PROTOCOL

Intervention study of children at high risk of chronic lung disease

Principal Investigators:
Dr Adrian Trenholme (CMDHB) and Dr Catherine Byrnes (Starship Children's Health)

Version: 5

Date: 17th April 2013

PROTOCOL SYNOPSIS

The following synopsis is provided as an overview of the study.

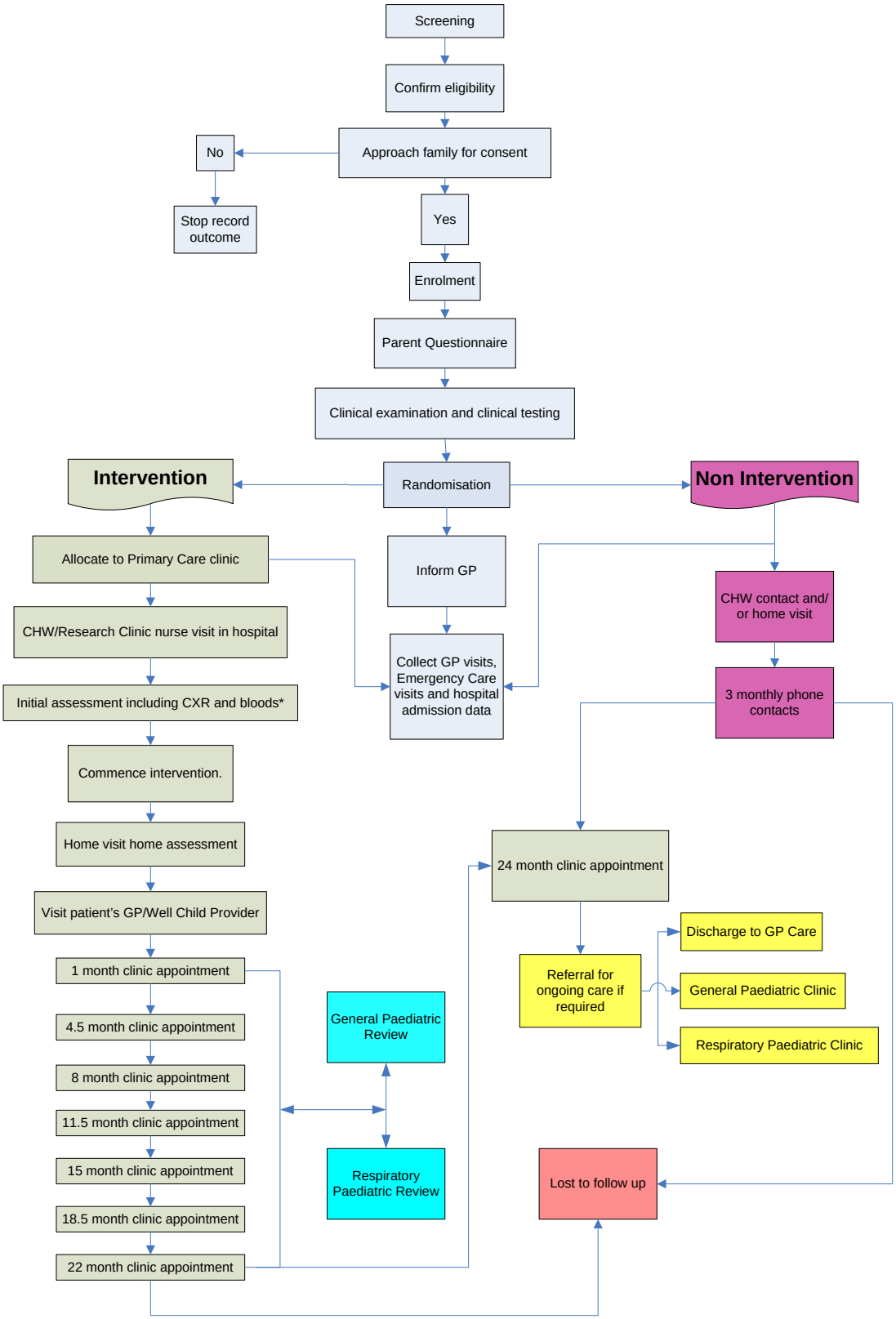
Name of Sponsor:	Health Research Council (HRC)	*(For National Authority Use Only)*
Title of Study:	Intervention study of children at high risk of chronic lung disease	
Principal Investigator(s):	Dr Adrian Trenholme and Dr Catherine Byrnes	
Co Investigators	Dr Harley Aish Karen Hoare Dr Dinny Lennon William Leung Mr Henare Mason Charissa McBride Dr Russell Metcalfe Joanna Stewart	
Aims:	To reduce respiratory morbidity in the predominantly Māori and Pacific children of South Auckland (SA) which develops subsequent to an admission for severe lower respiratory infection (LRI) by adapting the model of care employed for children with CF.	
Study Design		
Background:	Lower respiratory infection (LRI) is a significant problem for NZ children and the proposed intervention is a programme of change with regular clinical follow-up combining two approaches that have been successful in other areas.	
Participants:	Children <2 years age admitted to SA with ***severe*** LRI (pneumonia and/or bronchiolitis - admission ≥4 days and/or supplemental oxygen for > 36 hours and/or admission to Intensive care unit, and/or consolidation on CXR), and/or admitted ≥6 days over 3 a month period between 1st Aug 2010 & 31st Oct 2012.	
Design:	A randomised controlled study enrolling 400 children to either 'intervention' or 'control' groups. All children will have an initial assessment during the index admission and will complete a 24 month final outcome visit with clinical assessment, standard questionnaire, examination, CXR, upper airway or sputum cultures.	
Methodology:	A randomised controlled study enrolling 400 children to either 'intervention' or 'control' groups. All children will have an initial assessment during the index admission and will complete a 24 month final outcome visit with clinical assessment, standard questionnaire, examination, CXR, upper airway or sputum cultures.	
Number of Subjects:	400 participants – 200 randomised to the intervention group and 200 in the control group.	
Inclusion Criteria:	Children <2 years age admitted to SA with ***severe*** LRI (pneumonia and/or bronchiolitis - admission ≥4 days and/or supplemental oxygen for > 48 hours and/or admission to Intensive care unit, and/or consolidation on CXR) between 1st Aug 2010 & 31st Oct 2012.	

Exclusion Criteria:	Exclusions: • Children with more than two prior admissions to hospital with severe LRI as defined by study eligibility criteria • Prematurity <32 weeks gestation • Children with a diagnosis of chronic lung disease • Children known to have chronic health problems of clinical significance affecting daily life: o cardiovascular o neurological o immunodeficiency o multiple congenital abnormalities o enteral feeding
Intervention:	The intervention programme is based on the CF model of care for early childhood with regular clinic review for any deviation from normal health and to institute early treatment and/or preventative care. Reviews will be undertaken as a minimum at ,1, 4.5, 8, 12, 15, 18, 22 and 24 months after the day 0 assessment and as required in one of four community centres (Otara, Mangere, Manurewa, Pukekohe) staffed by the nominated general practitioner (GP) or nurse practitioner and practice nurse. Any child with ongoing respiratory problems will be referred to the Paediatrician clinic for further management and immediate discussion/transfer to paediatric respiratory specialist care as needed. Co-ordination will be undertaken by the study respiratory nurse who will attend all clinics and will undertake follow up in the community of any non-attenders.
Control:	The families will receive the current 'usual care' which is GP review for family directed health concerns with re-referral to paediatric services as necessary. These families will be followed up with a three monthly phone call to ensure contact details are maintained, a home visit prior to the 24 month clinic may be necessary if phone contact is unsuccessful.
Duration of Treatment:	24 month follow-up is required for participants in both study groups.
Assessments / Study Procedures	See the attached Schedule of Assessments for details of the assessments to be conducted at each study visit.
Study Endpoints: **Primary:**	Evidence of respiratory morbidity at 24 month follow up during a time of stability, as assessed by: • Abnormal CXR Brasfield score of ≤ 22/25 (25/25 = normal). • And/or abnormal clinical examination (defined as clubbing and/or MCIC and/or crackles on auscultation).
Secondary:	• Readmissions with LRI, medically attended LRI/wheezing episodes/asthma diagnosis • All CXR changes

- Bx on HRCT if indicated
- Nasal swab/sputum cultures
- Estimation of direct health costs of intervention
- CMC on history (defined as daily moist cough for >3 months or 3 or more episodes of moist cough for > 1 month).

Health Economic Sub-study:	95% confidence intervals for incremental cost-effectiveness ratios and cost-effectiveness acceptability curves will be calculated for endpoints to compare the intervention with usual care. Only direct costs of health care will be included.
Statistical Methods:	**Sample Size Determinations:** 400 children will be randomised 1:1 to intervention and control groups. Assuming 80% retention, 160 per group will be available at 2 year follow up. Note that this retention has been demonstrated in our previous SA studies[33,42]. With this sample size and assuming 40% of the controls have chronic respiratory symptoms (less than seen in the one year follow up study) there will be 91% power to detect a 50% reduction at the 1% level of significance (i.e. 20% of the intervention group having chronic respiratory symptoms). There will be 80% power to detect 45% reduction, at the 1% level. Should the rate in the control group only be 30%, there will still be 90% power to detect a 50% reduction at the 5% level of significance. The SA area includes 113,000 children< 15 years of age including 26% Maori and 29% Pacific with 71% of children living in the lowest socioeconomic quintile[35] **Analysis:** The primary hypothesis of a difference in chronic respiratory morbidity at 24 months post index hospital admission between the intervention and control groups will be tested using logistic regression with chronic respiratory morbidity, present or absent as the outcome and age, ethnicity, deprivation index, and group as explanatory variables. The "intention to treat" population will be used for all those completing the 24 month follow up. A further exploratory analysis will be done including the interactions of the other variables with group to ensure there is no evidence indicating the possibility of a differential effect of the intervention. Other outcomes will be investigated with the same explanatory variables using binary or ordinal logistic regression or linear regression, depending on the distribution of the variable.

Intervention Study of Children at High Risk of Chronic Lung Disease



STUDY PROCEDURES: Schedule of Assessments – Intervention Group

Procedure	Screening and Enrolment	Visit 1 (Month 1) [b]	Visit 2 (Month 4.5) [b]	Visit 3 (Month 8) [b]	Visit 4 (Month 11.5) [b]	Visit 5 (Month 15) [b]	Visit 6 (Month 18.5) [b]	Visit 7 (Month 22) [b]	Final Visit (Month 24)
Medical Assessment	X	X	X	X	X	X	X	X	X
Medical Treatment	X	X	X	X	X	X	X	X	X
Social/Housing Assessment	X	X[d]	X[d]	X[d]	X[d]	X[d]	X[d]	X[d]	
Immunisation		X[d]	X[d]	X[d]	X[d]	X[d]	X[d]	X[d]	
Education		X	X	X	X	X	X	X	
Chest Physio therapy		X[d]	X[d]	X[d]	X[d]	X[d]	X[d]	X[d]	
Smoking Cessation		X[d]	X[d]	X[d]	X[d]	X[d]	X[d]	X[d]	
Nutritional Assessment		X	X	X	X	X	X	X	X
Dental Review		X	X	X	X	X	X	X	X
Treatment Follow-up		X	X	X	X	X	X	X	
Blood test		X[a]							X[e]
Nasopharyngeal Swab									X[f]
Chest X-ray	X[a]	X[c]	X[c]	X[c]	X[c]	X[c]	X[c]	X[c]	X[c]
Collect GP, ED and hospital visits	X	X	X	X	X	X	X	X	

a. If not already taken as part of routine care while in hospital.
b. If concerns are raised during routine visit child/whanau may be brought back earlier for assessment of intervention effect. This will be decided by attending physician. At anytime discussion with or a referral to the general paediatrician or respiratory paediatrician depending on need can occur.
c. If the child is symptomatic at this visit delay clearance chest x-ray until stable/or clinically indicated – decision by attending physician.
d. As required
e. Blood sample taken for both immediate testing for iron, full blood count and storage for later Vitamin D and IgE testing.
f. Nasopharyngeal Swab sample to be stored for later virus and bacteria testing,

STUDY PROCEDURES: Schedule of Assessments – Non Intervention Group

Procedure	Screening and Enrolment	Visit 1 (Month 1)	Visit 2 (Month 4.5)	Visit 3 (Month 8)	Visit 4 (Month 11.5)	Visit 5 (Month 15)	Visit 6 (Month 18.5)	Visit 7 (Month 22)	Final Visit (Month 24)
Medical Assessment	X								X
Medical Treatment									X
Blood test									X[e]
Nasopharyngeal Swab									X[f]
Chest X-ray									X
Phone contact by CHW and/or Research Nurse		X	X	X	X	X	X	X	
Collect GP, ED and hospital visits	X	X	X	X	X	X	X	X	

e. Blood sample taken for both immediate testing for iron, full blood count and storage for later Vitamin D and IgE testing.
f. Nasopharyngeal Swab sample to be stored for later virus and bacteria testing,

Study Background:

Lower respiratory infection (LRI) is a significant problem for NZ children and the proposed intervention is a programme of change with regular clinical follow-up combining two approaches that have been successful in other areas, firstly early intervention in children with cystic fibrosis (CF) internationally and secondly community based care in adults with chronic lung disease in South Auckland (SA). This type of randomised interventional study has never been previously undertaken. It will provide health benefit whilst determining the feasibility of instituting a new health care delivery model in the community and also collecting informative data for this disadvantaged population within the next five years.

LRI admission for NZ children: The NZ rate of hospital admissions for LRI (predominantly bronchiolitis or pneumonia) from 1996 to 2006 was 10.9/1000 for children <15 years, and for SA was 18.3/1000 - both very high by international standards[1]. In the < 2 year age group admissions for LRI are 103/1000 nationally but are again higher in SA at 177/1000. The relative risk of admission for LRI is 1 European, 5.2 Pacific and 2.9 Māori, in addition there was a 4.9 relative risk for those in the lowest socioeconomic quintile. When compared to population studies in the US and UK, this is an increase of 2.5 x overall, 4.5 x for Pacific, 3.5 x for Māori, and 4 x for those in decile 10 [2,3,4,5,6,7]. In 2000-2004 respiratory diseases in Māori children were the first to third most common reason for admission to hospital in the age groups <1year age, 1-4 years age, 5-14 years age, 15-24 years age[8]. Admission rates for LRI in the early age groups are also increasing over time and increasing in severity i.e. not associated with an increased admission of less severe disease. Bronchiolitis admissions increased 118% over a decade (1988-1998), accompanied by an increase in severity; from 25% requiring any support to 59% requiring oxygen, 21% nasogastric fluids, 22% intravenous fluids, 8% admitted with apnoea and 3.1% requiring ventilation[9]. Pneumonia also had an annual increase of 5% over 7 years (to 1995) with increased severity and again admissions were skewed towards the younger age group[10]. In the Pacific Island Family Study following 1398 children has shown that breathing problems (cough and wheeze) are the most frequent symptoms complained of by Pacific parents[11,12]. Elliot et al in 1971 surveyed 2143 pre-school Rarotongan children performing a chest x-ray (CXR) on every third child with abnormalities seen in 37% and peak age of abnormality 24 months[13].

Progression from LRI to Chronic moist cough (CMC), Chronic suppurative lung disease (CSLD) and Bronchiectasis (Bx): While the exact pathway from LRI to persistent and chronic respiratory symptoms and ultimately irreversible lung disease is not yet understood, cohort studies of Alaskan and Australian Aboriginal children have clearly demonstrated that early admission to hospital with severe LRI is strongly linked to later development of CSLD/Bx[14,15]. A follow-up study of Alaskan children subsequent to hospital admission with RSV bronchiolitis or pneumonia < 3years age demonstrated 46% with productive cough, 22% with chronic bronchitis and 10% with Bx at age 5 years. The relative risks were 3.9 if their CXR had shown parenchymal densities and 3.0 if there were persistent parenchymal densities for great than 6 months. A case control study of Aboriginal children in Australia demonstrated that a history of hospitalised pneumonia gave an odds ratio of 15.2 for developing Bx. Two studies have described the high rates of Bx in NZ children with 80% being Māori and/or Pacifica[16,17]. A prospective national surveillance study for all new cases diagnosed in 2001-2003 describe an incidence of 3.7 per 100,000 which is 3-18 times higher than described in other western countries[18,19] If all the children live to 15 years, this gives a prevalence of 1 in 3,000 overall, but 1 in 1700 in Māori and 1 in 650 in Pacifica. This means that the incidence in Pacifica is four times more common that CF in the general NZ population. The disease is more severe in our population than any other populations described with 81% bilateral disease and 64% having 4 or more lobes involved[20]. Ethnicity and deprivation are also strongly linked to morbidity and premature mortality for Bx in the SA adult population[21,22]. In both our NZ paediatric studies, the first hospital admission for respiratory disease had occurred 4 years prior, and mean duration of CMC 2 years prior to the

diagnosis[16,17,20]. Despite extensive investigation only 10% had a specific underlying immune problem, again a smaller percentage than any other population described. It is therefore increasingly realised that a proportion of children progress from early, severe LRI to CMC, CSLD and/or Bx[23,24,25]. While we currently have trials of management underway to treat children with Bx, prevention of irreversible disease should be possible[26,27]. This has been the subject of a recent Thoracic Society of Australia and New Zealand task force in 2009 with the recommendations to be published[28].

Cystic Fibrosis Model of Care: CF is a genetically determined disease seen predominantly in European populations which also results in repeated and progressive lung disease. An increasing life expectancy with reduced respiratory and nutritional morbidity has already been achieved in children with CF using a clinical model of care with regular review from infancy, early detection of deviation from normal health and early intervention to prevent ongoing disease this has now been published as "Standards of Care" [29,39,31,32]. Leading research groups (NZ, Australia, Alaska, UK)[24,26,27,] have recommended a CF style approach for non-CF Bx, but this is already too late to prevent the actual disease. *We believe that by commencing this early intervention programme when the risk factors for developing the disease rather than the disease itself appears* we will prevent respiratory morbidity and irreversible disease. This also requires taking the model outside of the specialised hospital clinics in which it is currently practised and basing it in the community[29,30]. We have the at risk population within a geographically constrained area, with known high end-disease prevalence of greater severity than those in other areas (suggesting under-estimation), and the connected multi-disciplinary team with which to conduct this research. This has been confirmed by our pilot study.

LRI follow up study of SA children: We conducted a prospective epidemiology study of LRI in children hospitalised in SA from August to December 2007 and found that 223 of 489 had a discharge diagnosis of pneumonia or severe bronchiolitis as defined for this application[33]. These were approached in order of enrolment for one year follow up. The first 130 were contacted and 94 (with a demographic profile the same as the study group overall) were able to be seen with a clinical review, examination, questionnaire and CXR. We found 50% had a significantly abnormal CXR, 30% had CMC and 30% had moist cough in clinic (MCIC) with only 20% well. In summary two thirds had evidence of continuing respiratory morbidity with one or more of these abnormalities 12 months after the index event of hospital admission even when reviewed at a time of stability.

Study Timelines

This study has a 24 month follow-up for all children enrolled. Allowing for recruitment of suitable participants the study is due to proceed for 48 months.

Study Sites

This study will be conducted at four community centres in the Counties-Manukau catchment area – Otara, Mangere, Manurewa and Pukekohe.

Research activities will be centrally coordinated by the study team at Kidz First Childrens Hospital.

Ethical Requirements and Annual Reporting

Ethical approval has been received from Northern X regional ethics committee (reference NTX/10/09/094) An annual report will be provided to the ethics committee and the Health Research Council.

Adverse Events and Serious Adverse Events

As this study is assessing two methods of providing care rather than specific drug interventions we do not envisage the programme will create adverse or serious adverse events however, all adverse experiences either observed by the investigator or one study staff, or reported by the patient's parents/guardians spontaneously or in response to a direct question, that occur during the study period or a need for a change in therapy, will be evaluated by the investigator and noted in the study file. Events after the study period also thought to be due to a study intervention will be included.

A serious adverse event (SAE) is generally defined as any event that is fatal, life-threatening, permanently disabling, incapacitating or results in hospitalisation, prolongs a hospital stay or is associated with congenital abnormality, carcinoma or overdose.
Serious adverse events:
For this trial, serious adverse events are the following:

1. death during the study period
2. Any other event not mentioned above that is life threatening event or jeopardises the patient or requires medical or surgical intervention

Reporting SAEs

SAEs will be reviewed and reported by the principal investigators in accordance with NZ regional ethics reporting period.

Patient Withdrawals

Whanau/Families are able to withdraw their child from the study at anytime.

Study Monitoring Group

A study monitoring group will be established for this study who the study team will report to and will receive feedback on cultural and ethical behaviour. It will comprise of Maori and Pacific representatives and a public health consultant.

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Health and Disability Ethics Committees

Northern X Regional Ethics Committee
Ministry of Health
3rd Floor, Unisys Building
650 Great South Road, Penrose
Private Bag 92 522
Wellesley Street, Auckland
Phone (09) 580 9105
Fax (09) 580 9001

30 September 2010

Dr Adrian Trenholme
Kidz First
Middlemore Hospital
Private Bag 93 311
Otahuhu

Dear Adrian

Ethics ref:	**NTX/10/09/094** (please quote in all correspondence)
Study title:	**Randomised control trial of an intervention programme based on the cystic fibrosis model of care in children less than two years of age admitted to hospital with severe lower respiratory tract infection to prevent chronic lung disease: Protocol V#1, 23/08/10: PIS/Cons V#2/23/09/10**
Principal Investigator:	Dr Adrian Trenholme
Co-Investigators:	Dr Cass Byrnes, Dr Harley Aish, Mr Henare Mason, Ms Karen Hoare, Professor Diana Lennon, Mrs Joanna Stewart, Professor William Leung
Localities:	Counties-Manukau DHB, Bairds Rd Family & Christian Health Centre Otara, Greenstone Family Clinic Manurewa, Mangere Family Doctors Mangere

Thank you for your letter and Committee requirements, received 27 September 2010. This study has now been given ethical approval by the Northern X Regional Ethics Committee. A list of members of the Committee is attached.

Approved Documents

- Protocol V#1 dated 23 August 2010
- Participant Information Sheet/Consent Form V#2 dated 23 September 2010
- etc

This approval is valid until 31 July 2013, provided that Annual Progress Reports are submitted (see below).

Access to ACC

For the purposes of section 32 of the Accident Compensation Act 2001, the Committee is satisfied that this study is not being conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the trial is being carried out. Participants injured as a result of treatment received in this trial will therefore be eligible to be considered for compensation in respect of those injuries under the ACC scheme.

Amendments and Protocol Deviations

All significant amendments to this proposal must receive prior approval from the Committee. Significant amendments include (but are not limited to) changes to:

- the researcher responsible for the conduct of the study at a study site
- the addition of an extra study site
- the design or duration of the study
- the method of recruitment
- information sheets and informed consent procedures.

Significant deviations from the approved protocol must be reported to the Committee as soon as possible.

Annual Progress Reports and Final Reports

The first Annual Progress Report for this study is due to the Committee by **30 September 2011**. The Annual Report Form that should be used is available at www.ethicscommittees.health.govt.nz. Please note that if you do not provide a progress report by this date, ethical approval may be withdrawn.

A **Final** Report is also required at the conclusion of the study. The Final Report Form is also available at www.ethicscommittees.health.govt.nz.

Requirements for the Reporting of Serious Adverse Events (SAEs)

SAEs occurring in this study must be individually reported to the Committee within 7-15 days only where they:

- are *unexpected* because they are not outlined in the investigator's brochure, and
- are not defined study end-points (e.g. death or hospitalisation), and
- occur in patients located in New Zealand, and
- if the study involves blinding, result in a decision to break the study code.

Please see www.ethicscommittees.health.govt.nz for more information on the reporting of SAEs. and to download the SAE Report Form.

We wish you all the best with your study.

Yours sincerely

Pat Chainey
Administrator
Northern X Regional Ethics Committee
Email: pat_chainey@moh.govt.nz

Cc: CMDHB Research Office

Health and Disability Ethics Committees

Northern X Regional Ethics Committee
Private Bag 92522
Wellesley Street
Auckland 1141
Phone: (09) 580 9105
Fax (09) 580 9001
Email: northernx_ethicscommittee@moh.govt.nz

22 March 2012

Dr Adrian Trenholme c/- Ms Lyndsay Le Comte
CCRep
Private Bag 93 311 Otahuhu
Auckland 1640

Dear Adrian

Re:	Ethics ref:	**NTX/10/09/094** (please quote in all correspondence)
	Study title:	Randomised control trial of an intervention programme based on the cystic fibrosis model of care in children less than two years of age admitted to hospital with severe lower respiratory tract infection to prevent chronic lung disease: Protocol V#1, 23/08/10: PIS/Cons V#2/23/09/10: Prot/amend V#2, 3/02/11: Prot/amend V#3, 27/6/11; Prot/amend V#4, 12/03/12; PIS/Cons V#4, 12/03/12
	Investigators:	Dr Adrian Trenholme, Dr Cass Byrnes, Dr Harley Aish, Mr Henare Mason, Ms Karen Hoare, Professor Diana Lennon, Dr Joanna Stewart, Professor William Leung

Thank you for your letter received with Lyndsay's of email 13 March 2012 with changes to the study.

The protocol amendment and documentation were reviewed by the Chairperson of the Northern X Regional Ethics Committee under delegated authority.

Ethical approval is granted to:

- addition of Pukekohe Family Health Centre as study site
- Protocol Amendment version 4 [dated 12 March 2012]
- Information sheet/Consent Form [version 4, dated 12 March 2012]
- Patient Brochure [version 2 dated 12 March 2012]

It should be noted that Ethics Committee ethical approval does not imply any resource commitment or administrative facilitation by any healthcare provider, within whose facility the research is to be carried out. Where applicable, authority for this must be obtained separately from the appropriate manager within the organisation.

Yours sincerely

Cheh Chua
Administrator
Northern X Regional Ethics Committee

cc: CMDHB Research Office

Health and Disability Ethics Committees

Northern X Regional Ethics Committee
Ministry of Health
3rd Floor, Unisys Building
650 Great South Road, Penrose
Private Bag 92 522
Wellesley Street, Auckland
Phone (09) 580 9105
Fax (09) 580 9001

7 March 2011

Dr Adrian Trenholme
Kidz First
Middlemore Hospital
Private Bag 93 311
Otahuhu
Auckland 1640

Dear Adrian

Ethics ref:	**NTX/10/09/094** (please quote in all correspondence)
Study title:	**Randomised control trial of an intervention programme based on the cystic fibrosis model of care in children less than two years of age admitted to hospital with severe lower respiratory tract infection to prevent chronic lung disease: Protocol V#1, 23/08/10: PIS/Cons V#2/23/09/10: Prot/amend V#2, 3/02/11: PIS/Cons V#3, 1/02/11**
Principal Investigator:	Dr Adrian Trenholme
Co-Investigators:	Dr Cass Byrnes, Dr Harley Aish, Mr Henare Mason, Ms Karen Hoare, Professor Diana Lennon, Mrs Joanna Stewart, Professor William Leung
Localities:	Counties-Manukau DHB, Bairds Rd Family & Christian Health Centre Otara, Greenstone Family Clinic Manurewa, Mangere Family Doctors Mangere

Thank you for your letter dated 14 February 2011

The following amendment was reviewed by the Chairperson of the Northern X Regional Ethics Committee under delegated authority.

Ethical approval has been given for :

- Protocol amendment V#2 dated 3 February 2011
- Participant Information Sheet/Consent Form V#3 dated 1 February 2011
- Participant brochure
- Participant contact card

Yours sincerely,

Pat Chainey
Administrator
Northern X Regional Ethics Committee

Cc: CMDHB Research Office – Alison Robertson

Health and Disability Ethics Committees

4 July 2011

Northern X Regional Ethics Committee
Ministry of Health
3rd Floor, Unisys Building
650 Great South Road, Penrose
Private Bag 92 522
Wellesley Street, Auckland
Phone (09) 580 9105
Fax (09) 580 9001

Mailing Address:
Private Bag 92 522
Wellesley Street
Auckland 1141

email address
northernx_ethicscommittee@moh.govt.nz

Dr Adrian Trenholme
Kidz First
Middlemore Hospital
Private Bag 93 311 Otahuhu
Auckland 1640

Dear Adrian

Ethics ref:	**NTX/10/09/094** (please quote in all correspondence)
Study title:	Randomised control trial of an intervention programme based on the cystic fibrosis model of care in children less than two years of age admitted to hospital with severe lower respiratory tract infection to prevent chronic lung disease: Protocol V#1, 23/08/10: PIS/Cons V#2/23/09/10: Prot/amend V#2, 3/02/11: Prot/amend V#3, 27/6/11; PIS/Cons V#3, 1/02/11
Principal Investigator:	Dr Adrian Trenholme
Co-Investigators:	Dr Cass Byrnes, Dr Harley Aish, Mr Henare Mason, Ms Karen Hoare, Professor Diana Lennon, Mrs Joanna Stewart, Professor William Leung

Thank you for your letter dated 27 June 2011.

The protocol amendment to the study was reviewed by the Deputy Chairperson of the Northern X Regional Ethics Committee under delegated authority.

Ethical approval is granted to:

- Study Protocol (version 3 dated 27 June 2011)

In view of the change in timeframe, ethical approval is now valid to 31 July 2014, subject to annual reports received. The next progress report is due on **4 July 2012.**

Yours sincerely

Cheh Chua
Northern X Regional Ethics Committee

cc: CMDHB Research Office #

Appendix B
Statement of compliance and list of members

Statement of compliance

The Northern A Health and Disability Ethics Committee:

- is constituted in accordance with its Terms of Reference
- operates in accordance with the *Standard Operating Procedures for Health and Disability Ethics Committees*, and with the principles of international good clinical practice (GCP)
- is approved by the Health Research Council of New Zealand's Ethics Committee for the purposes of section 25(1)(c) of the Health Research Council Act 1990
- is registered (number 00008714) with the US Department of Health and Human Services' Office for Human Research Protection (OHRP).

List of members

Name	*Category*	*Appointed*	*Term Expires*
Dr Brian Fergus	Lay (consumer/community perspectives)	01/07/2012	01/07/2015
Ms Susan Buckland	Lay (consumer/community perspectives)	01/07/2012	01/07/2015
Ms Shamim Chagani	Non-lay (health/disability service provision)	01/07/2012	01/07/2014
Mr Kerry Hiini	Lay (consumer/community perspectives)	01/07/2012	01/07/2014
Assoc Prof Wayne Miles	Non-lay (intervention studies), Non-lay (health/disability service provision)	01/07/2012	01/07/2013
Dr Etuate Saafi	Non-lay (intervention studies)	01/07/2012	01/07/2014
Ms Michele Stanton	Lay (the law)	01/07/2012	01/07/2014

http://www.ethics.health.govt.nz

Health and Disability Ethics Committees
Ministry of Health
1 the Terrace
PO Box 5013
Wellington
6011

0800 4 ETHICS
hdecs@moh.govt.nz

21 May 2013

Dr Adrian Trenholme
Kidz First
Middlemore Hospital Private Bag 93 311
Otahuhu 1640

Dear Dr Trenholme

Re:	**Ethics ref:**	**NTX/10/09/094/AM02**
	Study title:	Randomised control trial of an intervention programme based on the cystic fibrosis model of care in children less than two years of age admitted to hospital with sever lower respiratory tract infection to prevent chronic lung disease.

I am pleased to advise that this amendment has been *approved* by the Northern A Health and Disability Ethics Committee. This decision was made through the HDEC Expedited Review pathway.

Please don't hesitate to contact the HDEC secretariat for further information. We wish you all the best for your study.

Yours sincerely,

BJ Fergus

Dr Brian Fergus
Chairperson
Northern A Health and Disability Ethics Committee

Encl: appendix A: documents submitted
appendix B: statement of compliance and list of members

Appendix A
Documents submitted

Document	Version	Date
Protocol	5	17 April 2013
Protocol: No track changes	5	17 April 2013
PIS/CF for persons interested in welfare of non-consenting participant: No track changes	5	17 April 2013
PIS/CF for persons interested in welfare of non-consenting participant: track changes	5	17 April 2013
Post Approval Form		02 May 2013

Study reference number:	NTX/10/09/094
Short title:	Healthy Lungs
Co-ordinating Investigator (CI):	Dr Adrian Trenholme
Date approved:	

Post-approval Form Filter

Filter. Which of the following post-approval items would you like to submit?

- (•) an amendment
- ( ) a progress report
- ( ) a protocol deviation or violation
- ( ) a report of a serious adverse event (to SCOTT only)
- ( ) notification of conclusion of the study
- ( ) a final report.

Amendment

A1. Please describe the amendment you wish to make to your study.

[< 2000 characters]

Additional information is to be collected at the final two year clinics. The participant information sheet has been changed to ask parents for consent to store a blood sample for future testing including; Vitamin D, immunoglobulin E and markers of inflamation.

Parents will also be asked to consent to a Nasopharyngeal Swab and for permission to contact them for a further follow up visit or visits.

A2. Please explain why this amendment is being made.

[< 2000 characters]

The blood tests are to ascertain factors which may indicate the risk or presence of chronic suppurative lung disease. The study budget does not include sufficient funds to perform these tests, at the time of this amendment. We await the results of funding applications.

The Nasopharyngeal Swab is to be taken to identify bacterial and viral load which may be linked to chronic suppurative lung disease. This was included in the original protocol but omitted from the participant information sheet.

The children reviewed at the final clinic will be between two and four years of age, the peak age of diagnosis of clinical bronchiectasis in New Zealand children is well over four years of age, we wish to review all children between four and six years of age to evaluate later presentation of bronchiectasis.

A3. Please indicate whether the amendment:

- ( ) concerns urgent safety measures that have already been implemented
- ( ) notifies the HDEC/SCOTT of a temporary halt of your study
- ( ) requests that your study re-commence following a temporary halt or suspension of approval
- (•) none of the above

A4. Please briefly explain the effect that you consider that this amendment may have on the following ethical aspects of your study.

Benefits:	[< 600 characters] This amendment will enable improved understanding of the aetiology of chronic suppurative lung disease in this age group and evaluate the impact of the intervention in both the 2-4 year old and 4-6year old age groups.
Risks:	[< 600 characters] The samples will be stored securely and de-identified. Following testing the samples will be disposed in the appropriate method by the laboratory.
Respect for persons and populations:	[< 600 characters] Stored blood will not be tested for anything other than the stated purposes. Parents/caregivers will be asked for consent to the storage of the blood and nasopharyngeal samples and for further follow up. It will be explained to parents that they do not have to consent to this.
Fairness:	[< 600 characters] All children in the study will be asked to re-consent to the storage of blood and nasophryngeal samples and further study follow up. It will be explained to parents that their consent is voluntary and they can still participate in the study without consenting to this amendment.

A5. *Only substantial amendments, as defined in section 11 of the Standard Operating Procedures for HDECs, need to be submitted to HDECs.*

Is this amendment substantial?

- (•) Yes
- ( ) No

A6. Please explain your answer above

[< 1200 characters]

The amendment meets 187.2.of the operational standards as it will impact on the scientific value of the study.

In addition parents/caregivers will be asked to provide consent.

Please upload amended versions of all relevant study documents in the "Documents" tab.