STUDY PROTOCOL

Improved Respiratory Support in Rural and Remote Settings for Children: A Paediatric Acute Respiratory Study (PARIS), PARIS on Country

A Multicentre Science Implementation Study

Protocol Version 3

Trial registry:

This trial is registered with the Australian New Zealand Trials Registry ACTRN12623000527662.

Simple Description:
Respiratory illnesses are the most frequent reason for non-elective hospital admissions in children aged less than 5 years, with a high global health burden. Acute respiratory failure (ARF) is the common endpoint for many underlying specific diagnoses such as bronchiolitis, asthma and pneumonia. In Australia and New Zealand, 28% of intensive care admissions for children are due to ARF. Whilst mortality due to ARF has improved in high-income countries (1-2%), mortality remains between 13-20% in less well-resourced settings. In Far North Queensland 50%, mostly indigenous children with ARF, require transfer to a metropolitan/tertiary hospital due to higher care and management care, whereas in South-East Queensland only 9-12% of these children require inter-hospital transfer. To address this inequality, we aim to evaluate a measured model of care using a comprehensive *Respiratory Care Bundle* for children with ARF in rural and remote hospitals in Queensland. This includes the implementation of nasal high-flow therapy, which is a standard therapy used in the past decade in regional and urban hospitals in Australia, but yet to be offered in a large number of rural and remote settings. The aim of this project is to reduce the number of transfers and offload the pressure on the emergency departments and retrieval systems in remote settings. Notably, keeping indigenous community members in their country/community environment has not only positive psychological and social-emotional impacts, but it also has significant health care economical savings.

CONFIDENTIAL

Statement of Compliance

This clinical trial will be conducted in compliance with all stipulation of this protocol, the conditions of the ethics committee approval, the NHMRC National Statement on ethical Conduct in Human Research (2007 and all updates), the Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice E6 (R2), dated 9 November 2016 annotated with TGA comments and the NHMRC guidance Safety monitoring and reporting in clinical trials involving therapeutic goods (EH59, 2016); and NHMRC Ethical conduct in research with Aboriginal and Torres Strait Islander People and communities: Guideline for researched and stakeholders 2018.

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Revision Chronology:

Date of change	Summary of changes
11 July 2023 Protocol V2.0	• Removal of Parent Brochure – Research Information Sheet V1.0 dated 31.10.2022 due to duplication in PICF • Removal of implied consent wording for parents due to informed written consent for parents in place. • Addition of Dr Andreas Schibler's affiliation change • Addition of Dr Andrew White for TUH investigator • Update of record retention section following Data Custodians feedback.
24 July 2024 Protocol V3.0	• Removal of all THHS sites, reducing the project to 14 sites across three HHSs. • Removal of all THHS investigators (Dr. Andrew White, Dr. Greg Wiseman, and Dr. Arjun Chavan). • Updated sample size calculation to reflect the reduced number of sites and an extension of one month control phase to complete the sample size (as outlined in the milestones). • Reduction of SpO2 threshold from 92% to 90%, aligning with standards at tertiary and regional centers across Australia and ensuring equitable care in remote settings.

TABLE OF CONTENTS

PROTOCOL SYNOPSIS

Respiratory illnesses are the most frequent reason for non-elective hospital admissions in children aged less than 5 years, with a high global health burden. Acute respiratory failure (ARF) is the common endpoint for many underlying specific diagnoses such as bronchiolitis, asthma and pneumonia. In Australia and New Zealand, 28% of intensive care admissions for children are due to ARF. Whilst mortality due to ARF has improved in high-income countries, mortality remains between 13-20% in less well-resourced settings. In Far North Queensland, 50% of mostly indigenous children with ARF require transfer to a tertiary hospital due to higher care needs, whereas in South-East Queensland only 9-12% of these children require transfer. To address this inequality, we aim to introduce an evaluation of a measured model of care using a comprehensive respiratory care bundle for children with ARF in rural and remote hospitals in Queensland. This includes the implementation of nasal high-flow therapy, which is a standard therapy used in regional and urban hospitals in Australia, but yet to be offered in a large number of rural and remote settings. Notably, this project uses only existing respiratory care pathways currently provided by Queensland Health and aims to implement these pathways similarly as it has occurred in Southeast Queensland. The key element is to empower local community members and local health care providers to care for children with ARF in their local settings and provide strict safety boundaries for the clinical care. The aim of this project is to reduce the number of transfers and offload the pressure on the emergency and retrieval systems in remote settings. Notably, keeping indigenous community members in their country/community environment has not just positive psychological and social-emotional impacts, but it also has significant economical savings.

Title	Improved Respiratory Support for children: A Paediatric Respiratory Intervention Study (PARIS) - ***PARIS on country***
Aim	To demonstrate that the implementation of an acute respiratory care bundle in children presenting to rural and remote hospitals with acute respiratory failure leads to service delivery improvements and reduced hospital transfers of these children.
Objectives	1.) To evaluate the implementation of a respiratory care bundle using existing Queensland Health clinical guidelines adapted to each individual context in existing acute paediatric care services in remote and rural hospitals to reduce the proportion of children transferred to a tertiary hospital and reduce health care costs. 2.) Evaluation and implementation of the respiratory care bundle reduces the length of stay in acute care settings and health care costs. 3.) To assess and measure the acceptance and compliance of the clinical staff of the respiratory care package. 4.) To demonstrate sustainability of the respiratory care bundle beyond the study.
Design	A stepped wedge cluster-randomised study design will be used to investigate the structured implementation of a respiratory care bundle (the intervention) for paediatric ARF including bronchiolitis. **NB:** This trial will allocate in random order the implementation of the respiratory care bundle to each hospital. There will be 3-4 hospitals in each clustered randomisation. *No individual clinical patient/participant randomisation will be required.*
Interventions	The intervention is a ***respiratory care bundle***. The respiratory care bundle is a comprehensive educational bundle that is based on current standard QH guidelines for bronchiolitis and ARF and use of nasal high-flow therapy in infants and children. The bundle incorporates evidence based on the recent RCT's in Australia and New Zealand on these cohorts of infants and children.
Primary outcome	The ***primary outcome*** is the proportion of yearly hospital transfers of infants and children aged 0-4 years with ARF including bronchiolitis cared for with the new respiratory care bundle in comparison to numbers under the existing respiratory pathways.
Inclusion Criteria	***Infants with bronchiolitis*** admitted to hospital, aged <12 months with or without oxygen requirement, defined as acute onset of respiratory disease, presenting with increased respiratory rate, cough, increased work

	of breathing, rhinorrhoea, increased body temperature, widespread crackles or wheeze and reduced fluid intake. ***Children admitted to hospital aged 0-4 years with acute respiratory symptoms***, presenting with increased respiratory rate, with or without oxygen requirement, with or without increased work of breathing and wheeze, increased body temperature and reduced fluid intake. Note, there are only few infants <12 months of age that are presenting to hospital with respiratory symptoms other than bronchiolitis.
Exclusion Criteria	There are no formal patient exclusion criteria as the intent of the study is to observe and audit all episodes when a child presents with acute respiratory failure, including bronchiolitis to one of the participating hospitals.
Number of Participants	1260 patients
Length of study	5 years

GLOSSARY OF ABBREVIATIONS

ABBREVIATION	TERM
NHF	Nasal High-Flow
SOT	Standard Oxygen therapy
CPAP	Continuous positive airway pressure
IV	Invasive Ventilation
PICU	Paediatric Intensive Care Unit
CPAP	Continuous Positive Airway Pressure
QALY	Quality adjusted life year
NIV	Non-invasive ventilation
PARIS	Paediatric Acute Respiratory Intervention Study

1. ADMINISTRATIVE INFORMATION

1.1. Trial registration

This trial is registered with the Australian New Zealand Trials Registry ACTRN12623000527662.

1.2. Sponsor

Study Sponsor	Gold Coast Hospital and Health Services
Contact name	Office for Research Governance & Development
Address	Gold Coast University Hospital Level 2 Block E Pathology and Education Building 1 Hospital Boulevard Southport QLD 4215 E: GCHResearch@health.qld.gov.au P: 07 – 5687 3880
Funding Bodies	A$ 1.6M by MRFF A$ 272,283 by EMF

1.3. Expected duration of study

1 October 2022 to 30 Sept 2027

2. INTRODUCTION AND BACKGROUND

2.1. Background and Rationale

Acute respiratory distress in children is the most common reason for emergency department (ED) presentations in Australia and is the most common reason for hospital admission in children less than 1 year of age (56% of all admissions to hospital) and the most common reason for paediatric aeromedical transfer in remote Australia [1, 2]. If high level of respiratory support is required, children require admission to a paediatric intensive care unit (PICU) in a tertiary hospital, necessitating a costly transfer by a retrieval service and impacting on families as they must care for their child outside their regular environment. Many rural and remote Australian hospitals experience delays in retrieval due to the distances involved, available assets to undertake the transport and impacts of weather conditions on safe transport. These transfers have an intrinsic risk associated with them. The delay in retrieval often results in an extended stay in the emergency department for these children, placing increased burden on ED staff and resources. To reduce this burden, staff in rural and remote hospitals may be able to safely deliver acute respiratory support to these children in the inpatient setting, building on evidence and research that has been undertaken in metropolitan centres by our research group.

On a global scale, the respiratory disease remains the leading cause of death in children. In under resourced countries, children presenting to hospitals with severe pneumonia have a mortality rate between 13-20% and most deaths occurring with hypoxaemia before therapeutic benefit of antimicrobials [3]. In developed countries in contrast, the mortality due to severe respiratory disease is relatively low, accounting for 1.1 % of deaths in PICU [1, 4]. In Australia, 28% of non-elective intensive care admissions for children are due to acute respiratory failure (ARF), with bronchiolitis representing 15%, pneumonia 7% and asthma 6% [1]. The direct cost due to Australia/New Zealand hospitalisation increased fourfold from A$ 11.4 M in 2002 to A$ 44.3 million in 2014 (indexed for inflation), due to severe bronchiolitis alone [5-7].

Vulnerability in rural and remote settings. Rural and remote Queenslander's account for approximately 38% of Queensland's total population with approximately 47% of First Nations people living in rural and remote regions. Aboriginal and Torres Strait Islander children, especially in remote communities, have a higher incidence rate of ARF including bronchiolitis than non-Indigenous children. The gap in the burden of disease between Indigenous and non-Indigenous populations is well-known. Paediatric respiratory disease remains a significant health problem in this remote population. Indigenous children are more likely to be hospitalised, have more severe illness, have more comorbidities and be susceptible to comparatively poorer outcomes [8].

> *This project was conceived out of the desire of a collective group of remote Indigenous mothers and is the result of this community feedback by parents, whose children were transferred out of remote settings, for care that the parents thought could be provided locally.*

There is a widely acknowledged gap of health outcomes between urban and rural and remote populations. Life expectancy is a decade less than their urban counterparts. Higher rates of disease and injury and less access to healthcare is the harsh reality for rural and remote Australians [9]. The Queensland Health Department announced in February 2022 their ***strategic goals*** for the next five years which are to ***improve rural and remote health & wellbeing***, and to ***promote equity of health outcomes*** with ***strong partnerships*** and ***sustainable skilled and supported workforce***. This proposal aligns with the initiative by the State's Health Department, and we presently work in line with these goals with the local Hospital and Health Services. In the past, children with ARF in SEQ used to be treated in resuscitation bays in ED, spent significant hours until either a retrieval occurred or were sent to the ward with 1:1 nursing, blocking valuable ED resources. Following the implementation of our RCT findings in SEQ, these children stay 1-2 hours in a standard ED observational bay on Nasal High-Flow (NHF) therapy and are now sent to the ward with 1:4 nursing. Our objective therefore is to demonstrate this can occur in any hospital covering 24/7 paediatric acute care and reducing bed block in ED.

The ***socio-economic implications*** of a respiratory care bundle that reduces the need for emergency retrieval for rural, remote and especially Indigenous families cannot be understated. The child and parent are removed from a community and flown up to 900kms away into a significantly larger hospital environment, and in the case of Indigenous families the significant cultural differences between staff and families contributes to feelings of powerlessness, fear and isolation [10]. Indigenous communities have repeatedly reported the importance of receiving care on country as it is intrinsically linked with health and wellbeing [11]. Ultimately, it is estimated with a reduction of the high retrieval costs that the savings within this project will surpass the costs of this project alone. The annual transfer rate of 273 (year 2018 and 2019) children in North Queensland per year at an average cost of $24,500 including back transfer results in $ 6.1 M expenditure/year and if successful in this project would lead to a yearly cost saving of $ 2-3 M /year (***Figure 1***).

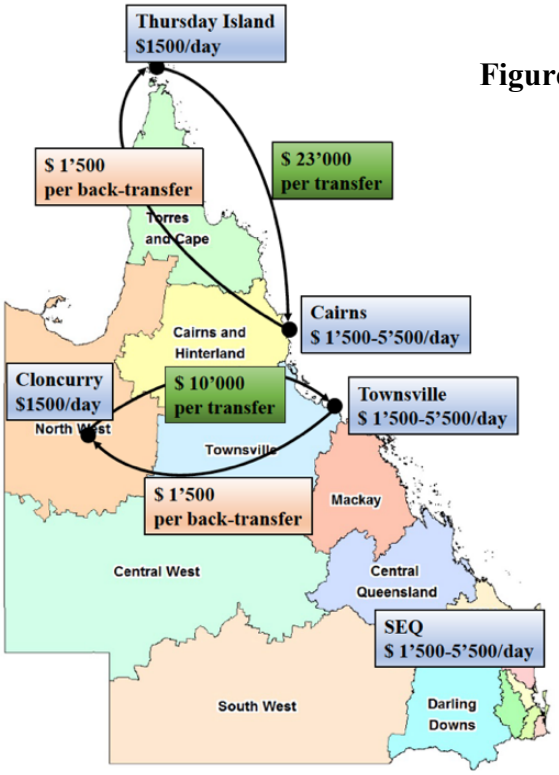

Figure 1

2.2. Impact

Impact on emergency services. A significant proportion of emergency paediatric aeromedical retrievals in rural and remote areas are due to respiratory conditions. The Torres Strait and Cape York Hospitals (Thursday Island, Weipa and Cooktown) reported that between July 2016-June 2018 a total of 216 infants (<12 months of age) were admitted with bronchiolitis, and in this timeframe 108 (50%) infants were airlifted to tertiary hospitals due to higher care needs at an average cost of $24,500/patient for the transport (cost of back transfer included). This compares to the significantly lower transport rates and costs and PICU admissions observed in our 2 recent large RCTs (GNT1081736, GNT1139903) for similar ARF including bronchiolitis children in South-East Queensland (SEQ) (6% transfers for bronchiolitis infants <12months and 2.2% for children with ARF aged 0-4 years) [12-14].

2.3. Preliminary data

A ***pilot phase*** of this project in Torres Strait and Cape York, Far North QLD (FNQ) is currently successfully in progress in 3 remote hospitals since 2021 (seed funding by Children's Health Foundation, Emergency Medical Foundation, Tropical Australian Academic Health Centre).

We aim to upscale the research question to 14 hospitals (mostly Level 2 CSCF services) and to deliver evidence with the success of the new respiratory care bundle in children with ARF in rural/remote settings. Current evidence by extensive literature review was used in conjunction with an expert panel in the context of the clinical application, health service delivery, governance, and community integration to develop locally adapted guidelines for a respiratory care bundle. The expert panel consisted of the Executive Director of Medical Services TCHHS, local nursing and medical representatives for the remote hospitals, Royal Flying Doctors Service (RFDS) and Retrieval Services QLD (RSQ), Simulation Training on Resuscitation for Kids (SToRK) team, Emergency and PICU services in Cairns and Townsville, tertiary and clinical researchers based in Townsville and Brisbane (including the previous PARIS studies clinical researchers), and Indigenous Community Representatives with support of their local Indigenous council. The pilot work has already demonstrated an initial reduction in retrievals for children and improved staff confidence in managing the acute phase of respiratory illnesses in these hospitals. Parents have reported to the local principal investigator (CI West) their relief in being able to receive care in their local communities. This foundation work has demonstrated a) the feasibility of implementing a remote-specific respiratory care bundle through the collaboration between academic and clinical services and b) high levels of community engagement directly responding to one of the key priorities for rural and remote communities' health care (equitable access).

2.4. Addressing Indigenous Aspects

Investigators on this project live, work and conduct research in locations where up to 65% of the population are Aboriginal and Torres Strait Islander people (The Torres Strait Islands and

Cape York specifically) and understand their needs. Considerable community consultation was conducted during a pilot phase for this project which informed the research methodology and processes. Consumer needs and outcomes are at the centre for this project and are paramount to the success of the project. An Indigenous advisory group with representation from each hospital and health service, will be formed and will provide advice as to cultural value of project to community, and will be involved in procedures and processes, interpretation of preliminary results from a consumer perspective, dissemination of results to consumers. Using this framework, we are able to disseminate research outputs to the stakeholders involved throughout the consultation process (addressing NHMRC indigenous core values, ***Respect*** and ***Cultural Continuity***).

The pilot project and current project have been conceived out of a collective group of remote Indigenous females who had themselves had children with respiratory illnesses resulting in frequent retrievals away from home. These mothers approached members of our research team with these concerns of not having the care for their children provided in their community (addressing NHMRC indigenous core value, ***Spirit and Integrity***). This has led to additional consultation work and the need to investigate options to reduce the proportion of children transferred to higher level of care. With the support of a senior clinical research nurse and medical officers within the Torres & Cape Hospital and Health Service the discrepancy between the respiratory care provided in South-East Queensland compared to remote and rural settings was highlighted and led to the development of the pilot and now the current project.

This project has been developed with an Indigenous Australian nurse and a prominent researcher in Aboriginal and Torres Strait Islander Health and an Aboriginal & Torres Strait Island Liaison Officer within TCHHS (addressing NHMRC indigenous core value, ***Reciprocity***). Multiple Aboriginal and Torres Strait Islander stakeholders were consulted within Thursday Island and Cape York and final consultation was sought through the Executive Director of Aboriginal and Torres Strait Island Health with TCHHS. The project has a dedicated role for an Indigenous Community Liaison officer. This role is appointed to a new researcher who is developing her research skills and knowledge with the collaboration and support of the larger research group, some of which have had more than three decades working in clinical and academic research. Stewardship will increase as this role evolves and grows with its importance to the project.

Dissemination of the research within the health care setting of TCHHS for the pilot phase has been overwhelmingly positive and very much anticipated by the health service's clinicians. A remote guideline for the management of NHF therapy for children was developed and implemented, multiple education sessions, training manuals, an online learning package and training resources have been provided to the health service. Dissemination about the research outside of the health service has predominately occurred through conference events and by attending social community events within the Cape York community such as setting up stands at the Bullrides, Running Festivals. These social events are paramount in describing current research works and answering questions to the community of which the research is

being conducted (addressing NHMRC indigenous core value, ***Cultural Continuity*** and ***Spirit and Integrity***). Overwhelming positive support for the project has been emphasised by the community and people in-general have described their own experiences within the health service with having an unwell remote child.

2.5. Benefit

Aboriginal and Torres Strait Islander infants, especially in remote communities, have a higher incidence rate of bronchiolitis than non-Indigenous Australians. Cape York and the Torres Strait Islands have the highest proportion of indigenous residents compared to the rest of Queensland. The gap in the burden of disease between Indigenous and non-Indigenous populations is well-known. Paediatric respiratory disease remains a significant health problem in this population, particularly in remote communities. Indigenous infants are more likely to be hospitalised, have more severe illness, and be susceptible to comparatively poorer outcomes. A significant proportion (31%) of paediatric aeromedical retrievals in rural and remote areas are due to infectious respiratory conditions. The three pilot phase hospitals in the Torres Strait and Cape York reported that 216 infants were admitted with bronchiolitis within a two-year period from July 2016 – June 2018; in the same timeframe, 108 (50%) of these infants were retrieved to tertiary hospitals due to higher care needs. This compares to the significantly lower transport rates and PICU admissions for bronchiolitis in Southeast QLD as reported in our 2 large RCT's (6% for bronchiolitis infants <12months and 2.2% for children with AHRF aged 0-4 years). This project will address this discrepancy aiming to reduce the transfer of infants and children to Cairns or Townsville tertiary hospitals (addressing NHMRC indigenous core value, ***Equity***). Overall, we expect a significant reduction in health care costs due to a reduced number of transfers of these children to a tertiary facility and more importantly these infants and children can be cared for in their communities which will lead to socio-economic benefit of their families.

2.6. Sustainability

This project is supported by a wide range of established experts in the field of acute respiratory failure (ARF) research. The group has successfully performed 2 large, randomised trials investigating the role of NHF within a respiratory support package in Australia and New Zealand with the Paris I study (bronchiolitis) published in one of the major medical journals (NEJM 2018) and Paris II study (AHRF) currently in submission. Our group also performed a large knowledge translation study in QLD investigating the current evidence in local practice change in SEQ following the PARIS I study. Additionally, we have been able to transfer this knowledge into practice and have introduced a similar respiratory support education package in 3 hospitals in FNQLD in 2021 (pilot phase). The introduction of the package was supported by an expert panel consisting of key stakeholders and community members (addressing NHMRC indigenous core value, ***Responsibility***). The package is using readily available resources, nursing and medical skills and expertise, hence there is no risk that the study intervention as proposed will not be sustainable long-term.

Using methods adapted from the PARIS I & II trials, implementation science was the framework used by the pilot phase team to establish how the full suite of training would be implemented across the pilot sites. The individual hospitals established their best implementation methods using clinical champions, directing an individual focus on what resources should go where. The pilot research ensured that the Torres & Cape Hospital and Health Service led the guideline formulation so that TCHHS had ownership and sustainability of this guideline in the management of children with acute respiratory failure. Local sites developing the guideline means the best people who understand and can address the remote context's needs is translated into practice (addressing NHMRC indigenous core value, ***Responsibility***). The PARIS Remote method of developing remote-specific policy/guidelines/training has now been discussed as the optimal method for addressing other health topics unique to the remote context such as: 'How to address the context issues involved in re-introducing birthing to the remote site'.

2.7. Building Capacity

The pilot phase of this proposed study has led to new research activity collaboratively through the James Cook University. This included new research nurses and medical team. The collaboration using the academic background of the Brisbane and Gold Coast based research team with extensive track record in the field of ARF research has been established and resulted in the funding of the pilot phase by the Children's Health Foundation and by the Medical Research Future Fund (MRFF) for the current study. Further collaboration and capacity building has been achieved with a network of researchers including local indigenous stake holders, remote health services, retrieval services and metropolitan/tertiary hospitals in Cairns and Townsville. It is anticipated with the expansion to additional sites that this network will expand and increased contribution by local communities and indigenous researchers will be achieved.

Aboriginal and Torres Strait Islander people represent a large workforce within TCHHS and this workforce has been relied upon throughout the entire process of implementing research on-the-ground. Without this assistance the pilot phase would not have been able to conduct the research to its entirety. The pilot phase provided education to and received support from all clinical health streams such as physiotherapy, occupational therapy, dietitians, speech pathology, pharmacy, nursing and medicine; however, support has also included administration, stores and hospital courier services in assistance with the research.

From being present and developing research capacity within the predominant Aboriginal Torres Strait Island population community, further contacts and discussion around potential future research projects that would benefit this community have now occurred and this effect will snowball into developing further capacity and beneficial impact for the health of Aboriginal and Torres Strait Islander people. Further collaborations with other research groups have been a result in the betterment of the planning, conduct and dissemination of research throughout these connections. Being present within the community makes a

significant difference and very much matters to the community in improving trust, reliability and further collaborations/consultations together (addressing NHMRC indigenous core value, ***Respect***).

2.8. Summary

In summary this project is governed by the following overarching principles:

1.) This project is ***driven by consumer request*** and will reduce pressure on North Queensland rural and remote emergency departments by ***reducing emergency transfers*** of children with ARF allowing for admission to a local ward rather than prolonged stay in the ED awaiting transfer to higher level of care.
2.) This project will ***reduce length of stay in ED (bed block)*** and free up hospital beds.
3.) This project will ***reduce the gap in respiratory care*** for ***Indigenous children*** with ARF in rural and remote health care settings from the time of presentation to discharge using existing resources of existing guidelines adopted in regional and metropolitan hospitals in Queensland (equality of care). This will build knowledge, skillset and confidence of local remote clinicians in caring for a young child in the emergency setting with the appropriate management which can reduce the risk of escalation and transfer.
4.) This project will ***reduce health care costs*** driven by a reduced need for aeromedical transport; greater patient satisfaction and reduced socio-economic burden on families (acute care can be provided safely in their remote hospital).

3. STUDY AIMS

3.1. The aim of this study is to evaluate that the implementation of an acute respiratory care bundle using current existing Queensland Health standards of care in children presenting to rural and remote hospitals with acute respiratory failure leads to service delivery improvements and reduced hospital transfers of these children.

3.2. Objectives

1. To evaluate the implementation of a respiratory care bundle, using existing current best Queensland Health practice guidelines that are adapted to each individual context in existing acute paediatric care services in remote and rural hospitals to reduce the proportion of children transferred to a tertiary hospital and reduce health care costs.
2. To demonstrate that the implementation of the respiratory care bundle reduces the length of stay in acute care settings and health care costs.
3. To assess and measure the acceptance and compliance of the clinical staff of the respiratory care package.
4. To demonstrate sustainability of the respiratory care bundle beyond the study.

3.3. Hypotheses

The primary hypothesis of this study is that the implementation of an acute respiratory care bundle reduces the proportion of children transferred to higher level of care compared to existing care pathways.

3.4. Primary Outcome

The ***primary outcome*** is the proportion of yearly hospital transfers of infants and children aged 0-4 years with ARF including bronchiolitis cared for with the new respiratory care bundle in comparison to numbers under the existing respiratory pathways.

3.5. Secondary Clinical Outcomes

The ***secondary clinical outcomes*** are:

1. length of stay in hospital
2. length of oxygen therapy
3. health care costs including transport costs and social opportunity costs (including back transfer)
4. sustainability and adherence to the respiratory care bundle beyond the intervention period measured with the Normalisation Process Theory
5. measurement of the proportion of infants and children transferred to a tertiary hospital post implementation
6. consumer satisfaction survey – includes staff and parents/carers

3.6. Secondary Health Service Research Outcomes

The ***health service research outcomes*** are:

1. Reduced health care resource utilisation in the form of reduced hospital transfers for higher level of care.
2. Satisfaction with education and competencies associated with ARF management
3. Electronic medical record prompts are operational
4. Use of evidence-based-practice (EBP) is cost-effective
5. Patient/Carer satisfaction
6. Availability of the associated materials, which are cost-effective
7. Reduced adverse effects for children with ARF or other outcomes.

3.7. Secondary Implementation Outcomes

The ***evaluation of the implementation outcomes*** will be measured using the Society for Implementation Research Instrument Toolkit (SIRC). Outcomes assessed will include acceptability, feasibility, adoption, penetration, adaptability and sustainability measures. Furthermore, the engaging, executing, planning, reflecting and evaluation measures will be captured. We will investigate the following specific Implementation Outcomes:

1. Use of the new respiratory care bundle as a routine treatment
2. Feasibility of the implemented changes
3. Acceptability of the EBP
4. Satisfaction with the use of EBP (all stakeholders)
5. Satisfaction with the implementation process
6. Evaluation of the EBP implementation is shown as acceptable and commendable/highly valued
7. Recommended for further implementation in other healthcare settings

3.8. Eligibility, Inclusion and Exclusion Criteria

3.8.1 Inclusion Criteria for Data Capture

- ***Infants with bronchiolitis admitted to hospital, aged < 12 months*** with or without oxygen requirement, defined as acute onset of respiratory disease, presenting with increased respiratory rate, cough, increased work of breathing, rhinorrhoea, increased body temperature, widespread crackles or wheeze and reduced fluid intake. Observational data will be obtained for these infants.
- ***Children admitted to hospital aged 0-4 years with acute respiratory symptoms,*** presenting with increased respiratory rate, with or without oxygen requirement, with or

without increased work of breathing and wheeze, increased body temperature and reduced fluid intake. Note, there are only few infants <12 months of age that are presenting to hospital with respiratory symptoms other than bronchiolitis. Observational data will be obtained for these children.

3.8.2 Eligible hospitals

Existing capacity to provide the following services: acute paediatric care services 24/7 covered by medical and nursing staff, radiology service, capacity to administer intravenous fluids and antibiotics and basic pathology or standard remote pathology services (point-of-care).

3.8.3 Exclusion Criteria

There are no formal patient exclusion criteria as the intent of the study is to observe and monitor all episodes when a child presents with acute respiratory failure (including bronchiolitis) to one of the participating hospitals.

4. STUDY DESIGN

4.1. Type of Study

A stepped wedge cluster-randomised study design will be used to investigate evaluation of the structured implementation of a respiratory care bundle (the intervention) for paediatric ARF including bronchiolitis in rural and remote hospitals in North Queensland. A stepped wedge design is a type of crossover design in which different clusters cross over from the control group to the intervention group at different time points. All clusters are measured at each time point (Figure 2). The first time point corresponds to a baseline measurement where none of the clusters receive the intervention of interest; at the last time point all clusters receive the intervention. After intermediate time points, clusters initiate the intervention. A transition period of one month will occur prior to intervention phase for medical and nursing staff to receive education. More than one cluster may start the intervention at a time point, but the time a cluster begins the intervention is randomised. This way, both comparisons between units and within units are possible, making the design powerful. [15, 16]
There will be no individual clinical participant randomisation for this trial design.

Cluster	Site	2023				2024												2025												2026		
		Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
1	1	C	C	C	C	C	C	T	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
	2	C	C	C	C	C	C	T	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
	3	C	C	C	C	C	C	T	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
2	4	C	C	C	C	C	C	C	C	C	C	C	C	T	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
	5	C	C	C	C	C	C	C	C	C	C	C	C	T	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
	6	C	C	C	C	C	C	C	C	C	C	C	C	T	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
	7	C	C	C	C	C	C	C	C	C	C	C	C	T	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
3	8	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	T	I	I	I	I	I	I	I	I	I	I	I	I
	9	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	T	I	I	I	I	I	I	I	I	I	I	I	I
	10	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	T	I	I	I	I	I	I	I	I	I	I	I	I
	11	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	T	I	I	I	I	I	I	I	I	I	I	I	I
4	12	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	T	I	I	I	I	I	I
	13	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	T	I	I	I	I	I	I
	14	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	T	I	I	I	I	I	I

Stepped wedge cluster randomised design

- Performed across 31 months with 4 clusters of 3-4 hospitals randomised at each step with 6-month intervals
- C – Cluster unexposed to intervention (Control phase) –> collection of data from all levels (service, health providers, parents/caregivers)
- T – Cluster in transition period while health providers receive training
- I – Cluster exposed to intervention (Intervention phase) –> collection of data from all levels (service, health providers, parents/caregivers)

* Data will be captured over the entire duration of the study including Control and Intervention phases which includes:
(a) Service – Clinical data; (b) Health providers and Parents/Caregivers - Health Economy and Implementation Science data.
* Intervention is the *Implementation of the Respiratory Care Bundle*

Figure 2 – Stepped Wedge Cluster-randomised study design

Because the design ensures that all participants receive the intervention before the end of the study, it is especially useful for interventions with elements that have been shown to be effective in explanatory research. Conducting the intervention in all participants is an important ethical consideration for interventions that are believed to be superior compared to the control condition, and this may increase the motivation for participating in the study. Gradual crossing over to the intervention condition will occur, which is inherent to the

stepped-wedge design, and may, in fact, provide additional information about the influence of contextual changes. Because the period of the intervention varies per group, researchers can account for the interaction effect of different time points with changing context and the duration of the intervention.

Additionally, the sequential introduction of the respiratory care bundle allows a more efficient allocation of the research resources. Simultaneous introduction of the bundle in the context of the rural and remote hospitals is logistically difficult (distance, staff shortages, local governance processes).

4.2. Study Setting

14 rural and remote North QLD hospitals who provide 24/7 nursing and medical acute care for infants and children and are linked with RSQ and RFDS services to a metropolitan/tertiary hospital in Cairns or Townsville.

Sites include:

Hospital Health Service (HHS)	**Hospital**	**Clinical Services Capability Framework level of paediatric emergency service**	**Clinical Services Capability Framework level of paediatric medical inpatient service**
Torres and Cape HHS	Weipa Hospital	Nil for ED	2
	Thursday Island Hospital	Nil for ED	2
	Cooktown Hospital	Nil for ED	2
	Bamaga Hospital	Nil for ED	2
North West HHS	Mt Isa Base Hospital	4	4
	Cloncurry Hospital	Nil for ED	2
	Doomadgee Hospital	Nil for ED	2
	Normanton Hospital	Nil for ED	2
	Mornington Island Hospital	Nil for ED	2
Cairns and Hinterland HHS	Atherton Hospital	Nil for ED	2
	Innisfail Hospital	Nil for ED	2
	Mareeba Hospital	Nil for ED	2
	Mossman Hospital	Nil for ED	2
	Tully Hospital	Nil for ED	2

4.2.1 <u>Site requirements:</u>

- Acute paediatric care services 24/7 covered by medical and nursing staff according to the local CSCF level
- Radiology service as part of standard service delivery

- Capacity to administer intravenous fluids and antibiotics
- Basic pathology or standard 'point-of-care' remote pathology services as part of standard service delivery
- Compliance with all requirements of the acute paediatric respiratory care bundle as part of standard service delivery

4.2.2 Site responsibilities:

- Identify a Principal Investigator (PI) to lead the trial within the health district
- Identify a doctor and nurse/allied health professional champion in each hospital
- Agree to incorporate the study into routine paediatric acute care clinical practice,
- Highlighting the importance of adherence to the bundle within the boundaries of best clinical care
- Agree to optimally monitor and document clinical care as part of standard service delivery
- ***No Good Clinical Practice (GCP) training is required*** for this trial design

The following must be in place prior to a site being activated for implementation:

- A complete site initiation visit (pending COVID-19 restrictions)
- all relevant institutional approvals (e.g. local confirmation of capacity and capability)
- Governance approval, which is proceeded by local community engagement (site specific)
- Fully signed Clinical Trial Site Agreement
- Fully signed Delegation Log

Once the overarching lead Chief Investigator of this study has confirmed that all necessary approvals and documentation is in place, a site activation email will be issued to the local research team, at which point, the site may start the Implementation process (phase II). Once the site has been activated, the local research team is responsible for ensuring:

- Adherence with the most recent approved version of acute paediatric respiratory care bundle
- Training of relevant site staff in accordance with the trial protocol and, if overseeing the study, Good Clinical Practice (GCP) requirements
- Timely data collection, entry and validation; and
- Prompt notification of all adverse events.

All local staff (i.e. PI, local investigators, research teams) involved in the conduct of the trial must be trained to carry out their assigned roles. Site research staff should be signed off on the Delegation Log, once trained, and the Delegation Log should be copied and sent to the lead Chief Investigator whenever changes are made.

5. RECRUITMENT, RANDOMISATION AND CONSENT

5.1. Recruitment and randomisation

This project is a science implementation evaluation study implementing an existing clinical respiratory care bundle for children with ARF using a stepped wedge cluster randomised trial design. Each participating hospital is the unit of randomisation, and target for primary analysis. There is no individual participant randomisation required. Clinical indication will dictate medical care. The implementation start date will be randomly allocated to each hospital using a computer-generated sequence and using a stratification per hospital and health services (HHS). Therefore, no individual patient recruitment will occur, however outcome data of individual data of children presenting with and admitted/transferred with ARF obtained during and after the implementation will be used in comparison to historical data of children with ARF previously presented/admitted and/or retrieved at the participating hospitals. We therefore only seek a Public Health Act (PHA) approval to include all participating hospitals and enable the research team to collect and review patient information during the hospital admission period or where relevant data on transfer to higher level of care occurs. All individual patient data will be de-identified for the purpose of study analysis.

The study investigators will remain blinded to outcome data until the study database is locked for analysis.

5.2. Consent

For clarification of consent requirements see Figure 3.

- For children admitted to hospital with the diagnosis of ARF in the historical data set and in the data set of the observational period post the step wedged study period, we seek a waiver of consent. Contacting parents/guardians could be stressful considering there could have been a negative outcome. Such a burden of stress would not add any value to the study outcome. An informed consent process would also impose a selection bias of the analysed data as certain socio-economic groups will be unlikely to be willing to participate and difficult to approach due to frequent loss of contact post follow-up. Having robust processes in place guaranteeing data safety, deidentification and confidentiality, there is minimal risk imposed on the individual participant. No parent interviews will occur for these patients.
- During the step wedge phase of the study we seek a waiver of consent for patients admitted with ARF. This project aims to evaluate the implementation of an acute respiratory care bundle which is based on current best practice recommended by Queensland Health, hence a structured best evidence-based standardised approach to treat and manage acute respiratory failure in children. The project does not evaluate a new intervention nor a new care pathway. The intention is to streamline

the current QH Bronchiolitis guidelines, the current QH Asthma guidelines, the current QH Community Acquired Pneumonia (CAP) guidelines and the current Nasal High-Flow guidelines (all outlined on page 34 of the protocol).

- We will obtain written informed consent from parents of patients (n=12) for a parent interview per hospital in the control phase and n=12 in the implementation phase. The candidates for the interview will be indentfied by the clinical team during hospital admission.
- Clinician interviews: we will use implied consent.

A Public Health Act (PHA) signed by all relevant Data Custodians will be required to access the childs health information data and deidentify for study purposes/collection.

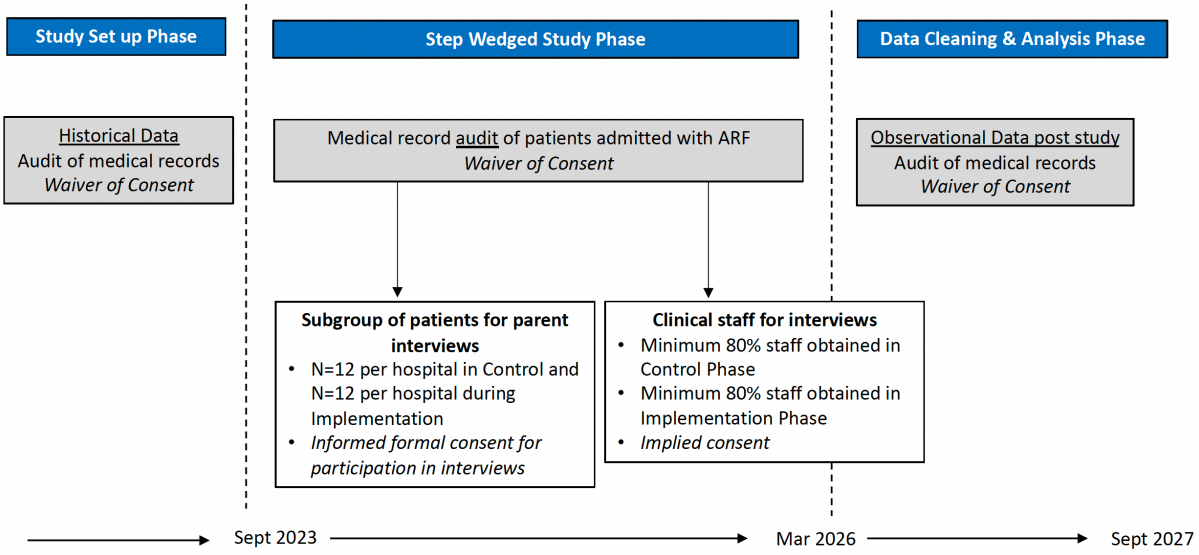

Figure 3. Consent process aligned with Study Milestones (**Figure 4)**

5.2.1 Consent of consumers/parents for the interview

In contrast to data collection on a patient level, we will perform structured interviews with selected consumers/parents and clinicians working in the participating hospitals to obtain information regarding socio-economic factors and their experience during the study.

Potential parent participants will be provided with a participant information sheet either in person or by email or mail.The parent information sheet exists with the Parent Information and Consent Form (PICF) document. Parents will be provided with the information and the interviewer/study coordinator will meet potential participants in person, talk them through the project and invite them to join the project by asking them to formally consent to taking part in an interview. Participation acceptance in the interview is via informed and written consent. Potential participants will be flagged by the clinical staff to the interviewer/study coordinator during the hospital admission of their child. The explanation of the project will be covered in the content of the Parent Information Sheet, for example: what participation involves, confidentiality, and what will happen with the data. Following this explanation and an opportunity for questions to be answered. Written informed consent wil be obtained and participants will be asked if a suitable time could be arranged to participate in a face-to-face

interview or telephone/video interview that may take up to one hour. Potential participants will be provided with contact details for the study coordinator if they wish to take time to consider participation.

All participants will be informed of their right to not participate or to withdraw from the project without prejudice, and to withdraw unprocessed data. Participants will be invited to provide a mailing or email address if they would like their interview transcript returned to them so they can review, approve or correct it prior to processing, and/or if they would like to have copies of the project results sent directly to them upon conclusion, analysis and write up of the project.

We acknowledge that the interview process may cause some distress to parents/carers. Potential participants will be flagged by the clinical staff with the understanding of the current emotional and social situation of the participant. For indigenous participants we anticipate to have an Indigenous interviewer. We will also use the Indigenous Liaison Officer in each hospital. The interviewer will inform participants that if the interview causes them distress to please let the interviewer know. The interview can be stopped at any time and they can be referred to a counsellor or someone else to talk to. If they become distressed after the interview, contact details for available services are listed on their information sheet.

The parent information sheet (information section of the PICF) will be distributed to parents of children with ARF to inform them that some parents may be interviewed, and questions asked in relation to their experience in hospital. The parent information sheet explains the aim of this interview to capture quality of life information from the parent/guardians (for the child by proxy) and to determine the burden and impact which takes place when their child is admitted to hospital. The interview may occur whilst the child is in hospital or after discharge home (within 4 weeks preferentially).

5.2.2 Consent of clinicians

In each of the 14 sites, all clinical staff (medical and nursing) from both ED and the general ward settings, will be invited to complete a questionnaire just prior to implementation and again every 6 months when implementation commences. The aim of these survey questionnaires is to determine if facilitated educational support promotes greater knowledge and skill level and will also explore factors that may influence how clinicians manage children with ARF. The survey will also collect information on the time spent in developing the skills (training and engagement - post) and the time spent with patients (pre and post). Surveys to staff will be delivered either by email or by using an online survey tool. Consent will be implied if a completed survey is returned.

Townsville Hospital and Health Services Human Research Ethics Committees (Townsville HHS HREC) approval will be obtained as is the HREC accredited for multisite study approval in these HHS's. All participating centres will follow suit in line with their local Ethics and governance practices (subject to local governance additional requirements) with most centres using the Townsville HHS HREC approval.

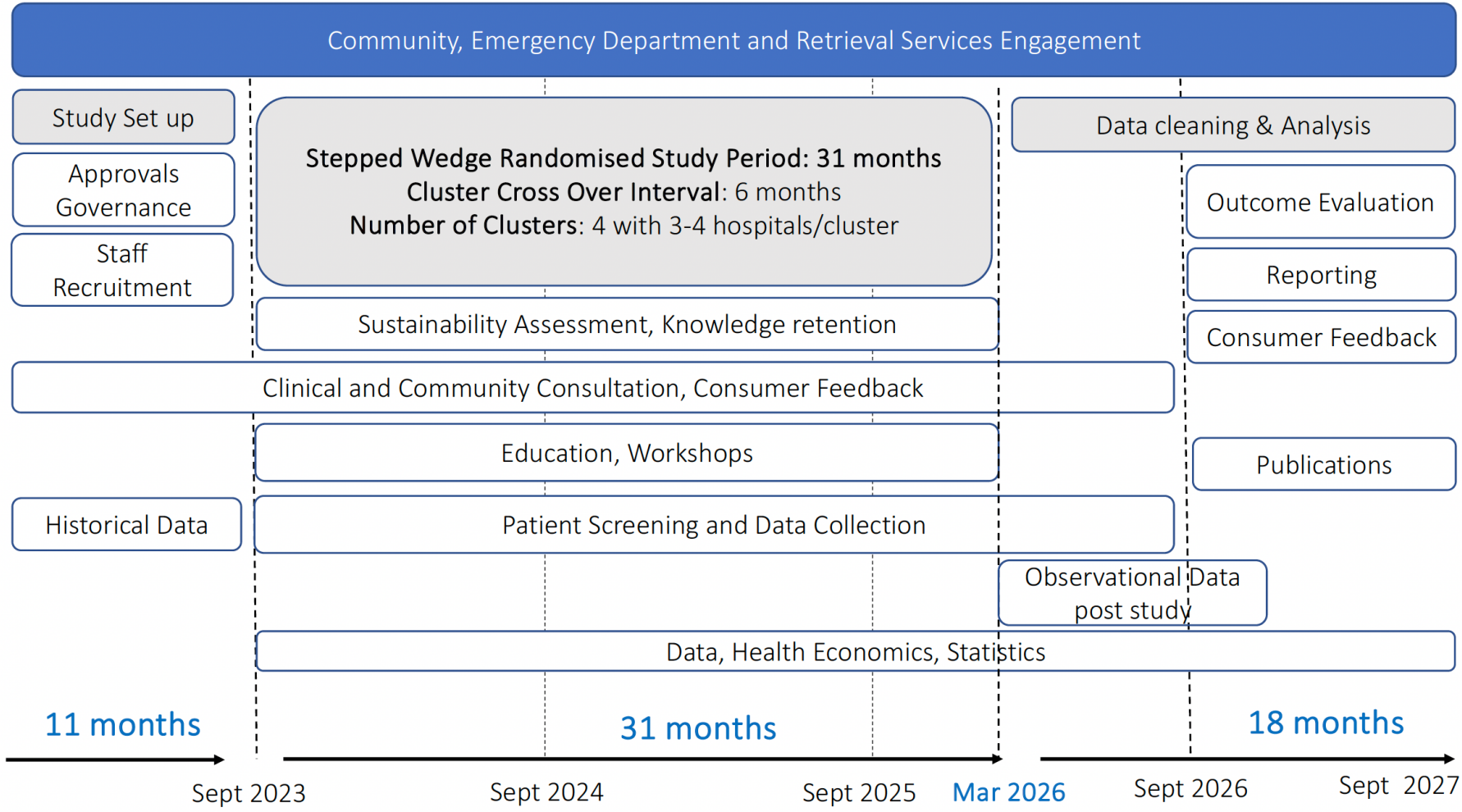

Figure 4 - Milestones over 5 years

6. INTERVENTION AND PROCEDURES

This project will include the following evaluation of intervention and procedures:

1. Evaluation of the implementation of a current respiratory care bundle used to educate and guide clinicians in the care and management of ARF in children.
2. Assessment of the implementation procedure for the respiratory care bundle for infants and children 0-4 years of age and assessment of the health service resources required for the implementation.

6.1 Clinical Intervention: Respiratory Care Bundle, the existing standard practice in South-East Queensland

6.1.1 Bronchiolitis (<12 months) Bundle

<u>For eligible patients meeting the inclusion criteria (see section 3.8)</u>

The respiratory care bundle will encompass all elements of the Australian and New Zealand Bronchiolitis Management Guidelines, Queensland Health Bronchiolitis and NHF guidelines. In short, they encompass: 1.) Diagnostic assessment and measurement of vital signs as per local guidelines and recording the score in the QLD children's early warning tool (CEWT). 2.) Measurement of transcutaneous oxygen saturation (optimal if continuous). 3.) Assessment of the work of breathing. 4.) Chest X ray and pathology (blood gases) only if uncertainty with initial diagnosis of bronchiolitis. 5.) Hydration: either orally, nasogastric tube or iv fluids. 6.) Oxygen therapy: administration of O_2 if saturations less than 90%. 7.) Nasal high-flow at weight specific flows if trial of standard oxygen is ineffective (**Appendix 1**).

<u>*Disposition/Escalation*</u>: if the infant improves with the initial treatment, then continue initiated therapies and monitoring of progress.
Escalation of respiratory support from SOT to NHF should be considered if one or more of the following is present:

i. increased work of breathing requiring escalation of respiratory support and assessed as moderate to severe respiratory failure (**Appendix 2**),
ii. heart rate remains unchanged or increased compared to admission/enrolment observations,
iii. respiratory rate remains unchanged or increased compared to admission/enrolment observations,
iv. oxygen requirement in standard subnasal oxygen therapy exceeds >2L/min to maintain SpO2 ≥90%,
v. hospital internal Children's Early Warning Tool (CEWT) calls for medical review and escalation of care,
vi. decreased conscious level,
vii. deterioration of cardiovascular function with impaired peripheral perfusion,
viii. clinical judgment of attending (senior) medical officer triggers escalation of treatment and care.

<u>*Consider transfer to higher level of care*</u> if on NHF if one or more of the following is present:

i. increased work of breathing requiring escalation of respiratory support and assessed as severe respiratory failure (**Appendix 2**),
ii. heart rate remains unchanged or has increased compared to time period prior to change from SOT to NHF application,
iii. respiratory rate remains unchanged or has increased compared to time period prior to change from SOT to NHF application,
iv. oxygen requirement in NHF exceeds FiO2 ≥ 40% to maintain SpO2 ≥90%
v. hospital internal Early Warning Tool (CEWT) calls for medical review and escalation of care,
vi. decreased conscious level,
vii. deterioration of cardiovascular function with impaired peripheral perfusion,
viii. clinical judgment of attending (senior) medical officer triggers escalation of treatment and care.

Consider transfer if local staffing and expertise is inadequate. Relevant communication with RSQ/RFDS and accepting base hospital. The use of Telehealth is encouraged.

6.1.2 Acute Respiratory Failure (0-4 years of age) Bundle

For eligible patients meeting the inclusion criteria (see section 3.8)

The respiratory care bundle in short will encompass the following elements, including asthma guidelines: 1.) Diagnostic assessment and measurement of vital signs as per local guidelines and QLD children's early warning tool. 2.) Measurement of transcutaneous oxygen saturation (optimal if continuous). 3.) Assessment of the work of breathing. 4.) Oxygen therapy: administration of O_2 if saturations less than 90%. 5.) Nasal high-flow at weight specific flows if trial of standard oxygen is ineffective. 6.) Use Salbutamol by MDI/Spacer if wheeze present, consider oral prednisolone and magnesium sulphate. 7.) Consider iv antibiotics if bacterial infection is suspected and consider chest X ray and other pathology tests if required. Careful assessment of cardiovascular function to exclude sepsis. Assess the patient using the QLD paediatric sepsis pathway for rural and remote hospitals.

Disposition/Escalation: if the infant improves with the initial treatment, then continue monitoring progress.
Escalation of respiratory support from SOT to NHF should be considered if one or more of the following is present:

i. heart rate remains >160/min for longer than 2 hours
ii. respiratory rate remains >45/min for longer than 2 hours
iii. oxygen requirement on SOT exceeds standard oxygen therapy (2 L/min by nasal prong, or 8L/min by face mask) to maintain SpO_2 ≥90%
iv. the hospital internal Early Warning Tool (CEWT) calls for medical review
v. increased work of breathing requiring escalation of respiratory support and assessed as moderate to severe respiratory failure (**Appendix 2**).

Consider transfer to higher level of care if on NHF and if one or more of the following is present:

i. heart rate remains >160/min for longer than 2 hours since start of NHF,
ii. respiratory rate remains >45/min for longer than 2 hours since start of NHF

iii. oxygen requirement on NHF exceeds FiO_2 > 40% (dependant on hospital standard policy) to maintain SpO_2 ≥90%,
iv. the hospital internal Early Warning Tool (CEWT) calls for medical review
v. increased work of breathing requiring escalation of respiratory support and assessed as severe respiratory failure (**Appendix 2**)

Consider transfer if local staffing and expertise is inadequate. Relevant communication with RSQ/RFDS and accepting base hospital. The use of Telehealth is encouraged.

Consultation with higher level of service for all NHF patients
Consultation with the level ≥4 hospital (normally the accepting hospital if transfer is required) will be at 2hrs post commencement of NHF therapy or sooner if required using standard QH video call resources. Communication throughout the tertiary consultations will use the ISBAR technique (standardised within Queensland Health) in conjunction with the Advice/Retrieval Record Paediatrics (MR262) procedures.

6.2 Implementation Procedures

6.2.1 *Respiratory Care Bundle, the existing standard practice in Southeast Queensland (ARF Flow Chart – Appendix 3)*
The proposed evaluation of the respiratory care bundle encompasses current best practice recommended by Queensland Health.
Queensland Health has published dedicated guidelines for the treatment of infants with bronchiolitis, asthma guidelines, pneumonia/sepsis guidelines and NHF guidelines (as per QHEPS). For some of these guidelines an adapted form has been published for rural and remote settings (Procedure titled: *The remote management of high flow nasal cannula therapy in paediatric and adolescent patients* (TCHHS-CLIN-1,6,8-PRO-0573). The implementation process in this study will use these guidelines without any further adaptations. The proposed respiratory care bundles for Bronchiolitis and Acute Respiratory failure include the QH guidelines and are specifying in greater detail the potential indicators when escalation of care is considered. They reflect distinct clinical boundaries ensuring safe application and adherence to the existing QH guidelines.

6.2.2 Facilitation and Education
A comprehensive educational bundle including onsite tutoring will be implemented accessing local resources and knowledge to achieve sustainability of the respiratory care bundle. This facilitation and education program will be costed for health economy analysis. In our previous 2 RCTS and in the implementation period thereafter in SEQ, we demonstrated the success of the proposed education elements and materials. The education material will be adapted to local needs where necessary. Education will be delivered using the following elements:

1.) Train the trainer program will train local educators using face-to-face workshops
2.) eLearning courses (developed by Griffith University Institute for Educational Research), dissemination of local guidelines and education material utilising Queensland Health educational modalities such as PARROT
3.) Equipment training (oxygen delivery methods and monitoring)
4.) Facilitation of local continuous education of local clinical staff
5.) Integration of the respiratory care bundle into local mandatory education

Transient staffing is a concern in these settings, such that education needs to be easily accessible and simple to use. Education will be underpinned by a solid theoretical and practical foundation in the care of a child presenting with a respiratory illness. Staff will have training in particular devices and therapies which requires development and competency of where nurses and doctors are able to make deliberate choices by using and integrating knowledge, skills, judgement attitudes and personal values. Educational materials in different modalities and format, information and medium used will aim to meet the transient staffing that occurs in these settings. In some instances, the educational material can be provided prior to the new staff commencing such that they have access prior to starting on their first day.

During the implementation phase data on resource allocation will be collected from the trainers and trainees – (e.g. training materials, staff time (and at what level), travel and other expenditures). The number of tasks completed and to what level they were completed will also be collected.

Delivery of training

In the first year of this project the existing training capacity of each hospital will be assessed, and gaps identified. The training will occur on two levels. The first level is provided by the local research nurse allocated to each site. The local research nurse will be provided with their training by the lead investigator and study coordinator to ensure consistency. This will be a 'Train the Trainer' model. In collaboration with the local nurse educator the local research nurse (now fully educated and trained) will apply the relevant training material and continue education throughout the project. The second level of training will be provided by SToRK (Simulation Training on Resuscitation for Kids), using resources already available and new training material. We will use online training material using the QHEPS platform, which includes training videos and access to the current Queensland Health guidelines via Queensland Paediatric Emergency Guidelines (QPEC). The training package will be adapted to the local context for maximum impact and sustainability.

6.2.3 Development Process of an Acute Respiratory Care Bundle for the local context in rural and remote hospitals:

A QLD Health led working group which will include members from the Remote PARIS expert panel will meet for round table discussions for the purpose of reaching consensus on a Respiratory Care Bundle for the safe management of patients less than five years of age (4yrs + 364 days) presenting with ARF at any of the participating hospitals. The working group participants will be provided with verbal and written information about this research project and invited to participate in the working group.

Working Group members will be drawn from key local stakeholders as well as those involved in retrieval, and clinical governance. These will include:

- Medical Superintendents/Director of Paediatrics and/or Emergency Department of each Hospital and Health Service
- RFDS and Retrieval Services Queensland
- SToRK
- Cairns and Townsville Base Hospital: Emergency, Paediatrics, Intensive Care Unit
- Children's Critical Care and Emergency Research Group, Gold Coast University Hospital, Brisbane (earlier PARIS RCT clinical research leaders)
- Local nurse/medical representation

The expert working group panel will be facilitated by the Steering Committee and the Trial Management Group who will lead the discussion of each topic within the already existing clinical guidelines and question these sections with what the experts recommend for the remote and rural context Respiratory Care Bundle. Scientific content of panel deliberations will be informed by existing guidelines and literature:

1. Australasian Bronchiolitis Guideline;[17]
   Australasian bronchiolitis guideline - PubMed (nih.gov)
2. Children's Health Queensland Hospital and Health Service Bronchiolitis - Emergency management in children
   Bronchiolitis – Emergency management in children | CHQ (health.qld.gov.au)
   Bronchiolitis - Emergency management in children (health.qld.gov.au)
   Bronchiolitis – Emergency management in children – Flowchart (health.qld.gov.au)
3. Children's Health Queensland Hospital and Health Service Pre-school wheeze – Emergency Management in Children
   Pre-school Wheeze - Emergency guideline | Children's Health Queensland
   Pre-school wheeze – Emergency management in children – Flowchart (health.qld.gov.au)
4. Children's Health Queensland Hospital and Health Service Asthma – Emergency Management in Children (ref)
   Asthma - Emergency guideline | Children's Health Queensland
   Asthma – Emergency management in children – Flowchart (health.qld.gov.au)
5. Children's Health Queensland Hospital and Health Service Community Acquired Pneumonia – Emergency Management in Children
   Community Acquired Pneumonia - Emergency management in children (health.qld.gov.au)
6. Children's Health Queensland Hospital and Health Service's Guideline on High Flow Nasal Cannula Therapy. [18] This guideline was formulated as a result of existing research pertaining to the Paediatric Research in Emergency Departments International Collaborative (PREDICT) where the Australasian Bronchiolitis Guideline was published.[17] This guideline is consistent with teaching from the Queensland-wide Stork Team education programs who carry out expert education in Cape York, therefore it was considered significant to include as literature for the expert panel to refer to.
   High Flow Nasal Therapy (health.qld.gov.au)
7. Queensland Government's Cairns and Hinterland Hospital and Health Service Procedure: Remote Management of High Flow Nasal Cannula Therapy in Paediatric and Adolescent Patients. [19]
   https://qheps.health.qld.gov.au/__data/assets/pdf_file/0016/2210317/procedure-0573.pdf
8. TCHHS Procedure on Management of high flow nasal cannula therapy in paediatric and adolescent patients.[20]
9. Children's Health Queensland Hospital and Health Service Febrile illness – Emergency management in children
   Febrile illness – Emergency guideline | Children's Health Queensland
   Febrile illness – Emergency management in children more than 3 months – Flowchart (health.qld.gov.au)
   Febrile Illness – Emergency Management in Child ren < 3 months – Flowchart (health.qld.gov.au)
10. Children's Health Queensland Hospital and Health Service Sepsis Pathway for rural and remote facilities
    Sepsis clinical guidelines and tools | Children's Health Queensland

Emergency Department Paediatric Sepsis Pathway – Rural and Remote | Queensland Health (clinicalexcellence.qld.gov.au)
Sepsis – Recognition and emergency guideline | Children's Health Queensland
Sepsis – Emergency management in children – Flowchart (health.qld.gov.au)

11. Children's Health Queensland Hospital and Health Service Escalation and advice outside of ED in Queensland
    Queensland Paediatric Transport Triage Tool – Medical (health.qld.gov.au)
12. TCHHS Procedure on escalation and transfer of the deteriorating patient;[21]
    https://qheps.health.qld.gov.au/__data/assets/pdf_file/0025/2255209/procedure-0184.pdf

The expert working party will be provided with detailed information derived from the literature and other documented NHF therapy protocols prior to the first meeting. A meeting will be held with the use of videoconference where a panel discussion would be conducive to get answers and discuss in real time. For the most part, the existing guidelines/care pathways used by the rural and remote hospital and the metropolitan/tertiary sites such as Cairns and Townsville address the majority of the physiological decision-making when applying NHF therapy. The expert working group may therefore find it easier to not change these sections within the guideline and purely focus on the contextual components of the guideline that have not been addressed prior by metropolitan/tertiary sites. The expert working group will be asked to discuss relevant clinical requirements for the management of infants on NHF therapy in the remote study settings. They will be asked to consider any implementation/ remote contextual/ operational factors that may impact on the utility and/or feasibility of using NHF therapy and strategies for achieving consistent application of the therapy. This may include discussion around:

- Is there adequate staffing?
- Are there competent/skilled/educated staff for use of NHF therapy in paediatrics?
- Where will the child be cared for? (eg. Emergency, ward)
- Will this child's retrieval be delayed/cancelled due to NHF therapy being available and possibly lead to delayed best clinical care?
- Does NHF therapy commencement elicit an immediate retrieval response?
- Could videoconferencing be a sufficient means of tertiary review?

From these discussions, a draft respiratory care bundle and an implementation plan will be developed which will be considered through a series of iterations by the expert working party until reasonable consensus is obtained. The respiratory care bundle will be drafted taking on the results from expert opinion at the time of the meeting. [22] Involvement of all key stakeholders particularly in the decision making of a respiratory care bundle to guide clinical practice not only achieves agreement with consistency, but it also brings together knowledge from the people best placed to answer the questions.[22]

An analysis of relevant documents will be used to describe the process of the respiratory care bundle development. e.g. minutes of expert working group meetings, analysis of literature provided to the working group, written notes regarding the process kept by the study co-ordinator.

This expert working group will be retained throughout the entire research process to act as a stakeholder reference group to guide any modifications to the respiratory care bundle or research process, on a needs basis, throughout the action research process.

For this project, the ***Normalisation Process Theory (NPT)*** was selected to guide the implementation process [23]. NTP sought to explain the operationalisation of complex interventions in health care settings. It focuses on how 'new material practices' (e.g., evidence-based-practice, EBP) that are embedded into the social practices of everyday work, considering individual, group, and organisational levels of practice. The four components of NPT are: coherence or sense making; cognitive participation or engagement; collective action; and reflexive monitoring [23]. In all of the four domains the process is expected to be non-linear, co-occurring and dynamic. NPT has been extensively used to explain the implementation of clinical guidelines in clinical practice [24]. The Expert Recommendation for Implementing Change (ERIC) study will inform the choice of specific implementation strategies. The Stages of Implementation Completion (SIC) framework will be applied to monitor the roll out of the EBP [25].

Based on the implementation plan outlined above a number of strategies are reported on how to deal with the quantitative or qualitative data collection. However, it needs to be stated that the data management is generally led by the teams involved in the changes. As such the information provided in the **Table 1** below is a guiding principle.

After each data collection and analysis cycle, a joint team meeting will occur to discuss the results, provide feedback, and set new targets or goals for fidelity and sustainability. This is an iterative process and a collaborative team approach from those involved is required. Implementation costs including stakeholder engagement, hospital staff commitment, educators and trainee time, and travel for educators will be assessed. This is a hybrid 2-implementation design, which means that the study assesses the effectiveness and the implementation outcomes simultaneously.

Phase	Activities
Orientation	Awareness of Acute Respiratory Bundle Interest and involvement
Insight	Understanding Insight into own routines
Acceptance	+ve attitude, motivation to change +ve intention or decision to change
Change	Actual adoption of Acute Respiratory Bundle Confirmation of benefit or value of change
Maintenance	Integration of new practice into routines Embedding of new practice in the HSS/hospitals

Table 1: 5 phases of implementation

Identification and Description of Evidence Based Practice (EBP)

Structured implementation of a local context specific respiratory care bundle for infants and children with ARF including bronchiolitis presenting to an emergency department in rural and remote setting in North and Northwest Queensland.

Evidence. The existing evidence produced by our research team and others will inform the composition of a local context specific respiratory care bundle (successfully established for FNQ and SEQ). Evidence gained from the recent cluster randomised trial implementing bronchiolitis in Australia, and data from our knowledge translation study in SEQ, and data from the pilot phase of

this study will inform the context, which considers the community, the local medical culture, nursing and medical leadership [26].

Previous context development in pilot phase. In each participating site, local community members, medical and nursing leadership and existing local health care resources capacity will be identified. The pilot phase for this study, involved community engagement with an Indigenous Nurse and a prominent researcher in Aboriginal and Torres Strait Islander Health (A/Prof Sandy Campbell) and an Aboriginal & Torres Strait Island Liaison Officer within TCHHS (Mr Rexie Burke). Multiple Aboriginal and Torres Strait Islander stakeholders were consulted within Thursday Island and Cape York and final consultation was sought through the Executive Director of Aboriginal and Torres Strait Island Health with TCHHS. The concept and study design were further developed by representatives of the hospitals (Western Cape Medical Superintendent, Dr Marlow Coates), RFDS team members (Mr Lee Poole), RSQ (Dr Clinton Gibbs), Cairns Hospital and Townsville University Hospital (Dr Neil Archer and Dr Greg Wiseman) and clinical research representative of the PARIS trials and Queensland Statewide NHF paediatric clinical guideline (Dr Donna Franklin). For the upscaling of this project the same approach with emphasis to value the local context and culture will be taken. SToRK and Griffith Institute for Educational Research will provide a pedagogically robust e-learning solution, facilitate local delivery of face-to-face training and develop simulation tools to support iterative improvement of locally delivered procedures.

7. DATA

7.1 Data Collection

The precise data to be collected and their sources for the study are given as per the below Clinical Research Forms (CRF) and datasets:

CRF 1	***Clinical data***
Source for Clinical data: Patient's medical records, including observations and medical/nursing notes, discharge summary and admission form. Includes EDIS export to locate the relevant patients to obtain data from.	
CRF 2	***Health Economy data*** (specifically aimed at out-of-pocket costs for families and measures of quality of life)
Source for Health Economy data: Use of the GenPrem instrument will be for the parent as proxy for the child and as the parent for their own experience with their childs admission to hospital.	
CRF 3	***Implementation Science data*** (specifically aimed at knowledge, skill retention and fidelity)
Source for Implementation Science data: The Normalisation Process Theory tool will be used and adapted for the staff survey. This survey will be in paper and electronic format depending on what is most suitable for the local team.	

Other Datasets & Collection includes:
Health Economy data (specifically aimed at health care and transportation costs) – sourced as per current Qld Health per day admission costings for the ward and/or Intensive Care and transfer/retrieval costs.
Health Economy data (specifically aimed at implementation costs which includes education costs) – sourced by capturing all education records and monitoring/capturing data on the movement of the transient staff in these regions.

Data will be collected in an online REDCap database. In each site the emergency admissions will be screened for children 0-4 years of age presenting with respiratory symptoms. Data on the baseline demographics, physiology at presentation and initial medical management will be captured. Length of hospital stay, length of oxygen therapy, type of oxygen therapy, and amount of oxygen resources will be captured. Further information will be captured on methods of oxygen therapy. Adverse events will be recorded. For children who required transfer to high level of care, vital signs and clinical diagnosis and medical therapy provided at time of decision to transfer will be collected. Data on respiratory support during transfer, mode and length of transport and data on treatment in accepting hospital and length of hospital stay will be collected. Adherence to the respiratory care bundle will be measured by the number of frequency of deviations from the protocol.

Twelve parents per hospital using a face-to-face structured interview will complete a paediatric proxy health related quality of life measurer (PedsQL).

Historical Control. Admissions (HBCIS) to the participating hospitals in year 2016-2022 will be screened using the same screening log as in the main protocol (Year 2020-2022 will be separately analysed due to impact of COVID-19 pandemic) and the same data collection as above used.

Time Points for Data Collection*.* All physiological (heart and respiratory rate, temperature) and blood parameters (arterial gases) that are captured in the medical records during the hospital admission and where relevant during the transfer for higher level of care. If admitted to a tertiary hospital, data on respiratory support provided will be captured.

Specific data
The specific data set mirrors in its basic form the data captured in our previous 3 large RCT's using nasal high-flow in children with ARF or bronchiolitis. Additional data on out-of-pocket expenses and lost income will be recorded.

Background data:
Background data collection will be collected as per the CRF. Below outlines some of the specifics which continue the same data collection of the 3 large RCT's.

Demographics:

- Age (on admission)
- Gender
- Weight (on admission)
- Ethnicity
- Diagnosis at admission
- History and risk factors
    - Prematurity (<37 weeks at birth)
    - Previous neonatal respiratory support post delivery
    - Previous Intensive Care admission post delivery
    - Previous hospital admission for respiratory support postnatal period
    - Complex patient
    - Previous Intensive Care admission postnatal period
    - History of chronic lung disease
    - History of congenital lung disease
    - Family history of allergies, asthma, wheeze

7.2 Implementation Science Data and Health economy Data

Several methods including interviews and questionnaires will occur across the study period to capture relevant data on the consumer/s (parents/guardians/carers), health practitioners and health care leaders experience.

Clinical Staff Interviews:

Knowledge and skill retention: Structured face-to-face interviews/questionnaires with local clinical staff to measure knowledge retention prior to implementation and six months post implementation for 12 months. Adherence audit of the respiratory care bundle will be measured comparing actual practice against recommended practice [26] on a 6 monthly interval during the 31 month implementation phase.

The following 5-6 key knowledge domains will be measured:

- Recognition of bronchiolitis or ARF and use of existing guidelines/source of truth
- Oxygen therapy thresholds
- Indication for high-flow
- Indication for escalation of care
- Correct use of high-flow
- Weaning of high-flow

Interviews with open ended questions: Perform structured interviews with selected consumers/parents and clinicians working in the participating hospitals to obtain information regarding socio-economic factors and experience during the study. There will be specific and open ended questions to capture the full image of concerns raised by the local stake holders. A post hoc categorisation will occur.

Hospital System interviews: Standardised interviews with leadership roles to measure adaptation of EBP in the local hospital context, including staff turnover management.

Parent interviews:

A structured interview with 12 parents per hospital in the Control Phase and 12 parents in the Implementation phase will be conducted after obtaining written formal consent (**Figure 3**). The following key domains will be covered:

- Previous experience with hospital admission or transfer
- Socioeconomic data
- Living conditions
- Work interruption, income interruption
- Out of pocket costs, accommodation, transfers

Economic evaluation of the implementation process will be conducted with the aim to evaluate the association between cost of implementation, depth of implementation and how this affects the key primary outcome. An alongside trial cost analysis will be carried out, with the effect of implementation depth and cost regressed against the key primary outcome (adjusting for covariates).

8. STATISTICAL METHOD

8.1. Sample Size

Pre COVID-19, the participating 14 hospitals in Far North QLD have admitted over 4 years (2016-2019) a total of 2532 children with ARF. The transfer rate in these hospitals was during this period 25%. With the implemented intervention of the full study in 14 hospitals, we aim to achieve a reduction in transfers from 25% under the existing respiratory care pathways to 12.5% under the intervention condition (for all children with ARF aged 0-4 years). Our sample size of minimal eligible participants of 90 patients per hospital (1,260 patients in total) achieves over 85% power to detect this difference in transfer rates assuming an intracluster correlation coefficient of 0.1 and using a two-sided test at the 5% level of significance with the Stata function “stepped wedge”. [15, 16] Our calculation under a stepped wedge design assumes a sequential rollout schedule of the intervention that has 4 steps, with 3 or 4 hospitals randomised at each step and an average of 18 patients per hospital per time point within a 6-month interval (i.e. a total of 90 patients per hospital including baseline recruitment). The total trial duration will be 31 months including a 1-month transition period for each hospital.

8.2 Data Analysis

Generalised linear mixed models (GLMMs) will be used to account for cluster hospital effects with adjustment for the rollout time of the intervention and potential district effect and estimate the change in the proportions of PICU transfers (using a logistic link function) as well as the length of stay in acute care settings (using Poisson or negative binomial distributions) under the intervention condition, compared with those under the control condition. Model fit and assumption testing will

be conducted as appropriate within the GLMM framework and significance will be set at $p<0.05$. The GLMM can handle missing data in the outcome variable under the ignorable mechanism (such as missing completely at random).

8.3 Methods for health economics evaluation

Economic evaluation of the intervention will be conducted using standard approaches and will be from a health care provider and societal perspective. An alongside trial economic evaluation will be undertaken, with primary outcomes of cost benefit/net benefit analysis and cost effectiveness analysis (formulated as the incremental cost-effectiveness ratio [ICER]) in the form of the incremental cost per air transport avoided.

The ICER is the ratio between the incremental cost and the incremental outcome. Incremental cost is the cost difference between the intervention and usual care. Incremental outcome is the outcome difference between the intervention and usual care. The economic evaluation will compare any incremental costs of the intervention (costs accrued in the intervention arm compared to those in the control arm) to the full list of incremental primary and secondary outcome endpoints, all expressed in their natural units of measurement. Given the pilot data and reductions in cost associated with it, a net monetary benefit and return on investment approach will be applied to estimate the potential value of the new NHF model. The net monetary benefit of an intervention is specified as: $\Delta Cost_{intervention} - \Delta Cost_{consequences}$. Where a net monetary benefit of greater than 0 represents a positive return on investment (where a reduction in cost consequences associated with the intervention is specified as a negative). With respect to return on investment, the direct incremental costs of the intervention ($Cost_{inv}$) are separated from the incremental cost consequences ($Cost_{con}$) associated having made the intervention.

Costs will be measured from activity data with pathway analysis to fully specify all activities in both intervention and control arms. Health service utilisation, adverse reactions, length of stays and associated costs will be obtained from linking the study patient data to QLD health data bases (e.g., T2 costing system). Data on social cost offsets will be collected directly from the patients' carers. Standard discounting will be applied to both cost and outcomes, with uncertainty in the cost and outcome data subjected to sensitivity analyses.

Consumer satisfaction: Data on consumer satisfaction with 12 parents/carers per hospital using a face-to-face structured interview with local clinical staff will be recorded with the GenPrem instrument. The GenPrem is an 8 dimension, 41 item. Patient reported experience measure which explores the domains of Convenience; Communication; Quality; Environment and facilities; Integration; Involvement; Discomfort; and Patient-centred care.

Evaluation of the Implementation outcomes measures:

Implementation Outcomes	**Data analysis**
Implementation outcomes	***Society for the Implementation Research Instrument tool kit.***
Use of EBP as a routine treatment locally.	SIRC acceptability measure.
Feasibility of the implemented changes.	SIRC Feasibility measure.
Acceptability of the EBP.	SIRC Adoption measure.
Satisfaction with the use of EBP (all stakeholders).	SIRC Penetration, Adaptability, and Sustainability measures.
Satisfaction with the implementation process.	SIRC Engaging measures (implementation leaders, opinion leaders, champions, external agents).
Evaluation of the EBP implementation is good.	SIRC Executing, Planning, Reflecting and Evaluating Measures.
Recommended for further implementation in other healthcare settings.	SIRC satisfaction and client outcome measures.
Service/Research Outcomes	
Satisfaction with education and competencies associated with AFR management.	SIRC Knowledge and beliefs about the intervention, Individual stage of change, Self-efficacy, Individual stage of change.
Aeroevacuation use is reduced.	Cost analysis of reduced high intensity care.
Electronic medical record prompts are operational.	Audit of electronic records.

Economic evaluation of implementation process

Economic evaluation of implementation strategies for NHF therapy will be examined. Economic evaluations of the implementation will revolve around the costs of different implementation strategies employed in the project and will focus on outcomes relevant to implementation research questions (e.g., acceptability, fidelity, reach) instead of health reported outcomes. Adherence to the respiratory care bundle will be measured by the number of frequency of deviations from the protocol. Specifically, we will consider implementation costs (see **Appendix 4**) to include all processes and strategies required to implement. Depending on how the implementation occurs at each site, implementation cost may vary. The economic evaluation of implementation will be based on a costing study, depending on the differences in implementation strategies used a regression analysis will be conducted to explore the differences between implementation success and depth of strategies used.

Milestones	Deliverables	Performance Indicator	Activity Timeframe
Study Set up Period			
PHASE I Oct 2022 – Sept 2023 **(11mths)**	Approvals Ethics application Governance application Trial Steering Committee and other relevant investigator meetings/groups established	All legislative requirements met June 2023.	0-9 month
	Personnel recruitment: Project Manager Appointment Educator Appointment	April 2023	0-6 month
	Indigenous Community Officer engagement Staff Interviews for current practice Parent interviews	April 2023	0-6 month
	Clinical consultation Process Local Context Assessment Workshops readiness for Staff Interviews for local Guidelines Approval of local Guidelines Site logistics fact finding visits	August 2023	0-11 month
	Education Material Workshop Development Digital Platform	Griffith Digital Education finalised August 2023	0-11 month
	Database Development	August 2023	0-11 month
	HE Model Development	August 2023	0-11 month
	Randomisation of units (hospitals)	August 2023	10-11month

	Data collection of paediatric ARF admissions in participating sites (historical)	September 2024	0-24 month
Study Implementation Period			
PHASE II Sept 2023 – Mar 2026 **31 mths)**	Staff Readiness Assessment for Implementation of Respiratory Care Bundle per site	Sept 2023-Mar 2026	At time of site commencement according to randomisation
	Start-up and Ongoing Training Workshops driven by study team	Sept 2023-Mar 2026	At time of site commencement according to randomisation
	Workshops for train the trainer eLearning courses	Sept 2023-Feb 2026	11-39 month according to randomisation of site
	Consultation Feedback (Guideline)	Sept 2023	6-11 month
	Consumer Feedback (Parents)	Sept 2023	6-12 month
	Historical Data collection	Oct 2022-Sept 2025	6-30 month
	Patient screening, data capturing, data cleaning	Sept 2023-Mar 2026	11-40 month
	Measurement of Knowledge Retention (Staff Interviews)	Sept 2023-Mar 2026	11-40 month
	Measurement of Health Economy (Parent interview/questionnaire)	Sept 2023-Mar 2026	11-40 month
	Measurement of Parent Satisfaction (Parent interview/questionnaire)	Sept 2023-Mar2026	11-40 month
	Continuous Education driven locally and by study team	Sept 2023-Mar 2026	11-40 month
Study Analysis			
PHASE III Mar 2026– Sept 2027 **(18 mths)**	Observational Data post study collection	Apr 2026-Apr 2027	41-51 month
	Assessment of Sustainability Staff Interviews Consumer Interviews	March 2027	40-52 month
	Reporting/Manuscripts: Main paper HE Paper Implementation Paper Consumer perspective Paper	March 2027	40-60 month
	Conference presentations		52-60 month

9. ADVERSE EVENTS AND RISKS

9.1 Adverse Event Definitions

Adverse Event (AE)
Adverse event data is collected as part of the study design and will form part of the secondary outcomes of the study. Conditions that are present at screening and do not deteriorate will not be considered adverse events. These outcomes will be routinely reported via standard hospital internal reporting methods/risk management processes. If any of the attending clinicians suspect an adverse event that is related to the study design, such an adverse event will be immediately reported to the Chief Investigator and Townsville HHS HREC.

For the purposes of this study the site investigator is responsible for recording all AEs, regardless of their relationship to study intervention. Conditions that are present at screening and do not deteriorate will not be considered AEs.

Serious adverse event (SAE)
SAEs for this study are defined as:

- Hypoxaemia leading to cardiac massage which the clinician believes is related to one of the study interventions
- Cardiac arrest: Loss of spontaneous cardiac output
- Mortality (all events will be reported)
- OR any life-threatening medical event or reaction which the clinician believes may be study related

Adverse event (AE)
AEs are defined as but limited to the following:

- Severe hypoxaemia with saturations <80% for longer than 1 minute
- Pneumothorax
- Unexpected need for endotracheal tube placement
- Bradycardia: bradycardia not requiring treatment; bradycardia of <60/min [27, 28]

9.2 Reporting of SAEs

All SAE data will be recorded on a SAE form on the CRF and submitted to the Townsville HHS HREC within 24-72hrs, in accordance with the safety reporting policy of HREC. Information reported will include: patient initials and study number, nature of the event, start and end time of the event, investigators opinion of relationship between implementation of the respiratory care bundle and the event (unrelated, possibly, probably or definitely related). Notification to the Townsville HHS HREC and their response may require amendment/s to the respiratory care bundle. If this occurs the necessary changes will be made.

9.3 Assessment and documentation of adverse events

The description of each AE on the CRF will include all of the following:

- Description of the AE
- Onset date, duration, date of resolution
- Severity (mild, moderate or severe)
- Seriousness
- Treatment/Management/Action taken
- Outcome (recovery, death, continuing, worsening)
- Likelihood of relationship of AE to the study treatment (Unrelated, Possible, Probable, Definite).

Changes in the severity of an AE will be recorded on the CRF.
AEs characterised as intermittent will be documented for each episode.
All AEs will be followed to adequate resolution or stabilisation, where possible.

9.4 Eliciting adverse event information

AEs will be documented from physical examination findings, clinically significant lab results or other documents that are relevant to patient safety.

9.5 Risk/benefit analysis

Individual patient care will be driven by standard practice before and after implementation of the respiratory bundle. An independent data safety monitoring board (DSMB) will be tasked to monitor study progression and assess trajectory of study outcome.

Potential risks.

This study is performed in a health care setting with a relatively high staff turnover. This may lead to decreased adherence to the respiratory care bundle. Mitigation: the education will be part of the required mandatory education in each hospital.
A delay in the transfer of patients who definitively require high level of care. Mitigation: the bundle sets robust boundaries and thresholds of when escalation must occur and hence this is unlikely to occur. Patient care will occur within the standard clinical treatment framework.

Potential benefits.

Reduction of unnecessary transfers to higher level of care. Increased clinical staff knowledge, confidence and skillset caring for children less than 5 years with acute respiratory failure. Increased clinical staff and consumer satisfaction.

10. DATA SECURITY

10.1 Data Storage

Data will be stored and locked by the investigating site in a locked cupboard in a secured location. Electronic data will be securely stored on the RedCAP databased, hosted by

Griffith University, Queensland. Following analysis, data will be transferred to a password protected computer file and stored on the secured and backed up drive at Griffith University, Brisbane.

10.2 Record Retention

As required by the Queensland State Archivist, and in keeping with the QH Retention and Disposal Schedule 2DAN546 v3 (Clinical research records for minors – Section 2659), all study information and documentation will be securely stored until the patient reaches one of the following retention age periods, before being securely destroyed. This also complies with the Australian Code for the Responsible Conduct of Research Section 2.1.1

- Retain until patient/client attains 18 years of age AND
- Retain for 15 years from completion of clinical research/trial or after date of publication or termination of the study AND
- 10 years after last patient/client service provision or legal action, whichever is the later.

11. STUDY OVERSIGHT

Oversight and Governance.

The trial will be overseen by a ***Trial Steering Committee (TSC)***, the membership of which will include: the CIA, and at least 2 further CIs. The role of the TSC will be to: monitor and supervise progress of the trial; review at regular intervals relevant information from other sources.

The ***Trial Management Team*** consists of the chief investigator, the project manager, and the lead educator.

Site trial management will be coordinated within each Hospital and Health Service (HHS) by a Site Trial Management Team consisting of the HHS PI and an HHS research nurse. The site PI will be responsible for local oversight of the study including: monitoring safety; ensuring that the study is conducted according to the protocol; and ensuring data integrity. The site PI will review the data for safety concerns and data trends at regular intervals and will promptly report to the Townsville HHS HREC and the central coordinating team any significant protocol deviation or any other significant event or problem that arises during the conduct of the study.

Quality Control and Quality Assurance

To standardise the collection of data by local research nurses, training of the research nurse will be undertaken by the lead educator; the research nurse will train the remaining local clinical team in particular the senior medical staff.

12. ETHICS AND DISSEMINATION

Research Ethics Approval

This protocol and any subsequent modifications will be reviewed and approved by the Townsville Hospital and Health Services Human Research and Ethics Committee. A letter of protocol approval by Townsville HHS HREC will be obtained prior to the commencement of the study, including approval for other study related documents for Townsville HHS HREC review and approval.

Site-specific agreement (governance) will be obtained for each site by the site chief investigator. This study will be performed in accordance with the ethical principles of the Declaration of Helsinki, ICH GCP for Guidance on Good Clinical Practice and NHMRC National Statement on Ethical Conduct in Research Involving Humans.

Modifications to the protocol

This study will be conducted in compliance with the current version of the protocol. Any change to the protocol document or Informed Consent Form that affects the scientific intent, study design, patient safety, or may affect a participant's willingness to continue participation in the study is considered an amendment, and therefore will be written and filed as an amendment to this protocol and/or informed consent form. All such amendments will be submitted to the Townsville HHS HREC, for approval prior to becoming effective.

Protocol Deviations

All protocol deviations must be recorded in the patient record (source document) and on the CRF (including REDCap) and must be reported to the PI. Protocol deviations will be assessed for significance by the Principal Investigator. Those deviations deemed to have a potential impact on the integrity of the study results, patient safety or the ethical acceptability of the trial will be reported to the Townsville HHS HREC in a timely manner. Where deviations to the protocol identify issues for protocol review, the protocol will be amended as per section 12.2.

Confidentiality

Participant confidentiality is strictly held in trust by the participating investigators, research staff, and the sponsoring institution and their agents. The study protocol, documentation, data and all other information generated will be held in strict confidence. No information concerning the study, or the data will be released to any unauthorised third party, without prior written approval of the sponsoring institution. Clinical information will not be released without written permission of the participant, except as necessary for monitoring by Townsville HHS HREC or regulatory agencies.

Dissemination and translation plan

Given the lead role of the investigators in the paediatric acute medicine health care sector; their role in regional and state-wide guideline development processes; their involvement in

professional colleges and at key educational conferences it is likely that the findings will have nationwide impact across Australia and New Zealand.
Publication in high impact peer-reviewed journals will be sought and presentation at national and international conferences is anticipated. Novel and modern information dissemination strategies will also be used including social media, podcast presentations and Free Open Access Medical education (FOAM) resources to generate discussion and disseminate the outcomes of the study.
The preliminary outcomes will be summarised and presented orally to community health action groups and other relevant consumer group and at local hospital staff meetings and emailed to management staff for dissemination. Local formal dissemination will occur at the end of the project via research scientific symposiums in each of the hospital and health care services. All publication/s will be disseminated and shared with each participating site and made available to health care providers and executives in their health service.

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APPENDICES

Appendix 1

NHF therapy minimum flow rates

Weight	NHF Flow rates
0-12 kg	2L/kg/min
13-15kg	30L/min
16-30 kg	35L/min
31-50 kg	40L/min
>50 kg	50L/min

These flows are indicative and should serve as a starting point but can be varied according to clinical need.

Appendix 2

Assessment of the severity of respiratory failure

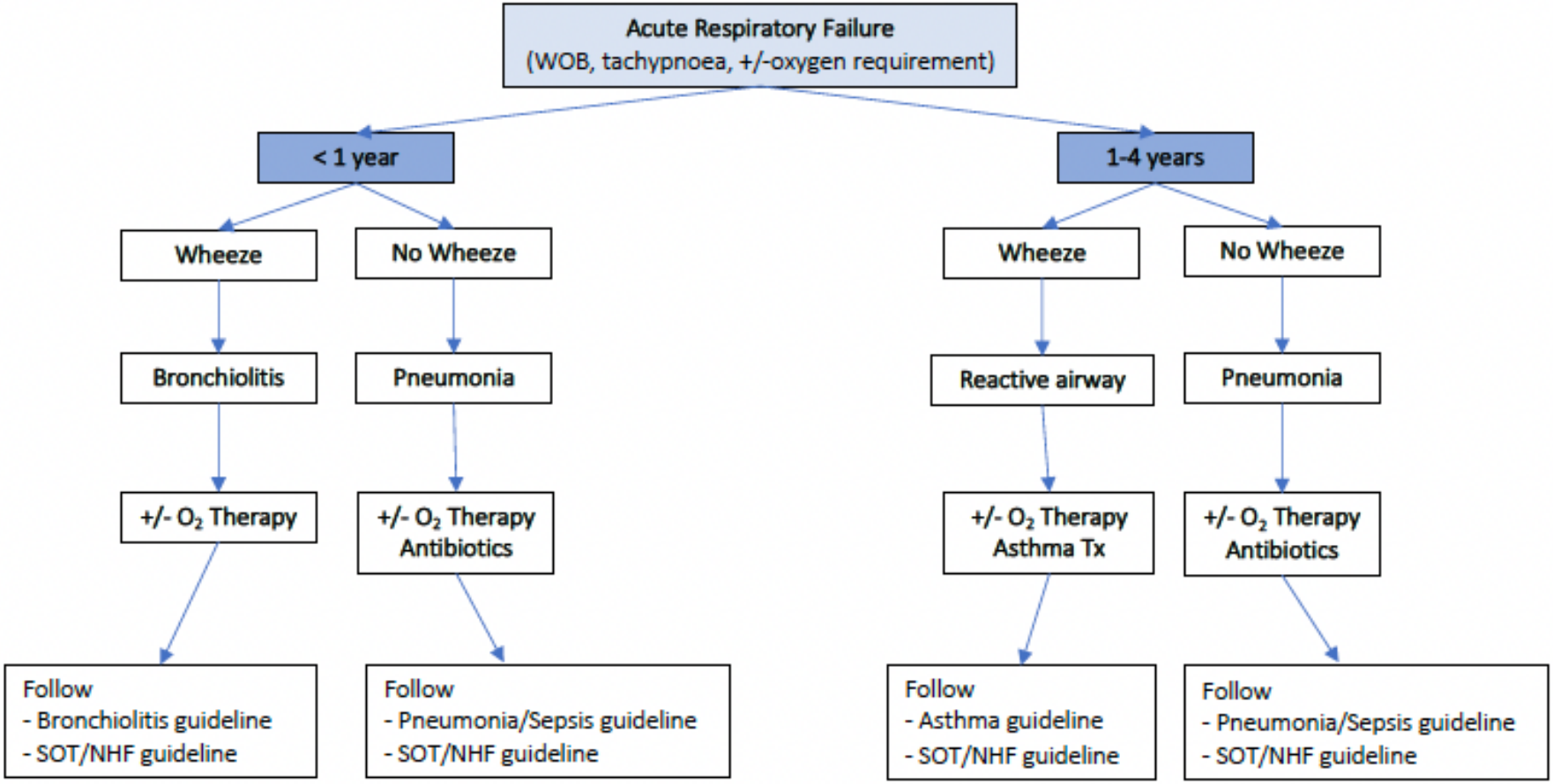
Assessment

	Mild	Moderate	Severe
Behaviour	Normal Able to talk normally	Some / intermittent irritability Some limitation of ability to talk	Increasing irritability and / or lethargy Marked limitation of ability to talk or unable to talk
Tachypnoea* (at rest - ie not crying)	Normal or mildly increase respiratory rate *(normal values by age)*	Increased respiratory rate	Increased or markedly reduced respiratory rate as the child tires.
Signs of increased work of breathing **Retraction** *(intercostal, suprasternal, costal margin)* *Paradoxical abdominal breathing* **Accessory muscle use** *Nasal flaring* *Sternomastoid contraction (head bobbing)* *Forward posture*	None or minimal	Moderate retractions and / or accessory muscle use	Marked increase in accessory muscle use with prominent chest retraction.
Oxygenation Oxygenation is only of limited utility in judging severity in many paediatric respiratory conditions. Don't just focus on the SaO_2 monitor. Look at the other signs.			O_2 saturations less than 90% (in room air) Any O_2 requirement in croup is classed as severe Cyanosis
Heart Rate	Normal or slight increase	Mildly increased	Significantly increased or bradycardia
Blood Pressure	Normal	Increased	Increased or decreased late.

Source: The Royal Children's Hospital Melbourne Assessment of severity of respiratory conditions
https://www.rch.org.au/clinicalguide/guideline_index/Assessment_of_Severity_of_Respiratory_Conditions/

Appendix 3

ARF Flow Chart



Clinicians' guide to the relevant Queensland Health guidelines

Appendix 4

All below will be costed for sustainability.

Implementation Strategies	2024/25	2025/26 @ 6 month intervals (4 x six month measurements/hospital)					What to measure?
	Pre-Impl	#1	#2	#3	#4	S	
Phase One Approvals						**Post**	
What needs to be approved and by whom? System thinking diagram?							
Community engagement							No. of meetings, who was present (staff), how long it took
Who needs to be engaged?							Need to decide on parameter of measurements HSS – individual hospitals Who is doing the measurement of engagement?
Healthcare professionals? First nations?							
First nations?							
Recruitment							
Who needs to be recruited? Staff hired?							
Who needs to be trained?							Measure: Time for training, no of sessions to achieve effectiveness and sustainability;
Mode of training per location							Online, face to face? Costing? Length of session;

Implementation Strategies	2024/25	2025/26 @ 6 month intervals (4 x six month measurements/hospital)				POST	What to measure?
	Pre-Impl	#1	#2	#3	#4	S	
Who is doing the training?							
Who is developing the educational materials? Time of training (e.g. 2 x1 hour etc).							
Readiness planning							
Feasibility: data collection & analysis of monitoring the implementation (barriers and facilitators + real time feedback to team so it can be addressed as it happens or shortly after) – Qualitative – reporting system							
Phase Two							
Staff hired & trained – so ready to implement							
Who is doing a face to face education – Is this continuous? How is this different from Phase 1?							
Services & consultation begins							
On-going services, consultation, fidelity monitoring & feedback							
Competency							
Up-scaling planning to different parts of the remote rural areas							
Phase Three							

Implementation Strategies	2024/25	2025/26 @ 6 month intervals (4 x six month measurements/hospital)				POST	What to measure?
	Pre-Impl	#1	#2	#3	#4	S	
Observational period – it was unclear to me what is going to be observed							
Data acquisition? What is going to be collected here?							
Interviews with whom and why?							
Healthcare cost data acquisition – I would include health equity calculation here. Not often used by health economists, but they should use it here. – distributional cost effective analysis							
Phase Four							
What exactly is happening in this period? what is going to be monitored? Why and how often?							
Phase Five							
What data is being analysed – as data analysis should be ongoing from phase one regarding barriers and facilitators of the process.							

Implementation Strategies	2024/25	2025/26 @ 6 month intervals (4 x six month measurements/hospital)				POST	What to measure?
	Pre-Impl	#1	#2	#3	#4	S	
Sustainability – what does this mean in this project? Once defined, then it can be measures (Network analysis? System change? Less Staff turnover?)							
Measurement of knowledge retention doesn't make sense here. It should be ongoing, and within 5 years, there might be changes							
What about community engagement – service and care model improvements and so on?							

N.B. S=Sustainability