less costly
Equipment costs

• Oximeters - £ 500 - £ 1000 each

• Reusable probes - £ 150 each
Cost of positive test

- HTA analysis assumed a cardiac centre echocardiogram for each test positive case
- Only echo those with unexplained hypoxaemia
- In-house echo increasingly common
- Additional repeat test likely to reduce test positives with transitional circulation
Cost savings from screening

- Majority of TP infants would need admission anyway

- Reduction in intensive care days as a result of early detection of CCHD, early-onset sepsis and other respiratory conditions
Postnatal pathway for Pulse Oximetry Screening for Critical Congenital Heart Defects in the Newborn

Apparently well newborn in the Postnatal Nursery
Pre-discharge pulse oximetry screening to commence at 4-8 hours (depending on local circumstances)

Right hand (Pre-Ductal) and either foot (Post-Ductal) saturations measured until consistent reading obtained (PO1)

- Both readings >94% and difference <3%
  - TEST NEGATIVE
    - No further action
    - Routine Care

- Either reading 90-94% or >2% difference
  - If asymptomatic repeat test in 2 hours (PO2)
  - Either reading 90-94% or >2% difference
    - If asymptomatic repeat test in 2 hours (PO3)
      - Either reading <95% or >2% difference
        - TEST POSITIVE
          - Urgent Paediatric Assessment
      - If nearing "out of hours" service when PO3 is required, then screen PO3 earlier to enable optimum time for contact of alternative services as may be required e.g. Paediatric Cardiology.
Positive Pulse Oximetry Screen
Saturation measurement <90%
3 saturation measurements 90-94% or >2% difference
Symptomatic or abnormal examination findings

Assessment by the most senior paediatric staff available or telephone discussion with senior paediatric cardiology staff

Asymptomatic
Saturations spontaneously improving in air or minimal oxygen

Observe on NNU
Continuous saturation monitoring

Minimal respiratory symptoms and/or abnormal CVS examination and/or minimal improvement in saturations with oxygen

Consider Urgent in-house echocardiogram or discussion with Paediatric Cardiologist
Consider starting Prostaglandin Infusion
Continuous saturation monitoring

Saturations remain abnormal in air without diagnosis

Respiratory / infective symptoms and/or saturations improve in oxygen

Investigate and treat respiratory or infective illness
Continuous saturation monitoring

Saturations normal in air

Repeat examination of CVS
Consider discharge if normal and baby asymptomatic
UK progress

• NIPE to present case for addition of pulse oximetry screening to NSC in early 2013
Routine pulse oximetry screening

- is feasible, cost-effective and acceptable to parents and staff
- adds value to existing screening procedures
- is likely to identify cases of CCHD which would otherwise go undetected
- has the additional advantage of detecting other serious (non-cardiac) illnesses
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- Askar Kukkadi.

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