Health and disability research

These screening questions will help determine whether HDEC review is required for your study. They are based on the rules contained in section three of the *Standard Operating Procedures for Health and Disability Ethics Committees*.

Don't hesitate to contact us if you'd like help answering these questions, or any others in the HDEC form.

A. Health and disability research

Does your study aim to improve health outcomes, or outcomes for disabled people?

- (•) Yes
- ( ) No

Human reproductive research

B. Will your study involve the creation or use of a human gamete, a human embryo or a hybrid embryo?

- ( ) Yes
- (•) No

Type of study

C. Is your study:

- ( ) an intervention study?

In intervention studies, the investigator controls and studies the preventive, diagnostic or therapeutic intervention(s) provided to participants for the purpose of adding to knowledge of the health effects of the intervention(s). Many intervention studies are clinical trials.

- (•) an observational study?

In observational studies the researcher has no control over study variables, and merely observes outcomes.

Main Criteria

D. Will your study involve **human participants** recruited in their capacity as:

- consumers of health or disability support services, or
- relatives and/or caregivers of consumers of health or disability support services, or
- volunteers in clinical trials (including bioequivalence and bioavailability studies)?

- (•) Yes
- ( ) No

E. Does your study involve the use, collection or storage of **human tissue** (as defined by section 7 of the Human Tissue Act 2008)?

Examples of human tissue include:

- *all or any part of a body*
- *whole human organs or parts of them*
- *human stem cells or other human cells*
- *human blood*
- *human bone marrow*
- *human hair, nails, and skin*
- *human mucus, sputum, or urine.*

◯ Yes

◉ No

G. Will your study involve the use or disclosure of **health information** (as defined by section 4(1) of the Health Information Privacy Code 1996)?

Health information is about identifiable individuals. It includes:

- *information about the health of an individual, including his or her medical history*
- *information about any disabilities that individual has, or has had*
- *information about any health services or disability services that are being provided, or have been provided, to that individual*
- *information in connection with the donation of any body part or any bodily substance of that individual*
- *information derived from the testing or examination of any body part, or any bodily substance of that individual*
- *information about the individual which is collected before or in the course of, and incidental to, the provision of any health service or disability service to that individual.*

◉ Yes

◯ No

H. *You don't need HDEC approval to use health information for research if:*

- *informed consent to this use has already been obtained*
  or
- *the health information won't be disclosed* to researchers in a form that would allow them to identify the individual(s) concerned, or to match the information with other datasets through a non-encrypted identifier (eg, an NHI number).*

Does one of these exceptions to the need to obtain HDEC approval apply to your study?

◯ Yes

◉ No

* See rule 11 of the Health Information Privacy Code 1996.

Exemptions

I. ***Exemption for low risk medical devices***

Does your study involve evaluating a low-risk (class I) medical device?

Low-risk (class I) medical devices are defined from page 77 of the Australian Therapeutic Goods Administration's Australian Regulatory Guidelines for Medical Devices.

◯ yes

◉ no

J. *Exemption for audits and related activities*

i. Is your observational study an audit or related activity?

The term "audit and related activity" is defined in the Ethical Guidelines for Observational Studies.

- ○ yes
- ◉ no

K. *Exemption for minimal risk observational studies*

Does your study involve more than minimal risk?

A study involves more than minimal risk if the probability and magnitude of possible harms resulting from participation in the study is greater than those encountered in everyday life.

A study always involves more than minimal risk if it involves one or more of the following:

- *one or more participants who will not have given informed consent to participate*
- *one or more participants are vulnerable*
- *standard treatment being withheld from one or more participants*
- *the storage, preservation or use of human tissue without consent*
- *the disclosure* of health information without authorisation.*

- ◉ yes
- ○ no

* See rule 11 of the Health Information Privacy Code 1996.

Kb. Please briefly explain your answer above.

[< 1200 characters]

The participants of the study will be neonates and are therefore unable to give informed consent themselves. Consent will be given by their primary caregivers. Some participants will be vulnerable because of other co-morbidity, e.g. chronic lung disease, intraventricular haemorrhage

L. *Exemption for some student research*

Is your study being done at or below Masters level?

- ○ yes
- ◉ no

INCLUSIONS

HDEC REVIEW

O. Your study requires HDEC review

The question below will determine the review pathway appropriate to your study.

Does your study involve any of the following? (select all that apply)

- [ ] a new medicine
- [ ] an approved medicine being used for a new indication or through a new mode of administration
- [ ] a medical device that is or would be classified as a class IIb, class III, or active implantable medical device by the Therapeutic Goods Administration (TGA)
- [ ] a new surgical intervention
- [ ] one or more participants who will not have given informed consent to participate
- [x] one or more participants who are vulnerable (that is, who have a restricted ability to make independent decisions about their participation)
- [ ] standard treatment being withheld from one or more participants
- [ ] the storage, preservation or use of human tissue without consent
- [ ] Future Unspecified Use of Tissue
- [ ] none

Ob. Please briefly explain why you believe that one or more participants in your study are vulnerable.

[< 1200 characters]

The participants of the study will be neonates and are therefore unable to give informed consent themselves. Consent will be obtained from their caregivers instead. Some participants will be vulnerable because of other co-morbidities, e.g. chronic lung disease, severe intraventricular haemorrhage (highly predictive of cerebral palsy)

Full. *Your study will be reviewed by the **full review** pathway described at section 5 of the Standard Operating Procedures for Health and Disability Ethics Committees.*

a.1 Title and summary

a.1.1.

Short study title: Effect of elective blood transfusion on regional oxygenation and cardiorespiratory stability of neonates

a.1.2.

Formal study title: Effect of elective blood transfusion on cerebral, hepatic and muscle regional oxygenation and cardiorespiratory stability in neonates

a.1.3. A protocol must be uploaded in the “Documents” tab before submission to an HDEC.

If this protocol has a unique identifier, please enter this below.

Protocol number (if applicable): Protocol_V6

a.1.4. Please provide the dates on which you plan to commence and conclude your study in New Zealand

Planned commencement date: 01/03/2016
Planned conclusion date: 30/06/2016

a.1.5. Please provide a brief, plain English summary of your study.

[< 2000 characters]

Newborn babies in neonatal intensive care units are prone to developing anaemia because of their immature bone marrow and frequent blood sampling required for ongoing monitoring. Anaemia in these infants, if left untreated, can result in lethargy, suboptimal growth and nutrition, ongoing requirement for respiratory support, and cardiovascular instability. Currently elective (i.e. non-urgent) blood transfusion is the treatment of choice for anaemia in these infants; however, there is no consensus in the literature on the ideal treatment threshold.

This study aims to develop better understanding of the mechanism by which elective blood transfusion benefits neonates with anaemia. More specifically it will examine whether elective blood transfusion increases availability of oxygen to the brain, liver and muscle. It also aims to examine whether such changes are sustained beyond the initial 24hrs of transfusion, and correlate such findings to markers of cardiorespiratory stability (frequency of peripheral desaturation, blood pressure stability and heart rate).

This is an observational study, and the decision to give elective blood transfusion will be made only by the attending clinicians. Once the decision to give transfusion is made, potential participants' caregivers will be approached for enrollment in the study.

The study involves use of non-invasive devices to measure physiological parameters. The oxygen levels in the brain, liver and muscle will be measured using near-infrared spectroscopy (NIRS), a portable and non-invasive device that is increasingly used in neonatal research and clinical practice. Parameters of cardiorespiratory stability will be measured using a pulse oximeter and a Human NIBP (non-invasive continuous blood pressure cuffs). Measurements will be taken before, during and immediately after a blood transfusion, as well as at 24hrs and 5 days post-transfusion.

a.1.6. Please provide a brief summary of the main ethical issues that you believe your study may raise.

[< 1200 characters]

Informed consent will have to be obtained from primary caregivers, as the study participants will be neonates.

a.2.1. Does your study aim to improve knowledge of:

- ○ diagnosis
- ○ early detection / screening
- ○ prevention
- ◉ treatment
  - ○ medicines
  - ○ devices
  - ○ surgery
  - ○ radiotherapy
  - ◉ other: Blood transfusion
- ○ rehabilitation
- ○ lifestyle/behaviour
- ○ other:

a.2.1.4. Which of the following best describes your observational study?

- ○ case control study
- ○ cohort study

- ○ cross-sectional study
- ○ case report
- ○ case series
- ◉ descriptive study
- ○ audit or related activity
- ○ device usability assessment
- ○ other

a.2.2. Please select the ANZSRC field of research that best describes your study from the drop-down menus.

Level 1: 11 Medical and Health Sciences

Level 2: Paediatrics and Reproductive Medicine

Level 3: Paediatrics

a.3 Investigators

Co-ordinating Investigator (CI)

The CI has overall responsibility for the conduct of the study, including adherence to established ethical standards.

In student research, the student him- or herself is the CI.

a.3.1. Are you the CI for this study?

- ◉ Yes
- ○ No

a.3.1.1. *The CI must authorise this application (through the "Authorisations" tab) before it can be submitted to an HDEC for review. You should request authorisation once you have completed all questions in the Online Form, or sign this form as the Co-ordinating Investigator in the Authorisations tab.*

Please provide the following information on the study's CI.

	Title:	Forename/Initials:	Surname:
	Dr	Maria	Saito Benz
Mailing Address:	Department of Paediatrics		
	University of Otago, Wellington		
	PO Box 7343		
Suburb/Town:	Wellington South		
Postcode:	6242		
Country:	New Zealand		
Organisation:	University of Otago, Wellington		
Department*:	Department of Paediatrics and Child Health		
Position:	PhD student		
E-mail:	maria_saito_benz@hotmail.com		
Phone (BH):	021570609		
Phone (AH)*:			
Mobile*:			
Fax:			

Other Investigator(s)

Other than the Co-ordinating Investigator, Investigators at all localities in a multi-centre intervention study must be listed as Investigators. Supervisors of student research must also be listed as Investigators.

You may list any other Investigators at your discretion.

a.3.2. Will any co-investigators be involved in conducting your study?

- (•) Yes
- ( ) No

a.3.2.1. *You should request authorisation from each Investigator in your study (using the "Authorisations" tab) once you have completed all questions in the Online Form.*

(For each co-investigator:)

Other CI 1

	Title:	Forename/Initials:	Surname:
	Dr	Max	Berry
Mailing Address:	Department of Paediatrics		
	University of Otago		
	PO Box 7343		
Suburb/Town:	Wellington South		
Postcode:	6242		
Country:	New Zealand		
Organisation:	University of Otago, Wellington		
Department*:	Department of Paediatrics and Child Health		
Position:	Senior lecturer		
E-mail:	max.berry@otago.ac.nz		
Phone (BH):	0212449929		
Phone (AH)*:			
Mobile*:			
Fax:			

Other CI 2

	Title:	Forename/Initials:	Surname:
	Professor	Dawn	Elder
Mailing Address:	Department of Paediatrics		
	University of Otago		
	PO Box 7343		
Suburb/Town:	Wellington South		
Postcode:	6242		
Country:	New Zealand		
Organisation:	University of Otago, Wellington		
Department*:	Department of Paediatrics and Child Health		
Position:	Head of Department of Paediatrics		
E-mail:	dawn.elder@otago.ac.nz		
Phone (BH):	+64 4 918 6145		
Phone (AH)*:			
Mobile*:	+64 21279 6140		

Fax:	+64 4 385 5898

Other CI 3

Title:	Forename/Initials:	Surname:
Dr.	Shieak	Tzeng

Mailing Address:	Centre for Translational Physiology
	University of Otago
	PO Box 7343
Suburb/Town:	Wellington South
Postcode:	6242
Country:	New Zealand
Organisation:	University of Otago
Department*:	Centre of Translational Physiology
Position:	Director
E-mail:	shieak.tzeng@otago.ac.nz
Phone (BH):	+64 4 806 1504
Phone (AH)*:	
Mobile*:	
Fax:	

a.4 Primary contact person

a.4.1. Are you the primary contact person for this study?

- (●) Yes
- ( ) No

Title:	Forename/Initials:	Surname:
Dr	Maria	Saito Benz

Mailing Address:	Department of Paediatrics
	University of Otago, Wellington
	PO Box 7343
Suburb/Town:	Wellington South
Postcode:	6242
Country:	New Zealand
Organisation:	University of Otago, Wellington
Department*:	Department of Paediatrics and Child Health
Position:	PhD student
E-mail:	maria_saito_benz@hotmail.com
Phone (BH):	021570609
Phone (AH)*:	
Mobile*:	
Fax:	

a.5 Sponsor

The sponsor has overall responsibility for the initiation, management, and financing arrangements of a study.

a.5.1. Which of the following best describe the sponsor(s) of your study?

- [ ] pharmaceutical company

- ☐ medical device company
- ☐ academic institution
- ☐ collaborative research group
- ☑ district health board (DHB)
- ☐ other government agency
- ☐ non-governmental organisation (NGO)
- ☐ other

- ☐ no sponsor

a.5.2. ***The sponsor(s) must authorise this application (through the "Authorisations" tab) before it can be submitted to an HDEC for review. You should request authorisation once you have completed all questions in the Online Form.***

Please provide the following details for your study's sponsor(s).

Sponsor 1

	Title:	Forename/Initials:	Surname:
	Ms	Marina	Dzhelali
Mailing Address:	Research Office		
	Capital and Coast DHB		
	Riddiford Street		
Suburb/Town:	Wellington		
Postcode:	6021		
Country:	New Zealand		
Organisation:	Capital and Coast DHB		
Department*:	Research Office		
Position:			
E-mail:	marina.dzhelali@dhb.org.nz		
Phone (BH):	644 918 5117		
Phone (AH)*:			
Mobile*:			
Fax:			

Sponsor 2

	Title:	Forename/Initials:	Surname:
Mailing Address:			
Suburb/Town:			
Postcode:			
Country:			
Organisation:			
Department*:			
Position:			
E-mail:			
Phone (BH):			
Phone (AH)*:			
Mobile*:			
Fax:			

Third party performing sponsor's duties or functions in New Zealand

a.5.3. Will a third party (such as a contract research organisation) perform one or more of the sponsor's duties or functions in relation to this study in New Zealand?

- ○ Yes
- ◉ No

a.6 Localities and participants

New Zealand

It is a standard condition of HDEC approval that locality authorisation be obtained (through the "Authorisations" tab) ***before a study commences at a locality****. This authorisation confirms that the locality has addressed research governance issues that may arise as a result of the study.*

However, locality authorisation ***does not*** *have to be obtained prior to submission of your application to an HDEC.*

Other organisations involved in studies may prefer or require that their involvement in studies be recorded as an authorisation. You should check with these organisations before proceeding with your study.

Contact details for DHB research offices are available here

a.6.1. At which type(s) of locality do you intend to conduct your study?

- ☑ district health board
- ☐ tertiary education institution
- ☐ primary health care centre
- ☐ private organisation
- ☐ other - please specify:

a.6.2. Approximately how many participants do you intend to recruit in New Zealand?

24

Other countries

a.6.3. Will your study also involve participants recruited in countries other than New Zealand?

- ○ Yes
- ◉ No

a.7 Prior review

a.7.1. Is this application related to one or more previous applications for HDEC review?

- ○ Yes
- ◉ No

a.7.2. Has an application for this study (or a substantially similar study) previously been declined approval by an HDEC in New Zealand?

- ○ Yes
- ◉ No

a.7.3. Has an application for this study (or a substantially similar study) previously been declined approval by an overseas ethics committee?

- ○ Yes
- ◉ No

a.8 Clinical trials of new medicines

a.9 Open/closed meeting

HDECs are public administrative bodies, and their meetings are open to the public. Your study may be reviewed in a closed meeting only if grounds may exist to withhold information about it under the Official Information Act 1982.

a.9.1. Do you want your application to be considered in a closed meeting?

- ○ Yes
- ◉ No

a.10 HDEC review preference

a.10.1. Please indicate your review preference.

- ○ I request that this application be reviewed **as soon as possible**.
  I understand that this may mean that this application is not reviewed by the HDEC nearest to the CI
- ◉ I request that this application be reviewed by the HDEC that meets **nearest to the CI.**

b.1 Research should be based around a clear study question that can produce benefits.

b.1.1. Briefly and in plain English, what is the principal study question (hypothesis) that your study will test?
You can refer to page numbers of your study's protocol for further detail if you need to.

[< 2000 characters]

We hypothesise the following:

1. Elective blood transfusion in anaemic neonates will result in improvements in tissue oxygenation in the brain, liver and muscle by at least 10%.
2. The improvements in tissue oxygenation in these organs will be sustained for 5 days after blood transfusion
3. Elective blood transfusion in anaemic neonates will result in improvements in the cardiorespiratory stability (i.e. heart rate, blood pressure, and peripheral arterial saturation)

b.1.2. Please briefly describe the scientific basis for your study (including, where appropriate, brief discussion of previous research).

You can refer to page numbers of your study's protocol for further detail if you need to.

[< 2000 characters]

Neonates have immature bone marrow and as a result have a slow rate of red blood cell production. This puts them at risk of developing anaemia if they are born premature ('Anaemia of Prematurity'), or have other co-morbidities which require them to have frequent blood sampling. Even if they appear asymptomatic, if left untreated, anaemia can slow down their growth and they may take longer to come off respiratory support such as CPAP and low flow oxygen.

It is generally accepted that anaemia in neonates should be treated electively with blood transfusion even if they appear clinically stable. However, the optimal threshold at which this should be performed is not fully understood [1], and as a result practice varies significantly between neonatal intensive care units (NICUs). In Wellington NICU, the transfusion guideline is adopted from the PINT study and is based on the haemoglobin count, postnatal age and requirement for respiratory support of each patient.

The primary function of red blood cell is to carry oxygen to vital organs. Therefore, it is plausible that those who would benefit from blood transfusion experience improvement in tissue oxygenation after elective blood transfusion. Seidel et al. showed that, using their haematocrit-based guideline, elective blood transfusion resulted in significant improvements in cerebral tissue oxygenation and episodes of peripheral desaturation in neonates[2]. Other studies have also showed a short-term (immediately post-transfusion and at 24hrs) improvement in tissue oxygenation in other organs such as kidney and small intestines.

References:
1. Whyte R, Kirpalani H. Low versus high haemoglobin concentration threshold for blood transfusion for preventing morbidity and mortality in very low birth weight infants. Cochrane Review 2011
2. Seidel D, Blaser A, Gebauer C, et al. Changes in regional tissue oxygenation saturation and desaturations after red blood cell transfusion in preterm infants

b.1.3. Please briefly explain how your study will contribute to new knowledge and improve health outcomes.

[< 2000 characters]

Previous studies have not examined whether:
1. Use of a more liberal transfusion guideline based on haemoglobin count result in a significant improvement in tissue oxygenation in vital organs
2. Such improvement can be sustained beyond 24hrs
3. Elective transfusion results in improved tissue oxygenation in muscle (which may be related to growth)

This study therefore aims to address these questions, and at the same time correlate these findings to cardiorespiratory stability of neonates before and after blood transfusion.

Better understanding of how elective blood transfusion confers benefits to anaemic neonates could facilitate development a more targeted transfusion guideline. Development of such guideline may enable clinicians to selectively give blood transfusion to those who are most likely to benefit from the treatment, and avoid giving transfusion to those who are less likely to benefit.

b.2 Research should be well-designed, so that it can answer the study question.

b.2.1. Please briefly describe and justify the design of your study.

[< 1200 characters]

This is a prospective, single-centre, observational study. Parental consent will be obtained before any data collection.

Patient characteristics collected as part of the study:
• Gestational/postnatal age
• Ethnicity
• Sex
• Birth weight /weight at time of transfusion
• Haemoglobin and Haematocrit count prior to transfusion

• Respiratory support
• Caffeine treatment

Tissue oxygenation in the brain, liver and muscle will be measured using a portable, non-invasive device, near-infrared spectroscopy (NIRS). Tissue oxygenation will be measured for 3hrs pre-, during and immediately post transfusion, and at 24hrs and 5 days post transfusion.

Cardiorespiratory stability will be measured using a Human NIBP and a pulse oximeter, both of which are portable and non-invasive. Heart rate, blood pressure and peripheral arterial saturation will be monitored for 12hrs prior to transfusion, during transfusion and again for 12hrs at 24hrs and 5 days post transfusion.

The study aims to recruit 24 infants, a sample size needed to detect a significant increase (10%) in brain oxygenation 24hrs post transfusion with 80% power using p-value of 0.05.

b.2.2. Please indicate whether peer review of the scientific and statistical quality of your study has been obtained from one or more of the following.

- [ ] the Standing Committee on Therapeutic Trials (SCOTT)
- [ ] the study's funder (e.g. the Health Research Council)
- [ ] the study's sponsor
- [x] experts within the research team
- [x] senior colleague(s) in the field
- [x] other

b.2.2.1. *Evidence of favourable peer review for this study must be uploaded in the "Documents" tab before submission to an HDEC.*

Please briefly describe the peer review process that has been carried out for your study.

[< 1200 characters]

The study protocol has been reviewed by the co-investigators and all consultant neonatologists in the Wellington neonatal intensive care unit. It has also been reviewed by a statistician, who assisted us in calculating the minimum sample size for the study.

b.3 Research should be conducted by an appropriate Principal Investigator, to ensure that the study protocol is respected and followed.

b.3.1. *A CV for the study's Co-ordinating Investigator must be uploaded in the "Documents" tab before submission to an HDEC.*

Please briefly summarise the Co-ordinating Investigator's qualifications and experience relating to conducting studies of this nature.

[< 1200 characters]

My most recent research experience is an observational clinical audit on the outcomes of extremely preterm infants in Wellington NICU. Under supervision of Dr Max Berry and Professor Dawn Elder, I assisted in designing of the study, collecting and analysing data, and manuscript preparation. Our manuscript titled 'Expectant management for periviable infants: A 10-year single-centre New Zealand perspective' has been submitted for publication to Journal of Paediatrics and Child Health and is currently under review. I have presented the findings at the 35th Annual Scientific Meeting of the Perinatal Society of New Zealand.

In 2010-11 I also designed and implemented my own observational study on the effect of HIV on diarrhoeal diseases in children in rural South Africa. I applied for and obtained a local ethics approval for the study. I presented my findings at the Royal College of Paediatrics and Child Health annual conference in Glasgow, UK, and also won the First Prize in Trainees' oral presentation at the Wessex Regional Paediatric Meeting at the University of Southampton, UK.

b.4 Where possible, research should generate material that is useful for future research.

Reporting and dissemination of results

b.4.1. How do you intend to report or disseminate the results of your study?

- [x] article(s) in peer-reviewed scientific journals
- [x] internal reports
- [x] conference presentations
- [ ] publication on website
- [ ] other publications
- [ ] submission to regulatory authorities (e.g. Medsafe, TGA, FDA, EMA)
- [ ] other
- [ ] no plans to report or disseminate results

b.4.2. Will any restrictions be placed (for example, by your study's sponsor or funder) on the publication of the results of your study?

- ○ Yes
- ◉ No

Future research using data generated in your study

b.4.4.

Might data generated in your study be made available for use in future research?

- ◉ Yes
- ○ No

b.4.4.1. *You should explain this clearly to potential participants.*

Which of the following best describes the form in which data generated by your study might be made available to other researchers?

- ○ identified
- ○ potentially identifiable
- ○ partially de-identified
- ○ de-identified
- ◉ anonymous
- ○ other – describe:

r.1 Risk of physical harm to participants

r.1.1. Briefly and in plain English, please describe:

- the procedures to be undertaken by participants in your study, and
- any risks associated with these procedures that potential participants may reasonably wish to be informed of.

Do not *describe procedures that will be undertaken as part of normal clinical care regardless of participation in your study, or the risks of such procedures.*

[< 2500 characters]

There is no invasive procedure to be performed to any of the participants in this study.

Following non-invasive equipment will be used as part of this study:

1. Near infrared spectroscopy (NIRS): Small (55mm x 30mm) NIRS probes (Nonin Equanox Advance Neonatal/Pediatric 9004CB) will be placed on skin overlying frontal lobe of the brain, liver and a limb muscle (gastrocnemius unless there is a clinical reason to use a different position). Non-adhesive neonatal probes will be used, and they have the advantage of being soft and flat to avoid any pressure-related injury. Each probe has two LED light emitters and two receivers built in. The probes will be connected to one portable bedside NIRS machine.

2. Pulse oximeter: MassimoRadical8TM will be used and a pulse oximeter probe will be attached to a hand, wrist, or foot.

3. Continuous blood pressure monitor: Human NIBP SetTM will be used to measure blood pressure non-invasively and continuously. A soft blood pressure cuff will be placed on the wrist and the cuff will be connected to a portable bedside device.

NIRS and pulse oximeter are used safely for preterm and term neonates in both clinical and research settings. Human NIBP Set has been used safely for preterm and term neonates in research setting.

We do not anticipate any significant risks with the use of these equipment. However, we will be informing parents of potential participants that due to multiple probes being attached, taking participating infants out of their cots for cuddle, particularly during NIRS data recording, will be more clumsy compared to usual.

We anticipate that the majority of our study cohort will be long-term patients in Wellington NICU (i.e. preterm infants, or infants with significant surgical condition) Enrollment in the study is therefore unlikely to prolong their inpatient stay. However, if the attending clinicians decide that a study participant is ready for discharge prior to completion of data collection, remaining data collection will be abandoned to ensure timely discharge.

r.1.2. Will you seek consent from participants to inform health practitioners with responsibility for their health care that they are taking part in your study?

(•) Yes ( ) No

r.1.3. Will your study involve withholding standard treatment from participants?

( ) Yes (•) No

Compensation for injury to participants

r.1.7. Will any participants seek or be given treatment by or at the direction of a registered health professional (as defined in the Accident Compensation Act 2001) as part of your intervention study?

( ) Yes (•) No

Ionising radiation not needed for normal clinical management

r.1.13. Will your study involve the administration of ionising radiation that is not needed for participants' normal clinical management?

◯ Yes ◉ No

r.2 Risk of breach of privacy and confidentiality

Before the study

r.2.1. Will your study involve reviewing or screening health information, for example in order to identify potential participants?

The term "health information" is defined in the Health Information Privacy Code

◉ Yes ◯ No

r.2.1.1. Please briefly explain how you will ensure the confidentiality of this health information before the study.

[< 600 characters]

To identify potential participants, I will verbally discuss with clinicians in Wellington NICU whether any patients are receiving elective blood transfusion. There will be no written documentation of the potential participants, and I will be responsible for ensuring the confidentiality of this information.

During the study

r.2.2. During your study, who will have access to health information used in your study?

[< 600 characters]

Myself (CI) and co-investigators.

r.2.3. Please briefly explain how you will ensure the confidentiality of this health information during the study.

[< 600 characters]

All health information will be recorded using Research Electronic Data Capture (REDCap) application, a secure online database system specifically designed to support handling of confidential information in research studies.

r.2.3.1. Will your study involve the use of surveys or questionnaires?

◯ Yes ◉ No

After the study

r.2.4. Which of the following best describes the form in which data generated in your study will be stored after the study has finished?

◯ identified
◯ potentially identifiable
◯ partially de-identified
◯ de-identified
◉ anonymous
◯ other – describe:

r.2.4.1. Please briefly explain your answer above.

[< 600 characters]

Study number will be assigned to every participant recruited. All health information will be stored securely in a Research Electronic Data Capture (REDCap) application anonymously with only the study numbers as their identifier.

r.2.5. *The Health (Retention of Health Information) Regulations 1996 require that **some** health information be retained for a period of ten years.*

For how long will health information generated in your study be stored?
[< 600 characters]

Until participants are 16 years old.

Publication of results

r.2.6. Will the results of your study be published in a form that identifies (or could reasonably be expected to identify) individual participants?

○ Yes ◉ No

r.3 Risks associated with the use of human tissue

r.4 Risk of unexpected clinically significant findings

r.4.1. Might any aspect of your study produce findings that may be both unexpected and clinically significant for participants, donors of existing stored human tissue, or their families?

○ Yes ◉ No

r.5 Risk of potential conflict of interest

Funding and remuneration

r.5.1. Please briefly describe the main source(s) of funding for your study.

[< 600 characters]

All equipment necessary for the investigation are already available from the Department of Paediatrics, University of Otago. CI is funded to do full-time research by the Freemasons (NZ).

r.5.2. Does the Co-ordinating Investigator, any Co-Investigator, or any direct member of their families have any commercial interest in the intervention(s) to be studied, or any financial relationship to the study sponsor or funder(s), that may inappropriately influence his or her conduct in the study?

○ Yes ◉ No

r.5.3. Will the Co-ordinating Investigator or any Co-Investigator be remunerated for their involvement in the study in a way that may inappropriately influence his or her conduct in the study (for instance, bonuses for favourable results or high recruitment rates)?

○ Yes ◉ No

Health or disability support service providers

r.5.4. Will the Co-ordinating Investigator or any Co-Investigator also be the usual health or disability support service provider for one or more participants in your study?

(•) Yes ( ) No

r.5.4.1. Please briefly describe how the risk of a conflict of interest between the research and clinical roles of such Investigators will be minimised and managed.

[< 600 characters]

Dr Saito-Benz (Co-ordinating investigator) will be a full-time researcher for the duration of the study, and will be in charge of recruitment and data collection.

Dr Berry (co-investigator) is a part-time neonatologist in Wellington NICU and she will be regularly looking after patients who are recruited in the study. However, her role in the study will be primarily to supervise and to assist with data interpretation.

Professor Elder and Dr Tzeng do not have a clinical responsibility in Wellington NICU.

r.5.5. Will the usual health or disability service provider for one or more participants in your study receive any remuneration (or any other valuable consideration) for referring potential participants to the research team in your study?

( ) Yes (•) No

Other potential conflicts of interest

r.5.6. Please briefly describe any other potential conflicts of interest that may arise for researchers in your study, and describe how they will be minimised and managed.

[< 600 characters]

There is no potential conflict of interest in this study.

r.6 Risk of stigmatisation

r.6.1. Please briefly indicate whether the results of your study may risk stigmatising individuals or population groups, and if so, how this risk will be minimised and managed.

[< 600 characters]

The results of our study is extremely unlikely to stigmatise individuals or population groups, as elective blood transfusion for anaemic neonates is a well recognised, standard treatment in neonatal intensive care units across the world.

r.7 Risks to researchers and third parties

r.7.1. Please briefly indicate whether your study may pose any significant risks to researchers and/or third parties, and briefly explain how such risks will be minimised and managed.

[< 600 characters]

Extra monitoring for study participants may potentially increase workload for nursing staff. To minimise the additional workload, the coordinating investigator will be available on-site at all time for trouble-shooting and data collection. Extra training opportunities have been provided for nursing staff, and the study has been approved by the charge nurse manager in Wellington NICU.

r.8 Summary: the risks of research should be proportional to its expected benefits.

r.8.1. Please briefly explain why you consider the risks of your study to be proportional to its expected benefits.

[< 1200 characters]

This study is not expected to have any direct risk or benefit to the participants.

Participants should consent to their participation in research.

p.1.1. Briefly and in plain English, please describe what taking part in your study will involve for participants.

[< 1200 characters]

Participants' parents will be approached for enrollment in the study prior to elective blood transfusion.

Once consent is obtained, participants will be monitored overnight (approximately 6pm-6am) using a pulse oximeter (a probe on hand or foot) and Human NIBP (blood pressure cuffs on wrists) prior to elective blood transfusion the following morning.

Around 3am three NIRS probes will be placed, one on forehead, one on abdomen, and one on a leg or an arm.

Around 6am when pre-transfusion data recording is completed, blood transfusion transfusion will be given. During this period and for 3hrs post transfusion, NIRS data recording will continue. NIRS probes will be removed at 3hrs post transfusion.

Pulse oximeter and blood pressure recording will be continued during transfusion and 12hrs after transfusion. All study monitors will be removed at 12hrs post transfusion.

NIRS, pulse oximeter and plethysmograph will be connected again approximately 24hrs and 5 days post transfusion (NIRS for 3hrs and the other two devices for 12hrs).

p.1.2. Will **all** participants in your study give their informed consent to participate?

- (•) yes, all participants will give informed consent
- ( ) no, one or more participants will not give informed consent

p.1.9. Will informed consent be recorded in writing?

(•) Yes ( ) No

Consent should be informed by adequate understanding of relevant information.

p.2.1. Briefly explain the process by which potential participants in your study will be provided with information on the study, have the opportunity to ask questions, and asked to give their informed consent.

[< 1200 characters]

The parents of potential participants will be identified based on the trend of haemoglobin count in a few days leading up to elective transfusion. I will arrange to meet them in person on the Neonatal Unit and explain about the study. They will be provided with a written information sheet and an opportunity to ask questions at this stage. A signed consent form will be collected by myself prior to start of data collection, and parents will be given a further opportunity to ask questions then.

p.2.2. A **generic** version of the participant information sheet and consent form (PIS/CF) that you will provide to potential participants must be uploaded in the "Documents" tab before submission to an HDEC. You don't need to submit information sheets specific to each study locality.
A suggested pro forma for your PIS/CF can be found here.

p.2.3. How have you checked that the participant information sheet is appropriate for your study population?

[< 600 characters]

The participant information sheet has been proof-read by two parents without any medical background, whose children had previously been on the neonatal intensive care unit.

p.2.4. How many words does your participant information sheet contain?

1999

p.2.5. What is the Flesch Reading Ease Score for your participant infornation sheet?
You can use Microsoft Word to calculate this score.
While there are no hard and fast rules for the readability of information sheets, a score of 65 or above usually indicates that a document is written in plain English.

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Withholding or concealing information from participants

p.2.6. Does your study involve deliberately withholding or concealing information from participants?
Blinding procedures in randomised controlled trials are not normally considered to involve withholding or concealing information from participants.

○ Yes ◉ No

Information that becomes available during the study and that may be relevant to continued participation

p.2.7. How will you ensure that participants receive information that becomes available during the study and that may be relevant to their continued participation?

[< 1200 characters]

As this is a non-invasive observational study, and because the optimal range of tissue oxygenation in neonates is not fully understood yet, it is unlikely that results of this study will affect their continued participation. However, if any unanticipated, untoward effect from the use of monitoring devices were to occur then CI (myself) would communicate this immediately to all participants (past, present and future).

Information about the results of the study

p.2.8. Will you inform participants of the results of your study?

◉ Yes ○ No

p.2.9. Please *either* explain how you will inform participants or explain why you do not intend to do so.

[< 600 characters]

Parents of participants, if they wish, will be provided with a written lay summary of the study findings. The written lay summary will be prepared by the CI (myself) after data collection is completed for the study. Parents will also be informed of any publication based on the study.

Consent should be voluntary.

p.3.1. *Generic copies of any advertising that you intend to use to encourage potential participants to take part in your study must be uploaded in the "Documents" tab before submission to an HDEC.*
Please explain how potential participants will be identified and approached in a way that ensures they can give informed consent free from undue influence.

[< 1200 characters]

Potential participants will be identified through daily communication with the clinical team whether any of their patients are likely to receive elective blood transfusion in the next few days (i.e. their haemoglobin count is trending towards the guideline threshold). I (CI) will then arrange to meet with parents of potential participants on the neonatal unit as they come in to do daily care for their infants. To avoid undue influence, I (CI) will be taking consent from the parents as I will be a full-time researcher for the duration of the study and I will not be a regular clinician looking after their infants.

It will be emphasised to the parents that whether they take part in the study or will have no bearing on the clinical care that their infants will receive. As this is an observational study, it will also be explained to them that taking part in the study will not directly benefit their infants.

To raise awareness about the study, a poster will be placed in the parents' communal room in Wellington NICU and also in Ronald McDonald House (accommodation for parents).

Potentially vulnerable people

p.3.2. Will your study involve potentially vulnerable people – that is, people who may have a restricted ability to make independent decisions about their participation?

◉ Yes ○ No

p.3.2.1. Please explain how your study's informed consent process takes the needs of these potentially vulnerable people into account.

[< 600 characters]

Neonates cannot give consent. Informed consent will therefore be sought from parents, or caregivers with a parental right, of potential participants. Informed consent will be obtained by CI (myself) who will be a full-time researcher and not a regular clinician of the potential participants.

p.3.2.2. Will informed assent also be sought from people responsible for the welfare of potentially vulnerable people involved in your study?

◉ Yes ○ No

p.3.2.2.2. *A **generic** version of the information sheet that will be provided to people interested in or responsible for the welfare of potentially vulnerable people involved in your study must be uploaded in the "Documents" tab before submission to an HDEC. You don't need to submit information sheets specific to each study locality.*

Please explain how informed assent will be obtained.

[< 600 characters]

Participants' information sheet will be available to parents as well as to those who are interested in or responsible for the welfare of potential participants. An opportunity for questions will also be provided to them.

Inducements

p.3.3. Will participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in your study?

○ Yes ◉ No

P.4 Population groups, particularly Māori, should be consulted in the design and conduct of research that is of relevance to them.

Consultation with Māori

p.4.1. Please describe whether and how your study may benefit Māori.

[< 1200 characters]

According to our local audit data, Māori infants are over-represented in Wellington NICU. Māori infants account for 35% of extreme premature births despite representing only 13% of total birth (ref the PSNZ presentation). Preterm infants are particularly at risk of anaemia because of their immature bone marrow, and as a result they frequently require elective blood transfusion.

This study aims to improve understanding of how elective blood transfusion benefits neonates, with the intention that this knowledge would help us develop a more individualised, evidence-based treatment guideline for elective blood transfusion in NICUs. Such guideline would benefit all infants, but particularly Māori infants who form a significant proportion of NICU inpatients.

p.4.2. Please identify the main cultural issues that may arise for Māori who may participate in your study, and explain how these issues will be managed.

If Māori will be excluded from participating, please state this. You will be asked to explain your inclusion/exclusion criteria in the next section of the Form.

[< 1200 characters]

Whilst most parents welcome the opportunity to participate in observational studies, this study involves non-standard physiological monitoring that could affect our recruitment rates, particularly of Māori where the head is considered tapu (sacred). To optimise recruitment we are working with Capital & Coast DHB Research Advisory Groups for Māori and their advice will be incorporated into the study. We also have a long-standing clinical relationship with Wellington hospitals' Whanau care services, which provide cultural advocacy and support for whanau and families with infants requiring NICU care. We are working with them to develop recruitment strategies to mitigate any systemic recruitment barriers.

p.4.3. According to the Health Research Council's Guidelines for Researchers on Health Research Involving Māori, is formal consultation with Māori required for your study?

(•) Yes ( ) No

p.4.3.1. Please either describe your study's consultation process, or explain why you do not consider that formal consultation with Māori is required.

[< 1200 characters]

One of our overarching objectives is to help achieve equitable health status between Māori and non-Māori. In accord with Otago University's policy for Research Consultation with Māori, we will submit the proposal to the Ngäi Tahu Research Consultation Committee and all recommendations will be incorporated.

p.4.4. Does your study involve kaupapa Māori research methodologies?

( ) Yes (•) No

Consultation with other relevant population groups

p.4.5. Will any other population groups be specifically targeted for recruitment into your study?

( ) Yes (•) No

Collection of ethnicity status

p.4.6. Will participants' ethnicity status be collected as part of your study?

(•) Yes ( ) No

f.1 Where possible, research should reduce health inequalities.

f.1.1. Might your intervention study contribute to reducing inequalities in health outcomes between different populations, and particularly between Māori, Pacific peoples and other New Zealanders?

( ) Yes (•) No

f.1.2. Please explain your answer above.

[< 1200 characters]

This is an observational study and not an intervention study.

f.2 Participants and non-participants should be treated fairly compared to each other

Inclusion and exclusion criteria

f.2.1. Please briefly describe the inclusion and exclusion criteria for your study.
You can refer to page numbers of your study's protocol where further detail is required.

[< 2000 characters]

Infants will be considered for recruitment into the study if the clinical team in Wellington NICU makes a decision to give elective (non-urgent) red blood cell transfusion to inpatients in Wellington NICU.

Patients with following criteria will be excluded from the study if:
1. Urgent blood transfusion is required
2. Mechanically ventilated at the time of transfusion
3. Undergoing treatment for systemic infection with broad spectrum antibiotics
4. Receiving medical treatment or are awaiting surgery for a haemodynamically significant patent ductus arteriosus (PDA)
5. Significantly oedematous

Exclusion criteria 1 and 2 are to ensure that unwell neonates receive blood transfusion without any delay.

Criteria 3 and 4 are to ensure that other conditions known to affect tissue perfusion and/or tissue oxygen consumption in neonates (i.e. systemic infection and haemodynamically significant PDA) do not interfere with the effect of blood transfusion on tissue oxygenation.

Criterion 5 is to ensure that the tissue oxygenation measured using NIRS reflects tissue oxygenation of the organs of interest instead of oedematous cutaneous tissue.

f.2.2. Please explain how these inclusion and exclusion criteria ensure that the risks and benefits of your study are distributed fairly.

[< 1200 characters]

As this is an observational study using non-invasive monitoring devices, we do not anticipate any direct benefit or risk to the participants.

Placebo-controlled Studies

f.2.3. Does your study involve the use of placebo?

○ Yes ◉ No

Impact on health and disability support service provision

f.2.4. Might your study adversely impact on the provision of health and disability services?

○ Yes ◉ No

f.3 Different groups of participants should be treated fairly compared to each other