Institution: University of Birmingham

Unit of Assessment: UoA2

Title of case study: PulseOx: Detecting heart disease in newborn babies through pulse oximetry screening

1. Summary of the impact

Congenital heart defects are a leading cause of infant death, accounting for more deaths than any other type of malformation and up to 7.5% of all infant deaths. Timely diagnosis is crucial for the best possible outcome for these children. However, the accuracy of current methods for screening newborn babies for critical congenital heart defects (CCHD) is variable and currently only detects these issues in between 35-50% of babies before birth. Although some cases are picked up after birth, up to a third of children with these problems are sent home undiagnosed, where they may become unwell or die. Research at the University of Birmingham has demonstrated that pulse oximetry is a rapid, safe, non-invasive, painless method of detecting the low blood oxygen levels associated with CCHD, and is also a cost-effective approach. As a result of our research, pulse oximetry was recommended for adoption across the US in 2011 by the Secretary for Health and Human Services. In the UK, our research is prompting a national review of screening for these conditions and some units are already using the approach, meaning that some patients are already benefitting.

2. Underpinning research

Congenital heart defects (i.e. issues existing at birth or during pregnancy) are the most common group of congenital malformations, affecting up to 9/1000 live born babies, and accounting for 40% of all deaths from congenital malformations. They are a leading cause of infant deaths in the developed world, with most deaths occurring in the first year of life. Critical congenital heart defects (CCHD) are a key subset; affecting around 2/1000 babies, they are have significant implications for the child's survival. If they are not detected early, risks for circulatory collapse increase. Although surgery can greatly improve survival, if diagnosis is not timely, the risk of surgical mortality also increases. Screening for congenital heart defects at the time of the research relied on antenatal ultrasonography and postnatal clinical examination. However, these methods are not very accurate for detecting CCHD, identifying before birth only 35-50% of babies for whom it is a problem. For the remaining babies, these defects are then either identified after birth or remain undetected when children are sent home. Overall, around one third of children with these potentially life-threatening heart defects are discharged from hospital without being diagnosed.

A team from the University of Birmingham UoA2 (Professor Jon **Deeks**, Professor of Health Statistics, UoB; Professor Tracy **Roberts**, Professor of Health Economics, UoB; Dr Pelham **Barton**, Reader in Mathematical Modelling, UoB; Dr Jane **Daniels**, Senior Research Fellow, UoB, Alexandra **Furmston**; Trial Co-ordinator, UoB, Lee **Middleton**, Statistician, UoB; Peter ***Auguste***, Research Associate, UoB until December 2012) with clinical colleagues in UoB UoA1 (Bhoyar, Ewer, Khan, Thangaratinam) and others (Edwards, Birmingham Women's Hospital; Pattison, Aston; University, Wright, Birmingham Children's Hospital) has worked since 2007 to conduct a programme of research around the use of pulse oximetry to better identify babies with these problems.

It is well established that blood oxygen levels are often low in CCHD and so one way of identifying these defects might be to identify those babies with low blood oxygen levels. Pulse oximetry is a method of measuring blood oxygen levels by placing a sensor on part of the patient's body (such as a fingertip or earlobe), not requiring any invasive techniques. The sensor can detect the baby's oxygenation levels during labour. The technique was developed in the 1970s and explored for monitoring fetal oxygenation, but results had been inconclusive. The University of Birmingham team conducted a systematic review in 2007 which showed encouraging results but drew attention to various difficulties in assessing the accuracy of pulse oximetry including variations in patient selection, timing of measurement, cut-offs for a positive result, types of congenital heart defects screened for, rigour of follow-up, and type of oximeters used [1]. The systematic review demonstrated a clear need for a larger, robust, well-conducted study to confirm the value, acceptability and cost effectiveness of such a screening programme.

In 2007, the National Institute of Health Research funded the PulseOx study (Ewer, **Daniels, Roberts,** Thangaratinam, Khan, **Deeks,** Pattison, Wright, NIHR HTA; £947k 2007-10). This large, multi-centre study assessed the accuracy of pulse oximetry for screening major congenital heart defects in newborn babies. It was the largest UK study in this field, screening 20,055 newborn babies between February 2008 and January 2009, and the first to assess the added value of pulse oximetry screening in modern healthcare systems where antenatal ultrasound screening was widely available. The study used robust methods to generate precise estimates of the accuracy [2,3], cost-effectiveness [2,4] and acceptability [2,5] of pulse oximetry. The test accuracy paper [2,3] demonstrated that the addition of pulse oximetry screening to the routine anomaly scan and newborn physical examination resulted in 92% of babies with critical congenital heart defects being detected prior to discharge; no baby died with unidentified congenital heart defects. The study found that pulse oximetry is a safe, feasible (i.e. easy to undertake and simple to adopt into routine practice) test that complements and adds value to existing screening by identifying more issues at birth, including cases of CCHD that would go undetected with antenatal ultrasonography. The team also demonstrated that pulse oximetry screening in combination with clinical examination identified almost 30 additional CCHD cases per 100,000 live births with a timely diagnosis compared with routine clinical examination alone, with a very high likelihood (over 90%) that this would be regarded as 'cost-effective', i.e. worth the extra investment needed to identify these cases [2,4]. The acceptability research undertaken clearly showed that both parents and health professionals felt the test was not painful, difficult to perform or inconvenient [2,5]. False-positive results did not significantly increase anxiety. Overall, the results substantially enhanced the evidence that indicates the potential benefits of the introduction of pre-discharge pulse oximetry screening as a routine procedure.

Media coverage of the work has included print newspapers (Guardian, Independent, Scotsman, Express, Star; reach 319,300), Radio (Heart FM, Classic FM, BBC Radio WM; reach 97,300) and online (Mail, Guardian, Telegraph, Independent; reach 4,888,400).

3. References to the research

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4. Details of the impact

This work has had major impacts on international policy and practice – including patient groups who wish to campaign on this topic – as well as directly for children and their parents where the test has been implemented as a result. The research was described as 'a new milestone in the history of congenital heart disease' in a Lancet editorial [1].

Impact on international policy

The Lancet paper (2011), HTA report (2012) and subsequent international media attention led to a

demand from policy makers internationally for advice on implementation of pulse oximetry. In the USA, where CCHD affects about 4,800 babies born every year, Dr Ewer was invited in 2011 to advise a working group of the Secretary's Advisory Committee on Heritable Diseases in Newborns' and Children (SACHDNC) in Washington, USA with his data described as 'instrumental in creating recommendations for the screening algorithm' [2] . Following this meeting, the group issued a statement advocating the introduction of pulse oximetry screening endorsed by the American Academy of Pediatrics [3] and the American Heart Association [4]. As a direct result, in 2011 the US Secretary for Health and Human Services recommended the addition of pulse oximetry screening for CCHD across the US [5,6], with the chosen strategy [7] referencing just the work of the Birmingham team (reference 14) and one Swedish study. Seven US states (including New Jersey, Michigan) currently perform routine screening; 27 others have passed legislation towards this goal, with 3 having active legislation in process. Current information on progress towards legislation can be obtained at [8] and an example of guidance on screening referencing the Birmingham team's work for the state of Alabama at [9].

The research has also impacted on provision in Ireland, where the Royal College of Physicians in 2011 recommended that pulse oximetry 'should be undertaken in all Units across the country', citing the 'seminal research' of the Birmingham team as the basis for the decision, and indicating that screening would identify 99 babies per year with the condition [10].

Impact on UK policy

The UK National Screening Committee (NSC) assesses evidence for programmes against a set of internationally recognised screening criteria, advises ministers/the NHS on all aspects of screening and supports implementation of screening programmes. The UK NSC will shortly conduct a public consultation over whether to add pulse oximetry to the assessment of newborn babies. The consultation highlights the *'…considerable research evidence to demonstrate that pulse oximetry, as an adjunct to clinical examination, increases the detection rate of critical or life-threatening CHDs at the newborn screening opportunity'* and that *'routine pulse oximetry is probably the most promising additional newborn screening modality'* under consideration, for which the University of Birmingham's work provides the bulk of the underpinning rationale and evidence [11].

Impact on UK clinical practice and patient health

Although the UK policy situation is still developing, changes in clinical practice are already occurring. A 2010 national survey found that only 7% of UK neonatal units were undertaking routine pulse oximetry screening. A survey of 204 units in 2012 indicated a rise in these figures, with 18% of units utilising pulse oximetry routinely and 4% in the process of introducing it [12]. Of non-screening units, 70% were considering its introduction. This survey and associated correspondence clearly indicates a shift of opinion among UK neonatologists about pulse oximetry screening, with a substantial majority now in favour, albeit with reservations about cost.

One centre adopting pulse oximetry screening is Birmingham Women's Hospital, with 8000 live births per year. With screening, over a three year period (2010-13) there were 187 admissions as a result of an abnormal screening test. This equates to approximately 60/year, 0.8% of all live births. Of the 187 babies admitted, seven had a critical congenital heart defect unsuspected prior to screening. Five further babies had an unsuspected non-critical congenital heart defect. Further, for those 180 babies who did not have critical congenital heart defects, many other serious health conditions (including congenital pneumonia, sepsis and pulmonary hypertension) were identified through the positive pulse oximetry screening, and only 36/180 (20%) admitted babies had no health issues. This indicates the additional benefits obtained through incorporating this screening into routine practice. If it is assumed that the 18% of units currently applying pulse oximetry screening look after 18% of the 700,000 babies born annually in the UK and that the rates for Birmingham Women's Hospital are typical, then an additional 63 babies with congenital heart defects were detected by pulse oximetry screening in 2012, including 37 babies with critical defects

International campaign groups

A significant impact of the work has been its use by lobbying groups, who were quick to recognise the potential benefits of pulse oximetry for screening newborns and have actively campaigned for its routine use nationally. These UK groups all cite the Birmingham Pulse Ox study as the most

important piece of evidence for their campaigns, and letters of support have been provided by:[13]

- **Children's Heart Federation** (*"The extensive and compelling research… has been crucial to our understanding and work around the issue. It has allowed us to strongly make the case that this test should be introduced for newborns in the UK."*);
- **Little Hearts Matter** (*"Little Hearts Matter has been able to use the findings to add credence to our call for better diagnosis of congenital heart disease with NIPE"*);
- **Tiny Tickers** ("*This research highlights the possibility of a timely and cost-effective neonatal solution and has resulted in Tiny Tickers lobbying of NIPE… it is likely to be enormously important to babies with undetected heart disease and their families and community"*).

Internationally, campaign groups also commonly recognise the value of Birmingham's work. A US website exists for parents to lobby for the use of pulse oximetry and cites the PulseOx study as one of "the most compelling pieces of evidence", which "should be part of any advocacy work" [14].

5. Sources to corroborate the impact

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