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Newborn Pulse Oximetry Screening in New Zealand

Feasibility Study Steering Committee Report and Recommendations

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Steering committee members

Frank Bloomfield (chair)	Professor of Neonatology, University of Auckland
Elza Cloete (secretary)	Neonatologist and Senior Research Fellow, University of Auckland
Tom Gentles	Paediatric Cardiologist, Starship Children's Hospital
Lesley Dixon	Midwifery Advisor, New Zealand College of Midwives
Dianne Webster	Clinical Scientist, Auckland District Health Board
Jane Alsweiler	Neonatologist and Senior Lecturer, University of Auckland
Sarka Davidkova	Paediatrician, Rotorua Hospital
Joshua Agnew	Pasifika representative and Paediatrician, Tauranga Hospital
Chris McKinlay	Neonatologist and Senior Lecturer, University of Auckland
Rob Lutter	Former CEO Heart Kids New Zealand
Kelly Richards	Consumer Representative
Jenny Rogers	Māori Representative, Kaiārahi, Liggins Institute
Julena Ardern	Neonatal Nurse Specialist, Middlemore Hospital
Donna Foote	Midwife

Conflict of interest

None to declare.

Acknowledgements

Chief investigators
Prof Frank Bloomfield
Dr Elza Cloete
Dr Tom Gentles

Co-investigators
Dr Lesley Dixon
Dr Dianne Webster
Dr Jane Alsweiler

Regional representatives
Dr Sarka Davidkova
Dr Chris McKinlay
Julena Ardern

Non-committee author contributors
Dr Lynn Sadler
Dr Kirsten Finucane
Dr Monique Stein-de Laat
Dr Kim Ward
Sharnie Cassells

Economic evaluation
Dr Richard Edlin

Consumer advisors
Rob Lutter
Kelly Richards

Graphic design
Diane Stephenson

Data managers
Safayet Hossin
Grace McKnight

Research administrators
Genevieve Morris
Erin Eydt
Renee Rialton

Research assistants
Sabine Huth
Dr Deborah Rowe
Jackie Mutu

Māori and Pasifika advisors
Jenny Rogers
Dr Sue Crengle
Dr Helen Wihongi
Dr Joshua Agnew
Dr Tueila Percival

Midwifery leaders
Nikki Edwards
Isabelle Eadie
Helenmary Walker
Lynn Austerberry
Robynne Hubbard
Raewyn Taylor
Corli Roodt
Sue Finch

Participating paediatric services
Cardiac Services, Starship Hospital
Newborn Services, Starship Hospital
Neonatal Unit, KidzFirst Hospital
Paediatric Department, Rotorua Hospital

Participating maternity units
Women's Health, Auckland City Hospital
Birthcare Maternity Unit
Botany Maternity Unit
Papakura Maternity Unit
Pukekohe Maternity Unit
Rotorua Hospital
Taupo Hospital

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This research project was led from:

The Liggins Institute, University of Auckland
Private Bag 92019
Auckland, 1142
New Zealand
www.liggins.auckland.ac.nz

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Abstract

Pulse oximetry has been utilised internationally as a screening tool for the detection of congenital heart disease in newborn infants for more than a decade. A research study was conducted to establish whether it is feasible for New Zealand to introduce nationwide pulse oximetry screening for the detection of critical congenital heart disease (CCHD) in newborns.

An intervention study of pulse oximetry screening was introduced at hospitals and primary maternity units in three District Health Boards. The study was conducted over a 2-year period and was preceded by consultation with stakeholder groups. Well infants with a gestation of ≥35 weeks were eligible for screening. An oxygen saturation ≥95% was a pass result. Participant demographics, test results and medical care following a failed test were recorded. Consumer satisfaction was assessed with a survey and healthcare provider satisfaction with focus group discussions.

Oximetry screening was performed on 16,644 of 27,172 (61%) eligible infants, with screening rates exceeding 80% in one centre. The overall screening rate was adversely affected by the inability of one tertiary hospital with a large number of births to take part. Forty-eight (0.3%) infants failed to reach saturation targets: 3 had critical cardiac disease; 34 had significant other pathology, and no pathology could be identified in 11. There were significant associations between screening rates and demographic variables with lower rates recorded for Māori, Pasifika, the socioeconomically deprived and those not registered with a maternity care provider. Consumers were satisfied with the screening procedure and the quality of information provided. Healthcare providers were positive about the screening test, but raised concerns that the lack of material and human resources will impede universal access to the test.

The introduction of pulse oximetry screening can identify infants with cardiac and other hypoxaemic conditions, but sector-led initiatives may perpetuate inequity. A nationally-led screening programme is most likely to optimise health outcomes for infants born with critical cardiac anomalies and will be well received by consumers.

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List of abbreviations

ADHB	Auckland District Health Board
BW	Birth weight
CCHD	Critical congenital heart disease
CHD	Congenital heart disease
CI	Confidence interval
CMDHB	Counties Manukau District Health Board
CRF	Case report form
CYMRC	Child and Youth Mortality Review Committee
DHB	District Health Board
d-TGA	d-loop Transposition of the great arteries
ECG	Electrocardiogram
GA	Gestational age
LMC	Lead maternity carer
MAS	Meconium aspiration syndrome
MAT	National Maternity Collection
MCIS	Maternity Clinical Information System
MERAS	Midwifery Employee Representation and Advisory Services
NHI	National Health Index
NICU	Neonatal intensive care unit
NSAC	National Screening Advisory Committee
NSU	National Screening Unit
NZ Dep	New Zealand deprivation index
OR	Odds ratio
PaO_2	Partial pressure of arterial oxygen
PMMRC	Perinatal and Maternal Mortality Review Committee
PPHN	Persistent pulmonary hypertension
RDS	Respiratory distress syndrome
SpO_2	Peripheral capillary oxygen saturation
SVT	Supraventricular tachycardia
TAPVD	Total anomalous pulmonary venous drainage
TTN	Transient tachypnoea of the newborn
UK	United Kingdom

Executive summary

Background

Congenital heart disease is the most common group of congenital malformations and the leading cause of infant mortality from birth defects. Most cardiac anomalies are amenable to surgery, but delayed diagnosis is a barrier to the timely initiation of potentially life-preserving interventions. Antenatal ultrasound and newborn physical examination have been used to detect cardiac disease. Both these strategies have limitations and therefore critical cardiac disease may remain undiagnosed by the time a newborn is discharged from the place of birth. In recent years pulse oximetry has been utilised in various jurisdictions as a screening tool for the detection of cardiac anomalies and it has become evident that the number of late diagnosed infants can be reduced significantly when pulse oximetry is used in conjunction with other screening strategies.

In New Zealand, there currently is no national approach to newborn pulse oximetry screening. Until recently there have been no reports in the literature of New Zealand-specific data relating to pulse oximetry that can contribute towards an evidence-informed decision regarding implementation of a nationwide screening programme.

Aims

We undertook a research study of pulse oximetry screening in the New Zealand maternity setting with the aim to assess the feasibility of delivering a nationwide screening programme. The study assessed: local patient and institutional factors that may impede universal access to the test; the impact of universal pulse oximetry screening on maternity, paediatric and cardiac services in New Zealand; acceptability among consumers and healthcare professionals, and the economic implications of delivering a national screening programme.

Methods

Following the establishment of a steering committee, stakeholder engagement, and the development of guidelines and resources the study was conducted over a 2-year period at hospitals and primary maternity units from the Auckland District Health Board (ADHB), Counties Manukau District Health Board (CMDHB) and Lakes District Health Board (Lakes DHB). One quaternary hospital, two regional hospitals and four primary maternity units participated in the study.

Post-ductal oxygen saturations were measured on well newborn infants with a gestational age of ≥35 weeks. The recommended time for entering the screening algorithm was between 2 and 24 hours after birth. Infants achieving an oxygen saturation of 95% or greater passed the test. Results were recorded on a case report form and transferred to an electronic database. Study data were supplemented with Ministry of Health data sources and clinical records.

Consumer acceptability was assessed with an anonymous survey and focus groups discussions were held to assess acceptability among healthcare professionals.

Main findings of pulse oximetry screening feasibility study

Pulse oximetry screening was performed on 16,644 of 27,172 (61%) eligible infants. Forty-eight (0.3%) infants failed to reach saturation targets, of whom three had critical cardiac disease. A further 34 infants had significant respiratory or infective diseases. Pathology could not be identified in the remaining 11 infants with a positive screen.

Screening practices varied significantly among participating centres. The median age at which the screening algorithm was commenced varied from 3 to 31 hours. Earlier screening was associated with a higher false-positive rate. The yield from pulse oximetry screening does, however, appear to be inversely related to time. In this study one pathology was identified for every 245 tests that were performed <4 hours after birth compared with one pathology for every 309 tests performed between 4 and 12 hours. One pathology was identified among the 6,197 tested after 12 hours.

Infants that were unsettled or asleep at the time of testing were less likely to pass compared with awake and settled infants ($p < 0.001$ and $p = 0.002$ respectively). Breastfeeding during the recording did not result in lower oxygen saturation levels demonstrating that screening does not have to interfere with the bonding between a mother and her infant.

Screening rates improved over time but were significantly influenced by the place of birth, with the highest rate achieved among those born at Auckland's quaternary hospital and the lowest rate recorded for home births (81% and 6%, respectively). Infants born in the CMDHB region (adjusted OR = 0.29; 95% CI 0.27 – 0.32) and Lakes DHB region (adjusted OR = 0.75; 95% CI 0.67 – 0.83) were significantly less likely to receive pulse oximetry screening compared to those born in the ADHB region. Only approximately half of Māori and Pasifika babies were screened compared with three-quarters of Asian and European babies. There was also a significant association between screening rates and deprivation, with higher odds of screening recorded for babies born to families living in the least deprived areas (quintile one) compared with those living in the most deprived areas (quintile five) (adjusted OR = 1.39; 95% CI 1.25 – 1.54). Failure to register with a maternity care provider was associated with lower odds of infant screening (adjusted OR 0.61; 95% CI 0.55 – 0.68) compared with care provided by an LMC midwife.

Equity

Quality improvement initiatives have the potential to benefit some population groups more than others. In this study, participation was voluntary and dictated by individual perceptions as well as institutional constraints. This resulted in inequitable service delivery with lower screening rates achieved for Māori and Pasifika, those living in the most deprived areas, and those born at home, in primary maternity units or in CMDHB. No ethnic or socioeconomic disparity was evident in the context of high screening rates.

A pulse oximetry screening programme that is sector-led is likely to perpetuate inequality as human and material resource constraints may prohibit access to the test. If equal participation in screening can be reached, pulse oximetry screening will likely result in greater health gains for Māori, Pasifika and those living in the most deprived areas of New Zealand. This relates to the lower lead maternity carer registration rates reported among women living in the most deprived areas as well as Pacific women. Māori women are also less likely to register with a maternity care provider compared to European women. Engagement with antenatal maternity care providers is directly related to the likelihood of detecting abnormalities during pregnancy.

Economic evaluation

The analysis compared a national screening programme for CCHD in the newborn utilising pulse oximetry against New Zealand's historic standard of postnatal screening, namely the newborn physical examination. Short-term outcomes of timely (pre-discharge) diagnosis and quality-adjusted life year (QALY) outcomes alongside 2-year healthcare costs were considered.

Pulse oximetry screening was estimated to detect 23.75 infants with CCHD before discharge from the place of birth each year, compared with 19.76 in the New Zealand historic standard of care (clinical examination). This equates to 0.52 additional timely diagnoses each year for infants with single ventricle anomalies (Group A) and 3.47 for infants with critical biventricular anomalies (Group B).

Diagnosis before discharge from the place of birth was associated with a 5% reduction in mortality for Group A and 3.7% for Group B. With a lower mortality rate amongst the earlier detected cases, the infants identified with pulse oximetry screening would correspond to an expected gain of approximately 3.74 QALYs per year. It is estimated that pulse oximetry screening will improve health at a cost exceeding $195,000 per QALY. However, this analysis does not take into account the potential benefit of timely diagnosis on neurodevelopmental outcome, nor the health benefits of earlier diagnosis of other hypoxaemic conditions such as neonatal sepsis.

Midwifery perspective

Midwives' involvement with mothers and infants in the first few hours after the birth place them in an ideal position to perform pulse oximetry screening. The majority of screening in this study was indeed undertaken by midwives. As such, they were given the opportunity to provide their perspectives and to share their experiences through focus group discussions. Hospital and community midwives from all participating regions contributed to the discussions.

Midwives were overwhelmingly positive about their experiences of pulse oximetry screening. They considered that identifying an unwell baby before it became clinically unwell was important, not just for the health of the baby but also for the parents, wider family/whānau, and the midwives caring for that family. However, they also identified several barriers that may impede equitable and universal access to the test. Workload and lack of material and human resources were regarded as key constraints. An overstretched and undervalued midwifery workforce is likely to detract from an equitable screening service. Furthermore, place of birth was regarded as a potential barrier as equipment is not currently accessible to all midwives overseeing home births. Discussion with the midwifery professional body will be necessary before the additional demands of a screening programme are placed on midwives.

Paediatric services perspective

The benefits of pulse oximetry screening can be achieved with minimal impact on neonatal, paediatric and cardiac services. In most infants with a positive screen, a diagnosis is established after clinical examination, basic laboratory tests and radiographs, and less than a quarter require echocardiography. Because New Zealand has a well-developed system for paediatric echocardiography by credentialled secondary care providers, the impact of pulse oximetry screening on tertiary cardiac services will be negligible. When required, a 24-hour on call paediatric cardiology service is available at Starship Hospital for consultation and review of echocardiograms to support regional paediatricians.

Although early pulse oximetry screening would potentially result in approximately 41 infants per annum failing screening due to delayed birth transition in the absence of underlying pathology (rate 0.7/1,000), these infants can be managed by secondary paediatric services, with only approximately half of these cases requiring additional assessment other than clinical examination. It is recognised that some infants with false-positive screening results may need to travel a considerable distance to a secondary or tertiary centre for a paediatric assessment. This could be mitigated against if, in the case of inconclusive test results, the third screening test is delayed until the infant is at least 12 hours of age. Overall, the workload associated with the review of these infants by regional paediatric services is likely to be negligible.

Consumer perspective

Pulse oximetry screening was well received and understood by consumers and is considered to be an important health check for newborn infants. The effective dissemination of information to consumers is important on many levels. First, parents wish to be well informed and involved with matters that relate to their newborn child. The anxiety associated with positive test results can be limited if parents have a good understanding of the test and its potential outcomes. Furthermore, information should be provided during pregnancy as many will not retain information that is shared in the period immediately before or after the birth of the child.

Conclusion

Pulse oximetry is a safe, easy-to-use and effective tool that can identify serious diseases in the newborn before the onset of symptoms. The research conducted in New Zealand supports the introduction of a national screening programme.

Recommendations

1. New Zealand should introduce a nationwide pulse oximetry screening programme for the detection of critical congenital heart disease and other hypoxaemic conditions in the newborn.
2. All newborn infants should receive equitable access to pulse oximetry screening, whether they are born in a hospital, primary maternity unit or at home. To achieve this, uniform guidelines, based on the algorithm used in the feasibility study, should be developed.
3. We recommend pulse oximetry screening in all infants, between 2 and 24 hours after birth using a post-ductal (foot) assessment of oxygen saturations.
4. The pulse oximetry screening programme should be performed by midwives caring for the infants and their mothers.
5. It is essential that midwives be adequately resourced, with both equipment, consumables and funded time in order to perform pulse oximetry screening.
6. It is also essential that the pulse oximetry screening programme be monitored in order to ensure quality is maintained.
7. Awareness of pulse oximetry screening should be raised in both healthcare providers and consumers for both the benefits and limitations of pulse oximetry screening to be appreciated.

Publications arising from the New Zealand feasibility study

1. Should New Zealand introduce nationwide pulse oximetry screening for the detection of critical congenital heart disease in newborn infants? Cloete E, Gentles TL, Alsweiler JM, Dixon LA, Webster DR, Rowe DL, Bloomfield FH. *New Zealand Medical Journal* 2017; 130:64-69.
2. Newborn pulse oximetry screening in the context of a high antenatal detection rate of critical congenital heart disease. Cloete E, Bloomfield FH, Cassells SA, de Laat MWM, Sadler S, Gentles TL. *Acta Paediatrica*. 2019 Jul 23. DOI: 10.1111/apa.14946.
3. Pulse oximetry screening in a midwifery-led maternity setting with high antenatal detection of congenital heart disease. Cloete E, Gentles TL, Webster DR, Davidkova S, Dixon LA, Alsweiler JM, Bloomfield FH. *Acta Paediatrica*. 2019 Jul 12. DOI: 10.1111/apa.14934.
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6. Comment on Kluckow M. Barriers to the implementation of newborn pulse oximetry screening: A different perspective. Gentles TL, Cloete E, Mellander M. *International Journal of Neonatal Screening* 2018; 4(2):13.
7. Antenatal detection of treatable critical congenital heart disease is associated with lower morbidity and mortality. Cloete E, Bloomfield FH, Sadler L, de Laat MWM, Finucane AK, Gentles TL. *The Journal of Pediatrics* 2019; 204:66-70.
8. Congenital left heart obstruction: ethnic variation in incidence and infant survival. Cloete E, Sadler L, Bloomfield FH, Crengle S, Percival T, Gentles TL. *Archives of Disease in Childhood*. 2019 Sep; 104(9):857-862. DOI: 10.1136/archdischild-2018-315887.
9. New Zealand should introduce nationwide pulse oximetry screening for the detection of critical congenital heart disease and other hypoxaemic conditions. Cloete E, Gentles TL, Bloomfield FH. *New Zealand Medical Journal*. In press.
10. Health professionals' view of newborn pulse oximetry screening in a midwifery-led maternity setting. "It's a good thing to do, but fund it!" Ward K, Dixon LA, Cloete E, Gentles TL, Bloomfield FH. Under review.

Introduction

Congenital heart defects are the most common group of congenital malformations, with an incidence of between four and ten per 1,000 live-born infants. Surgery and cardiac catheter interventions have resulted in marked improvements in survival, particularly for those infants with life-threatening conditions (K L Brown et al., 2006; D E Fixler et al., 2014; D Tobler et al., 2010). Successful intervention is dependent on timely diagnosis; if such defects are not detected early, severe hypoxaemia, shock, acidosis and death are potential sequelae. Detecting infants with severe cardiac malformations before or immediately after birth is therefore of the utmost importance.

Pulse oximetry has been utilised as a screening tool for the detection of congenital heart defects in newborn infants for more than a decade (A F Bakr et al., 2005; R I Koppel et al., 2003; J D Reich et al., 2003; E Rosati et al., 2005). In recent years this practice has been widely introduced in various jurisdictions as it became evident that the number of late diagnosed infants can be reduced significantly when pulse oximetry is used in conjunction with other screening strategies, namely antenatal ultrasound and newborn physical examination (A de-Wahl Granelli et al., 2009; J L Oakley et al., 2015; A Turska Kmiec et al., 2012; Q M Zhao et al., 2014). In New Zealand, there currently is no national approach to newborn pulse oximetry screening for critical congenital heart disease (CCHD). However, some District Health Boards (DHB) have begun screening led at hospital level. Given the existing regional and demographic variation in maternity care (Ministry of Health, 2015, 2016) hospital-led approaches to screening are, however, unlikely to improve health outcomes in an equitable way.

Until recently there have been no reports in the literature of New Zealand-specific data relating to pulse oximetry that can contribute towards an evidence-informed decision regarding implementation of a nationwide screening programme.

Aims

We undertook research exploring the feasibility of pulse oximetry screening in the New Zealand maternity setting. The research aimed to assess:

1) local patient and institutional factors that may impede universal access to the test;
2) the impact of universal pulse oximetry screening on maternity, paediatric and cardiac services in New Zealand;
3) the economic implications of a national screening programme, and
4) acceptability of the test to consumers and healthcare professionals.

Methods

Governance and stakeholder engagement

A Pulse Oximetry Screening Steering Committee was established in August 2014. This committee is comprised of paediatricians, midwives, nurses, Māori and Pasifika representatives, consumer representatives, a screening expert, a general practitioner and an obstetrician. Members aided in the development of the study design and oversaw the research and activities related to the project. Furthermore, the following stakeholder groups were collaborators in this work: National Paediatric Cardiac Service; New Zealand College of Midwives; Newborn Clinical Network, and Heart Kids New Zealand. The Ministry of Health's National Screening Unit (NSU) was consulted from the outset. The NSU is responsible for the development, management and monitoring of nationally organised population-based screening in New Zealand.

The study was approved by the Health and Disability Ethics Committees of New Zealand (15/NTA/168) and each District Health Board provided institutional approval.

Feasibility study

An intervention study of pulse oximetry screening was conducted at hospitals and primary maternity units affiliated with the Auckland District Health Board (ADHB), Counties Manukau District Health Board (CMDHB) and Lakes District Health Board. Screening was introduced at Auckland City Hospital and Birthcare maternity unit in May 2016 followed by Rotorua and Taupo Hospitals in June 2016. Three primary maternity units from CMDHB joined the study in November 2016. Middlemore Hospital was unable to overcome institutional constraints preventing participation in the study, but infants born at the hospital were screened if they transferred to a participating regional primary maternity unit for postnatal care. Data were collected up to 30 April 2018.

Study guidelines and resources were developed prior to the introduction of screening. Appendices I – VII were developed specifically for the feasibility study. Post-ductal oxygen saturations were measured on well newborn infants with a gestational age of ≥35 weeks. The recommended time for entering the screening algorithm was between 2 and 24 hours after birth. Infants with a prenatal diagnosis of a congenital anomaly and other infants admitted to the Neonatal Intensive Care Unit (NICU) within 2 hours from birth were excluded from the study.

Identical handheld pulse oximeters (Masimo, Radical SET, version 5 with reusable sensors; Irvine CA, USA) with an averaging time of 8 seconds were provided to all participating centres. Infants achieving an oxygen saturation of 95% or greater passed the test and required no further evaluation provided that they remained clinically well. Results below 90% warranted a referral to the nearest paediatric service for telephonic advice and/or clinical assessment. Saturations between 90 and 94% were regarded as an inconclusive result and therefore repeat testing had to be performed one to two hours later. Three consecutive results in the inconclusive range also warranted a paediatric referral (Appendix III). The relationship between oxygen saturation, infant activity and the infant's age at the time of the first screening test have been explored with the aim of informing the design of a screening strategy that will minimise saturation readings <95% in the context of no underlying pathology. The screening tests were primarily performed by community midwives or self-employed midwives. In some cases, nurses working on postnatal wards undertook the screening test.

Data sources

Pulse oximetry screening test results were recorded on a case report form (Appendix IV & V). Information was transferred to an electronic database that assigned a unique identification code to each participant.

Birth data for infants with a gestational age of ≥35 weeks were obtained from hospitals and birthing units. The following demographic information was extracted from the Ministry of Health's National Maternity (MAT) collection for each infant: a) prioritised ethnicity; b) maternity care provider, and c) deprivation index. The National Health Index (NHI) number was used as a unique identifier. The national paediatric cardiac centre's databases were interrogated to identify all infants with CCHD, not identified on antenatal ultrasound screening or with pulse oximetry screening.

Assessment of acceptability

1) Consumers

Parents of infants who underwent pulse oximetry screening were invited to complete a survey, which was distributed and collected prior to discharge home following the birth of the child. Participation was voluntary and anonymous. Extending invitations to parents to complete a survey was at the discretion of participating centres. A written survey was designed in collaboration with consumers with the aim of

investigating satisfaction with the screening test, and to determine whether information about the test was useful and disseminated effectively (Appendix IX). The first five questions related to participant demographics. The following eight statements related to the screening test or the information/resources provided. Respondents were asked to rank their satisfaction with the test and information resources on a five-level Likert scale ranging from "strongly agree" to "strongly disagree". A free text space was provided where any additional comments could be added. Quantitative and qualitative data were then synthesised into three main themes.

2) Healthcare professionals

Health professionals who worked in a birth care setting caring for mothers and infants enrolled in the feasibility study participated in nine focus groups. Participants were recruited through local and national maternity networks and via unit managers at each location.

Data generated during focus groups about the use of pulse oximetry screening were audio recorded and transcribed verbatim. Participants shared their views on oximetry screening including barriers and enablers to a successful national screening initiative. Thematic analysis was done using an inductive coding approach where the content of the data directed coding and theme development.

Economic evaluation

The analysis compared a national screening programme for CCHD in the newborn utilising pulse oximetry against New Zealand's historic standard of clinical postnatal screening, namely, the newborn physical examination. Short-term outcomes of timely (pre-discharge) diagnosis and quality-adjusted life year (QALY) outcomes alongside 2-year healthcare costs were considered. The economic modelling employed a decision tree comparing the two options. Findings are presented as incremental cost-effectiveness ratios (ICER) and budget impact based on a probabilistic sensitivity analysis. Infants diagnosed with CCHD before birth were excluded from the analysis. Sensitivity analyses of time taken to perform the test, oximeter use and comparison with antenatal diagnostic costs were performed.

Clinical information was obtained from the National Paediatric Cardiac Service and cost estimates for inpatient and outpatient services provided in the first 2 years were obtained from Ministry of Health datasets. Infants were grouped into two categories: Group A) single ventricle anomalies, and Group B) biventricular anomalies that resulted in death or that required an intervention within the first 28 days from birth.

Sensitivity and specificity figures for pulse oximetry screening were obtained from the literature (M N Plana et al., 2018) where 76.3% of babies with CCHD were reportedly detected by pulse oximetry (95%CI 69.5 to 82.0%). The specificity of pulse oximetry screening was reported as 99.9% (95%CI 99.7 to 99.9%). For the New Zealand historic standard of care, sensitivity figures were calculated from the proportion of cases in Groups A and B that were identified in a timely fashion.

QALYs were estimated based on infant survival broken down by diagnostic group and timing of diagnosis. There were no prospective quality of life data in survivors of congenital heart disease detected by screening compared with those detected without screening to inform the QALY estimations. Life expectancy for avoided mortality was calculated using NZ projections at 1 year of age, where 2017 life expectancy was 93.3 for female babies and 91.2 for male babies (StatsNZ, 2019). Discounted life expectancy was calculated at 1 year by assuming this life expectancy and discounting each year of life until the stated life expectancy was reached, with discounted figures of 28.33 and 28.42 years. Given a sex ratio of 1.05:1 for boys to girls at birth (CIA Factbook, 2019) and incorporating a half cycle correction, each death averted gains 27.87 years. Based on New Zealand population norms this translates to a gain of 24.57 QALYs per death averted (Appendix VIII).

Results

Screening rates

During the course of the study there were 27,172 live-born infants in participating regions that satisfied the study's inclusion criteria. The largest number of births occurred in a hospital setting (24,826; 91.4%). Four hundred and twelve (1.5%) births took place at home and 1,812 (6.7%) at a primary birthing unit. A total of 16,644 (61%) infants received pulse oximetry screening. The screening rate was significantly influenced by the place of birth, with the highest rate achieved among those born at a quaternary hospital and the lowest rate recorded for home births (81% and 6% respectively). Infants born at Lakes DHB (adjusted OR = 0.75; 95% CI 0.67 – 0.83) and CMDHB (adjusted OR = 0.29; 95% CI 0.27 – 0.32) were significantly less likely to receive pulse oximetry screening compared to those born at the ADHB (Table 1).

There was a significant association between screening rates and deprivation, with higher odds of screening recorded for babies born to families living in the least deprived areas (NZ Dep quintile 1) compared with those living in the most deprived areas (NZ Dep quintile 5) (adjusted OR = 1.39; 95% CI 1.25 – 1.54). Furthermore, failure to register with a maternity care provider was associated with lower odds of infant screening (Table 1).

Only approximately half of Māori and Pasifika babies were screened compared with three-quarters of Asian and European babies (p <0.0001). Ethnic variation in screening rates were most pronounced for CMDHB. At the ADHB there was little variation in screening rates with the lowest screening rate recorded for European infants (78%) and the highest for Asian infants (81%).

Screening strategy

Infants entered the screening pathway at a median age of 7 hours (range 1 – 472). A pulse oximetry test prior to 4 hours of age resulted in a higher proportion of infants failing to achieve a saturation level of at least 95% compared to those undergoing testing more than 24 hours after birth (2.8% v. 1.9%; p = 0.005). Infants that were unsettled or asleep at the time of testing were less likely to pass compared with awake and settled infants (p <0.001 and p = 0.002 respectively). However, breastfeeding during the recording did not result in lower oxygen saturation levels (Table 2).

The probability of achieving a test result of ≥95% in the context of no underlying pathology ranged from 0.94 for an unsettled infant screened prior to 4 hours of age to 0.99 (p <0.001) when the test was performed after 24 hours on a settled infant (Figure 1).

Figure 1. Probability of achieving saturation ≥95% in context of no pathology

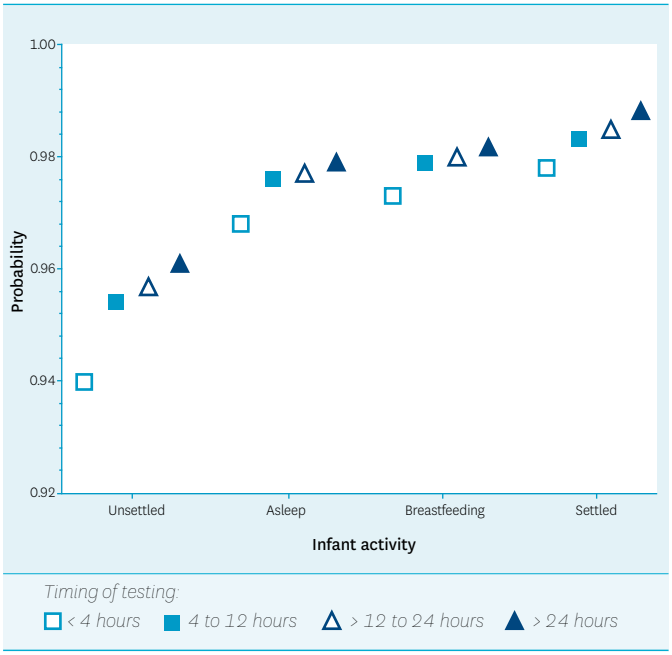

Table 1. Factors influencing screening rates

	All Regions			
	Unadjusted OR (95% CI)	p value	Adjusted OR (95% CI)	p value
Region				
Region A	1		1	
Region B	0.50 (0.46 - 0.55)	< 0.0001	0.75 (0.67 - 0.83)	< 0.0001
Region C	0.16 (0.15 - 0.17)	< 0.0001	0.29 (0.27 - 0.32)	< 0.0001
Ethnicity				
Māori	1		1	
European	2.38 (2.21 - 2.56)	< 0.0001	1.44 (1.32 - 1.57)	< 0.0001
Pacific Peoples	0.62 (0.57 - 0.67)	< 0.0001	0.77 (0.70 - 0.84)	< 0.0001
Asian	2.43 (2.24 - 2.65)	< 0.0001	1.46 (1.32 - 1.61)	< 0.0001
Indian	1.31 (1.20 - 1.43)	< 0.0001	1.21 (1.10 - 1.34)	0.0002
MELAA	1.84 (1.58 - 2.16)	< 0.0001	1.17 (0.98 - 1.40)	NS
Maternity care provider				
LMC midwife	1		1	
Obstetrician	3.50 (3.20 - 3.84)	< 0.0001	1.42 (1.28 - 1.58)	< 0.0001
Community midwife	3.50 (3.15 - 3.89)	< 0.0001	2.02 (1.79 - 2.27)	< 0.0001
General practitioner	2.15 (1.05 - 4.40)	0.04	1.01 (0.49 - 2.09)	NS
No provider	0.31 (0.28 - 0.34)	< 0.0001	0.61 (0.55 - 0.68)	< 0.0001
Deprivation quintile				
Five	1		1	
Four	1.98 (1.84 - 2.13)	< 0.0001	1.13 (1.04 - 1.23)	0.004
Three	2.93 (2.71 - 3.17)	< 0.0001	1.30 (1.18 - 1.42)	< 0.0001
Two	2.78 (2.58 - 3.00)	< 0.0001	1.34 (1.22 - 1.46)	< 0.0001
One	3.58 (3.28 - 3.91)	< 0.0001	1.39 (1.25 - 1.54)	< 0.0001
Study time epoch				
First	1		1	
Second	1.24 (1.17 - 1.32)	< 0.0001	1.38 (1.29 - 1.48)	< 0.0001
Third	1.28 (1.21 - 1.36)	< 0.0001	1.44 (1.35 - 1.55)	< 0.0001

OR – odds ratio
CI – confidence interval
LMC – lead maternity carer
MELAA – Middle Eastern, Latin American and African
NS – not significant

For adjusted OR all variables are included in the model

Table 2. Relationship between saturation levels, timing of first test and infant activity

	Total (n)	Median (range)	First saturation <95%, n (%)	Pathology (n)	No pathology n (%)	p value
Timing of testing#:						
< 4 hours	6,122	98 (77 – 100)	198 (3.2)	25	173 (2.8)	0.005
4 – 12 hours	3,092	99 (55 – 100)	78 (2.5)	10	68 (2.2)	0.4
> 12 – 24 hours	2,580	99 (85 – 100)	54 (2.1)	-	54 (2.1)	0.6
> 24 hours	3,617	98 (78 – 100)	70 (1.9)	1	69 (1.9)	*
Activity[d]:						
Asleep	5,365	99 (55 – 100)	144 (2.7)	9	135 (2.5)	0.002
Breastfeeding	2,448	99 (77 – 100)	53 (2.2)	4	49 (2.0)	0.3
Awake settled	6,408	99 (77 – 100)	122 (1.9)	14	108 (1.7)	*
Awake unsettled	1,030	98 (81 – 100)	53 (5.1)	1	52 (5.0)	<0.001

 # Exclusions applied to 1,233 due to insufficient data.

d Exclusions applied to 1,393 due to insufficient data. Infant activity not recorded for 8 infants with pathology.

** Reference for making individual comparison with other variables in realtion to the proportion of readings <95% in the context of no pathology.*

Pathology detected and resource implications

Forty-eight infants (0.3%) ultimately did not achieve oximetry screening targets, forty-one of whom (85%) were admitted to a newborn unit as a result. Eleven (23%) infants were transferred to a larger medical centre for assessment and investigations. The median (range) distance travelled for an assessment was 43 (1 – 80) km. CCHD was detected in three infants. A review of cardiac surgical data revealed a further three infants with congenital cardiac disease who required intervention in the first 28 days after birth. Two of these had d-loop transposition of the great arteries, for which pulse oximetry has excellent sensitivity but which were diagnosed post-discharge, and one infant had atrial and ventricular septal defects. Pulse oximetry screening was, however, not performed on these infants prior to discharge.

A further three infants had persistent pulmonary hypertension and one newborn was diagnosed with supraventricular tachycardia. Respiratory disease was responsible for the majority of positive screening results. There were 13 infants with congenital pneumonia, eight with transient tachypnoea of the newborn, four with meconium exposure, and one with a pneumothorax. Three infants were diagnosed and treated for sepsis. One infant had an ongoing unexplained oxygen requirement (presumably related to respiratory pathology) and was discharged home on supplemental oxygen after 15 days. He remained on oxygen for a further 2 weeks after discharge.

No pathology could be identified in a further 11 (23%) infants who failed to reach saturation targets. Four (36%) of these infants were admitted to a neonatal unit for investigation and observation. The median (range) duration of admission was 1 (0 – 2) day. Seven infants failed the test as a result of saturation levels persistently in the 90–94% range and four had saturations below 90%. Testing was conducted at an early stage in the majority of these infants with the algorithm completed at a median (range) age of 5 (3 – 36) hours.

A summary is provided of the investigations performed on all infants who failed to reach oxygen saturation targets (Table 3).

Acceptability

1) Consumers

Six hundred and fifty-seven surveys were completed and returned to the research team, which represents 4% of pulse oximetry screening study participants. Primary and secondary birthing facilities were better represented amongst survey responders; ethnic spread was similar in survey responders and the whole cohort. The characteristics of survey participants and that of infants that underwent screening are summarised in Table 4.

Analysis of survey results and comments revealed three themes: 1) parents were satisfied with the screening procedure; 2) the quality of the available information was good, but not all received sufficient information, and 3) the timing of information delivery influenced retention of information.

The vast majority (94%) of parents either agreed or strongly agreed that pulse oximetry is an important health check for newborns and 90% found it reassuring that their child had the screening test. Free text comments reflected participants' views that the test was simple and fast, and they supported the importance of identifying issues early.

Parents reported that they understand why the pulse oximetry test was offered to them and agreed that the result of the test was explained adequately. A third of participants indicated a wish for more information. There was positive feedback for the parent information brochure with 74% agreeing that the content was helpful, but 100 (15%) of respondents did not receive this source of information. The parent information video was not well distributed with the majority (64%) reporting that they had not viewed it.

Although the survey did not ask specifically about the timing of provision of information, 12 participants made a written comment addressing this topic. They described poor recollection of the test and of the information that was provided. Some indicated that they were fatigued following the birth of their child and therefore could not retain the information.

Table 3. Investigations

	CHD n 3	SVT n 1	PPHN n 3	Respiratory n 27	Sepsis pathology n 3	Slow transition / No pathology n 11	Total n 48
Full blood count, n (%)	3 (100)	1 (100)	3 (100)	27 (100)	3 (100)	6 (55)	43 (90)
Blood culture, n (%)	2 (67)	-	2 (67)	26 (96)	3 (100)	2 (18)	35 (73)
C-reactive protein, n (%)	2 (67)	-	1 (33)	13 (48)	3 (100)	4 (36)	23 (48)
Blood gas, n (%)	3 (100)	1 (100)	3 (100)	27 (100)	3 (100)	5 (45)	42 (88)
Chest radiograph, n (%)	3 (100)	1 (100)	3 (100)	27 (100)	3 (100)	7 (64)	44 (92)
Electrocardiogram, n (%)	3 (100)	1 (100)	-	5 (19)	1 (33)	-	10 (21)
Echocardiogram, n (%)	3 (100)	1 (100)	3 (100)	3 (11)	-	1 (9)	11 (23)

CHD – congenital heart disease; SVT – supraventricular tachycardia; PPHN – persistent pulmonary hypertension.

2) Healthcare professionals

There were 45 participants in the focus groups (Table 5). Thematic data analysis yielded three themes: 1) oximetry screening for newborns is reassuring, practical and worthwhile; 2) midwifery services workload expectations and under-resourcing will hinder universal oximetry screening; and 3) location of the baby at the time of screening could impede universal access.

Table 5. Focus group participants

Setting	Participants, n	Duration (minutes)
1. Main centre hospital	3	61
2. Primary maternity unit (urban)	6	69
3. Primary maternity unit (rural)	7	50
4. Midwife LMC (rural)	1	42
5. Main centre hospital and linked maternity unit (rural)	5	74
6. Mixed group at a national meeting	8	20
7. Mixed group at a national meeting	9	35
8. Main centre hospital	2	48
9. Midwife LMCs	4	45
Participant work role		
DHB midwife	22	
Midwife LMC	15	
DHB midwife and LMC	1	
Paediatrician	1	
Managers**	6	1

LMC – lead maternity carer; DHB – District Health Board
*** Managers included charge midwives and Women's Health mangers*

Overwhelmingly, participants agreed that neonatal pulse oximetry screening for newborns is reassuring, practical and useful. Participants described screening as simple, non-invasive and reassuring for both them and the parents. Despite participants' initial misgivings about the increased workload that extra screening might impose, most commented that it was quickly integrated into care, becoming easy and "straightforward" to administer. Being able to identify an unwell baby before it became clinically unwell was considered important, not just for the baby and whānau, but also for the midwives and health professionals caring for that family.

Midwives did, however, express anxiety about their current workload expectations and the pressure they experience individually and as a service. Each focus group identified high workload as a major barrier to a successful pulse oximetry screening programme. Concerns were also raised over the cost of equipment and consumables.

Participants stressed the importance of offering screening for all births and that the location of the baby at the time of the screening became a significant factor in achieving that, particularly for those discharged early to a satellite unit or home, and for home and rurally located births. There were concerns that the screening may be forgotten or missed when an infant is transferred to another location. Access to equipment was considered to be an important factor that can enable screening within the recommended timeframe.

Economic evaluation

During the period 2006 to 2014 there were 544,046 births in New Zealand. There were 453 antenatally detected cases of CCHD. Twenty-two infants with a single ventricle cardiac anomaly (Group A) and 260 with a critical biventricular anomaly (Group B) were diagnosed in the postnatal period. With the New Zealand historic standard of care, 12 of 22 (54.5%) infants in Group A and 167 of 260 (62.7%) infants in Group B were detected pre-discharge. Based on sensitivity figures, pulse oximetry screening is estimated to detect 23.75 infants with CCHD before discharge from the place of birth each year, compared with 19.76 in the New Zealand historic standard of care. This equates to 0.52 additional timely diagnoses each year in Group A and 3.47 in Group B.

There is a lack of relevant data to identify the specificity of testing in the New Zealand historic standard of care. Taking a conservative assumption, we assume a specificity of 1 for pulse oximetry screening in the base case analysis.

The combined 2-year in-patient and out-patient costs are summarised in Table 6. These figures also provide estimates of mortality in each group based on the timing of diagnosis. Diagnosis before discharge from the place of birth was associated with decreased infant mortality in both Groups A and B with a 5% reduction in mortality for Group A and 3.7% for Group B.

The incremental analysis for base case and sensitivity is presented in Table 7.

Table 6. Combined 2-year in-patient and out-patient costs by group, timing of diagnosis and outcome

Group	Timing of diagnosis	Status	n	Mean	SD of Mean
A	Pre-discharge	Dead	3	$22,057	$14,723
		Alive	9	$180,616	$17,251
	Post-discharge	Dead	3	$62,334	$54,613
		Alive	7	$139,131	$21,867
B	Pre-discharge	Dead	19	$69,947	$19,702
		Alive	148	$119,117	$5,349
	Post-discharge	Dead	14	$57,755	$22,619
		Alive	79	$99,741	$3,887

A – single ventricle anomalies; B – critical biventricular anomalies
SD – standard deviation

With a lower mortality rate amongst the earlier detected cases, the infants identified with pulse oximetry screening would correspond to an expected gain of approximately 3.74 QALYs per year. The estimated cost of pulse oximetry screening (including inpatient and outpatient costs) was $4.1 million compared to $3.37 million within the historic

Table 7. Incremental analysis for base case and sensitivity cases

	Incremental Analysis			Likelihood of cost-effectiveness at:		
	QALYs	Costs	ICER	$10k per QALY	$30k per QALY	$50k per QALY
Base Case	3.74	$730,495	$195,125 per QALY	0.00%	0.04%	2.08%
False positives in historical standard of care	3.75	$755,771	$201,769 per QALY	0.00%	0.03%	1.70%
Pulse oximetry time increased	3.78	$1,007,607	$266,658 per QALY	0.00%	0.00%	0.28%
Pulse oximetry time decreased	3.73	$591,915	$158,749 per QALY	0.00%	0.23%	5.17%
Decreased cases per oximeter	3.78	$832,850	$220,616 per QALY	0.00%	0.03%	1.76%
Increased cases per oximeter	3.78	$679,172	$179,468 per QALY	0.00%	0.12%	2.99%
Antenatal costs as alternative for detected cases	3.77	$747,174	$198,109 per QALY	0.00%	0.03%	1.76%
QALY benefits not discounted	11.73	$730,785	$62,322 per QALY	0.00%	17.74%	38.05%
QALY benefits discounted at 6%	2.36	$730,879	$309,672 per QALY	0.00%	0.00%	0.07%

QALY – quality adjusted life year; ICER – incremental cost-effectiveness ratio

standard of care (Appendix VIII). With pulse oximetry providing more QALYs at an increased cost of $730,495 it would be expected to improve health at a cost exceeding $195,000 per QALY.

Sensitivity analyses suggest that a national screening programme at a DHB level would likely have total costs of between $500,000 and $1,000,000. This does not include administration costs related to a nationwide screening programme. A sensitivity analysis using antenatal costs as a proxy leads to more expensive estimates but the ICER is largely unchanged ($198,000 per QALY). In a sensitivity analysis modifying discounting based on the assumption that discounting rates for newborn interventions with potential life-long effects for benefit are not well substantiated, shows that with no discounting the ICER falls to $62,000 per QALY.

Discussion

The evidence for pulse oximetry screening for the detection of CCHD is sufficient

The first research in this field emerged in the early 2000s (T R Hoke et al., 2002; R I Koppel et al., 2003; S Richmond et al., 2002) and now, nearly 20 years later, the value of pulse oximetry as a screening tool for CCHD has been firmly established. A Cochrane systematic review of 21 studies that included 457,202 participants was published in 2018 (M N Plana et al., 2018). Pulse oximetry was found to be highly specific (99.9%; 95% confidence interval [CI] 99.7% to 99.9%) and moderately sensitive (76.3%; 95% CI 69.5% to 82.0%) for the detection of critical cardiac disease with a very low false-positive rate (0.14%). This review showed that six out of 10,000 apparently healthy late preterm and term infants will have CCHD and that pulse oximetry screening can detect five of them. The reviewers therefore concluded that current evidence supports the introduction of routine pulse oximetry screening for CCHD.

Importantly, there is also evidence to show that pulse oximetry screening improves survival for infants with congenital cardiac disease. Abouk et al. reported a 33.4% (95% CI, 10.6% – 50.3%) decline in cardiac related deaths in American states with mandatory screening policies between 2007 and 2013 (R Abouk et al., 2017).

As a result of the mounting evidence in favour of universal pulse oximetry screening, several developed countries have formulated a consensus statement in favour of its implementation. Perhaps the most widely cited is the recommendation made by the United States Secretary of Health and Human Services in 2011 to add pulse oximetry screening to the country's Recommended Uniform Screening Panel (W T Mahle et al., 2012). More recently statements have been published by a European workgroup (P Manzoni et al., 2017), and in Canada (K K Wong et al., 2017), Spain (M Sanchez Luna et al., 2017) and Nordic countries (A de-Wahl Granelli et al., 2014). Research has also been conducted in developing countries to investigate the feasibility and unique challenges associated with introducing pulse oximetry screening in those settings (P Nuntnarumit et al., 2018; A M Taksande et al., 2013; A M Van Niekerk et al., 2016; Q M Zhao et al., 2014).

Optimising test accuracy and limiting false-positive results

An ideal screening test has a high sensitivity, a high specificity and a low false-positive rate. In pulse oximetry screening, both the timing of screening and the site(s) used to do the test can impact on the accuracy of the test. The Cochrane review on pulse oximetry screening found greater variability in sensitivity than specificity across studies, but could not find an explanation for this heterogeneity in sensitivity (M N Plana et al., 2018). No significant difference in test accuracy was found when comparing measurements obtained from the foot alone (post-ductal) with measurements taken from both the foot and the right hand (post- and pre-ductal). Nonetheless, there are many advocates for two-limb testing as there are reports in the literature of infants diagnosed with coarctation of the aorta or interrupted aortic arch based solely on a difference between pre- and post-ductal oxygen saturation (A de-Wahl Granelli et al., 2009; A K Ewer et al., 2011). This difference, when present, is produced by right to left shunting across the ductus arteriosus as a result of the pressure gradient between the pulmonary circulation and the aortic arch beyond the level of obstruction. This is an important consideration in the New Zealand context where fewer than 40% of the 15 infants born each year with either coarctation of the aorta or an interrupted arch are diagnosed before birth (E Cloete, F H Bloomfield, S A Cassells, et al., 2019)

The incidence of specific cardiac anomalies among population groups and its relationship to the sensitivity of pulse oximetry has not been

investigated yet. It is well understood that cardiac anomalies produce varying degrees of hypoxaemia depending on the anatomy of the defect with, for instance, aortic arch anomalies less likely to produce hypoxaemia in the first few days after birth than transposition of the great arteries (S Prudhoe et al., 2013). The incidence of left heart obstructive lesions is significantly higher in the New Zealand European population compared with all other ethnic groups in the country (E Cloete, L Sadler, et al., 2019). The ethnic composition of communities and its relationship with disease incidence may therefore contribute to the variation in the test's sensitivity that has been reported.

Furthermore, test accuracy may be influenced by human error (C L Diller et al., 2018; L K Kochilas et al., 2013; M E Oster et al., 2014; B M Pflugeisen et al., 2015). Computer-based tools have been shown to result in improved accuracy compared with manual interpretation of screening algorithms. Oster et al. reported that 81.6% of mock screening scenarios (using a 2-limb strategy) were manually correctly interpreted compared with 98.3% when using a computer-based tool. This difference was most pronounced for "fail" scenarios (65.4% manual vs 96.1% computer) (M E Oster et al., 2014). A single-limb screening strategy was used in our feasibility study. The simplicity of performing the test on one limb was an important consideration in this setting where significant concerns were raised about the impact of the test on the workload of midwives. This factor, combined with the lack of evidence suggesting a higher sensitivity when using a two-limb strategy and in the absence of a computer-based programme that can store and interpret the test results, resulted in a decision by the Steering Committee that a single-limb strategy was most appropriate for the New Zealand setting (Appendix III).

Test accuracy studies have also investigated the impact of the timing of the test, with screening conducted <24 hours after birth reportedly resulting in higher false-positive rates, but with no significant impact on sensitivity or specificity (M N Plana et al., 2018). We have demonstrated a relationship between the false-positive rate and not only the timing of the test, but also infant activity. Infants tested <4 hours of age were significantly more likely to have a low oxygen saturation level in the absence of pathology (2.8%) compared with 1.9% that were tested after 24 hours ($p = 0.005$) (E Cloete, T L Gentles, D R Webster, et al., 2019). It is generally recommended that pulse oximetry should be conducted on infants that are calm and alert, but the relationship between infant activity and oxygen saturation levels has not previously been investigated. Our research showed that conducting the test while infants are unsettled or asleep will result in a significantly higher proportion of low oxygen saturation levels in the context of no underlying pathology when compared to tests conducted when infants are awake and settled. We were the first to demonstrate that breastfeeding does not result in a higher false-positive rate. This finding demonstrates that the bonding between a mother and infant does not have to be interrupted in order to perform the test. When pulse oximetry screening is conducted in the first 24 hours after birth, the number of false-positive results can be limited if the test is conducted after 4 hours and while infants are settled or breastfeeding (E Cloete, T L Gentles, D R Webster, et al., 2019). This is an important finding as infant activity is a variable that can be adjusted more easily than the timing of the test, which is often dictated by the setting in which screening is undertaken. Jurisdictions characterised by early postnatal discharges have to conform to an early screening strategy (E Cloete, T L Gentles, D R Webster, et al., 2019; I C Narayen et al., 2016).

Other hypoxaemic conditions

False-positive test results are to a large extent attributed to conditions such as respiratory or infective diseases that can also produce hypoxaemia. Early screening in particular presents an opportunity to detect and treat these conditions. The study we undertook showed that 33 of 48 (69%) infants with a positive screening result had a respiratory or infectious disease (E Cloete, T L Gentles, D R Webster, et al., 2019). This is in keeping with others that reported that pneumonia, septicaemia and transient tachypnoea are some of the most common causes of low oxygen saturations on the first day of life (A Meberg, 2015; A Singh et al., 2014). Detecting these 'false-positives' is of benefit to the affected infants as some of these conditions are potentially life-threatening if treatment is delayed. Undertaking pulse oximetry screening before discharging newborns home can also avert the morbidity, cost and anxiety associated with later urgent transfer. During the course of our study, pulse oximetry screening prevented the discharge of several infants with congenital pneumonia and sepsis, and an infant with supraventricular tachycardia (E Cloete, T L Gentles, D R Webster, et al., 2019). Clinicians are in agreement that no newborn with unexplained persistent hypoxaemia should be discharged home (A K Ewer et al., 2013). It is therefore surprising that the UK National Screening Committee recently decided not to recommend routine pulse oximetry screening in the UK due, among other reasons to concerns about potential overdiagnosis and treatment of infants with false-positive test results (Public Health England, 2019b). A pilot study conducted in the UK found that 7 out of every 1,000 infants that are screened will be healthy despite failing to reach target saturations on the first day. Contrary to this up to 80% of infants that are admitted to a neonatal unit following a positive test have a non-cardiac condition that requires treatment (Public Health England, 2019a). The decision in the UK will be reviewed after the completion of a public consultation process.

The New Zealand maternity setting

In the last decade New Zealand has made significant improvement in the antenatal detection of cardiac anomalies with >70% of fetuses with critical anomalies currently diagnosed during pregnancy (E Cloete, F H Bloomfield, S A Cassells, et al., 2019). The yield from pulse oximetry screening may be less than in other jurisdictions with lower antenatal detection rates. We have estimated that five previously undiagnosed infants can be identified each year if pulse oximetry screening is offered in New Zealand (E Cloete, F H Bloomfield, S A Cassells, et al., 2019). However small the number, the survival of these infants may depend on the introduction of universal pulse oximetry screening.

Different approaches have been used globally to introduce screening, ranging from hospital-led initiatives to mandatory state-wide policies (R Abouk et al., 2017; K Bhola et al., 2014; A de-Wahl Granelli et al., 2014; Q M Zhao et al., 2014). New Zealand has a midwifery-led model of maternity care and women can choose whether to give birth at home, a primary maternity unit or a hospital. Women who birth in a hospital are frequently discharged either home or to a primary unit within hours of the birth. Ensuring that pulse oximetry is offered to all, regardless of the chosen place of birth, will be an important determinant of the success of a screening programme.

Impact on clinical services

Midwives' central role in the care of mothers and babies on the first day post-partum place them in the ideal position to perform pulse oximetry screening. Consultation with New Zealand midwives revealed concerns over the impact on workload and additional resource requirements (K Ward et al., 2019). The New Zealand College of Midwives and Ministry of Health are working jointly to address the current midwifery workforce shortage and its impact on maternity services. The parties recently agreed to a process for the co-design of a new funding model and contracting of community Lead Maternity Carer midwives (Ministry of Health, 2019b). The recognition of the value of hospital midwives' work has also been stressed by the Midwifery Employee Representation and Advisory Services (MERAS) in their advocacy for pay equity for midwives (Midwifery Employee Representation and Advisory Services, 2019).

Work is underway to support improved midwifery staffing levels as part of the MERAS midwifery accord with the District Health Boards.

Staffing and resource constraints are likely to detract from equitable service delivery. We found significant ethnic and regional disparities in the delivery of pulse oximetry screening in a research setting. Screening rates were lowest among Māori and Pacific infants from the most deprived areas. Furthermore, only 6% of infants born at home were tested. There was also an association between the type of maternity carer and screening rates, with the lowest rates recorded for infants whose mothers failed to register with a carer (E Cloete, T L Gentles, L A Dixon, et al., 2019). The additional demands placed on midwives by a screening programme and the resource requirements therefore require careful consideration.

Reassuringly, we found no evidence to suggest that positive test results will place excessive pressure on child health services in New Zealand. Referral pathways are already in place to ensure that any infant suspected of cardiac or other diseases are assessed and treated appropriately. In our study, 48 of 16,644 (0.28%) infants that underwent pulse oximetry screening had a positive result. Eleven (23%) of those were found to have no underlying pathology. Four (36%) of these infants were admitted to a neonatal unit for investigations and/or observation. The median (range) duration of these admissions was 1 (0–2) day. Over the course of the study 11 echocardiograms were performed of which four may be considered unnecessary. These four scans were performed by paediatricians and neonatologists and did not impact on cardiac services (E Cloete, T L Gentles, D R Webster, et al., 2019).

Acceptability

Acceptability among consumers and healthcare providers is one of the key principles when making a decision on the delivery of screening programmes in New Zealand (National Health Committee, 2003). It was therefore important to assess acceptability as part of a feasibility study.

Pulse oximetry screening was well received and understood by consumers in our research setting and is considered to be an important health check for babies (E Cloete et al., 2018). The study highlighted parents' desire to be involved in the decision-making related to their newborn child and to be well informed. Importantly, several participants commented that they were unable to retain information that was given to them shortly after the birth and therefore careful consideration should go into the effective dissemination of information. Initiating discussions about the test in the third trimester may address this deficiency.

Despite the concerns raised by the UK National Screening Committee over the potential anxiety caused by false-positive test results (Public Health England, 2019b), there is no evidence to suggest that consumers would oppose a screening test based on this potential harm. Research have shown that parents who receive effective education enabling them to understand the different types of screening results and investigation pathways are psychologically better prepared in the event of a true- or false-positive result (J Hewlett et al., 2006; A M Vernooij-van Langen et al., 2014).

Midwives were very positive about their experience using pulse oximetry screening and described the test as reassuring, practical and worthwhile (K Ward et al., 2019). The quick and non-invasive nature of the test made it popular among midwives who also reported that parents are very accepting of the test. These findings are consistent with other reports in the literature (A K Ewer et al., 2012; R Powell et al., 2013).

The lack of human and material resources was regarded as the main barrier to the implementation of a universal screening programme.

Economic evaluation

The cost-effectiveness of pulse oximetry screening has been demonstrated in the United States (C Peterson et al., 2013; M R Reeder et al., 2015), the United Kingdom, (A K Ewer et al., 2012) and the Netherlands (I C Narayen et al., 2019). However, a study evaluating screening in Chinese regions with diverse socioeconomic status demonstrated cost-effectiveness only in affluent regions (R G Tobe et al., 2016), highlighting the importance of taking region-specific factors into consideration. In our setting, the number of infants born each year with CCHD is small and the majority are diagnosed in the antenatal period (E Cloete, F H Bloomfield, S A Cassells, et al., 2019). In the short-term, the addition of pulse oximetry screening therefore comes at a large economic cost relative to the QALYs that may be gained. A strength of the economic evaluation performed is that it included actual healthcare costs for the first two years of life at a population level. Limitations are that no data were available to estimate life-long costs nor to model potential differences in life-long morbidity and quality of life following timely diagnosis via pulse oximetry screening and late diagnosis upon clinical collapse. Late diagnosed CCHD may have a lifelong impact on the affected patient and their caregivers to a different degree than timely diagnosis, particularly related to neurological injury from cardiovascular collapse. The economic analysis therefore likely underestimates QALY gains and overestimates cost per QALY. Furthermore, the economic analysis did not take account of the health benefits of early diagnosis of other hypoxaemic conditions, such as sepsis. Future studies should consider the cost of pulse oximetry screening in the context of averted death as well as long-term healthcare implications.

Conclusion

Pulse oximetry is a safe, easy-to-use and effective tool that can identify serious diseases in the newborn before the onset of symptoms. The research conducted in New Zealand supports the introduction of a national screening programme.

Recommendations

Key recommendation

New Zealand should introduce a nationwide pulse oximetry screening programme for the detection of critical congenital heart disease and other hypoxaemic conditions in the newborn. Such a programme should be delivered in a uniform and equitable way that ensures access to the test for all newborn infants regardless of their place of birth. In order to achieve this, the following additional recommendations are made:

1) Develop uniform guidelines

National guidelines should be developed to guide screening practices in New Zealand based on the evidence obtained from the feasibility study. Consideration should be given to the following:

Timing of the test

The screening strategy used during the feasibility study (Appendix III) allowed infants to enter the algorithm from 2 hours of age. Screening before 4 hours of age resulted in a higher number of low oxygen saturation readings, although the number of false-positive results can be limited if infants are only tested when either awake and settled, or breastfeeding (E Cloete, T L Gentles, D R Webster, et al., 2019). Adjusting the earliest time screening can be performed to 4 hours would reduce the number of false positives; however, discharges often occur soon after birth in many of our busy maternity centres. Therefore, adjusting the algorithm to reduce false positives from early testing would have to be balanced against a greater number of babies missing screening. Mothers with an early discharge are likely to be different from those with a later discharge and are likely to include increased proportions of Māori mothers. We therefore recommend that the algorithm remains as is with the following caveat:

We recommend that in a baby in whom there are no clinical concerns with saturations in the inconclusive range for the first two screening tests, the third test is delayed until 12 hours of age. This will reduce unnecessary transfers to larger centres.

Pre- and post-ductal screening v. post-ductal screening alone

The lack of evidence suggesting a higher sensitivity when using a 2-limb strategy and in the absence of a computer-based programme that can store and interpret the test results, a single-limb test is currently the most appealing strategy for the New Zealand setting. This strategy should be reviewed once the Maternity Clinical Information System (MCIS) has been implemented at all DHBs.

2) The programme should be monitored

Quality is an integral part of screening programmes. Ongoing quality improvement activities should be undertaken to ensure that the programme remains safe and effective, and is delivered at a reasonable cost. Poor quality may have a negative impact on the relationship between the benefit and harm generated by the screening test. Failure to ensure equitable access to pulse oximetry screening in New Zealand will exacerbate already existing disparities in the healthcare system.

3) The availability of adequate human and material resources should be ensured

Midwives' involvement with mothers and infants in the days before and after the birth place them in an ideal position to perform pulse oximetry screening. Positive feedback has been received from midwives who described the test as 'reassuring, practical and worthwhile'. Significant concerns were, however, raised over the impact that a lack of human and material resources may have on a screening programme (K Ward et al., 2019). It is essential that equipment and consumables are provided at all birthing facilities as well as to lead maternity carers that oversee home births to ensure equitable access to the screening test. The Ministry of Health will need to work with the New Zealand College of Midwives (professional midwifery organisation) regarding the inclusion of pulse oximetry screening as part of care of the newborn baby to ensure midwives are resourced and supported in performing this test.

4) There should be ongoing efforts to improve antenatal ultrasound screening

The relationship between timing of diagnosis and outcomes for infants born with severe cardiac malformations have been demonstrated (E Cloete, F H Bloomfield, L Sadler, et al., 2019; L Eckersley et al., 2016). The antenatal period remains the optimal time to make a diagnosis of a congenital malformation. This allows an opportunity to discuss the diagnosis, prognosis and management plan with the parents before the birth of the child. If a critical cardiac anomaly has been identified arrangements will be made for the mother to birth at the cardiac centre in Auckland to enable immediate intervention if required. In the last decade significant work has gone into improving the quality of antenatal ultrasound screening in New Zealand, which has resulted in an improved antenatal detection rate of CCHD (E Cloete, F H Bloomfield, S A Cassells, et al., 2019). Ongoing quality improvement initiatives, such as the development of New Zealand Obstetric Ultrasound Guidelines (Ministry of Health, 2019a) and regular country-wide sonographer and clinician education days, will ensure that the current standard of mid-trimester screening is maintained and build upon.

5) Raise awareness

Newborn and maternity healthcare providers should have knowledge of the test, its purpose, the screening pathway and the potential harm associated with false-negative results. Sharing this information with consumers will promote trust in the provider by demonstrating transparency and knowledge. Furthermore, informed parents may experience less anxiety if their baby has an abnormal screening result. It is equally important to inform parents that the test will not detect all forms of cardiac and other diseases. Therefore, the signs and symptoms of an unwell baby should be discussed and parents should be encouraged to seek medical advice if they have any concerns about their baby. Discussions about the test should be initiated in the third trimester of the pregnancy. The timing of delivering information is an important factor for parent satisfaction. Our study showed that many were unable to retain information that was given to them shortly before or after the birth (E Cloete et al., 2018).

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Appendices

Appendix I: Pulse oximetry screening guideline

Background

Congenital heart defects are the most common group of congenital malformations, with a reported incidence of between 4 and 10 per 1,000 live-born infants (A K Ewer, 2014b; S Prudhoe et al., 2013). The term congenital heart disease (CHD) encompasses a variety of lesions with a wide range of clinical importance, ranging from those with no functional or clinical significance to potentially life-threatening lesions. If critical defects are not detected early, they can result in cardiovascular compromise resulting in death or significant long-term effects on neurodevelopment. Critical CHD refers to heart defects that require intervention or lead to death in the first 28 days after birth. Timely recognition of these conditions allows the possibility of early intervention that may influence the natural history of the condition and subsequent outcome.

Current screening strategies to detect CHD in New Zealand include antenatal ultrasound ('anatomy scan') and physical examination of the newborn. Both these investigations have only modest sensitivity. Nearly 20% of infants born in New Zealand with a critical heart defect are diagnosed after initial discharge from hospital. Pulse oximetry screening will detect hypoxaemic infants and has been shown to improve the early diagnosis of CHD in newborn infants.

Pulse oximetry screening does not replace the newborn clinical assessment for congenital heart disease. Auscultating for murmurs, detection of clinically visible cyanosis and palpation of pulses (femoral pulses in particular) remain an important part of the newborn and 6-week examination. Clinical concerns warrant an immediate referral to the paediatric team.

Eligibility criteria

All well newborn infants with a gestational age ≥35 weeks

Screening should be performed between 2 and 24 hours of age

Exclusion criteria

Parental refusal

Infants for palliative care

Infants with an antenatal diagnosis of congenital heart disease

Special considerations

Infants that are <35 weeks' gestation at birth will generally be admitted to a newborn unit where they will be monitored as part of standard care provided to premature infants. On the rare occasion that such an infant is admitted to the postnatal ward, pulse oximetry screening should be performed.

Unwell infants ≥35 weeks' gestation admitted to a newborn unit do not have to be screened. These infants are often haemodynamically unstable and will have routine on-going monitoring of oxygen saturations. It is the responsibility of the attending paediatric team to ensure that all infants have reached saturation targets prior to discharge from the unit. It should be documented in the patient's discharge letter that saturations ≥95% have been achieved.

An echocardiogram will often be part of the work-up for infants with severe hypoxaemia as a result of birth asphyxia and persistent pulmonary hypertension. Echocardiograms are also routinely performed on infants with Trisomy 21 and other chromosomal anomalies. If a cardiac anomaly is identified in these cases the findings should be recorded on the 'Hypoxaemia report' (Appendix V).

If screening did not take place in the first 24 hours in an otherwise healthy infant, the test should be performed at the earliest possible opportunity.

Screening before 2 hours of age is associated with higher false-positive rates. Early screening can therefore potentially delay discharge or transfer from hospital. Infants should remain in hospital until they have reached saturations of ≥95%.

Nearly 4% of New Zealand's babies are born at home (Ministry of Health, 2015). Midwives will usually stay with a mum and baby for 2 to 3 hours following a home birth and will return for a follow-up visit within the next 24 hours. Pulse oximetry screening should ideally be performed prior to the midwife's departure, but may have to be deferred until the return visit if an oximeter is not available at the time of the birth.

Screening pathway

- Obtain consent from parents or caregivers to perform the screening test.
- Ensure that the infant is calm and warm. Movement and crying can affect test accuracy. The test may be performed while the baby is feeding or sleeping.
- Obtain a saturation reading from one foot.
- Document the results on the 'Screening record' (Appendix IV).
- Refer to the screening algorithm to establish if further action is required.

What to do if there is an infant that does not reach oxygen saturation targets

- Refer the infant for a same-day paediatric assessment.
- A thorough clinical examination is indicated.
- Further investigations should be performed at the discretion of the paediatric team.
- Consideration should be given to respiratory, infective and metabolic conditions. Refer to the hypoxaemia guideline.
- An echocardiogram should only be requested via the children's heart specialist after consultation with the responsible neonatologist/paediatrician.
- The paediatric team should complete the 'Hypoxaemia report' if an infant failed to reach saturation targets.

Differential diagnosis

- Be aware that pulse oximetry screening has a false-positive rate of 0.14% (S Thangaratinam et al., 2012) and so the baby may not have CHD.
- Screening before 2 hours of age is associated with higher false-positive rates.
- Approximately two thirds of positive tests will not be attributed to congenital heart disease but may reveal alternative diagnoses.

Appendix II: Diagnostic approach to the hypoxaemic infant

Definitions

- Hypoxaemia is failure of normal blood oxygenation and is defined as low partial pressure of oxygen in the arterial blood (PaO_2). Causes of hypoxaemia include: hypoventilation; low inspired oxygen; right to left shunting, and ventilation-perfusion mismatch.
- Hypoxia is a failure of normal tissue oxygenation.
- SpO_2 refers to the oxygen saturation of arterial blood as measured by a pulse oximeter.

Background

Pulse oximetry is a biomarker for the detection of hypoxaemia, which would not necessarily produce visible cyanosis, in apparently healthy newborns. It has been shown to improve the early diagnosis of congenital heart disease (CHD) in newborn infant (A de-Wahl Granelli et al., 2009; A K Ewer, 2014a), as a degree of hypoxaemia is present in the majority of infants with CHD. Pulse oximetry screening will also detect other significant pathologies which produce hypoxaemia that may otherwise have gone undetected prior to discharge, for instance: sepsis; respiratory compromise, and metabolic disease. It has been reported that approximately two thirds of positive pulse oximetry screening results will be related to conditions other than CHD (K Bhola et al., 2014). Pulse oximetry has a false-positive rate of 0.14% (95% CI 0.06 – 0.33) (S Thangaratinam et al., 2012). We have adopted an early screening strategy that can potentiate the diagnosis of CHD prior to cardiovascular compromise and collapse; however, earlier screening is associated with higher false-positive rates.

The hypoxaemic newborn

An infant who has failed to reach oxygen saturation targets during pulse oximetry screening requires a paediatric assessment and, potentially, further investigations. A low SpO_2 reading can be normal in newborns adjusting to the extra-uterine environment.

Consideration should be given to the following diagnoses when assessing a hypoxaemic newborn infant:

- Transient tachypnoea of the newborn (TTN)
  TTN is a self-limiting disease commonly seen in newborn infants. It is the result of delayed clearance of fetal lung fluid.
- Persistent pulmonary hypertension (PPHN)
  PPHN is failure of normal circulatory transition after birth and is characterised by elevated pulmonary vascular resistance, right-to-left extrapulmonary shunting and severe hypoxaemia. Severe PPHN occurs in 2 per 1000 live born term infants and some degree of pulmonary hypertension complicates the course of approximately 10% of newborn infants with respiratory failure (G G Konduri et al., 2004). Right-to-left shunting will produce a gradient between pre- and post-ductal saturations (pre-ductal saturations will be higher).
- Respiratory distress syndrome (RDS)
  RDS is a result of inadequate surfactant production and release. The incidence of surfactant deficiency is inversely related to gestational age.
- Pneumonia
  Pneumonia can be congenital, intrapartum or nosocomial. The onset of congenital pneumonia will usually be within 6 hours after birth and intrapartum acquired pneumonia within 48 hours after birth.
- Meconium aspiration syndrome (MAS)
- Pulmonary air leak
  Pneumothoraces occur in up to 1% of otherwise healthy term infants (H Shaireen et al., 2014). It is more common in surfactant deficiency, MAS, pneumonia and pulmonary hypoplasia.
- Sepsis
- Congenital heart disease
  These infants are often asymptomatic in the first 24-48 hours when the ductus arteriosus is still patent. Hypoxaemia may be the only sign suggestive of underlying cardiac disease.
- Other less common causes for hypoxaemia include: pulmonary hypoplasia; trachea-oesophageal fistula; obstruction of the upper respiratory tract; metabolic disorders, and seizures.

Investigations

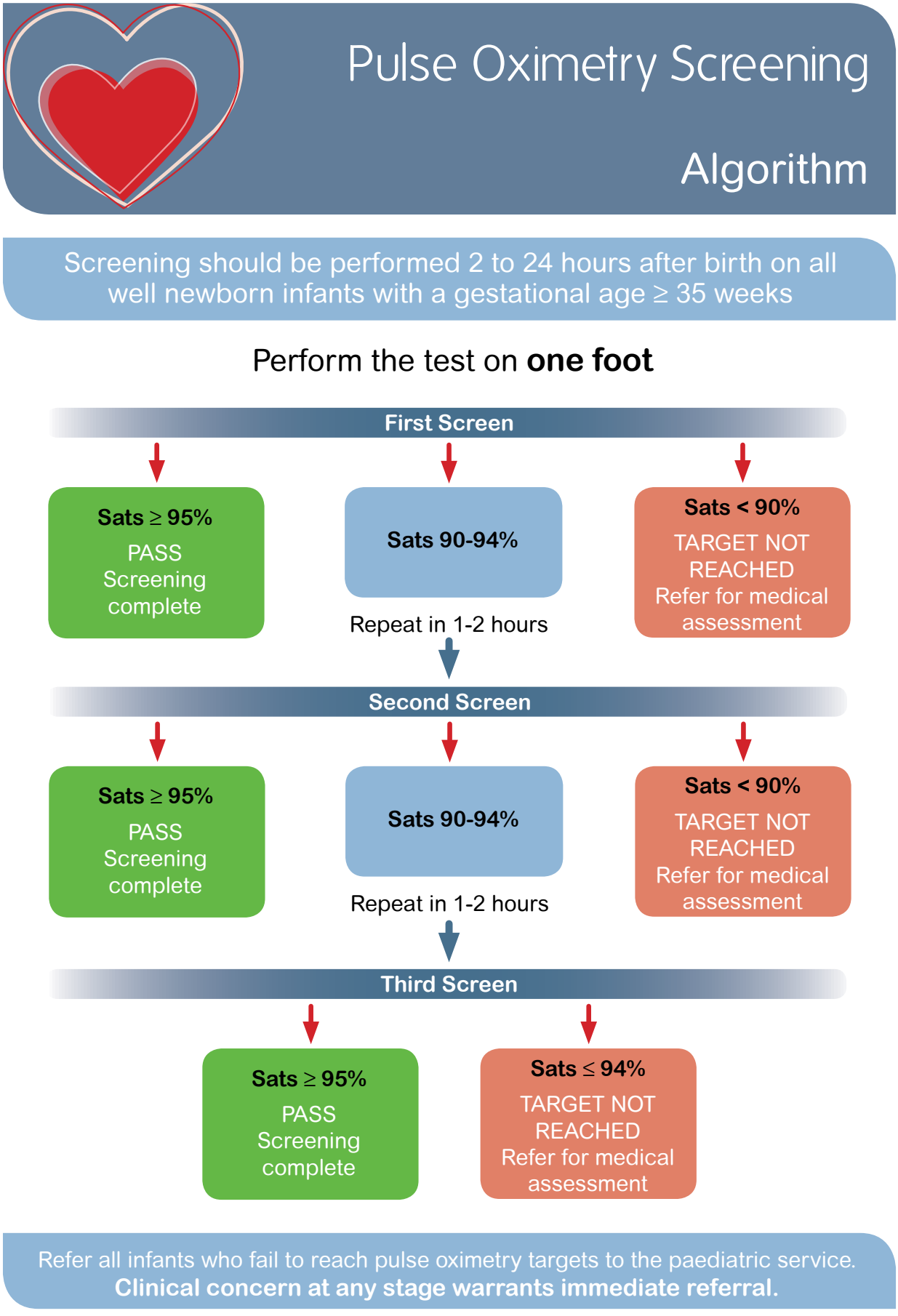
Investigations should be guided by the history and findings on clinical examination.

Consideration can be given to the following investigations:

- Chest X-ray
- Blood gas
- Full blood count, C-reactive protein, blood culture
- Electrolytes and glucose
- Lumbar puncture
- Echocardiogram
- Electrocardiogram (ECG)

The majority of hypoxaemic infants will have an underlying respiratory cause. Chest X-rays are inexpensive and easy to obtain and should therefore be considered as a first line investigation in hypoxaemic infants. Blood tests and cerebrospinal fluid can be particularly useful to identify infective or metabolic causes for hypoxaemia. Echocardiography is indicated if congenital heart disease is suspected or if no other cause for hypoxaemia can be identified. This test has to be performed by a skilled operator in consultation with the children's heart specialist. This may result in referral to a regional centre with echocardiography services.

Appendix III: Screening algorithm



Appendix IV: Screening record

AUCKLAND DISTRICT HEALTH BOARD
Te Toka Tumai

Screening Record (Form A)

MUST ATTACH PATIENT LABEL HERE

SURNAME: _____ NHI: _____

FIRST NAMES: _____ DOB: _____

Please ensure you attach the correct visit patient label

Office Use: Study ID	1	6	9	1	8	0	•					

Pulse Oximetry Screening

A1. Demographics

A1.1.Date and time of birth Date (dd-mm-yyyy)											Time (24h - min)				
							2	0					h		

A1.2. Gestational age at birth			weeks	+		days

A1.3. Maternal Ethnicity (tick one)		
	European	
	Maori	
	Pacific Islander	
	Chinese	
	Indian	
	Other Specify:	

A1.4. Parental Consent	I have received information on pulse oximetry screening and agree to participate.			
	Yes		No	

Completed by: Name _____ **Signature** _____ **Date** _____

A2. Guide to interpreting screening results

Pass

If saturation is ≥95% no further testing required

Repeat Screening (Inconclusive result)

If saturation is 90-94% mark 'inconclusive' and repeat the test in 1-2 hours

Medical assessment required

If the infant has three readings in the 'inconclusive' range with each measurement separated by 1-2 hours, contact a newborn health care provider
If saturation is <90% at any time contact a newborn health care provider immediately
Clinical concern at any stage warrants a referral to a newborn health care provider for a medical assessment

PULSE OXIMETRY SCREENING - FORM A - SCREENING RECORD

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PULSE OXIMETRY SCREENING - FORM A - SCREENING RECORD

AUCKLAND DISTRICT HEALTH BOARD
Te Toka Tumai

Screening Record (Form A)

MUST ATTACH PATIENT LABEL HERE

SURNAME: _____ NHI: _____

FIRST NAMES: _____ DOB: _____

Please ensure you attach the correct visit patient label

Office Use: Study ID	1	6	9	1	8	0	•					

Pulse Oximetry Screening

A3. Screening Results

A3.1. First Screen

A3.1.1. Performed at Date (dd-mm-yyyy)										Time (24h - min)					Location (circle one)				
						2	0					h			Delivery Suite	Postnatal Ward	Birthing Facility	NICU/ SCBU	Home

A3.1.2. Infant's status (tick one)							
Asleep		Breastfeeding		Awake & settled		Awake & unsettled	

A3.1.3 Saturation foot	**%**

Result	**Tick One**	**Action**
Pass		No further testing required
Inconclusive		Repeat screening in 1-2 hours
Target not reached		Contact a newborn health care provider

A3.1.4 Approximate duration of screening process:		min

A3.2. Second Screen

A3.2.1. Performed at Date (dd-mm-yyyy)										Time (24h - min)					Location (circle one)				
						2	0					h			Delivery Suite	Postnatal Ward	Birthing Facility	NICU/ SCBU	Home

A3.2.2. Infant's status (tick one)							
Asleep		Breastfeeding		Awake & settled		Awake & unsettled	

A3.2.3 Saturation foot	**%**

Result	**Tick One**	**Action**
Pass		No further testing required
Inconclusive		Repeat screening in 1-2 hours
Target not reached		Contact a newborn health care provider

A3.3. Third Screen

A3.3.1. Performed at Date (dd-mm-yyyy)										Time (24h - min)					Location (circle one)				
						2	0					h			Delivery Suite	Postnatal Ward	Birthing Facility	NICU/ SCBU	Home

A3.3.2. Infant's status (tick one)							
Asleep		Breastfeeding		Awake & settled		Awake & unsettled	

A3.3.3 Saturation foot	**%**

Result	**Tick One**	**Action**
Pass		No further testing required
Target not reached		Contact a newborn health care provider

CR9149

Appendix V: Hypoxaemia report

AUCKLAND DISTRICT HEALTH BOARD
Te Toka Tumai

Screening Record (Form B)

MUST ATTACH PATIENT LABEL HERE

SURNAME: _____ NHI: _____

FIRST NAMES: _____ DOB: _____

Please ensure you attach the correct visit patient label

Office Use: Study ID | | | | | | | • | | | | | |

Pulse Oximetry Screening

Paediatric health care providers complete this form for:
a) any infant who was referred for a medical assessment following failure to reach pulse oximetry screening targets, or
b) an infant displaying signs and symptoms of cardiac disease prior to screening

Send completed forms to: pulseox@adhb.govt.nz

B1. CLINICAL EXAMINATION

B1.1.Date and time of birth Date (dd-mm-yyyy)										Time (24h - min)				
						2	0					h		

B1.2.Date and time of examination Date (dd-mm-yyyy)										Time (24h - min)				
						2	0					h		

B1.3. Examination performed by (tick one)		
	House officer	
	Registrar	
	Nurse Specialist	
	Fellow	
	Paediatrician/Neonatologist	

B1.4. Were there signs and symptoms present prior to pulse oximetry screening?

Yes		No	

B1.5. Did the baby have signs of congenital heart disease on examination?

Yes		No	

B1.6 Which of the following were present on examination? (Tick all that apply)

Cyanosis		Bradycardia	
Murmur		Tachycardia	
Tachypnoea		Unresponsive	
Apnoea		Hypotonia	
Poor perfusion		Weak/absent femoral pulses	
Other Specify:			

Completed by: Name _____ **Signature** _____ **Date** _____

PULSE OXIMETRY SCREENING - FORM B - HYPOXAEMIA REPORT

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AUCKLAND DISTRICT HEALTH BOARD
Te Toka Tumai

Screening Record (Form B)

MUST ATTACH PATIENT LABEL HERE

SURNAME: _____ NHI: _____

FIRST NAMES: _____ DOB: _____

Please ensure you attach the correct visit patient label

Office Use: Study ID | | | | | | | • | | | | | |

Pulse Oximetry Screening

B2. INVESTIGATIONS

B2.1. Which of the following investigations were performed? (Tick all that apply)

Full blood count		Lumbar Puncture	
Blood Culture		Chest X-Ray	
CRP		ECG	
Blood gas		Echocardiogram	
Other Specify:			

B2.2. Complete this section if echocardiography was performed:

B2.2.1. Date of echocardiogram Date (dd-mm-yyyy)									
						2	0		

B2.2.2. Echocardiogram performed by:			
Neonatologist		Cardiologist	
Neonatal fellow		Cardiology fellow	
General paediatrician		Cardiac sonographer	

B3. DIAGNOSIS

B3.1. What is the diagnosis? (Tick one)

Congenital heart disease		Metabolic disease	
Respiratory disease		No cause found (false-positive result)	
Sepsis			
Other			

B3.2. Describe the diagnosis:

Completed by: Name _____ **Signature** _____ **Date** _____

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PULSE OXIMETRY SCREENING - FORM B - HYPOXAEMIA REPORT

CR9150

AUCKLAND DISTRICT HEALTH BOARD
Te Toka Tumai

Screening Record (Form B)

MUST ATTACH PATIENT LABEL HERE

SURNAME: _____ NHI: _____

FIRST NAMES: _____ DOB: _____

Please ensure you attach the correct visit patient label

Office Use: Study ID | | | | | | | . | | | | | |

Pulse Oximetry Screening

B4. ADMISSION SUMMARY

B4.1. District Health Board where infants was born:

B4.2. Was this infant admitted to the neonatal unit?

Yes		No	

B4.2.1. Date of admission to neonatal unit
Date (dd-mm-yyyy)

						2	0		

B4.3. Was this infant transferred from another hospital or birthing facility?

Yes		No	

B4.3.1. If yes, name the referring hospital or birthing facility:

B4.3.2. How many hours after the infant failed oximetry screening did he/she arrive at the referral centre?

	hours

B4.4. Was this infant transferred to another ward or hospital?

Yes		No	

B4.4.1. If yes, specify where this infant was transferred to:

B4.5. Date of discharge from neonatal unit
Date (dd-mm-yyyy)

						2	0		

Completed by: Name _____ **Signature** _____ **Date** _____

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PULSE OXIMETRY SCREENING - FORM B - HYPOXAEMIA REPORT

CR9150

Appendix VI: Parent information brochure

What information is collected and how will it be used?

As part of the screening, information will be collected about your baby's test results. Information identifying you and your baby will be removed prior to entering the results into a data system. No reports will identify you or your baby in any way. Information will be used to evaluate and improve pulse oximetry screening for newborn infants.

Your rights

If your baby was injured during the test, which is very unlikely, you would be eligible to apply for compensation from ACC just as you would be if an injury occurred at home.

If you do not want your baby to be screened you can inform your doctor or midwife when you are in hospital to deliver your baby. Your baby does not have to have the test.

More information

If you have any questions, please ask your midwife, doctor or the 'Healthy Heart Screening' investigators for more information. We can be reached at pulseox@adhb.govt.nz. You may also contact us if you wish to remove your baby's test results from the data system.

This initiative is supported by:

Healthy Heart Screening

Information for parents

Pulse Oximetry Screening

Screening is a tool used to detect a problem before it causes trouble. Pulse oximetry can be used to screen for heart and lung disease in newborn babies. The test will be offered to the parents of all newborn babies that are ≥ 35 weeks' gestation at birth.

What is pulse oximetry?

Pulse oximetry is a test that measures how much oxygen is in the blood. It is helpful in determining if an infant's heart and lungs are healthy.

What is congenital heart disease (CHD)?

CHD is a problem in the structure of the heart or the blood flow through the heart. Some forms of CHD need to be detected and repaired early in life; these are called 'critical' CHD. Every year nearly 100 babies are born in New Zealand with a critical heart defect.

Why is pulse oximetry used to screen for CHD?

CHD in some babies is discovered by ultrasound scans done before birth or at the time of the newborn baby check, but unfortunately not all CHD can be picked up this way.

Babies with CHD often have low levels of oxygen in their blood. When these levels are very low, a baby's skin and lips are blue. Pulse oximetry can diagnose babies with CHD before they become blue and sick.

How is pulse oximetry done?

A sensor with a small red light is placed around the baby's foot. The sensor is attached to a monitor that shows the oxygen levels in the blood. The test is painless. It takes just a few minutes to perform when the baby is quiet, calm and warm. You can comfort your baby while the test is being performed.

When will the screening be done?

The pulse oximetry screening test will be done in the first 24 hours after birth.

What does it mean if my baby's test shows a low oxygen level?

A low pulse oximetry reading can be normal in newborn babies whose heart and lungs are adjusting after birth. A health care provider will examine your baby and a recommendation will be made either to repeat the test in a couple of hours or to proceed with further investigations to check for a heart or lung problem. This may include an echocardiogram.

What is an echocardiogram?

An echocardiogram is an ultrasound of the heart that is used to diagnose heart disease.

Can all hospitals perform echocardiography?

No, not all hospitals can do this test. If your baby requires a heart ultrasound you and your baby may need to be transferred to a larger hospital for further assessment.

What if an abnormality in my baby's heart is found?

A children's heart specialist will advise your doctor how best to manage your baby. This might include transfer to Starship Children's Hospital.

Most babies can be treated successfully if the problem is found early.

Can a baby with CHD have a normal pulse oximetry reading?

The test will not detect all forms of CHD. Your baby should continue to have normal visits with his or her "Well-child Tamariki Ora" provider. If there are concerns, your baby will be referred for further assessment.

If you notice any of the following or have other concerns, you should get your baby checked: fast breathing when your baby is at rest or sleeping; sweating around the head; a bluish skin colour, or if your baby tires easily during feeds.

Appendix VII: Information for health care professionals

Information for health care professionals

Pulse Oximetry Screening

Every year nearly 100 babies are born in New Zealand with a critical heart defect. If not detected early, critical defects can result in death or neurodevelopmental impairment. Timely recognition of these conditions allows the possibility of intervention that may influence the natural history of the condition and subsequent outcome.

Current strategies to detect congenital heart disease (CHD) are antenatal ultrasound ('anatomy scans') and newborn physical examination. Up to 20% of newborns with critical CHD will not be detected by these screening methods. With the addition of pulse oximetry screening we will be able to identify some of these infants.

What is pulse oximetry?

Pulse oximetry is a test that measures how much oxygen is in the blood. The test will enable us to identify infants who are hypoxaemic secondary to cardiac, respiratory or other diseases such as infection. Detecting cyanotic congenital heart disease is the main target of pulse oximetry screening programmes.

Who should be screened?

Newborn infants with a gestational age ≥ 35 weeks' will be eligible for screening.

When will the screening be done?

The pulse oximetry screening test should be done between 2 and 24 hours after birth. If screening did not take place in the first 24 hours in healthy infants with a gestational age ≥ 35 weeks', for whatever reason, arrangements should be made to perform the test at the earliest possible time.

Screening before 2 hours of age is associated with higher false-positive rates. Very early screening can therefore potentially delay discharge or transfer from hospital. Infants should remain in hospital until they have reached saturations of ≥ 95%.

Babies with a gestational age ≥ 35 weeks' that are admitted to a neonatal unit will usually have ongoing saturation monitoring during their admission. It is the responsibility of the attending paediatric team to ensure that these babies have reached target saturations and that it has been recorded, prior to discharge from the unit.

Which limb will be used for screening?

The post-ductal saturation level should be measured. The sensor can be attached to the left or right foot to obtain this reading. Pre-ductal measurements from the right hand do not need to be obtained routinely, but may be requested for diagnostic purposes. A difference between pre- and post-ductal saturations may point towards persistent pulmonary hypertension or left outflow tract obstruction.

What can affect test accuracy?

Movement and crying may affect test accuracy. Ensure that the infant is calm and warm during the screening procedure. Promote parental involvement to comfort the infant. Screening may be performed while the baby is feeding or sleeping.

Bright light from phototherapy lamps can interfere with the accuracy of the test. Switch these lights off while the test is performed.

Reusable sensors must be cleaned with disinfectant solution or alcohol swabs before and after screening each infant. Dirty sensors can affect the accuracy of the reading and can transmit infection.

How often can a sensor and foam wrap be used?

All units are equipped with reusable sensors to perform cost-effective pulse oximetry screening. Do not discard these sensors; they can be used again after being cleaned.

Disposable sensors cannot be used again. Use a new, clean sensor for each infant. These sensors are also available, but should not be used for the purposes of screening on postnatal wards or in the community, as it will result in unnecessary costs.

Disposable and reusable sensors are secured to an infant's foot with a foam wrap. Foam wraps are disposable; a new one should be used for each infant. If the test has to be repeated on an infant, the foam wrap should be re-used on that infant.

What does it mean if a baby does not reach saturation targets?

A low oximetry reading can be normal in newborns adjusting to the extra-uterine environment. We have adopted an early screening strategy to ensure infants with CHD are diagnosed prior to cardiovascular compromise and collapse, but earlier screening can result in higher false-positive rates. It is important to accurately follow the steps in the screening algorithm if a baby with low saturations is identified.

Referral to paediatric services is indicated if an infant fails to reach target saturations or if there are clinical concerns at any stage. Further investigations, including echocardiography, will be at the discretion of the paediatric team.

Can a baby with CHD have a normal pulse oximetry reading?

The test will not detect all forms of CHD. Pulse oximetry can only identify cardiac anomalies that produce low oxygen saturation levels. Anomalies causing obstruction of the left outflow track, e.g. coarctation of the aorta or aortic valve stenosis will usually produce a normal pulse oximetry reading. Reduced or absent femoral pulses may be the only indicator of congenital heart disease in these cases. It is important to remain vigilant and to report any clinical concern.

Parents should be advised to seek medical advice if they notice any of the following: fast breathing when the baby is at rest or sleeping; sweating around the head; a bluish skin colour, or if the baby tires easily during feeds.

Informed consent

Consent has to be obtained prior to performing the screening test on a baby. The parent or guardian should be informed that the primary purpose of the test is to screen for serious heart defects in babies, but that other diseases may also be detected. Ensure that they understand that pulse oximetry screening will not detect all forms of cardiac disease.

Caregivers have the right to decline screening.

More information

Do not hesitate to approach a senior colleague for assistance with parental counselling or with performing pulse oximetry screening. Refer to the screening guidelines on the Starship Children's Hospital website for more information.

Appendix VIII: Economic evaluation

Pulse Oximetry Screening Economic Evaluation Report

Dr Richard Edlin, Health Economist, University of Auckland

Decision Problem

This analysis compares a potential national screening programme for the detection of hypoxaemia in the newborn using pulse oximetry in babies born at a gestational age ≥35 weeks within 24 hours of birth against New Zealand's historic standard of care. It considers only detection of critical congenital heart disease (CCHD) and not other hypoxaemic conditions for which early detection may be beneficial and considers the short term outcome of timely (pre-discharge) diagnosis and longer term quality-adjusted life years (QALY) outcomes alongside 2 year District Health Board (DHB) costs. Findings are presented in terms of cost-effectiveness (as incremental cost-effectiveness ratios [ICERs]) and budget impact based on a probabilistic sensitivity analysis, with cost-effectiveness acceptability curves used to identify the likely cost-effectiveness of treatment at $10,000 per QALY, $30,000 per QALY and $50,000 per QALY. Newborns previously diagnosed with CCHD were excluded from the analysis, as they were identified prior to birth and their care would not be directly affected by the decision made here.

The economic modelling employs a decision tree, since the uncertainty here relates to the timing of identification and this is resolved within the first year of life. This tree divides cases using two diagnostic subgroups with CCHD alongside one group considering both healthy and non-critical CHD together, timeliness of diagnosis (2 levels), and survivorship (deceased vs survivor). As the NZ screening data provides only data for those who were intended to receive screening, we used existing New Zealand data and economic evaluations to inform our counterfactual; where possible NZ data have been used. These data are from either the recent Pulse Oximetry feasibility (Cloete et al., 2019) study or the National Congenital Heart Disease dataset compiled by the Paediatric and Congenital Cardiac Service at Starship Children's Hospital for all infants with CHD regardless of outcome or treatment received between 2006 and 2014.

Methods

Epidemiology of diagnosis and casemix

A central question for the economic evaluation was the identification of likely prognosis, costs and benefits for infants. Since these are heterogeneous, we grouped infants with CCHD in the National Congenital Heart Disease Dataset. These groups were as follows:

- Group A: Single ventricle anomalies
- Group B: Critical biventricular anomalies causing death or requiring intervention ≤ 28 days

These groups exclude the antenatally-detected cases, since these infants fall outside our decision problem. We note that within the National Congenital Heart Disease Dataset 53.5% of these critical cases (i.e. Groups A and B) are detected antenatally. Within the modelling we employed a Group C to cover all other cases, including other non-cardiac and cardiac conditions causing hypoxaemia that would cause death or require intervention after 28 days.

As the National Congenital Heart Disease Dataset includes all New Zealand cases over a number of years, the dataset can be used to identify the incidence of CCHD within Groups A and B. The Ministry of Health records a total of 544,046 births in New Zealand between 2006 and 2014 (the period of this dataset), which includes 453 antenatally-detected cases of CHD. Thus within this timeframe we have:

		Cases Identified	Probability per life birth
Group A	Single ventricle anomalies	22	0.000040
Group B	Critical biventricle ≤28d	260	0.000478
Group C	All other	543,311	0.999481

Table 2: Postnatally-Detected Cases and Potential NZ Incidences

Sensitivity and Specificity of Pulse Oximetry Screening and historic standard of care

The most reliable current estimate for the sensitivity and specificity for pulse oximetry in CCHD, that is Groups A and B, comes from the recent Cochrane review (Plana et al., 2018). Here, 76.3% of babies with a CCHD have this defect detected by pulse oximetry testing (95%CI 69.5 to 82.0%). The specificity of pulse oximetry testing is also taken from this Cochrane study and was reported as 99.9% (95%CI 99.7 to 99.9%).

For the New Zealand historic standard of care, specificity figures are found by looking at the proportion of cases in Groups A and B that were identified in a timely fashion. Here, 12 of 22 cases in Group A (54.5%) and 167 of 260 cases in Group B (62.7%) were detected pre-discharge.

There is a lack of clearly-relevant data to identify the specificity of testing in the New Zealand historic standard of care. Where CHD is suspected in a newborn, this is likely to require a brief clinical examination, blood tests and a chest radiograph. If suspicion remains an echocardiogram will be performed. Taking a conservative assumption, we assume a specificity of 1 for pulse oximetry screening in the base case analysis.

Cost of Pulse Oximetry screening and historic standard of care

The cost of pulse oximetry testing is calculated based on the assumption that each test takes approximately 5 minutes, based on experience with in the NZ Pulse Oximetry screening study. We note that this is shorter than some estimates that appear in the literature, and this issue is addressed in sensitivity analyses. Assuming an estimated midwife earns $69,500 (MBIE, 2018) plus 3% Kiwisaver

and 50% overheads and works 48 weeks at 40 hours/week, each hour would cost approximately $55.38. At this cost, the labour costs per screen amounts to $4.62 per infant.

In equipment costs, we assume that each pulse oximeter costs $1,295 (ProMed Technologies) and lasts for 10 years (Peterson et al., 2014). Given discounting and yearly maintenance of $320, the average yearly cost per machine is estimated at $470.64. Within the screening study, 16,644 babies were screened using only 30 oximeters, which equates to around 277 infants per oximeter per year. The model used a figure of 275 infants per oximeter per year in the base case analysis, which equates to a cost of $1.71 per infant. In addition, each infant requires a foam wrap for the oximeter sensor, costing $4.00. Overall, then the cost per screen is calculated to be $10.33. In sensitivity analyses, the number of infants per machine per year is modified, as is the time taken per infant.

Where necessary, diagnostic echocardiography is assumed to cost $323 (ADHB, 2017) with this used to confirm CHD in all suspected cases. No additional costs are applied for the historic standard of care except where false-positives are considered in sensitivity analyses, where the echocardiography cost is applied. This is because opportunistic detections would be identified within the standard of care.

Mortality and costs from the New Zealand historic data

The analysis will consider the costs and consequences in terms of detections pre- and post-discharge, with first two years' costs assigned from a payer (i.e. DHB) perspective in 2017 New Zealand Dollars. The costs and consequences consider all hospital inpatient and outpatient costs in these first two years but do not consider costs to the patients or their whanau, subsequent DHB costs beyond the two year timeframe, other costs to the government (e.g. due to disability and on the educational system) or later indirect societal costs due to loss of productivity.

The National Congenital Heart Disease Dataset provides NHI information for infants diagnosed with CHD, including the cohort of most interest with CCHD. Resource utilisation was sourced from National Collections data (NMDS and NNPAC) using NHI data and this allows both inpatient and outpatient costs to be assessed. Inpatient utilisation was valued using WIESNZ weights, with outpatient events (including Emergency Department visits) using sources from New Zealand and overseas. Primary care community costs are not included in this analysis as they are not captured within the National Collection data. Unit costs for outpatient events were taken from a variety of sources, including ineligible DHB patient costs. This dataset allows costs to be assessed for both deceased and surviving infants in each of the groups. A summary of these figures is provided below in Table 3 below.

Group	Diagnosis	Status	n	Mean	SD of Mean
A	Pre-discharge	Deceased	3	$22,057	$14,723
		Survivor	9	$180,616	$17,251
	Post-discharge	Deceased	3	$62,334	$54,613
		Survivor	7	$139,131	$21,867
B	Pre-discharge	Deceased	19	$69,947	$19,702
		Survivor	148	$119,117	$5,349
	Post-discharge	Deceased	14	$57,755	$22,619
		Survivor	79	$99,741	$3,887

Table 3: Combined 2-Year Inpatient and Outpatient Costs by Group, Diagnosis Time and Decedence

These figures also provide estimates of mortality in each group both pre- and post-discharge. Here, early diagnosis is associated with decreased mortality in both Groups A and B, with mortality falling from 30% (as 3 of 10) to 25% (as 3 of 12) in single ventricle anomalies and from 15.1% (as 14 of 93) to 11.4% (as 19 of 167) in critical biventricular anomalies. Within our non-CHD group (Group C), first year mortality is estimated to be 0.0038 reflecting 228 deaths from a population of 59,610 (excluding CHD cases).

QALY figures from survivorship at 1 year

Life expectancy for avoided mortality was calculated using NZ projections at 1 year of age, where 2017 life expectancy was 93.3 for females and 91.2 for males (StatsNZ, 2019). Discounted life expectancy was calculated at 1 year by assuming this life expectancy and discounting each year of life until the stated life expectancy was reached, with discounted figures of 28.33 and 28.42 years. Given a sex ratio of 1.05:1 boys to girls at birth (CIA Factbook, 2019) and incorporating a half cycle correction, each death averted gains 27.87 years. Given NZ population norms for the EQ-5D, in each year (Janssen & Szende, 2014), this translates to a gain of 24.57 QALYs per death averted.

Transfer costs between NZ Hospitals

Transfer costs between locations were not considered due to both the difficulty of finding reliable cost estimates (these were considered commercially sensitive) and because the impact is likely to be very minor as almost all cases will require transport (with the exception of cases detected post-mortem). Where CHD is suspected (including false-positive cases), infants are locally examined prior to expensive transfers by air.

Base Case and Sensitivity Analyses

For the purposes of this analysis, we assume a birth cohort of 60,000 infants born alive in New Zealand per year. If not all infants are screened, then cost-effectiveness findings are likely to be identical but the budget impact is likely to be reduced proportionately. A probabilistic model provides the base case analysis by averaging estimates across for 50,000 runs of the model.

Within the probabilistic model, prevalence is drawn from a Dirichlet distribution based on the number of cases identified in the National Congenital Heart Disease Dataset. All mortality figures are drawn as Beta distributions. The combined outpatient/inpatient costing figures are drawn using lognormal distributions based on the reported mean/standard deviations provided here.

The sensitivity of pulse oximetry testing in Groups A and B are drawn from a beta distribution in the probabilistic model based on the presented figures. In the case of specificity, the stated mean and upper bound of a 95% CI are reported identically within the Cochrane review. In order to make this tractable, we have analysed these data as 99.86% (95% CI 99.74 to 99.96%) within the probabilistic model. For the New Zealand historical standard of care, sensitivity and specificity are again treated as beta distributions and based on the figures given above.

Our sensitivity analyses are summarised in Table 4. These include considering the impact of using sensitivity from the New Zealand Pulse Oximetry study, where 45 false-positives were found from a population of 16,644. Sensitivity analyses were also conducted in both the time taken to undertake the pulse oximetry test and the number of cases that each pulse oximeter would deal with on average in each year. In a final sensitivity test, we also consider the impact of using costs of antenatally-detected cases instead of observed pre-discharge cases for those identified pre-discharge, although these figures are similar (see Table 5). In this final case, it was felt that this might provide a proxy for early, ideal management.

Description	Parameter(s)	From	To
False positives in historical standard of care	Specificity of PO testing	(Plana et al., 2018)	Beta (16641, 45)
PO time increased	Minutes per PO test	5	10
PO time decreased	Minutes per PO test	5	2.5
Decreased cases per oximeter	PO bases per oximeter per year	275	138
Increased cases per oximeter	PO bases per oximeter per year	275	550
Antenatal costs used as an alternative for detected cases	PO Costs for Groups A and B, conditional on decadence	See Table 3	See below

Table 4: Base Case and Sensitivity Case Analyses

Group	Status	Pre-discharge Mean	SD	Antenatal Mean	SD
A	Deceased	$22,057	$14,723	$67,576	$14,643
	Survivor	$180,616	$17,251	$177,084	$8,106
B	Deceased	$69,947	$19,702	$55,428	$8,233
	Survivor	$119,117	$5,349	$124,758	$4,343

Table 5: Combined 2-Year Inpatient and Outpatient Costs by Group and Decedence; pre-discharge vs. antenatally-detected cases only.

Results

Within the base case analysis, pulse oximetry testing would detect 23.75 infants pre-discharge with CHD across Groups A and B each year across the 60,000 infants, as compared to 19.76 cases in the New Zealand historic standard of care. With a lower mortality rate amongst the earlier detected cases, the additional identified infants via pulse oximetry screening (0.52 additional in Group A, 3.47 additional in Group B) would correspond to an expected gain of around 3.74 additional QALYs per year. The estimated cost of the pulse oximetry screening (including inpatient and outpatient costs) amongst CCHD is $4.10 million, as compared to $3.37 million within the historic standard of care. With pulse oximetry providing more QALYs at an increased cost of $730,495 it would be expected to improve health at a cost exceeding $195,000 per QALY.

There is little decision uncertainty in the base case analysis as the cost-effectiveness threshold varies (Figure 1). Here, only 2% of the 50,000 model runs suggest that pulse oximetry is cost-effective at a threshold of $50,000, whilst even at $100,000 per QALY the probability of pulse oximetry being deemed cost-effective is only 20%.

The results of sensitivity analyses are presented below, alongside the base case figures. Since Table 6 includes figures for the full cohort of 60,000 infants, the numbers presented are large. An incremental analysis, as in Table 7, is more informative as it focusses on the differences between the two options presented.

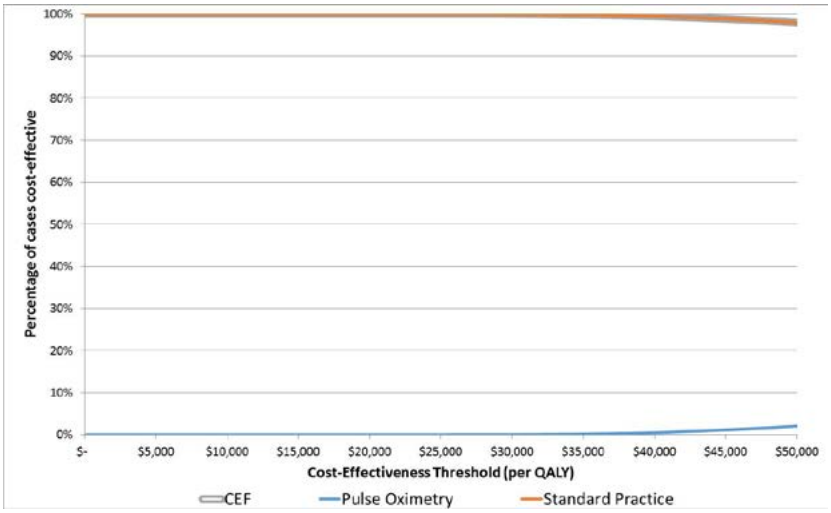

Figure 1: Cost-Effectiveness Acceptability Curve and Frontier - Base Case

Four of these cases relate to the cost of conducting the pulse oximetry screening – being either a modification of the time taken to conduct the screening or a change to the number of screening tests that each oximeter undertakes each year. Whilst the incremental costs do vary here (and in the expected directions), these cases suggest that a pulse oximetry screening programme (ignoring any national set up costs) would require resources to be reallocated at a DHB level and that the overall cost is likely to be between $500,000 to $1,000,000 in total. This cost does not include any administration costs of a nationwide pulse oximetry screening programme, which would be expected to increase the net cost of a pulse oximetry programme.

The sensitivity analysis using antenatal costs as a proxy for idealised care leads to slightly more expensive estimates for care but does not appear to substantively affect the results (ICER at $198,000 per QALY). Likewise, where the number of false-positives from the NZ Pulse Oximetry Screening Study is used to inform specificity, the costs increase by around $26,000 and the impact on overall cost-effectiveness is minor (ICER at $202,000 per QALY). The overall conclusion that pulse oximetry does not appear to be cost-effective at a 'typical' cost-effectiveness threshold persists across all the analyses presented. Indeed, the only sensitivity analyses that substantively change results is where the discounting on QALYs is modified. Where no discounting is applied to QALYs, the ICER falls to $62,000 per QALY.

	Pulse Oximetry			Historical Practice			Budget Impact
	Diagnoses	QALYs	Costs	Diagnoses	QALYs	Costs	
Base Case	23.75	1,468,651	$4,102,659	19.76	1,468,647	$3,372,164	$730,495
False positives in historical standard of care	23.75	1,468,385	$4,128,577	19.76	1,468,381	$3,372,806	$755,771
PO time increased	23.75	1,468,385	$4,379,511	19.76	1,468,382	$3,371,904	$1,007,607
PO time decreased	23.74	1,468,385	$3,962,402	19.75	1,468,381	$3,370,487	$591,915
Decreased cases per oximeter	23.76	1,468,386	$4,206,552	19.76	1,468,383	$3,373,702	$832,850
Increased cases per oximeter	23.76	1,468,385	$4,052,606	19.76	1,468,381	$3,373,434	$679,172
Antenatal costs used as an alternative for detected cases	23.75	1,468,389	$4,193,200	19.76	1,468,386	$3,446,026	$747,174
QALY benefits not discounted	23.75	4,526,525	$4,103,382	19.76	4,526,513	$3,372,597	$730,785
QALY benefits discounted at 6%	23.76	926,155	$4,105,636	19.76	926,152	$3,374,758	$730,879

Table 6: Overall Results for Base Case and Sensitivity Analyses

	Incremental Analysis			Likelihood of cost-effectiveness at		
	QALYs	Costs	ICER	$10k per QALY	$30k per QALY	$50k per QALY
Base Case	3.74	$730,495	$195,125 per QALY	0.00%	0.04%	2.08%
False positives in historical standard of care	3.75	$755,771	$201,769 per QALY	0.00%	0.03%	1.70%
PO time increased	3.78	$1,007,607	$266,658 per QALY	0.00%	0.00%	0.28%
PO time decreased	3.73	$591,915	$158,749 per QALY	0.00%	0.23%	5.17%
Decreased cases per oximeter	3.78	$832,850	$220,616 per QALY	0.00%	0.03%	1.76%
Increased cases per oximeter	3.78	$679,172	$179,468 per QALY	0.00%	0.12%	2.99%
Antenatal costs used as an alternative for detected cases	3.77	$747,174	$198,109 per QALY	0.00%	0.03%	1.76%
QALY benefits not discounted	11.73	$730,785	$62,322 per QALY	0.00%	17.74%	38.05%
QALY benefits discounted at 6%	2.36	$730,879	$309,672 per QALY	0.00%	0.00%	0.07%

Table 7: Incremental Analysis for Base Case and Sensitivity Cases

Discussion

In all cases considered except that removing discounting on QALY gains, the likelihood of pulse oximetry being cost-effective when health effects are valued at or below $50k per QALY remains at or below 5%. In this remaining undiscounted case, any appropriate cost-effectiveness threshold (as a marker for opportunity cost) would also be lower, so that it is unlikely that this could be argued to approach cost-effectiveness. As such, whilst pulse oximetry does provide for a higher detection of CCHD, there is a relatively low benefit expected in terms of QALYs. Here, with good quality management of even those cases detected late, the mortality risks associated with late detection are relatively small. This does not mean that other risks are avoided; the current analysis has not been able to consider the morbidity effects of earlier vs. later detection and treatment or the costs of treatment and support beyond the 2-year timeframe available for costing.

It is conceivable that there are benefits to pulse oximetry that this analysis has not been able to consider in terms of both morbidity and costs, particularly as these relate to neurological damage and subsequent chronic morbidity and dependence. Consistent with the lack of data in this area, the quality of life (QoL) multiplier applied to survival in both groups is the same, whereas if there are long-term morbidities from late diagnosis we would expect this to be different for the two groups. This is an area where prospective collection of data is likely to be both complex and costly, although there is potential to use the Integrated Data Infrastructure (IDI) to track known historic cases to identify some of the ongoing costs of treatment and some elements of morbidity through subsequent contacts with the health system (although not quality of life data). Linkages through the IDI may also, in time, allow some of the other impacts on government budgets outside of health to be considered, for example with respect to levels of educational and other supports.

This analysis has a key strength in that there are more data available to it than many previous analyses available in the literature, especially in relation to the potential costs and outcomes associated with early and late diagnosis in critical congenital heart defects. There is a lack of randomised controlled trial-based evidence in this literature, and this analysis shares that general weakness. A major weakness is that there are no data from QoL tools for survivors in the historic or pulse oximetry cases meaning that QALYs must be inferred only from survival.

There were areas where this study is likely to underestimate costs and/or overestimate benefits. Within the model reported here survival from 1 year was assumed to reflect mortality ratios from the general population. Grosse et al (2017) suggest that there is a shortened life expectancy amongst those with CCHD after infancy, with for instance a higher incidence of cancer even after removing individuals with chromosomal disorders. They suggest that life expectancy amongst individuals with CCHD may be 10-20% lower than the general population, with an impact of 3-6 discounted life years. Within our model, which assumes around 28 discounted life years per death averted at 1 year, so a reduction of 4.5

years suggests would increase ICERs to around 120% of the figures predicted here to figures approaching $250,000 per QALY.

Our model provides for benefit amongst, and considers outcomes only in, those with critical congenital heart disease. The majority of economic evaluations of pulse oximetry testing consider both CCHD and at least some non-critical CHD cases (e.g. Ewer et al (2012), Griebsch et al (2007), Knowles et al (2005), Roberts et al (2012), Tobe et al (2016), Tobe et al (2017) with Peterson et al (2013)an exception in considering only CCHD. The approach used here fits within the minority of existing studies, in that only CCHD cases are considered – in our case, this is due in part to limitations in the data available which are relevant to the NZ context. Narayen et al (2016) noted that when only CCHD are considered, this would increase the false-positive rate for CCHD, since cases that are non-critical CHD would also then be considered within this group. Contrastingly, they argue that a broader CHD group would decrease the sensitivity of CHD testing relative to looking only at CCHD. Within this study, we have focussed on the sensitivity and specificity figures provided by Plana et al (2018) and have not incorporated any costs or effects based on non-critical CHD or indeed other conditions causing hypoxia as 'false-positives'. It was suggested that many of these cases would by definition not be treated immediately and could be treated safely at a later stage, so that early identification by pulse oximetry testing would not provide any clear survival benefit – and the current model is only able to assess benefits where a survival benefit accrues. Any morbidity benefits that would accrue for babies with non-critical CHD could not have been captured within the current model and these non-critical CHD cases were thus grouped with the healthy non-CHD cohort.

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Appendix IX: Parent survey

Healthy Heart Screening Survey

Pulse oximetry is a test that can help to determine if a baby's heart and lungs are healthy. If your baby had this test we would like to invite you to complete this survey to help us better understand what parents think of the test. This survey will not collect any information that will identify you or your baby.

Q1. How old are you? _____

Q2. Which ethnic group do you belong to? Mark (x) all those that apply to you.

- ❑ New Zealand European
- ❑ Māori
- ❑ Samoan
- ❑ Cook Island Māori
- ❑ Tongan
- ❑ Niuean
- ❑ Chinese
- ❑ Indian
- ❑ Other - Please state: _____

Q3. How many children do you have (including this baby)? _____

Q4. What is the highest level of education you have completed?

- ❍ No qualification
- ❍ Primary school
- ❍ Secondary school
- ❍ Trade certificate
- ❍ Diploma
- ❍ University qualification
- ❍ Other - Please state: _____

Q5. Where did you deliver your baby?

- ❍ Home
- ❍ Auckland City Hospital
- ❍ Birthcare
- ❍ Middlemore Hospital
- ❍ Botany Maternity Unit
- ❍ Papakura Maternity Unit
- ❍ Pukekohe Maternity Unit
- ❍ Rotorua Hospital
- ❍ Taupo Hospital
- ❍ Other _____

Q6. What was the outcome of your baby's 'Healthy Heart Screening' test? Mark <u>all</u> those that apply to your baby.

- ❑ My baby passed the test
- ❑ My baby needed more tests
- ❑ My baby was transferred to another hospital
- ❑ My baby was admitted to the hospital's newborn unit / children's heart ward
- ❑ My baby has a heart problem
- ❑ My baby has a lung problem
- ❑ My baby has an infection
- ❑ I don't know

Q7. Do you agree with the following statements?

	Strongly Agree	Agree	Neither Agree nor Disagree	Disagree	Strongly Disagree
I understand why the 'Healthy Heart Screening' test was performed on my baby	❍	❍	❍	❍	❍
I would have liked to receive more information about the screening test	❍	❍	❍	❍	❍
The test is an important health check for babies	❍	❍	❍	❍	❍
The result of the test was explained to me	❍	❍	❍	❍	❍
I found it reassuring that my baby had the test	❍	❍	❍	❍	❍
Screening tests cause disruptions to babies and their families	❍	❍	❍	❍	❍

Q8. The information brochure and parent information video were helpful:

	Strongly Agree	Agree	Neither agree nor disagree	Disagree	Strongly Disagree	I didn't receive this information
'Healthy Heart Screening' brochure	❍	❍	❍	❍	❍	❍
Parent information video	❍	❍	❍	❍	❍	❍

Q9. If you have any other comments about the test, please add it here:

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Phone: +64 9 923 6691
Email: director@liggins.auckland.ac.nz
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Write to us

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University of Auckland
Private Bag 92019, Victoria Street West
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