DEPARTMENT FOR HEALTH AND AGEING

REVIEW OF THE NATIONALLY FUNDED CENTRES (NFC) PAEDIATRIC LUNG AND HEART-LUNG TRANSPANT PROGRAM

FINAL REPORT

29 JUNE 2016
Final Report
29 June 2016
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<th>Abbreviation</th>
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</thead>
<tbody>
<tr>
<td>2010 NFC Assessment</td>
<td>Health Technology Assessment of a Proposal to Establish Paediatric Lung and Heart-lung Transplantation Procedures as a Nationally Funded Centre (DLA Phillips Fox, no date included on document)</td>
</tr>
<tr>
<td>2015 Review submission</td>
<td>Review submission from AHM with RCH, dated September 2015 (received 28 September, 2015)</td>
</tr>
<tr>
<td>Q1 2015-16</td>
<td>Three months ended September 2015 (first quarter of the financial year)</td>
</tr>
<tr>
<td>ACT</td>
<td>Australian Capital Territory</td>
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<tr>
<td>AHM</td>
<td>The Alfred Hospital, Melbourne</td>
</tr>
<tr>
<td>AHM-revised costing</td>
<td>The revised AHM costing provided to the Review on 7 December 2015 (noting that this differs from the costs reported in the 2015 Review submission)</td>
</tr>
<tr>
<td>ANZCOTR</td>
<td>Australia and New Zealand Cardiothoracic Organ Transplant Registry</td>
</tr>
<tr>
<td>ANZOD Registry</td>
<td>Australia and New Zealand Organ Donation Registry</td>
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<tr>
<td>BOS</td>
<td>Bronchiolitis obliterans syndrome</td>
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<tr>
<td>CF</td>
<td>Cystic Fibrosis</td>
</tr>
<tr>
<td>CHD</td>
<td>Congenital Heart Disease</td>
</tr>
<tr>
<td>COAG</td>
<td>Council of Australian Governments</td>
</tr>
<tr>
<td>DBD</td>
<td>Donation after Brain Death</td>
</tr>
<tr>
<td>DCD</td>
<td>Donation after Cardiac Death</td>
</tr>
<tr>
<td>DRG</td>
<td>Diagnosis Related Group</td>
</tr>
<tr>
<td>ECMO</td>
<td>Extra-corporeal membranous oxygenation</td>
</tr>
<tr>
<td>ES</td>
<td>Eisenmenger’s syndrome</td>
</tr>
<tr>
<td>EVLP</td>
<td>Ex Vivo Lung Perfusion</td>
</tr>
<tr>
<td>FTE</td>
<td>Full Time Equivalent</td>
</tr>
<tr>
<td>HITH</td>
<td>Hospital in the Home</td>
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<tr>
<td>HOI</td>
<td>Health Outcomes International</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>ICU</td>
<td>Intensive Care Unit</td>
</tr>
<tr>
<td>IHPA</td>
<td>Independent Hospital Pricing Authority</td>
</tr>
<tr>
<td>IPAH</td>
<td>Idiopathic Pulmonary Arterial Hypertension</td>
</tr>
<tr>
<td>IPF</td>
<td>Idiopathic Pulmonary Fibrosis</td>
</tr>
<tr>
<td>IPLTC</td>
<td>International Paediatric Lung Transplant Collaborative</td>
</tr>
<tr>
<td>ISHLT</td>
<td>International Society for Heart and Lung Transplantation</td>
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<tr>
<td>LOS</td>
<td>Length of stay</td>
</tr>
<tr>
<td>NHCDC</td>
<td>National Hospital Cost Data Collection</td>
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<td>NHMRC</td>
<td>National Health and Medical Research Council</td>
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<tr>
<td>NFC</td>
<td>Nationally Funded Centre</td>
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<tr>
<td>NFC PLHLT Program</td>
<td>The Nationally Funded Centre Paediatric Lung and Heart-Lung Transplantation Program</td>
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<tr>
<td>NSW</td>
<td>New South Wales</td>
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<tr>
<td>NT</td>
<td>Northern Territory</td>
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<tr>
<td>PLHLT</td>
<td>Paediatric Lung and Heart-Lung Transplantation</td>
</tr>
<tr>
<td>PMG</td>
<td>Project Management Group</td>
</tr>
<tr>
<td>RCH</td>
<td>Royal Children’s Hospital, Melbourne</td>
</tr>
<tr>
<td>Review Period</td>
<td>The three financial years spanning the period 2011-12 to 2013-14.</td>
</tr>
<tr>
<td>SA</td>
<td>South Australia</td>
</tr>
<tr>
<td>SCHN</td>
<td>Sydney Children’s Hospital Network Westmead</td>
</tr>
<tr>
<td>SRTR</td>
<td>Scientific Registry of Transplant Recipients</td>
</tr>
<tr>
<td>TAS</td>
<td>Tasmania</td>
</tr>
<tr>
<td>The Review</td>
<td>This review, the review of the Nationally Funded Centre Paediatric Lung and Heart-Lung Transplant Program (the NFC PLHLT Program).</td>
</tr>
<tr>
<td>TSANZ</td>
<td>Transplantation Society of Australia and New Zealand</td>
</tr>
<tr>
<td>VIC</td>
<td>Victoria</td>
</tr>
<tr>
<td>WA</td>
<td>Western Australia</td>
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The South Australian Department for Health and Ageing appointed Health Outcomes International (HOI) in July 2015 on behalf of the Nationally Funded Centres (NFC) Reference Group to undertake a review of the NFC Paediatric Lung and Heart-Lung Transplantation (PLHLT) Program. The NFC PLHLT Program is currently delivered at The Alfred Hospital, Melbourne (AHM) in collaboration with The Royal Children’s Hospital (RCH), Melbourne.

### E.1 REVIEW OBJECTIVES

The primary objective of this review was to provide a comprehensive analysis of the delivery of the NFC PLHLT Program during the period 1 July 2011 to 30 June 2014, and where data are available for 1 July 2014 to 30 June 2015, in order to inform recommendations regarding the:

- current eligibility of this procedure for NFC status
- appropriate number of sites for the delivery of this procedure
- quality of the PLHLT Program in the context of the objectives of the NFC Program and international practice and benchmarks.

The review also recommends a price for the delivery of the procedure effective from 1 July 2015 and recommends improvements to the delivery of the NFC PLHLT Program as identified during the course of the review. In addition, HOI consulted with New South Wales clinicians regarding their interest in providing this procedure in the future.

### E.2 REVIEW METHODOLOGY

The review methodology designed by HOI included quantitative and qualitative analysis to address the review criteria as outlined in the *NFC Guidance for Governance, Management, Funding, Establishment, Review, September 2011* (the NFC Guidance). The review methodology was described in the Review Framework which established the review process, the review questions and approach to assessing the NFC Program at the NFC sites under the following assessment domains (based on the NFC Guidance):

- Access to the NFC
- Health outcomes
- Model of care & service delivery
- Non-inpatient services
- Quality and safety
- Teaching, Training and Research
- Clinical practice
- Projected demand for services
- Cost of services
• Risk Management
• Opportunities for improvement

The Review’s assessment included analysis of the submission provided by the NFC site to the NFC Reference Group, a comprehensive literature review of international trends in the provision of PLHLT, a case study visit to the NFC site, a visit to the SCHN as part of the consultation with New South Wales clinicians, telephone consultations with jurisdictional representatives, referrers and stakeholders, analysis of feedback from NFC Patient and Family Questionnaires from participants in the NFC PLHLT Program, and an analysis of the cost of the procedure’s care pathways.

At all stages of the review, HOI sought the advice and clinical input from two clinical experts who were an integral part of the review process:

• **Dr Melinda Solomon** (Medical Director, Lung Transplant Program; Director, Cystic Fibrosis Clinic; Director, Training Program-Respiratory Medicine; Hospital for Sick Children. Associate Professor, University of Toronto Hospital of Sick Children, Toronto, Canada) and

• **Dr Robert Justo** (Paediatric Cardiologist, Director of Cardiology, Queensland Paediatric Cardiac Service, Lady Cilento Children’s Hospital, Brisbane, Queensland). Dr Justo participated in the case study site visit to The Alfred and the consultations with clinicians from the Sydney Children’s Hospital Network, Westmead (SCHN).

**E.3 SUMMARY OF REVIEW FINDINGS**

The key findings of the review with respect to each of the review objectives are summarised below.

**E.3.1 Eligibility of this procedure for NFC status**

The NFC Program was established to implement a national policy for public sector provision of certain high cost, highly specialised clinical practices and technologies with limited demand, to ensure equitable access to these practices and technologies for all Australians. For a technology to be considered as a NFC, it must be an established clinical practice requiring a national population base for efficient and effective service provision.

The NFC PLHLT Program was established in 2011 at the existing AHM/RCH site. Based on the data assessed by this review (refer section E.3.3 below), the current and projected demand and required expertise support the continuation of the NFC PLHLT Program. It is the conclusion of this review that the NFC Reference Group should endorse continuation of the delivery of the NFC PLHLT Program.

**E.3.2 Number of sites for the delivery of this procedure**

Stakeholders consulted generally did not consider that demand would change significantly in the next three to five years. From this perspective, the estimated future demand for services was likely to stay the same or increase slightly to provide three to five lung or heart-lung transplants per year.

It is the conclusion of the review that the NFC PLHLT Program should be delivered at a single site and, based on performance, that site should be the exiting AHM/RCH site.

**E.3.3 Quality of the PLHLT Program against assessment domains**

The key findings of the review with respect to each assessment domain are summarised below.

**Access to the NFC**

A total of 31 patients were referred to the NFC PLHLT Program in the first three years, and 37 patients in total to the end of September 2015 (Q1 2015-16). This represents an average of 8-9 referrals per
year. Victorian patients were over-represented in referral numbers; and NSW patients were under-represented. While NSW referring clinicians considered distance from the NFC site was a challenge for NSW families, this rarely resulted in families electing not to proceed to transplantation (only one instance noted, and there were other complicating factors). The variance in referral rates is more likely explained by a higher proportion of Victorian patients with pulmonary hypertension being referred than in other states (61.5% vs 12.5% of total referrals respectively had diagnosis of pulmonary hypertension). Consultation with NSW clinicians treating paediatric patients with pulmonary hypertension suggested that the combined effects of improvements in the treatment outcomes achieved from intravenous epoprostenol may be reducing referral numbers. However, these clinicians emphasised that referrals were being made (where appropriate) and that due to the small numbers of patients involved a longer time series was required to identify difference in referral rates.

Criteria for referral aligned with international practice, and the NFC PLHLT team was very responsive to discussion regarding these criteria and particular patients with referring sites. Conditions that were previously considered as absolute contraindications are now considered on a case by case basis. The NFC PLHLT team will now consider acceptance of patients on ECMO, with Mycobacterium abscessus or *burkholderia cenocepacia* (see discussion in ‘clinical practice’ below). Psychosocial factors that may affect adherence to medical care are critical to success and considered in decision making.

The initial screening assessment is conducted by members of the NFC PLHLT team (either at the NFC site or at the home jurisdiction if patients are unwell to travel) to assess whether transplant is a feasible and appropriate option and whether/when the patient should proceed to formal assessment. A total of 17 patients progressed to formal assessment conducted at AHM/RCM and were subsequently accepted to the NFC PLHLT Program in the first three years, and 22 patients in total to Q1 2015-16. This represents an average of five to six patients per year accepted to the NFC PLHLT Program (54.8-59.5% of those referred).

A total of nine patients underwent lung or heart-lung transplant in the first three years, and a total of 15 patients in total to Q1 2015-16. This represents an average of three to four patients per year undergoing a lung or heart-lung transplant, with a range of up to six per year.

The majority of patients fell within the current target group for the program (children and adolescents aged six to 15 years typically weighing 20-40kg, noting that under the approved criteria it is stipulated that weight should not be an exclusion to transplant if the patient is in the right age range). One patient was five years old and one 16 years old and one patient was under 20kg and five patients over 40kg.

At 30 June 2014 there were four children on the NFC PLHLT Program waiting list. At the time of this review (September 2015) there were two children on the waiting list. The median waitlist time for lung transplantation is 57 days, ranging from 1-442 days. Two children (9.1%) have died on the waitlist since 1 July 2011. In an effort reduce waitlist time and to improve organ availability, the AHM/RCH is accepting more marginal organs (e.g. donation after cardiac death (DCD)) and conducting lobar transplants.

**Health outcomes**

Outcomes from the NFC PLHLT Program appear similar to international outcomes data collected by ISHLT. Since NFC status, four of the 15 children transplanted under the PLHLT Program have died as a consequence of complications related to transplantation (non-adherence, a common problem in adolescent health, was an important contributor to poor outcomes in two of the transplanted children). Comparison of one-year survival rates with ISHLT data are as follows:
6 to 10 year olds: NFC program 100% survival (three patients alive); ISHLT 95.2% (50 patients alive)

11 to 17 year olds: NFC program 75.0% survival (nine patients alive); ISHLT 81.1% (226 patients alive)

The AHM reported that since 2006, when the PLHLT service was first established (outside of the NFC Program), one year survival for the 29 transplant procedures has been 84% to September 2015, comparable to the global experience of 81.1% one year survival for 11-17 year olds reported by the ISHLT. The AHM commented that the more recent reduction on one year survival outcomes may be influenced by the acceptance of more marginal patients in recent years.

A specific adolescent-focused education program has now been developed and implemented in collaboration with the Adolescent Service at RCH to address issues with non-adherence in adolescence. The NFC PLHLT Program has also included a request and budget for a child psychologist to be added to the core NFC PLHLT team for the future.

Quality of life is an important outcome measure for children undergoing lung transplantation, and potential to improve quality of life was reported by the AHM to be a key consideration in decisions regarding transplant. Formal assessment of quality of life outcomes was not conducted in the first year of the program, but an ongoing research project was initiated in 2012-13 and results will become available in the next two years.

**Opportunities for improvement**

The key opportunities for improvement related to health outcomes include:

1. **Report outcomes of higher-risk patients.** The outcomes of higher risk patients (such as those supported with ECMO-bridge-to-transplant, or patients with Mycobacterium abscessus) should be separately reported to the NFC Reference Group as part of the annual reporting process.

2. **Build linkages to collect longer term complications data.** The NFC site should develop linkages to collect and document long-term complications such as diabetes, hypertension etc. and report these as part of the NFC annual reporting process.

3. **Reporting of readmissions.** The NFC reporting template should be amended to specifically require the number of patient readmissions to be reported.

**Model of care and service delivery**

A number of modifications and initiatives have been implemented to address limitations of delivering a paediatric service in an adult hospital. These include cross credentialing of staff, ongoing education program, combined paediatric and lung transplant physician input at all stages of the care pathway, and broad paediatric and lung transplant expertise to allow continuation of a viable and functional program in the absence of care staff.

The NFC PLHLT Program offers a continuum of care that extends from the point of referral to three months post-transplant. The care continuum includes the following stages:

1. **Initial referral:** This is generally from Paediatric Respiratory Physician or Paediatric Cardiologist in the home jurisdiction.

2. **Screening assessment:** Conducted by NFC PLHLT team (or local team in some cases) in patient’s home jurisdiction following initial telephone consultation with referring clinician, with the aim of deciding whether to progress patient to formal transplant assessment or defer transplant with ongoing outpatient review as required.
3. **Formal detailed transplant assessment**: Conducted over five days at RCH with two outpatient days at AHM (note that all patients proceeding to formal assessment to date have been accepted to the program).

4. **Care on waiting list**: The average length of time on the waiting list is 119 days (median is 57); during this period patients are able to live at home if they are within a four hour travel time to the NFC site, with care provided by the local paediatric team and reviewed NFC PLHLT team every six months. Patients relocating to Melbourne receive care at the RCH, and the waiting list review is conducted by NFC PLHLT team every six weeks.

5. **Lung transplant procedure**: The lung transplant operation is performed following organ retrieval by senior surgeons from the AHM’s Cardiothoracic Surgical Department, with attendance by RCH cardiothoracic surgeons if required. The mean ICU length of stay post-transplant is 12 days and the mean total hospital stay is 27 days, with accommodation provided for families if required.

6. **Post discharge care**: Post discharge care is provided for up to three months post discharge from hospital under the NFC PLHLT Program, and patients who do not live near Melbourne remain near AHM during this time. This involves clinic visits and investigations, review by Paediatric Respiratory Specialist at RCH, allied health program, education sessions, Hospital in the Home for antimicrobial therapy, and readmission if required.

Ongoing care is provided by the AHM/RCH Paediatric Lung Transplant Service for local Victorian patients outside of the NFC Program, with transition to AHM adult lung transplant program when the patient reaches 18 years old. Interstate patients are referred back to local state-based adult lung transplant programs with review by the NFC PLHLT team as required. Established long term follow-up clinics exist with clinicians in NSW, Queensland, Tasmania, SA and WA.

All jurisdictional stakeholders reported that the screening visit by the NFC PLHLT team in the patients’ home jurisdiction and/or the subsequent formal assessment undertaken at the NFC site are extremely valuable components of the program; and provides psychological support to patients and families, clinical assessment and upskilling of local practitioners.

Whilst the NFC PLHLT Program is inclusive of a small number of key back up staff, patients reported excellent transition experiences between core and back up staff. However, some concerns were raised regarding the ability to maintain services with this limited number of staff (noting that this issue was not raised by the NFC PLHLT team or patients).

**Non-inpatient services**

The NFC PLHLT Program provides non-inpatient services relevant to the provision of initial assessment and care whilst on waitlist, as well as post discharge care for the first three months post discharge from hospital during which time it is anticipated that patients will remain close to AHM/RCH.

Following discharge from the NFC PLHLT Program, care is transferred either to the PLHLT Program’s hospital-based clinic for patients in Victoria, or local services interstate including life-long support by a local transplant team. For those patients who live outside of Melbourne, the PLHLT Unit Head and the Paediatric Lung Transplant Coordinator meet with each patient and their family to answer any questions prior to them returning home.

Provision of post-discharge care in the home jurisdiction is provided by either adult or paediatric services (depending on patient need and the availability of local services and expertise). Stakeholders reported that the NFC PLHLT Program has a key role in facilitating discussions and for planning of post-discharge care in home jurisdictions. This includes supporting post-discharge care through videoconference or other approaches to ensure consistent support, irrespective of setting.
QUALITY AND SAFETY
The NFC site has well established plans, protocols and clinical guidelines to deliver the NFC PLHLT Program to a high standard of quality and safety. Adverse events have been documented and appropriately managed by the sites and referring practitioners.

TEACHING, TRAINING AND RESEARCH
Members of the NFC PLHLT Program multidisciplinary team at the NFC site actively contribute to teaching, training and research both locally and internationally.

CLINICAL PRACTICE
AHM/RCH are currently requesting an expansion of the NFC PLHLT Program to include patients four to 15 years with a minimum weight of 10kg\(^1\), and are exploring the possibility of providing a service to younger children (less than five year old) at the RCH with input from the PLHLT team in the future. A move to lowering the age to include younger patients was supported by our international expert in line with international practice. There is broad stakeholder support for lowering the minimum age limit for the NFC PLHLT Program based on international experience, as long as expertise is available to provide this care. All stakeholders reported that the upper age limit was appropriate but that flexibility was required for some patients aged 14-15 years who may be better managed under the local adult transplant service (i.e. based on psychosocial circumstances, emotional maturity, and size). This has already occurred in several jurisdictions.

In addition, the AHM/RCH are now accepting patients (where they meet the developed protocols) on ECMO-bridge-to-transplant and/or patients colonised with *Mycobacterium abscessus* or *burkholderia cenocepacia* who would previously have been contraindicated for transplant. The NFC PLHLT team is expecting that these patients are likely to comprise around 20–25% of new referrals in the future. While these changes have a minimal impact of the price per procedure recommended by this review (as ECMO-bridge-to-transplant costs are removed in full, and the funding patients colonised with *Mycobacterium abscessus* or *burkholderia cenocepacia* is approximately $5,600 per procedure), they do represent significant changes in the accepted indications for the procedure.

In October 2015, the NFC Reference Group submitted revisions to the Guidance document including the protocol for approval of new care pathways to AHMAC which were subsequently approved. The revised NFC Guidance states that it is a requirement for established NFC sites to notify of changes to the approved NFC programs. The review identified that this notification had not occurred in relation to these changes.

The Review has considered the recently published literature and consulted with our international clinical expert, and it is the conclusion of the Review that these practices (transplanting: patients four to 15 years with a minimum weight of 10kg; patients on ECMO bridge to transplant; and patients colonised with *Mycobacterium abscessus* or *burkholderia cenocepacia*) is considered established clinical practice in some centres (with relevant expertise) and is consistent with the NFC eligibility criteria.

Opportunities for improvement
The key opportunities for improvement related to clinical practice include:

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\(^1\) The NFC site for paediatric lung and heart-lung transplantation may also treat older adolescents (aged 15 years but less than 18 years) where they are smaller, of lower body weight, or have complex paediatric issues (including psychosocial issues).
1. **Expanded target cohort.** It is recommended that the NFC Reference Group endorse the expansion of the target cohort of patients to include children and adolescents 4 to 15 years typically weighing ≥10kg.

2. **Inclusion of previously contraindicated patients.** It is recommended that the NFC Reference Group endorse the practice of the NFC site to accept certain previously contraindicated patients (ECMO-bridge-to-transplant and/or patients colonised with *Mycobacterium abscessus* or *burkholderia cenocepacia*) on a case by case basis. Should the NFC Reference Group endorse these changes, it is recommended that the outcomes of higher risk patients be separately reported to the NFC Reference Group as part of the NFC annual reporting process.

**Projected demand for services**

Stakeholders consulted generally did not consider that demand would change significantly in the next three to five years. The estimated demand for services in the next three to five years is likely to stay the same or increase slightly to provide three to five lung or heart-lung transplants per year based on the following:

- Little overall change in number of referrals, with a decrease in number of patients with cystic fibrosis requiring transplant before adulthood but an increase in number of referrals of patients with other diagnoses (e.g. interstitial lung disease) or younger ages.
- Increase in number able to be transplanted, based on program acceptance of more marginal patients (e.g. patients on ECMO or with *Mycobacterium abscessus*) and more marginal donor organs.

Clinicians from Sydney Children’s Hospitals Network (Westmead) considered that for patients living in Sydney (and particularly in the western regions), the number of referrals for paediatric heart and/or lung transplantation may increase by an additional three to five per year if a local service were available at SCHN, with a commensurate increase in the number of local organ donations. However, subsequent consultation with referring clinicians in NSW did not identify any evidence to support this position.

**Assessment of number of sites**

With the exception of clinicians from SCHN in NSW, all referring clinicians consulted during the review process considered that a single site was appropriate to conduct the NFC PLHLT Program over the next three to five years and based on performance, and that the site should be the existing AHM/RCH site.

SCHN clinicians have expressed the view that the model of care (paediatric transplantation in an adult setting at only one national site) is inappropriate, and that the NFC PLHLT Program should reside in a paediatric hospital, and/or be supplemented with an additional site to better support the Australian population.

Based on our review of the evidence base and in consultation with our international clinical expert it is considered that the NFC Reference Group should continue to approve the delivery of PLHLT services at a single site.

**Cost of services**

The NFC PLHLT Program commenced on 1 July 2011 based on a single average price per procedure of $314,266. A summary of the NFC pricing structure since 2011 is presented in Table E.1 below.
Table E.1: Funded price per procedure by financial year

<table>
<thead>
<tr>
<th>Year</th>
<th>2011/12</th>
<th>2012/13</th>
<th>2013/14</th>
<th>2014/15</th>
<th>2015/16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Price per procedure</td>
<td>$314,266</td>
<td>$327,905</td>
<td>$339,480</td>
<td>$350,513</td>
<td>$361,975</td>
</tr>
</tbody>
</table>

**Indexation rate (a)**  
- 4.3%  
- 3.5%  
- 3.3%  
- 3.3%

(a) Indexed annually by an amount reflecting the Australian Institute of Health and Welfare health-specific cost index and the Productivity Commission derived index of technology growth.

The established 2011/12 price per procedure included funding for costs related to: screening of referrals ($13,354); pre-acceptance work-up and assessment ($52,358); and the decision to accept ($5,468). In total, 22.6% ($71,180) of the price per procedure funded items that are now not considered part of the defined NFC-funded episode of care.

HOI’s review of the reported costs has identified a number of proposed cost adjustments and the impact of these is presented in Table E.2 below. It should be noted that the adjusted comparative price column provides the adjusted 2015/16 price for items that were endorsed in 2010, but now determined to be outside the defined NFC-funded care pathway. As a consequence of the proposed adjustments, the revised cost is:

1. $98,854 (27%) less than the existing 2015/16 price per procedure, primarily attributed to the removal of cost components currently included in the price that are now outside of the defined NFC-funded care pathway.
2. $17,457 (7%) more than the ‘adjusted comparative price’ (i.e. the price amended to remove funded elements not within the defined NFC-funded episode of care) per procedure.

Table E.2: Summary of proposed adjustments to costs (2015/16) per procedure

<table>
<thead>
<tr>
<th>Item</th>
<th>AHM revised cost 2015/16</th>
<th>Adjusted comparative price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Submitted costs per procedure</td>
<td>$319,950</td>
<td>$361,975</td>
</tr>
<tr>
<td>Direct costs</td>
<td>$319,950</td>
<td>$361,975</td>
</tr>
<tr>
<td>On-costs</td>
<td>$26,265</td>
<td>$31,790</td>
</tr>
<tr>
<td>Overhead</td>
<td>$67,593</td>
<td>$71,910</td>
</tr>
<tr>
<td>Total</td>
<td>$413,808</td>
<td>$361,975</td>
</tr>
</tbody>
</table>

Adjustments:

1. Cost categories outside NFC pathway  
   ($56,675)  
   ($3,571)  
   ($11,664)  
   ($71,910)  
   ($86,660)

2. Program acceptance costs (volume adjustment)  
   ($1,059)  
   ($143)  
   ($240)  
   ($1,442)  
   -

3. Remove ECMO-bridge-to-transplant  
   ($9,683)  
   ($1,096)  
   ($1,961)  
   ($12,740)  
   -

4. Remove transport costs prior to admission  
   ($6,778)  
   -  
   ($1,356)  
   ($8,134)  
   ($7,187)

5. Remove local transport in outpatient pathway  
   ($336)  
   -  
   ($67)  
   ($403)  
   -

6. Remove WEIS funded investigations from outpatient pathway  
   ($5,148)  
   -  
   ($1,030)  
   ($6,178)  
   -

7. Remove PBS funded ‘drug costs’ from outpatient pathway  
   ($8,265)  
   -  
   ($1,653)  
   ($9,918)  
   ($8,763)
## Itemised Costs

<table>
<thead>
<tr>
<th>Item</th>
<th>AHM revised cost 2015/16</th>
<th>Adjusted to existing 2015/16 price</th>
<th>Adjusted to comparative 2015/16 price</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Direct costs</td>
<td>On-costs</td>
<td>Overhead</td>
</tr>
<tr>
<td>8.</td>
<td>($2,665)</td>
<td>($128)</td>
<td>($335)</td>
</tr>
<tr>
<td>9.</td>
<td>($4,080)</td>
<td>-</td>
<td>($816)</td>
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<tr>
<td>10.</td>
<td>($3,497)</td>
<td>-</td>
<td>($1,049)</td>
</tr>
<tr>
<td>11.</td>
<td>($11,659)</td>
<td>-</td>
<td>($2,332)</td>
</tr>
<tr>
<td>12.</td>
<td>($12,279)</td>
<td>($1,592)</td>
<td>($2,774)</td>
</tr>
<tr>
<td>Revised cost per procedure</td>
<td>$198,603</td>
<td>$19,735</td>
<td>$42,549</td>
</tr>
</tbody>
</table>

**Notes:**

(a) This increase effectively represents the impact of the changed methodology for on-cost and overhead charges. In the prior review on-costs (30%) and overheads (13%) were applied only to salary-based items in the costing. In the current costing, on-costs (13.5%) are applied to salary-based cost elements, and overheads (20%) applied to all costs. HOI has estimated the impact of this change, based on the accepted cost-items identified above, is an increase in costs per patient of approximately $28,800.

## Opportunities for Improvement

The key opportunities for improvement relating to the cost of services include:

1. **Definition of the NFC care pathway.** It is noted that the NFC Reference Group has an AHMAC approved review cycle for the NFC Guidance document every three years and it is recommended that this review includes definitions of the ‘care pathway’ and the circumstances where deviations from that care pathway require AHMAC approval.

2. **Regular review of NFC Guidance.** In addition, as part of the review cycle it is recommended that the review process should incorporate invitations to jurisdictions to provide feedback to ensure urgent or critical matters are addressed in an appropriate timeframe.

## Risk Management

Key risks arising from the provision of a paediatric service in an adult hospital were identified early in the establishment of the service at the AHM, and strategies were developed and implemented to largely mitigate these risks. These strategies include cross credentialing of staff, and appointments dedicated to the program at both the AHM and RCH. An education program specific to the needs of adolescent patients has recently been developed to address the particular needs of this group.

Stakeholders including patients, families, referring clinicians and other jurisdiction staff reported that the paediatric service was of a high standard at the AHM. However, SCHN medical staff and many of the referring respiratory physicians have indicated that the model of care (paediatric transplantation in an adult setting at only one national site) is inappropriate.
Research and risk assessments were undertaken prior to the decision to accept patients on ECMO as a bridge to transplant or patients with Mycobacterium abscessus colonisation who would previously have been contraindicated, and protocols developed for review and management of these groups.

E.4 CONCLUSION

Our assessment of the NFC PLHLT Program, has demonstrated that the program provides high quality services and delivers excellent patient outcomes that are comparable to international standards.

Based on our analysis of the data presented against the NFC Guidance criteria and with assessment of contemporary evidence base, it is recommended that the NFC PLHLT Program continue as a concentrated service as part of the NFC Program at a single site and, based on performance, that site should be the existing AHM/RCH site.
**CONSOLIDATED LIST OF RECOMMENDATIONS**

**Recommendations addressing the review’s Terms of Reference regarding the existing scope of the NFC PLHLT Program**

The following recommendations specifically address the review Terms of Reference and directly relate to the operations of the existing NFC PLHLT Program.

1. It is recommended that the NFC Reference Group endorse continuation of the delivery of the NFC PLHLT Program for an additional three years at a single site and, based on performance, that site should be the exiting AHM/RCH site, with a further review to be conducted at the end of that period.

2. It is recommended that the NFC Reference Group endorse the revised pricing structure from 1 July 2015 for the delivery of the NFC PLHLT Program of **$260,887 per procedure**. The price should be indexed in subsequent financial years in accordance with the NFC Guidance.

3. It is recommended that the NFC Reference Group endorse the expansion of the target cohort of patients to include children and adolescents 4-15 years typically weighing ≥10kg.

4. It is recommended that the NFC Reference Group endorse the practice of the NFC site to accept ECMO-bridge-to-transplant patients on a case by case basis in accordance with existing protocols. Should the NFC Reference Group endorse these changes, it is recommended that the outcomes of higher risk patients be separately reported to the NFC Reference Group as part of the NFC annual reporting process.

5. It is recommended that the NFC Reference Group endorse the practice of the NFC site to accept patients colonised with Mycobacterium abscessus or Burkholderia cenocepacia on a case by case basis in accordance with existing protocols. Should the NFC Reference Group endorse these changes, it is recommended that the outcomes of higher risk patients be separately reported to the NFC Reference Group as part of the NFC annual reporting process.

6. It is recommended that the NFC site develop linkages to collect and document long-term complications (such as hypertension, diabetes mellitus or bronchiolitis obliterans syndrome).

**Recommendations addressing other opportunities for improvement**

The following recommendations address opportunities to improve the NFC PLHLT Program but fall outside of the NFC episode of care and/or the NFC Guidance.

7. It is noted that the NFC Reference Group has an AHMAC approved review cycle for the NFC Guidance (every three years) and it is recommended that this include definitions of the ‘care pathway’ and the circumstances where deviations from that care pathway require AHMAC approval.

8. It is noted that the NFC Reference Group has an AHMAC approved review cycle for the NFC Guidance (every three years) and it is recommended that the review process should incorporate invitations to jurisdictions to provide feedback to ensure urgent or critical matters are addressed in an appropriate timeframe.

9. It is recommended that NFC site reviews the communication processes with referrers to provide information on contemporary treatment and outcomes data, explain referral, patient support and discharge protocols, and provide opportunities for referrers to provide feedback and recommendations to improve future program services.
10. It is recommended that as part of the standard discharge protocols for the Program that the NFC site facilitates a post-discharge videoconference or similar communication method involving all stakeholders (including the patient/family). The primary aim being to ensure consistency in the delivery of post-discharge support services by the Program and in the care provided by local services.

11. It is recommended that the NFC reporting template be amended to require the number of patient readmissions to be reported.
INTRODUCTION

The South Australian Department for Health and Ageing appointed Health Outcomes International (HOI) in July 2015 on behalf of the Nationally Funded Centres (NFC) Reference Group to undertake a review of the NFC Paediatric Lung and Heart-Lung Transplantation (PLHLT) Program. The NFC PLHLT Program is currently delivered at The Alfred Hospital, Melbourne (AHM) in collaboration with The Royal Children’s Hospital (RCH), Melbourne.

1.1 THE NFC PROGRAM

The NFC Program was established in 1990 by the Australian Health Ministers’ Conference (now Council of Australian Governments (COAG) Health Council) to implement a national policy for public sector provision of certain high cost, highly specialised clinical practices and technologies with limited demand, to ensure equitable access to these practices and technologies for all Australians.

The NFC Program is managed by the NFC Reference Group which reports through the Hospitals Principal Committee to the Australian Health Ministers’ Advisory Council (AHMAC). The NFC Reference Group comprises representation from all states and territories and the Australian Government, and is chaired by Professor Paddy Philips the Chief Medical Officer and Chief Public Health Officer, SA Health. The review of the NFC PLHLT Program was managed by the NFC Project Management Group (PMG), which is a sub-group of NFC Reference Group members from non-provider jurisdictions.

The objectives of the NFC Program are to ensure that:

- there is optimal access to certain high cost, low demand, new and emerging technologies regardless of geographical location, in the context of workforce and resource availability
- these technologies are provided efficiently and effectively
- requirements for high quality and safe introduction and ongoing provision of these technologies have been defined and implemented
- health and cost outcomes of these technologies are monitored and evaluated.

For a technology to be considered as a NFC, it must be an established clinical practice requiring a national population base for efficient and effective service provision.

A technology may also be considered if it is a clinical practice in the establishment phase and has yet to be incorporated into standard clinical practice, but has the potential for broader diffusion into the Australian health system.

1.2 REVIEW OBJECTIVES

The primary objective of the review was to provide a comprehensive analysis of the delivery of the NFC PLHLT Program during the period 1 July 2011 to 30 June 2014, and where data are available, for 1 July 2014 to 30 June 2015, in order to inform recommendations regarding the:
The review was also required to recommend a price for the delivery of the procedure effective from 1 July 2015, and improvements to the delivery of the NFC PLHLT Program that were identified during the course of the review. In addition, HOI was required to consult with New South Wales clinicians regarding their interest in delivering the procedure under the auspices of the NFC Program in the future.

1.3 Scope of the review

The review was conducted in accordance with the NFC Guidance for Governance, Management, Funding, Establishment and Review (September 2011) to assess NFC PLHLT Program activities undertaken in the period 1 July 2011 to 30 June 2014, encompassing the time this technology has been included in the NFC Program.

The scope of the review included the following:

1. **Assessment against the general criteria for NFC status** including:
   - clinical indications
   - clinical pathways and protocols
   - models of care
   - quality of care outcomes, morbidity and mortality
   - activity and demand in Australia and New Zealand and internationally
   - costs and financial modelling
   - new and emerging technologies in the field
   - teaching, training and research
   - evaluation activities
   - risk management.

2. **Assessment of specific issues for the NFC PLHLT Program** including:
   - whether the current target population for this NFC procedure is still appropriate or should be revised
   - whether procedural volumes and outcomes are consistent with international best practice
   - whether demand on services has impacts on access to the technology
   - equity of access across jurisdictions (and if it has improved since program introduction).

3. **Assessment of the cost of providing technology under the NFC Program** including a detailed financial analysis of the costs associated with the delivery of the PLHLT Program.

4. **Recommendations for improvements to the delivery of the NFC PLHLT Program** as identified through the review.
1.4 REVIEW METHODOLOGY

The review methodology designed by HOI included quantitative and qualitative analysis to address the review criteria as outlined in the NFC Guidance for Governance, Management, Funding, Establishment, Review, September 2011 (the NFC Guidance). The review methodology was described in the Review Framework which established the review process, the review questions and approach to assessing the NFC program at the sites under the following assessment domains (based on the NFC Guidance):

- Access to the NFC
- Health outcomes
- Model of care & service delivery
- Non-inpatient services
- Quality and safety
- Teaching, Training and Research
- Clinical practice
- Projected demand for services
- Cost of services
- Risk Management
- Opportunities for improvement.

The methodology designed by HOI comprised four stages as set out below.

1. **Project Planning.** HOI conducted a project initiation meeting with the project management group (PMG) which established the project work plan and timeframes, as well as agreeing relevant information which would inform the review, identifying the key stakeholders and agreed approaches, reporting, risk management strategy and broader communication strategy. A finalised Project Plan was subsequently presented and approved by the PMG.

2. **Situation Analysis.** The situation analysis was conducted to develop an understanding of the current operations relating to the NFC PLHLT Program and to establish an evidence base of contemporary international practices. The situation analysis included:
   - **Document review.** A review of available documentation that was provided to HOI by the site and by the NFC Secretariat at the commencement of the review.
   - **Literature review:** A literature review that was used to establish an evidence base to inform the identification of key findings and recommendations on the delivery of contemporary PLHLT service models.
   - **Development of a Review Framework.** A Review Framework was developed based on the NFC Guidance and in consultation with our expert clinical advisors HOI prepared a review framework that provided the blueprint for conducting the review including the issues to be addressed as part of the consultative and data analysis processes.
   - **Stakeholder consultations.** A consultation plan was developed for the structure of consultations with nominated stakeholders and referrers involved in the NFC PLHLT Program. The plan involved a series of telephone interviews. As part of this, HOI visited SCHN to consult with NSW clinicians.
Case study visits to the NFC site. A case study visit was conducted to the NFC site to obtain input from clinicians involved in delivering the program.

Desktop analysis. A desktop analysis of retrospective feedback from the NFC Patient and Family Questionnaires and data reported by the NFC PLHLT site with respect to the operations of the NFC PLHLT Program.

At the conclusion of this stage, a Situation Analysis Report was submitted to the NFC PMG on 26 November 2015. This provided a foundation for the conduct of a detailed assessment of the NFC PLHLT Program against the NFC Review Criteria. The literature review findings were incorporated into this report where relevant. For completeness the literature review has been included in Appendix A as a standalone document.

3. Data analysis. The objective of the data analysis (as specified in the Review Framework) was to facilitate a comprehensive analysis of the NFC PLHLT Program in accordance with the NFC Guidance. This stage included undertaking:

- Comparative analysis of the information collected
- Triangulating data collected during the review period
- Analysis of the costs reported by the NFC site
- Benchmark analysis of the performance of the site against the Review Framework.

4. Draft and Final Reports. The Draft and Final Reports were prepared from the consolidated analysis and findings from the preceding stages in accordance with the NFC PLHLT Program Review Framework. In collaboration with the clinical experts (see below), HOI prepared the First Draft Final Report and recommendations (this report).

1.5 Clinical expert review

The HOI consulting team included two clinical experts who have provided input across all stages of the review.

1. Dr Melinda Solomon Medical Director, Lung Transplant Program; Director, Cystic Fibrosis Clinic; Director, Training Program-Respiratory Medicine; Hospital for Sick Children. Associate Professor, University of Toronto Hospital of Sick Children, Toronto, Canada.

2. Dr Robert Justo Paediatric Cardiologist, Director of Cardiology, Queensland Paediatric Cardiac Service, Lady Cilento Children’s Hospital, Brisbane, Queensland. Dr Justo participated in the case study site visit to The Alfred and the consultations with clinicians from the Sydney Children’s Hospital Network, Westmead (SCHN).

1.6 Structure of the report

This document presents the consolidated findings of the review of the NFC PLHLT Program. Accordingly, the structure of the remainder of the report is as outlined below.
<table>
<thead>
<tr>
<th>Chapter 2</th>
<th>Presents a comprehensive assessment of the performance of the NFC PLHLT Program and the current NFC PLHLT site in accordance with the NFC Guidance Review Criteria.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chapter 3</td>
<td>Presents an assessment of considerations for the future NFC PLHLT Program including discussion regarding new technologies, forecast demand for the procedure, interest of alternate sites and factors for consideration in recommending an appropriate number of sites.</td>
</tr>
<tr>
<td>Chapter 4</td>
<td>Presents a discussion and analysis of the NFC PLHLT Program costs that were reported by the NFC site and recommendations regarding future program pricing.</td>
</tr>
<tr>
<td>Chapter 5</td>
<td>Presents a summary of the review findings and recommendations for future status of PLHLT Program under the NFC Program.</td>
</tr>
</tbody>
</table>
A S S E S S M E N T O F P E R F O R M A N C E

This chapter presents a comprehensive assessment of the performance of the NFC PLHLT Program for the current review period. The assessment has been undertaken in accordance with the NFC Guidance review criteria and addresses:

- Current clinical practice
- Access to the NFC
- Health outcomes
- Model of care and service delivery
- Non-inpatient services
- Quality and safety
- Teaching, training and research
- Risk management

Presentation of findings and discussion regarding the cost of the NFC PLHLT Program, new and emerging technologies, interest of alternative sites, and projected demand for the service are presented in subsequent chapters of this report.

Recommendations and opportunities for improvement have been integrated into relevant sections of this and subsequent chapters.

2.1 CURRENT CLINICAL PRACTICE

Since lung transplantation was pioneered in 1963, over 43,000 transplantations have been undertaken in adults across the globe. The first paediatric patient to undergo lung transplantation was a 16 year old boy presenting with familial pulmonary fibrosis in 1987. Between 1987 and 2014, 1,875 children (of all ages, including younger children (less than five years old)) have since received a lung transplant (Kirkby & Hayes, 2014). As a slightly newer procedure, the first adult heart-lung transplant was performed in 1981 followed by a paediatric heart-lung transplantation conducted in 1986 in a 15 year old girl (Orr, 2014).

Since 1986 there have been significant developments in surgical procedures, perioperative and postoperative management, recipient selection and organ allocation processes, which have resulted in steady improvements in short term survival of transplantation, amongst other outcomes.

2.1.1 TRANSPLANTATION ACTIVITY AND TIMING

In 2011, 43 transplant centres across the globe reported undertaking paediatric lung transplantation procedures with the majority of centres located in the United States and Europe (where ‘paediatric’ is defined as under 18 years of age). Between 2006 and 2011, although just over 100 children received a lung transplant each year, it is evident that most paediatric centres have very low procedure volumes
compared with adult programs (Kirkby & Hayes, 2014). Only five paediatric centres worldwide reported performing over five paediatric lung transplants annually in 2010 (Khan et al, 2015). Internationally the number of paediatric heart-lung transplantation procedures undertaken and reported to the International Society for Heart and Lung Transplantation (ISHLT) Registry has steadily increased over the last decade (Benden et al., 2013), from 73 in 2000 to 107 in 2011. The highest number of paediatric lung transplants performed internationally were reported in 2009 and 2010, with 125 in both years. The majority of these transplants are performed in older children 11-17 years.

Australia represents <3% of all PLHLTs conducted internationally. According to the ISHLT Registry, there were five paediatric lung or heart-lung transplants performed in Australia during the period 1 January 2013 through to 30 September 2014, one of which was a heart-lung transplant. These transplants represented 2.4% of all paediatric lung and heart-lung transplant activity reported through the ISHLT Registry during this time.

The timing of transplantation is heavily influenced by the availability of donor organs. Keeshan, et al. (2015) report that the number of lung transplants undertaken per year has risen in both paediatric and adult cohorts, and postulate that improvements in donor matching and allocation have resulted in this increase in volume where supply (donor pool) has not simultaneously increased. The Australian NFC PLHLT Program is currently challenged by a limited supply of younger donor organs. The AHM has developed strategies to support young children awaiting lung transplantations. One approach is to use lungs donated after cardiac death (DCD) in lieu of the use of lungs donated after brain death (DBD) which have historically been relied upon. The 2015 ANZOD Annual Report presents data that confirms that the number of lungs DCD (all aged groups) has been increasing since 2006.

2.1.2 CLINICAL INDICATORS AND CONTRAINDICATIONS

Clinical presentation for lung or heart-lung transplantation is usually dependent on the primary diagnosis. Children may present with respiratory insufficiency or respiratory failure, exercise intolerance, poor growth, hypoxemia, carbon dioxide retention, abnormal pulmonary function test findings, and frequent respiratory exacerbations that require antibiotics and/or anti-inflammatory medications. Children with underlying pulmonary vascular disorders may present with syncope, exercise intolerance, poor growth, cyanosis, and impaired quality of life (Faro & Visner, 2013).

Across all paediatric age groups combined, cystic fibrosis (CF) is the most common indication for lung transplantation worldwide, followed by idiopathic pulmonary arterial hypertension (IPAH). Other less common indications include idiopathic pulmonary fibrosis (IPF), surfactant protein deficiencies and other diseases now more uniformly classified as childhood interstitial lung diseases, congenital heart disease (CHD), and re-transplantation (Faro & Visner, 2013).

Contraindications for transplantation must also be considered in the process. In terms of contraindications for lung transplantation, Weill et al. (2015) explains that these are generally extrapolated from adult data and are therefore similar. However, these authors (amongst others) also explain that in the United States, medical and surgical contraindications for those under age 18 can vary between transplantation centres with some centres recognising absolute contraindications as relative contraindications and vice versa. ECMO support as a bridge to transplantation in children is considered a relative contraindication in some centres but recent literature indicates that this may not be the case if patients are selected carefully. Weill et al. (2015) also explains that the contraindications identified in relation to adult patients may not be as relevant in a paediatric setting.
2.1.3 TRANSPANTATION PROCESS

Once the allocation of donor organs is made, the transplantation process occurs over three distinct phases: (1) preoperative assessment and management; (2) perioperative management and transplantation; and, (3) postoperative management. The ISHLT has released a number of clinical guidelines and protocols to guide some of these processes.

1. **Preoperative management.** Whilst patients remain on the waiting list a range of preoperative management strategies can be put in place to optimise their medical care and promote optimal health in order to undergo transplantation and to address any medical issues arising through the evaluation. Preoperative approaches or bridges to transplant can include the following where considered appropriate (Faro & Visner, 2013):
   - improving the patient’s nutritional status
   - providing pulmonary rehabilitation
   - decreasing the number of pulmonary exacerbations for which intravenous antibiotics are required
   - applying medical therapies with epoprostenol or other pulmonary vasodilators, such as sildenafil and bosentan to patients with pulmonary hypertension
   - using ex vivo lung perfusion technology with acute respiratory failure as a bridge to transplant.

2. **Perioperative management and transplantation.** The application of an induction regime of immunosuppressive drugs to inhibit rejection of the lung allograft and in turn the development of bronchiolitis obliterans syndrome (BOS) can also be applied although this approach, and the drugs applied varies by transplant centre (Faro & Visner, 2013). Conrad and Cornfield (2014) indicate that around 60% of paediatric lung transplant recipients reported to the ISHLT received some form of induction therapy during the perioperative period.

   Currently, the most frequently performed procedure is a bilateral sequential lung transplant via median sternotomy. In this procedure, Conrad and Cornfield (2014) explain that the mainstem bronchi and left and right pulmonary arteries are connected via end-to-end anastomoses following which two pulmonary veins with intact atrial connections are harvested from each donor lung and each left atrial patch is connected to the recipient heart. The benefits of this particular approach are that cardiopulmonary bypass time is minimised which in turn can reduce the risk of surgical and post-surgical complications (Conrad & Cornfield, 2014).

3. **Postoperative management.** Where surgical complications have not arisen, most patients will expect to remain in hospital for two weeks post-surgery. Whilst they remain intubated, frequent bronchoscopy may be required in order to evaluate the anastomotic site and to clear the airway from debris and secretions.

   Intravenous antibiotics and other antimicrobials will be administered for two weeks and physical therapy will also be initiated and intensified as necessary. At this point the patient should be discharged to a post-transplantation centre close to the transplant centre’s grounds (although this can vary by centre with some centres preferring for patients to remain within the hospital) (Faro & Visner, 2013). According to a transplant centre’s protocol patients will undergo a surveillance bronchoscopy with transbronchial biopsy (Faro & Visner, 2013). Furthermore, patients will also undergo maintenance immunosuppression. Faro and Visner (2013) explain that the majority of centres prefer to apply tacrolimus-based regimes as the side effects are more manageable for paediatric patients which can in turn have a positive impact on adherence to the overall post-surgical regime.
Once discharged from the post-transplantation centre, patients require a suite of outpatient based care (Faro & Visner, 2013).

2.2 Access to the NFC

This section presents a discussion regarding access to the NFC PLHLT Program and considers numbers, referral sources and demographics of patients, criteria for patient selection and organ allocation, and equity of access to the program.

2.2.1 Patient referrals

Referrals to the NFC PLHLT Program are generally made by paediatric respiratory physicians or paediatric cardiologists. Referrals to the service are made to the Head of the Paediatric Lung Transplant Program at the AHM, Associate Professor Glen Westall. In jurisdictions with an adult lung transplant service, initial referral was in several instances made to the local adult service, and the adult service then referred appropriate patients on to the NFC PLHLT Program.

As presented in Table 2.1 below, a total of 37 patients have been formally referred to the NFC PLHLT Program between 1 July 2011 and 25 September 2015, representing an average referral rate of 8-9 patients per year. These numbers relate to written referrals only (noting the numbers reported in the NFC Annual Reports included telephone enquiries) and exclude two patients referred to the service from New Zealand, one of whom did not proceed to formal assessment, and the other who proceeded to formal assessment and transplant outside of NFC funding.

Table 2.1: NFC PLHLT Program referrals by jurisdiction, compared to population 5-14 years

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<th></th>
<th></th>
<th></th>
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</tbody>
</table>

% of referrals: 24.3% 35.1% 18.9% 10.8% 5.4% 5.4% 0% 0% 100%

% of population 5-14yrs(a): 31.9% 24.0% 21.4% 11.0% 6.8% 2.2% 1.6% 1.2% 100%

Source: NFC site submission to the review and subsequent information provided to the review
(a) Australian Bureau of Statistics, Estimated resident population by states and territories 2014, ages 5-14 years (stat.abs.gov.au)

Table 2.1 demonstrates that referrals to the NFC PLHLT Program broadly reflect birth populations across Australia, with the exception of NSW and Victoria. Victoria is over-represented in referral numbers and NSW is under-represented. The AHM/RCH suggested that reasons for over-representation of Victorian patients in referrals may be attributed to the fact that RCH operates Australia’s largest pulmonary hypertension service. This is supported by analysis of referral diagnoses, whereby eight of the 13 patients referred from Victoria had a diagnosis of pulmonary hypertension (61.5%), compared with only three of the 24 patients referred from outside Victoria (12.5%).
international clinical expert has advised that the rates of referral for PLHLT for patients diagnosed with pulmonary hypertension are also increasing in North America, but noted that rates can vary significantly from site to site depending on the availability of local pulmonary hypertension services. Note that further discussion regarding patient diagnoses is presented in section 2.2.4 below.

Reasons for the under-representation of NSW patients is mostly likely explained by the lower proportion of referrals on NSW patients with pulmonary hypertension. Consultation with NSW clinicians treating paediatric patients with pulmonary hypertension suggested that the combined effects of improvements in the treatment outcomes achieved from intravenous epoprostenol may be reducing referral numbers. However, these clinicians emphasised that referrals were being made (where appropriate) and that due to the small numbers of patients involved a longer time series was required to identify difference in referral rates.

While NSW referring clinicians considered distance from the NFC site was a challenge for NSW families, this rarely resulted in families electing not to proceed to transplantation (only one instance noted, and there were other complicating factors).

### 2.2.2 Criteria for patient referral and selection

Clinical criteria for referral have been established by AHM/RCH and reflect international evidence-based protocols supporting earlier rather than later referral, even where the outcome may be that the patient is deemed too well to transplant. This allows all parties involved with the case to become familiar with the patient particularly when time-critical decisions regarding transplant can arise in the future, and to make appropriate decisions regarding transplant suitability. Referral recommendations outlined by AHM/RCH include the following:

- Children with end-stage lung disease who demonstrate declining function despite optimal therapy, and in whom anticipated or predicted survival is limited
- Patient is breathless on minimal exertion (New York Heart Association class III or IV) and survival is expected to be limited to two to three years
- Lung transplantation is rarely appropriate in critically ill patients in desperate clinical situations (e.g. intubated patients).

Broadly, patients are accepted for transplantation based on a prognosis of end-stage lung disease with less than a two year median survival where there are no suitable alternative treatments. Such patients have pronounced and disabling breathlessness and very poor quality of life, which has the potential to be enhanced by transplantation. In their submission to this review, AHM/RCH reported that patient selection criteria to the program are in accordance with universally agreed guidelines that were previously detailed in the 2010 NFC Assessment Report, pages 28-31. These are reproduced in Table 2.2 below for reference.

#### Table 2.2: Guidelines for patient selection to the NFC PLHLT Program from 2010 NFC Assessment Report

<table>
<thead>
<tr>
<th>General selection criteria for listing for transplantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung or heart-lung transplantation is considered in selected children with end stage or progressive lung disease or life-threatening pulmonary vascular disease for which there is no other medical or surgical therapy. Usually, this</td>
</tr>
</tbody>
</table>

---

2 DLA Phillips Fox. Health Technology Assessment of a Proposal to Establish Paediatric Lung and Heart-lung Transplantation Procedures as a Nationally Funded Centre, 2010 (no date included on document)
means candidates are on full medical therapy, and in spite of full medical therapy the predicted life expectancy for the child is poor (i.e. have less than 50% chance of surviving two years without transplant intervention)\textsuperscript{3,4}. Each transplant centre has slightly different selection criteria, based on their experience and local preferences.

Irrespective of underlying diagnosis, all candidates should possess\textsuperscript{5,6,7}

- a clear diagnosis or adequately delineated trajectory of illness despite optimal medical therapy that puts the individual child at risk of dying without a lung transplant
- adequate family support
- adequate access to transplant services and medications after transplantation
- adequate evidence of willingness and ability on the part of patient and parent to adhere to the rigorous therapy, daily monitoring and re-evaluation schedule after transplant.

### Condition-specific guidelines

Selection guidelines have been published for some conditions only. For other clinical conditions there are no strict selection criteria\textsuperscript{8,9}. Condition specific guidelines include:

**Cystic fibrosis:**

- baseline FEV1 < 30% predicted
- hypoxia at rest (PaO\textsubscript{2} < 55mmHg)
- hypercapnia (PaCO\textsubscript{2} > 50mmHg)
- rapid clinical decline, or
- greater than two pulmonary exacerbations per year requiring hospital admission or home IV antibiotic therapy.

**Idiopathic pulmonary arterial hypertension:**

- New York Heart Association functional class III or IV
- unresponsive to medical management
- mean right atrial pressure > 10mmHg
- mean pulmonary arterial pressure > 50mmHg, or
- cardiac index < 2 l/min/m\textsuperscript{2}.

Lung transplantation is only considered when both medical and surgical management have already been fully optimised and cannot significantly improve lung function. There is no randomised controlled trial or systematic review of any form of lung transplantation. The management of severe lung disease by experienced teams, including appropriate use of therapies such as bi-level positive airway pressure (BiPAP), dornase alpha and azithromycin in patients with CF, may lead to a successful ‘bridge-to-transplant’. Similarly, intravenous prostacyclin, oral bosentan and sildenafil may bridge patients of all ages with severe pulmonary hypertension. These interventions are, however, ongoing, associated with risk and costly.

\textsuperscript{3} Huddleston C. Pediatric lung transplantation. Seminars in Pediatric Surgery 2006;15:199-207  
\textsuperscript{4} Doherty G, Aurora P. Update on paediatric lung transplantation. Paediatric Respiratory Review 2010;11:54-61  
\textsuperscript{8} Woo M. Overview of lung transplantation. Clinical Reviews in Allergy and Immunology 2008;35:154-63.  
Contraindications to transplantation

Contraindications to lung and heart-lung transplantation include anatomical, surgical, medical and psychological factors. However, there is a high degree of variability between treatment centres regarding relative and absolute contraindications for transplantation. Those most commonly agreed upon include\textsuperscript{10, 11, 12, 13, 14}.

Absolute:
- marked chest wall abnormalities (including severe scoliosis and severe tracheal abnormalities)
- active malignancy
- sepsis
- active tuberculosis
- severe neuromuscular disease
- documented, refractory non-adherence with clinical management
- multiple organ dysfunction, or
- hepatitis C with histological liver disease.

Relative:
- pleurodesis
- renal insufficiency
- markedly abnormal body mass index (BMI)
- mechanical ventilation
- scoliosis
- poorly controlled diabetes mellitus
- osteoporosis
- chronic airway infection with multiply resistant organisms
- fungal infection / colonisation, or
- hepatitis B surface antigen positive.

Talc pleurodesis is a contraindication in some surgical centres but not others. Formerly, history of pneumonectomy was also considered a strong contraindication due to altered thoracic anatomy. However recent success has been demonstrated in performing transplantation in carefully selected cases where anatomy permits lung transplant\textsuperscript{15}. Renal insufficiency (creatinine clearance less than 50 mL /1.73 m\textsuperscript{2}), hepatic insufficiency and left ventricular dysfunction are contraindications for isolated lung transplantation\textsuperscript{16}. However, transplantation is considered if combined with transplantation of the second failing organ. Heart-lung and lung-liver transplantation.

\textsuperscript{10} Woo M. Overview of lung transplantation. Clinical Reviews in Allergy and Immunology 2008;35:154-63.
\textsuperscript{11} Wells A. Special considerations in pediatric lung transplantation. Seminars in Respiratory and Critical Care Medicine 2006;27:552-60.
are established surgical clinical treatments for combined organ failure whereas simultaneous lung-kidney transplantation is rarely performed worldwide\textsuperscript{17}.

Children with cancer generally have to be in remission for one to five years, depending on the cancer type, prior to being listed for lung or heart-lung transplantation\textsuperscript{18}.

Virulent antibiotic resistant bacteria such as Mycobacterium abscessus and Burkholderia cenocepacia in patients with CF is considered an absolute contraindication in the majority of transplant centres. The presence of Burkholderia cenocepacia in particular is associated with early death and poor survival rates after lung transplantation. The presence of multi-resistant pseudomonas aeruginosa is also an absolute contraindication in some transplant centres\textsuperscript{19,20}.

Child psychologists and paediatric social workers assess children and their families as a routine component of pre-transplantation evaluation in order to determine whether families and children are likely to be able to comply with the rigorous requirements of management post-surgery. Uncontrolled psychiatric or behavioural disorders are a contraindication to lung transplantation in most treatment centres\textsuperscript{21}.

A history of poor compliance with medical care is a relative contraindication in most centres, and is an important consideration for some families.

The site submission to this review reported that there continues to be evolution as to what are regarded as contraindications to lung transplantation. Whilst malignancy (unless in remission for five years), serious incurable infection, other systemic illnesses and major psychiatric illness (such as uncontrolled psychosis or substance addiction) are still generally accepted absolute contraindications to lung transplantation, other conditions that were previously considered as absolute contraindications are now considered on a case by case basis at AHM. These include:

- PLHLT for patients on ECMO-bridge-to-transplant
- the presence of Burkholderia cenocepacia, atypical Mycobacteria (e.g. Mycobacterium abscessus) and fungi (such as Aspergillus spp)

While these changes have a minimal impact of the price per procedure recommended by this review (as ECMO-bridge-to-transplant costs are removed in full, and the funding patients colonised with Mycobacterium abscessus or burkholderia cenocepacia is approximately $5,600 per procedure), they do represent significant changes in the accepted indications for the procedure. As such, it is recommended that the NFC Reference Group formally consider this appropriateness of this change. These changes are discussed in detail in section 3.1 of this report.

The submission also noted that multiple relative contraindications may lead to a decision to not transplant if the assessment team consider that the likelihood of a sustained period of quality of life after transplantation is low. These factors may include previous surgery (particularly pleurectomy or pleurodesis) but also complex cardiac repairs and infections with significant pathogens that are difficult to control post-transplant. Other co-morbidities such as chronic liver disease, renal impairment and psychosocial aspects where there is demonstrably poor support, lack of commitment to transplantation, or poor compliance are also considered as relative contraindications. It was reported in the submission that for paediatric patients, psychosocial aspects may be critical to decision making.

\textsuperscript{17} Dishop M. Pediatric lung transplantation. Pediatric and Developmental Pathology 2008;11:85-105.
2.2.3 Number of Patients Accepted and Transplanted

Following patient referral, the referring clinician is contacted to discuss the patient if this has not already occurred prior to referral. Where required, an initial assessment is offered in the home jurisdiction either as an outpatient or inpatient in the local hospital. This initial assessment is conducted by members of the NFC PLHLT team (Head of the Program at AHM, Paediatric Respiratory Physician from RCH, and Paediatric Lung Transplant Coordinator from AHM). The initial telephone discussion and/or consultation visit allows the team to determine whether transplant is a feasible and appropriate option, and whether/when the patient should proceed to formal assessment.

Suitable patients progress for formal assessment conducted at AHM/RCH. Formal assessment is generally performed over five days as an in-patient at RCH where most tests are performed, with two outpatient days at AHM to meet members of the multi-disciplinary lung transplant team. Following this assessment, a decision is made regarding acceptance or non-acceptance to the NFC PLHLT Program, and patients are placed on the waiting list if accepted. The formal assessment allows the team to gain a complete picture of the child’s needs, determine the most appropriate intervention options, and determine when the patient should be put on the waiting list. In emergency situations or where the patient is very ill, the patient may be accepted to the program and waitlisted following initial assessment at the home jurisdiction.

During the review period, a total of 17 patients (in the first three years of the NFC PLHLT Program - 54.8% of total referrals), and 22 patients to September 2015 (59.5% of total referrals) progressed to formal assessment. Of the 17 patients who did not progress to formal assessment since the NFC PLHLT Program’s inception (including two patients referred from New Zealand who were included in data provided by the NFC site), reasons for not progressing were reported to include:

- Patient too well (n=8)
- Alternative therapies suggested (n=4)
- Concerns regarding non-adherence (n=3)
- Multiple co-morbidities (n=2).

An average of five to six patients per year accepted to the NFC PLHLT Program and placed on a waitlist for lung or heart-lung transplantation. At 30 June 2014 there were four children on the NFC PLHLT Program waiting list. At the time of this review (September 2015) there were two children on the waiting list. During this period patients are able to live at home if they are within a four hour travel time to the NFC site, with care provided by the local paediatric team and reviewed NFC PLHLT team every six months; patients relocating to Melbourne receive care at RCH, and waiting list review conducted by NFC PLHLT team every six weeks.

As presented in Table 2.3 below, a total of 15 patients have undergone PLHLT between 1 July 2011 and 25 September 2015 under the NFC PLHLT Program, including two patients accepted to the waitlist prior to NFC status, representing an average of three to four patients per year undergoing transplantation under the NFC PLHLT Program. Although small numbers limit the conclusions that can be drawn from any analysis of referral and transplant rates by referring jurisdiction, the annual transplant rate per million population in Victoria is four times that for NSW (2.03 per million compared with 0.51 per million). This may be influenced to some extent by the low referral rate from NSW to the program.
Table 2.3: Number of patients referred and undergoing transplant by state/territory of referral, July 2011 – September 2015

<table>
<thead>
<tr>
<th>No. patients</th>
<th>Referring jurisdiction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NSW</td>
</tr>
<tr>
<td>Referrals</td>
<td>9</td>
</tr>
<tr>
<td>Formal assessment and acceptance</td>
<td>4</td>
</tr>
<tr>
<td>Undergone transplant(a)</td>
<td>2</td>
</tr>
<tr>
<td>Population 5-14yrs (million)(b)</td>
<td>0.92</td>
</tr>
<tr>
<td>Average annual PLHLT rate per million population (5-14yrs)</td>
<td>0.51</td>
</tr>
</tbody>
</table>

Source: NFC site submission to the review and subsequent information provided to the review
(a) Number undergoing transplant refers to transplants conducted in the time period, and includes two patients who were accepted for transplant prior to the review period (NFC Annual Report 2011-12). Two patients accepted to the program in the review period are still on the waitlist, two patients died whilst on the waitlist, four patients were delisted (three due to subsequent clinical improvement and one due to persistent non-adherence to medical therapy), and one patient turned 18 and was transferred to the adult program.
(b) Australian Bureau of Statistics, Estimated resident population by states and territories 2014, ages 5-14 years, (stat.abs.gov.au)

Based on information provided by the NFC PLHLT Program there has been a slight increase in the number of patients per year accessing the program at AHM since receiving NFC status. Prior to NFC status, and noting that the service was only initiated in 2005, there was an average of two to three patients per year undergoing lung or heart-lung transplant. Following NFC status there has been an average of three to four patients per year. In the period 2007 to 2009 (immediately preceding the NFC status assessment) PLHLT were being undertaken by two sites (AHM and St Vincent’s Hospital Sydney). At that time NSW patients represented 33.3% of patients transplanted (now 13%), and no Victorian patients were transplanted in that period (now 40% of patients transplanted). Representation from other jurisdictions has remained relatively consistent.

As shown in Table 2.4 below, there were two patients transplanted under the program since 1 July 2011 who were accepted prior to NFC status. Of the 22 patients accepted to the program since 1 July 2011, 13 have undergone transplant and two are still on the waitlist. Of the patients still waitlisted, one is from NSW and the other is from Queensland, with the latter patient having been on the waitlist for 219 days and having to relocate to Victoria for this time. Two patients died whilst on the waitlist, one of these on ECMO following a liver transplant complicated by portopulmonary syndrome who died within 24 hours of listing, and the second who was listed for re-transplant and died from chronic rejection after being on waitlist for six months. Four patients were delisted (three due to subsequent clinical improvement and one due to persistent non-adherence to medical therapy), and one patient turned 18 whilst on the waitlist and was transferred to an adult program.
Table 2.4: Transplant status of patients accepted to and/or transplanted under the NFC PLHLT Program (July 2011 – September 2015)

<table>
<thead>
<tr>
<th>Status</th>
<th>Accepted to NFC (n=22)</th>
<th>Accepted pre-NFC (n=2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transplant undertaken</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>De-listed from NFC</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>Died on waitlist</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Still on waitlist</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Transferred to adult program</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>2</td>
</tr>
</tbody>
</table>

Source: (a) Submission to the review (b) Annual Report 2011-12

2.2.4 Patient demographics and year of transplant

The current target group for the NFC PLHLT Program is:

Children and adolescents 6–15 years typically weighing 20-40kg, noting that weight should not be an exclusion to treatment if the patient is in the right age range. The NFC site for paediatric lung and heart-lung transplantation may also treat older adolescents (aged 15 years but less than 18 years) where they are smaller, of lower body weight, or have complex paediatric issues (including psychosocial issues).

Patient demographic data for those undergoing transplantation since 1 July 2011 are summarised in Table 2.5 below and presented by case number in Table 2.6. These data indicate that whilst the majority of patients fell within the target group for the program, two fell outside the target age (13.3%; one patient was five and one 16 years old) and six patients fell outside the target weight (40.0%; one patient <20kg and five patients >40kg). The age range of patients undergoing transplantation under the NFC PLHLT Program was five to 16 years, with median age 14 years and mean age 12.7 years. The weight range of patients was 16–66kg, with median weight of 36kg and mean weight of 38.8kg. The majority of patients had a diagnosis of cystic fibrosis, with others having either pulmonary hypertension or pulmonary fibrosis. Most patients underwent bilateral sequential lung transplantation (n=10), with four patients undergoing lobar lung transplant and one five year old patient undergoing heart-lung transplantation. The average time on the waitlist was 119.3 days, with a median of 57 days and a range of 1–442 days.

Table 2.5 also indicates that there can be considerable variation in actual numbers of patients transplanted per year. Since NFC status, number of transplants conducted under the program ranged from one to six per year.
### Table 2.5: Summary of demographic characteristics of patients undergoing transplant (n=15)

<table>
<thead>
<tr>
<th>Year transplant conducted</th>
<th>No. patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011/12</td>
<td>6</td>
</tr>
<tr>
<td>2012/13</td>
<td>1</td>
</tr>
<tr>
<td>2013/14</td>
<td>2</td>
</tr>
<tr>
<td>2014/15</td>
<td>3</td>
</tr>
<tr>
<td>2015 Q1</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>5-16 years</td>
</tr>
<tr>
<td>Mean (median)</td>
<td>12.7 (14) years</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weight</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>16-66kg</td>
</tr>
<tr>
<td>Mean (median)</td>
<td>38.8kg (36kg)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystic fibrosis</td>
<td>9</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>3</td>
</tr>
<tr>
<td>Pulmonary fibrosis</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Transplant type</th>
<th>No. patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral sequential lung transplantation</td>
<td>10</td>
</tr>
<tr>
<td>Lobar lung transplantation</td>
<td>4</td>
</tr>
<tr>
<td>Heart-lung transplantation</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Waitlist days</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>1-442 days</td>
</tr>
<tr>
<td>Mean (median)</td>
<td>119.3 (57) days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other</th>
<th>No. patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transplant from ECMO</td>
<td>2</td>
</tr>
<tr>
<td>Pre-transplant Mycobacterium abscessus colonisation</td>
<td>2</td>
</tr>
</tbody>
</table>

Source: NFC site submission to the review and review presentation
Table 2.6: Demographic characteristics of patients undergoing transplant by patient (n=15) between July 2011 – September 2015 and status at 30 September 2015

<table>
<thead>
<tr>
<th>Year</th>
<th>Patient case no.</th>
<th>Age (yrs)</th>
<th>Weight (kg)</th>
<th>Diagnosis</th>
<th>State</th>
<th>Waitlist days</th>
<th>Transplant type</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011/12(a)</td>
<td>1</td>
<td>6</td>
<td>21</td>
<td>PF</td>
<td>NSW</td>
<td>153</td>
<td>Bilat. lung</td>
<td>Alive</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>13</td>
<td>28</td>
<td>CF</td>
<td>VIC</td>
<td>54</td>
<td>Bilat. lung</td>
<td>Deceased</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>14</td>
<td>58</td>
<td>CF</td>
<td>NSW</td>
<td>57</td>
<td>Bilat. lung</td>
<td>Deceased</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>14</td>
<td>32</td>
<td>CF</td>
<td>VIC</td>
<td>4</td>
<td>Bilat. lung</td>
<td>Deceased</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>14</td>
<td>36</td>
<td>CF</td>
<td>VIC</td>
<td>291</td>
<td>Lobar lung</td>
<td>Deceased</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>15</td>
<td>61</td>
<td>PHT</td>
<td>VIC</td>
<td>7</td>
<td>Lobar lung</td>
<td>Alive</td>
</tr>
<tr>
<td>2012/13</td>
<td>7</td>
<td>15</td>
<td>36</td>
<td>CF</td>
<td>QLD</td>
<td>371</td>
<td>Lobar lung</td>
<td>Alive</td>
</tr>
<tr>
<td>2013/14</td>
<td>8</td>
<td>14</td>
<td>40</td>
<td>CF</td>
<td>QLD</td>
<td>129</td>
<td>Bilat. lung</td>
<td>Alive</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>15</td>
<td>34</td>
<td>CF</td>
<td>TAS</td>
<td>442</td>
<td>Lobar lung</td>
<td>Alive</td>
</tr>
<tr>
<td>2014/15</td>
<td>10</td>
<td>15</td>
<td>47</td>
<td>PHT</td>
<td>VIC</td>
<td>23</td>
<td>Bilat. lung</td>
<td>Alive</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>5</td>
<td>16</td>
<td>PHT</td>
<td>VIC</td>
<td>172</td>
<td>Heart-lung</td>
<td>Alive</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>11</td>
<td>30</td>
<td>CF</td>
<td>WA</td>
<td>1</td>
<td>Bilat. lung</td>
<td>Alive</td>
</tr>
<tr>
<td>2015 Q1</td>
<td>13</td>
<td>14</td>
<td>47</td>
<td>CF</td>
<td>SA</td>
<td>22</td>
<td>Bilat. lung</td>
<td>Alive</td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>9</td>
<td>30</td>
<td>PF</td>
<td>QLD</td>
<td>1</td>
<td>Bilat. lung</td>
<td>Alive</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>16</td>
<td>66</td>
<td>PHT</td>
<td>SA</td>
<td>62</td>
<td>Bilat. lung</td>
<td>Alive</td>
</tr>
</tbody>
</table>

Source: Presentation by NFC site to reviewers, October 2015

PF=Pulmonary Fibrosis; CF=Cystic Fibrosis; PHT=Pulmonary Hypertension; Bilat lung=Bilateral sequential lung transplantation

(a) One patient from NZ underwent lung transplant at AHM in 2011-12 but has not been included in data as outside the NFC program.

The analysis also indicates that a small number of patients have undergone transplantation following ECMO or with a pre-transplant infection who may be contraindicated in other centres. Reasons for acceptance of patients outside the target age and/or weight group, and also acceptance of marginal patients or donors, were provided by AHM/RCH in their submission to the review as summarised below.

1. **Patients under six years and/or under 20kg.** The NFC PLHLT Program has accepted two children who were under six years and weighing less than 20kg to the waitlist (with one child being subsequently transplanted) following detailed multi-disciplinary assessment. This assessment involved cardiothoracic surgeons, respiratory physicians, anaesthetists and intensivists from both the AHM and the RCH, as well as consultation with, and agreement from, the NFC Reference Group. AHM/RCH has requested that the NFC PLHLT Program be expanded to include patients 4-15 years weighing minimum 10kg (the NFC site for paediatric lung and heart-lung transplantation may also treat older adolescents (aged 15 years but less than 18 years) where they are smaller, of lower body weight, or have complex paediatric issues (including psychosocial issues). This is discussed further in Chapter 3 of this report.

2. **Marginal recipients.** AHM/RCH will consider the following patients for acceptance to the program who would previously have been contra-indicated: patients on ECMO, and patients with *Mycobacterium abscessus* and *Burkholderia cenocepacia*. Since NFC status, protocols have been established by the NFC site for patients on ECMO as a bridge to transplant, and two patients on ECMO have been accepted to the program and transplanted including one from interstate (13.3%
of transplants undertaken). In addition, two patients with *Mycobacterium abscessus* who were able to tolerate intensive intravenous antimicrobial therapy for at least three months pre and post-transplant surgery were also accepted to the program and underwent transplant. AHM/RCH estimates that 20% of all paediatric lung or heart-lung transplants in the future will be done on patients who are being supported on ECMO at RCH, and/or on patients colonised with *Mycobacterium abscessus*. This is discussed further in Chapter 3 of this report.

3. **Marginal donors.** In order to address a limited supply of paediatric donor organs, the AHM reports it has pioneered approaches for use of donation after cardiac death (DCD) lungs and down-sizing adult lungs in order to perform lobar transplants, and now has the world’s largest elective lobar transplant program in children, the results of which have been extensively published and presented internationally (see Appendix C). AHM also has plans to introduce ex vivo lung perfusion (EVLP) to assess and repair the quality of extended or questionable donor lungs in the future. However, details regarding implementation of this approach are still under consideration by AHM (noting that other centres worldwide and all three of Australia’s other lung transplant units are now reported to be utilising EVLP). It is noted by HOI that organ retrieval and organ donation, and by extension the costs of EVLP technology, are outside of the scope of the NFC Program.

### 2.2.5 CRITERIA FOR ORGAN ALLOCATION

TSANZ has developed eligibility criteria not only for patients to be listed for organ transplantation but also protocols for the allocation of organs to patients once listed. Version 1.4 of these guidelines was released in April 2015 and contains allocation protocols relevant to lung transplantation. Based on the allocation protocols, and noting that there are no separate organ allocation guidelines for paediatric patients, AHM/RCH receive the majority of donor lung/heart-lung organs from Victoria. AHM/RCH report that they are in ongoing discussions with the lung advisory committee of TSANZ regarding this issue which impacts donor organ availability to the NFC PLHLT Program.

AHM reported that in order to improve the supply of paediatric organ donors, that it has pioneered approaches for use of donation after cardiac death (DCD) lungs and down-sizing adult lungs in order to perform lobar transplants, as discussed in section 2.2.4 above. With an increasing number of paediatric lung transplants involving DCD lungs at NFC PLHLT Program, the NFC site noted that there is currently an absence of DCD protocols in paediatric hospitals but that Donate Life is exploring this issue. Given the time critical nature of transplantation using DCD organs, the majority of these organs also come from Victoria.

It was reported by one jurisdictional stakeholder (Head, Adult Lung Transplant Service), that organ availability is the main limitation to PLHLT, and that different organ procurement and acceptance rates exist across different states and territories in Australia. EVLP may provide opportunities to increase the donor pool (refer further section 3.1.5).

### 2.2.6 COMMENTS FROM REFERRING CLINICIANS AND OTHER JURISDICTIONAL STAKEHOLDERS

Referring clinicians and other jurisdictional stakeholders generally reported no issues with access to the NFC PLHLT Program. Where patients were required to relocate to Melbourne, even for patients with over four hours travel time who had to relocate for the waiting list period (e.g. patients from WA and some from Queensland), it was generally reported by clinicians and families that this was a
reasonable expectation of a specialised national service. However, it was reported by NSW clinicians participating in the consultation at the SCHN that the inability to access a local paediatric lung transplantation service was a significant barrier to access for patients in this region. These clinicians stated that an additional three to five patients per year would access a PLHLT service if it was available locally (i.e. doubling the number of paediatric patients currently undergoing lung or heart-lung transplant per year across Australia).

Referring clinicians generally reported being sufficiently informed about the program and all commented that the NFC PLHLT team is very accessible to contact. Where clinicians were new or had previously had no contact with the service, they reported finding out about the service in several cases from their local adult lung transplant team. After then contacting the service, they were phoned back by the NFC PLHLT Program Unit Head (Associate Professor Glen Westall) within 24 hours, often earlier, and provided with all the information required. In some cases, the initial screening assessment was conducted by the local adult transplant team (e.g. in WA) with subsequent referral to the NFC PLHLT Program for formal assessment.

Areas where one or more referring clinicians commented that further information would be useful were the following:

1. **Guidelines for referral of patients on ECMO.** One interstate referring clinician was under the impression that until recently, patients on ECMO would not be accepted to the program, and had therefore referred such patients in the past to the local adult service. Guidelines for retrieval of patients on ECMO from other jurisdictions were not yet established, and it was noted that a paediatric ECMO retrieval service would be demanding on any institution providing this service. In the most recent case of a child from Queensland, there was discussion regarding AHM retrieving the patient, but on the day staff from Queensland provided this service due to availability.

2. **Patient costs.** Two interstate referrers were uncertain about the level of support, or the degree of flexibility in the provision of support, available to families travelling to Melbourne under the NFC PLHLT Program, and what out-of-pocket expenses would likely be incurred by families particularly during a protracted stay.

3. **Overall numbers and outcomes data.** No clinicians were aware of the total number of patients referred to the NFC PLHLT Program or the number of transplants undertaken. One requested that more regular provision of outcomes data be provided to referring clinicians and other jurisdictional stakeholders under the NFC Program as this would assist in pre-referral discussions and decision making.

There was no criticism of the waitlist management or organ allocation process undertaken by NFC PLHLT Program, with several stakeholders commenting that they were kept well-informed regarding waitlist status for patients they had referred.

**Recommendation:** It is recommended that NFC site reviews the communication processes with referrers to provide information on contemporary treatment and outcomes data, explain referral, patient support and discharge protocols, and provide opportunities for referrers to provide feedback and recommendations to improve future program services.

*(Consolidated list of recommendations 9)*

### 2.2.7 Comments from patients and families

Patients from Victoria and from other jurisdictions reported a high level of satisfaction with the NFC PLHLT Program and were very happy to travel and/or relocate as required in order to access a
specialised service. Where necessary, travel and accommodation arrangements had been organised by the PLHLT Program Coordinator and were reported to be much appreciated and to “take the load off families”. Accommodation was reported by families to be convenient to the hospital and much appreciated, with the logistics of organisation described by one family as “100% perfect”. However, one family commented that they had to find and fund their own accommodation prior to transplant as their child needed to relocate to undergo a course of three months intravenous antibiotics for Mycobacterium abscessus colonisation.

2.3 Health outcomes

The International Society for Heart and Lung Transplantation – United Network of Organ Sharing (ISHLT/UNOS) registry provides regular reports (updated on [www.ishlt.org](http://www.ishlt.org)) on the outcome for heart-lung transplantation, bilateral lung transplantation, and single lung transplantation in adults and paediatric patients. Survival outcomes for patients undergoing transplant in the NFC PLHLT Program are compared to international outcomes below, and an ongoing project to collect data on quality of life outcomes is described.

2.3.1 Survival outcomes

As presented in Table 2.6 above, since the provision of NFC status four of the 15 children transplanted under the NFC PLHLT Program have died as a consequence of complications related to transplantation. All these patients had undergone transplant in the first year of the NFC PLHLT Program in 2011/12. One of these patients died less than 30 days post-transplant, two between 30 days and one year post transplant, and one just under two years post-transplant.

One year survival for the first three years of the program was reported to be 70% in the NFC Annual Report 2013/14 (although these data included one patient from New Zealand who was not funded under the NFC Program). AHM reported in its submission to the review that since 2006, when the PLHLT service was first established at AHM, one year survival for the 29 transplant procedures has been 84% to September 2015.

Table 2.7 provides a breakdown of survival outcomes by age group and a comparison of these outcomes reported by the NFC PLHLT Program with international data from the ISHLT Registry. It is important to note that small numbers and variation in patient acceptance criteria mean that caution should be exercised in making comparisons across centres. Noting these caveats to data comparison, one year survival outcomes appear superior to international outcomes for younger patients, and slightly inferior for adolescent patients. A calculation of NFC PLHLT Program three year survival rates has not been included as the majority of patients were transplanted under three years ago making numbers for inclusion in analysis very small.
Table 2.7: Survival rates for patients undergoing PLHLT internationally (ages 6-17 years, 2010 to 2014) compared with NFC Program (ages 5-16 years, 2011 to 2014/15)

<table>
<thead>
<tr>
<th>Age at PLHLT (years)</th>
<th>Time post-transplant</th>
<th>ISLHT (a)</th>
<th>NFC Site Submission(b)</th>
<th>Survival rate</th>
<th>No. deaths (cumul.)</th>
<th>Survival rate</th>
<th>Time of death (days post Tx)</th>
<th>Cause of death</th>
<th>Contributing factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-10</td>
<td>30 days</td>
<td>Not provided</td>
<td>0</td>
<td>100.0%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>1 year</td>
<td>95.2%</td>
<td>0</td>
<td>100.0%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>3 years</td>
<td>80.8%</td>
<td>0</td>
<td>n/a</td>
<td>29</td>
<td>Aspergillus infection</td>
<td>CF, pre-Tx colonisation</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>11-17</td>
<td>30 days</td>
<td>Not provided</td>
<td>1</td>
<td>91.7%</td>
<td>317</td>
<td>Antibody-mediated rejection</td>
<td>Non-adherence</td>
<td>348</td>
<td>Antibody-mediated rejection</td>
</tr>
<tr>
<td></td>
<td>1 year</td>
<td>81.1%</td>
<td>3</td>
<td>75.0%</td>
<td>702</td>
<td>Chronic rejection</td>
<td>Non-adherence</td>
<td>348</td>
<td>B. cenocepacia infection and reduced immunosuppression</td>
</tr>
<tr>
<td></td>
<td>3 years</td>
<td>64.3%</td>
<td>4</td>
<td>n/a</td>
<td>702</td>
<td>Chronic rejection</td>
<td>Non-adherence</td>
<td>702</td>
<td>Chronic rejection</td>
</tr>
</tbody>
</table>

Sources:
(a) ISHLT Transplant Registry Quarterly Report for Lung – Survival rates for transplants performed between 1 October 2010 and 30 September 2014 (entire ISHLT Registry)
(b) NFC site submission to review for NFC PLHLT Program 2011/12-Q1 2015/16,

The AHM/RCH commented that contributing factors resulting in poorer outcomes compared to internationally, particularly in the adolescent age group, reflects known difficulties associated with taking on higher risk patients, including those who have pre-transplant colonisation or infection. Our international expert concurred with these comments.

In addition, the two patients where non-adherence was a contributing factor were both adolescents, where non-adherence is a common problem. The NFC PLHLT Program has now developed a specific adolescent-focussed education program to address this issue, in collaboration with the Adolescent Service at RCH. The NFC Program site also commented that children undergoing life-saving transplant surgery are likely to face significant long-term psychological challenges related to the chronic need to take life-saving immunosuppressant medications, and have included a request and budget for a child psychologist to be added to the core NFC PLHLT team for the future.

2.3.2 Quality of Life Outcomes

Quality of life is an important outcome measure for children undergoing lung transplantation, and potential to improve quality of life was reported by AHM to be a key consideration in decisions regarding transplant. Formal assessment of quality of life outcomes was not conducted in the first year of the program, but an ongoing research project was initiated in 2012-13 and results will become available in the next two years (Understanding the perceived lived experience: an exploration of the perceived quality of life in children post-bilateral transplantation (Living with new Lungs)). This research project is being led by the PLHLT occupational therapist, and so far five of the 15 patients have been...
recruited to the project. Quality of life is being assessed at 3, 6, 12 and 18 months post-transplant using the following tools:

- Pediatric Quality of Life Inventory, Version 4.0 Short Form[SF15] - Toddlers, Young Children, Child and Teen reports and matching Parent Reports at same time points
- Pediatric Quality of Life Inventory, Transplant Module Version 3 - Toddlers, Young Children, Child and Teen reports and matching Parent Reports at same time points
- Child Occupational Self-Assessment.

AHM/RCH reported that all patients who were discharged from the NFC PLHLT Program following the initial transplant operation were able to reengage with their education and returned to school within four months of the transplant surgery.

2.4 MODEL OF CARE AND SERVICE DELIVERY

The model of care and delivery of services provided by the NFC PLHLT Program are described in this section, including discussion regarding service development, workforce, continuum of care, and the adolescent program.

2.4.1 SERVICE DEVELOPMENT

The AHM adult lung transplant service is Australia’s and one of the world’s busiest lung transplant programs, having transplanted over 1200 patients since 1990. Currently more than 80 patients undergo lung transplantation at AHM each year and forecasts suggest that annual activity will rise to over 100 lung transplants per annum by 2018. This brings considerable multi-disciplinary experience to lung transplantation, and was the major driver in 2005 for the decision to base paediatric lung transplantation at AHM, albeit in close collaboration with the RCH. A number of modifications and initiatives have been implemented since the PLHLT service was established to address the obvious limitations of running a paediatric service within an adult institute. These have been reported by AHM/RCH in their submission to the review to include:

- Memorandum of understanding between the AHM and RCH that underpins the collaborative NFC PLHLT Program
- Cross-credentialing of identified staff members in the departments of lung transplantation, respiratory medicine, cardiothoracic surgery, anaesthetics, intensive care, and nursing between AHM and RCH
- A directed, extensive and on-going education program covering multiple aspects of paediatric care and lung transplantation continues to be provided at the RCH and AHM, respectively
- Combined paediatric and lung transplant physician input at all steps of the transplantation pathway (initial review, assessment, waiting list, post-transplant inpatient and outpatient care)
- Broad expertise in paediatrics and lung transplantation across the AHM and RCH, meaning that whilst the Paediatric Lung Transplant Service is primarily run by a focused group of medical, nursing and allied health staff, systems have been established so that the program remains viable and functional in the absence of core staff
- Dedicated paediatric lung transplant coordinator operating across both hospitals and identified as the first point-of-contact for patients and their families, as well as for the wider multi-disciplinary paediatric lung transplant team
- Recruitment at AHM of specific medical and allied health staff with background training and experience in the care of the paediatric patient
- Early post-transplant in-patient care on the ICU and respiratory ward provided by nurses trained in paediatrics and lung transplantation, respectively.

Whilst the established model has been developed to safely transplant children aged 6 to 15 years, as per the target group for the NFC Program, it also provides appropriate facilities and services to treat older adolescents (aged 15 to 18 years) where they are smaller, of lower body weight or have complex paediatric issues (including psychosocial issues).

2.4.2 Workforce

The NFC PLHLT Program at the AHM continues to exist under the umbrella of the adult lung transplant program and consists of a large multidisciplinary team. Since its inception, and reflecting the demands of managing children in an adult hospital, the following key appointments in the following have been made at the AHM:

- Medical: lead physician in paediatric lung transplantation (A/Prof Glen Westall)
- Nursing: paediatric lung transplant coordinator
- Allied health: physiotherapy, occupational therapy, nutrition.

Additionally, a fractional appointment for a coordinator has been appointed at the RCH to assist with paediatric lung transplant assessments and to liaise with AHM. Reflecting the fact that the NFC PLHLT Program is a collaboration between AHM and RCH, cross-credentialing of key medical personnel involved in the care of children has been arranged at both hospitals.

In addition to the core salaried positions, paediatric liaison staff members have been identified in key supporting specialities as outlined in Table 2.8 below. Reflecting the need for an around-the-clock 24/7 care provision for paediatric lung transplant patients, it was reported that all senior members of the adult lung transplant medical and surgical teams are available to provide back-up support, in the absence of any of the core team members.

<table>
<thead>
<tr>
<th>Core positions</th>
<th>Liaison staff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paediatric Lung Transplant Unit Head (Associate Professor Glen Westall)</td>
<td>Cardiothoracic Surgery</td>
</tr>
<tr>
<td>Paediatric Respiratory Physician (RCH)</td>
<td>Medical Head of Adult Lung Transplantation</td>
</tr>
<tr>
<td>Paediatric Lung Transplant Coordinator</td>
<td>Anaesthetics</td>
</tr>
<tr>
<td>Physiotherapist</td>
<td>Intensive Care Unit (ICU)</td>
</tr>
<tr>
<td>Occupational Therapist</td>
<td>ICU nursing</td>
</tr>
<tr>
<td>Dietitian</td>
<td>Perfusion services</td>
</tr>
<tr>
<td>Transplant Coordinator (RCH)</td>
<td>Adolescent/Transition Care</td>
</tr>
<tr>
<td></td>
<td>Endocrinology</td>
</tr>
<tr>
<td></td>
<td>Paediatric Cardiology (RCHM)</td>
</tr>
</tbody>
</table>

Source: NFC site submission to the review
2.4.3 **CONTINUUM OF CARE**

The NFC PLHLT Program offers a continuum of care that extends from the point of admission for the definitive treatment to three months post discharge from hospital after that treatment. For all of the transplanted children, care continues life-long outside of the NFC Program. For Victorian children care continues to be provided by the RCH in Melbourne until they transition to the adult lung transplant program. For interstate children, they are referred back to their local adult lung transplant team or other physician who has looked after lung transplant patients. The model of care that underpins the NFC PLHLT budget and costing proforma is provided below:

1. **Initial referral.** This is generally from Paediatric Respiratory Physician or Paediatric Cardiologist in the home jurisdiction.

2. **Screening assessment.** The patient and their parents travel to AHM for consultation after initial telephone discussion between the NFC PLHLT Program Unit Head and the referring clinician, or alternatively if the patient is too unwell to travel, the Unit Head, Paediatric Respiratory Physician and Paediatric Lung Transplant Coordinator will travel interstate. Following the initial review patients will either:
   - proceed to formal transplant assessment, or
   - defer transplant with ongoing outpatient review as required.

3. **Formal detailed transplant assessment.** The patient and a parent or carer travel to Melbourne and are admitted as an in-patient for five days at RCH where they undergo consultations and investigations, therapy optimisation, and two day visits to AHM to meet the team and become familiar with the facilities where the transplant will be undertaken. Following evaluation during this time by the transplant team, patients will either:
   - be listed for paediatric lung transplant, or
   - be declined or deferred transplant, with ongoing outpatient review as required.

4. **Care on waiting list.** The average length of time on the waiting list is 119 days (median 57). During this time patients are able to live at home if they are within a four hour travel time to the NFC site. For patients remaining at home during this time, care is provided by the local paediatric team and reviewed by the NFC PLHLT team at the AHM every six months. For patients who are not within four hours of the NFC site (historically, patients from WA, Queensland or other distant sites), patients are required to relocate to Melbourne where ambulatory and inpatient care is provided by the RCH, and waiting list review conducted by the NFC PLHLT team every six weeks. The NFC site reported that to date, two patients from Queensland who have since been transplanted had to relocate to Victoria for 129 and 371 days, and one child currently on the waitlist has also had to relocate from Queensland.

5. **Lung transplant procedure.** The lung transplant operation is performed following organ retrieval by senior surgeons from the AHM’s Cardiothoracic Surgical Department, with attendance by RCH cardiothoracic surgeons if required. Following the implant operation, patients are transferred to AHM’s Cardiothoracic Intensive Care Unit (ICU) where cross-credentialed adult and paediatric intensivists, primarily based at the AHM, oversee management of paediatric lung transplant recipients. After leaving ICU patients are transferred to the respiratory ward at the AHM. Mean length of ICU stay is 12 days and mean total hospital stay is 27 days (see Table 2.9 below). During this time, hospital or local accommodation is provided for families if required.
6. **Post discharge care.** Once transplanted, an individual’s progress determines when they are ready to be discharged from hospital. Post discharge care is provided for up to three months post discharge from hospital under the NFC PLHLT Program, and for patients who do not live near Melbourne, it is anticipated that they will remain near AHM during this time. Post discharge care generally involves the following:

- Three initial clinic visits per week at the AHM ambulatory Transplant Clinic, decreasing as the child’s condition stabilises
- Regular review by Paediatric Respiratory Specialist at the RCH
- Investigations including pathology, radiology, lung function, bronchoscopy with biopsy
- Allied health including physiotherapy three times per week, occupational therapy two sessions per week, weekly review by dietitian and psychosocial input for patient and family weekly or as needed
- Weekly education sessions for patients, parents and siblings if required, with education and information aimed at an appropriate level of understanding for each child (noting in particular the use of a specific adolescent-focussed education program, developed by the NFC PLHLT team in collaboration with the Adolescent Service at the RCH)
- Provision and monitoring of therapeutic drugs both PBS and non-PBS funded
- Readmission was reported to be frequently required, most commonly for infection in the lung allograft
- Hospital in the Home used extensively for extended antimicrobial therapy.

7. **Ongoing care.** Ongoing care is required for patients post discharge from the NFC PLHLT Program. This is provided by the AHM/RCH Paediatric Lung Transplant Service for local Victorian patients. Interstate patients are referred back to local state-based lung transplant programs (i.e. physician attached to the local adult lung transplant team or a physician who has looked after lung transplant patients before), with review by the NFC PLHLT team as required. Some states were reported to have established share care arrangements whereby both the local adult lung transplant physician and the referring paediatrician are equally responsible for long term care. The NFC PLHLT team reported that established long term follow-up clinics exist with clinicians in the following locations:

- NSW: Children’s Hospital Westmead and St Vincent’s Hospital
- Queensland: Prince Charles Hospital
- Tasmania: Royal Hobart Hospital
- SA: Royal Adelaide Hospital and Adelaide Women’s and Children’s Hospital
- WA: Royal Perth Hospital

SCHN consider that the dynamics of co-management pre and post-transplant are currently not satisfactory, and seem to vary considerably from state to state. They have reported that a significant burden of management is placed on the SCHN physicians who manage all of the family
issues, transplant education and clinical issues pre and post- transplant. This matter is addressed further in Section 2.5.

2.4.4 ADOLESCENT SERVICES

Dr Miranda Paraskeva is an AHM respiratory physician who joined the adult lung transplant service in 2011. She has a particular interest in adolescent and young adult (<26 years) health, and in partnership with the NFC PLHLT team and the Adolescent Service at the RCH, has developed an adult transition program. This program manages the cohort of lung transplant patients aged 25 years or younger and involves the following:

- Review by one of two named clinicians
- Follow up by a dedicated adolescent coordinator
- Occupational Therapy review with a focus on re-engagement in education and occupation
- Discussion and review of clinical condition and management at fortnightly multi-disciplinary meetings
- A dedicated early post-transplant education program that is age appropriate running parallel to the adult education
- Six monthly education mornings with other adolescent lung and heart-lung transplant recipients.

The two education sessions run in 2015 have covered the following topic areas:

- Medication adherence and how to manage prescriptions
- Physical activity and return to sport
- Nutrition and health eating
- Tattoos and piercings
- Travel
- Sexual health and reproduction.

They have also included three speakers who are transplant recipients who discussed life after transplant, travelling whilst immunosuppressed, and the experience of chronic rejection and retransplantation.

Future plans for the adolescent program include the following:

- Completion of a dedicated adolescent focused education resource
- Collaboration with the Centre of Adolescent Medicine and the Heart Transplant Service at RCH to develop a psychosocial assessment tool specific to adolescent transplant recipients
- Collaboration with the Education Institute RCH to improve transition back to education.

2.4.5 COMMENTS FROM REFERRING CLINICIANS AND OTHER JURISDICTIONAL STAKEHOLDERS

All jurisdictional stakeholders reported that the screening visit by NFC PLHLT team in the patients’ home jurisdiction and/or the subsequent formal assessment undertaken at the NFC site are extremely valuable components of the program. The pre-transplant assessment by the NFC PLHLT team was reported to have the following benefits:
1. **Psychological.** It was reported that the “visit from the big centre that does the transplant” not only provided reassurance to patients and families but also reinforced what was involved for patients and families where non-adherence was likely to be an issue (i.e. to assist with decisions regarding acceptance to the program or otherwise).

2. **Clinical.** It was reported that whilst local physicians may be able to do testing including bronchoscopies, the NFC PLHLT team “know what they are looking for” and it allows them to become familiar with the patient and their particular requirements. In addition, in some cases the visit by the NFC PLHLT team was conducted in the local adult lung transplant site and provided an opportunity for the family to meet the clinical team from both the adult and paediatric services who would be responsible for post-discharge care.

3. **Upskilling of local practitioners.** Referring clinicians without significant recent experience in lung transplantation reported that the visit was essential to provide expert advice regarding patient management and the need for or expected timing of transplant.

All referring clinicians reported having excellent working relationships with the NFC site, and that the team is very responsive and easy to contact. The NFC PLHLT team was also reported to be very adept at managing the waitlist and keeping referring sites informed as per the following comment:

“The [NFC PLHLT Program] team is proactive in managing complications, asking appropriate questions to facilitate best practice management, and anticipate issues which may occur pre and post discharge, as per what a mature and experienced service would provide.” (Referring clinician, October 2015)

One referring clinician reported that the level of support provided by the RCH whilst the patients were in the AHM was insufficient, and that the burden fell on the referring paediatric centre interstate to discuss specific issues with patients or families. However, this experience related to patients referred in the first year of the NFC Program, and was not raised by other referring clinicians or stakeholders.

Although the AHM/RCH report that all senior members of the adult lung transplant medical and surgical teams are available to provide back-up support to ensure a viable service in the absence of any of the core team members, one referring clinician raised concerns that “if Glen is not there, families don’t want to deal with other clinicians.” This was not raised as a concern by other stakeholders, but an issue raised by another jurisdiction stakeholder in relation to this and other transplant services was around ongoing staffing as per the comment below:

“The perennial issue is staffing. It’s all very well increasing organ donation but you need the transplant and retrieval and post-transplant care teams to run the services. Staff are all fatigued.” (Director of Adult Lung Transplant Services, non-Victorian jurisdiction, October 2015)

During the consultation with clinicians from the SCHN it was asserted that a paediatric lung transplant service may be better provided under a cardiothoracic unit at a paediatric hospital with a team experienced in other solid organ transplants. Our international expert commented that whilst there is benefit to being able to provide a paediatric lung transplant service under a paediatric cardiothoracic unit, as all paediatric subspecialties and appropriate paediatric equipment are immediately available if required, the key issue to providing such a service relates to staff experience. For example, at the Sick Kids Hospital in Toronto the adult lung transplant surgeons are cross appointed to the paediatric and adult hospitals which are across the street from each other. Cardiovascular surgeons are paediatric only and not cross appointed, there are two dedicated lung transplant respirologists and some of the paediatric allied health staff work across lung and cardiac transplant services. The assessment, surgery and post-operative care occurs at the paediatric hospital. High quality service delivery in low volume...
procedures, such as the NFC PLHLT Program relies on development of a flexible model delivered where expertise lies.

In general, clinical stakeholders were very supportive of the model of care provided by the NFC PLHLT Program.

2.4.6 Comments from patients and families

Supporting the comment by AHM/RCH that alternative staff have been identified to provide back up as required, patients report that their experience of transition of the PLHLT Program Coordinator position to a maternity leave locum was absolutely seamless and did not affect patient care in any way. All patients and families participating in the focus group commented that the provision of paediatric care in the adult service at AHM was excellent, and they had nothing but praise for the model of care provided from initial assessment to transplant and post-discharge care where they had progressed to this stage.

2.5 Non-inpatient services

The PLHLT service at AHM has been operating as a national service since 2005 and as an NFC since 2011. The NFC PLHLT team conducted an initial and ongoing awareness campaign that has involved presentations at local and national meetings. The NFC PLHLT team reported that they believed that all Australian Centres of Paediatric Respiratory Medicine are aware of the NFC PLHLT Program.

Post-transplant care following discharge from the hospital is provided to patients for the first three months following transplantation under the NFC Program (as outlined in section 2.4.3 above), and following this either at the NFC PLHLT Program’s hospital-based clinic or at local services interstate. For patients in Victoria, the frequency of clinic visits will decrease over time and after the first year patients are usually seen every two to three months depending on how well they are. In addition to the regular clinic visits, more detailed evaluations are performed at 3, 6, 9 and 12 months including blood tests, six minute walk tests, x-rays and bronchoscopies. All transplant recipients require life-long supervision by a transplant team within their home jurisdiction.

For those patients who live outside of Melbourne, the PLHLT Unit Head and the Paediatric Lung Transplant Coordinator meet with each patient and their family to answer any questions prior to them returning home. Each child is then referred either to a physician attached to the local adult lung transplant team in their home state where possible, or a physician who has looked after lung transplant patients before. Patients from NT and ACT will require specifically tailored follow up arrangements. Members of the NFC PLHLT Program remain available to provide advice and review patients as required.

Comprehensive transfer letters from the NFC PLHLT Program were reported by the NFC site to be sent to the accepting interstate adult transplant program. The NFC PLHLT Paediatric Lung Transplant Coordinator is also able to visit the interstate team to aide in the transition to the new service.

2.5.1 Comments from referring clinicians and other jurisdictional stakeholders

Several jurisdictions raised issues regarding provision of ongoing care once the patient is discharged from the program, particularly for patients transitioning to adolescence where non-adherence can become an increasing problem. The relative involvement of the paediatric and adult teams were reported to be considered on a case by case basis, with the following comments reflecting the importance of clear post-discharge transfer of care:
“Surgery is relatively easy. The key for these patients is good immediate post-transplant care and ongoing follow-up care post discharge as the patient’s condition may deteriorate over time.” (Jurisdiction stakeholder outside Victoria, October 2015)

“The most important thing post-transplant discharge is to know who has primary responsibility. We need a clear delineation of who is responsible for what.” (Head, Adult Lung Transplant Service outside Victoria, October 2015)

“The most important thing is to give the family a clear line on who is responsible for care once they return home.” (Referring clinician, October 2015)

“We had a 13 year old boy [transferred from the AHM/RCH PLHLT Program post-transplant to the local adult transplant service] a few years ago who was physiologically an adult. This caused such a kerfuffle with hospital management, nursing etc. because we weren’t credentialed for patients under 17 and all had to get police checks etc., that this model was unsustainable. Now primary care responsibility for patients under 17 years is at the paediatric hospital, and I go there to see the patient for transplant related issues.” (Head, Adult Lung Transplant Service outside Victoria, November 2015)

In several cases, referring jurisdictions reported that post-discharge care was dependent on patient age and other circumstances. In one state, it was reported that primary care for younger patients is provided by the paediatric team with input from the adult lung physician; while for older patients care may be more appropriately provided in an adult setting as long as paediatric team input is available if required. For example, the adult post-transplant service may be responsible for transplant related care and the paediatric service for non-transplant related care (e.g. diabetes, gastroenterology, psychosocial issues). Ongoing care provision may also depend on diagnosis and relationship with referring clinician. One confounding factor was reported to be a lack of consistency across jurisdictions in the cut off age for credentialing of adult or paediatric services.

Stakeholders reported that the NFC PLHLT Program has a role in facilitating or improving post discharge care for patients returning to home jurisdictions outside Victoria. It was suggested that the NFC site should organise a videoconference or similar approach involving all stakeholders to ensure consistency in messages to all follow-up services and patients/family. Jurisdictions are then responsible for provision of collaborative care between paediatric and adult services for these patients as required, noting that this can be complicated in some cases where several services are involved (e.g. AHM, RCH, local adult lung transplant service, paediatric service in referring jurisdiction capital city, regional services where patient resides). Further, SCHN consider that the dynamics of co-management pre and post- transplant are not satisfactory, and seem to vary considerably from state to state, placing a significant burden on referring clinicians.

Recommendation: It is recommended that as part of the standard discharge protocols for the Program that the NFC site facilitates a post-discharge videoconference or similar communication method involving all stakeholders (including the patient/family). The primary aim being to ensure consistency in the delivery of post-discharge support services by the Program and in the care provided by local services.

(Consolidated list of recommendations 10)

2.5.2 Comments from patients and families
Experiences regarding organisation of post-transplant care in the home jurisdiction were different depending on location, but all reported as positive by the five families participating in the focus group.
Patients and families from Victoria were very happy that ongoing care was able to continue with the same team of staff (i.e. at AHM and/or RCH). Patients and families from other jurisdictions who were yet to return home reported that meetings had already been facilitated by the NFC PLHLT Program Unit Head with local teams, either prior to them coming to Melbourne so that they could meet the local post-transplant team or post discharge.

2.6 Quality and Safety

This section outlines the protocols and procedures established to assess and maintain quality and safety standards, and presents data regarding complications and readmissions associated with the NFC PLHLT Program.

2.6.1 Quality and Safety Protocols and Assessment

Both the RCH and the AHM had implemented quality improvement policies and associated frameworks that integrate corporate and clinical risk, address clinical and non-clinical quality improvement, outline relevant supporting structures, processes and roles, and describe the culture required to deliver safe, high quality health care, provide good governance and maintain organisational sustainability. The quality improvement and risk management framework utilises the Victorian Department of Health and Human Services clinical governance framework with the clinical domains of consumer participation, clinical effectiveness, risk management and workforce effectiveness.

Quality and safety is monitored via a range of processes such as clinical indicators, audit, mortality and morbidity meetings, incident reporting, and consumer feedback. Monitoring and review of outcomes occurs at a hospital, divisional and unit level. Where appropriate, targets are set and risk ratings applied to results. Reporting occurs in accordance with the governance structure. Quality planning occurs within clinical areas, prioritising activities, focusing on valuation and sustainability and involving a wide range of staff.

Reflecting that paediatric lung transplant recipients are being predominantly cared for in an adult hospital (AHM), the NFC PLHLT Program reports making a number of specific endeavours to ensure that paediatric care is not compromised. These include:

- Regular input from paediatricians at all steps of the transplant pathway
- Specialised paediatric nursing available in both inpatient and outpatient settings
- Psychosocial expertise available from both RCH and the adult CF service at AHM to address issues of adolescence
- Access to the Child and Youth Mental Health Service (CYMHS) to provide age-appropriate counselling and support
- Access to paediatric patients who have already undergone lung transplantation at AHM
- Provision of age-appropriate rehabilitation equipment at AHM
- Provision of age-appropriate toys and games, and play therapists at AHM
- Recruitment of allied health staff with a background and experience in paediatric care.
- Access to in-patient schooling at AHM.

National guidelines on patient selection and donor utilisation have been established for lung transplantation, and are adhered to by the PLHLT NFC\textsuperscript{24}.

The NFC “Patient and Family Questionnaire” is provided to all patients treated under the PLHLT NFC and their families. The questionnaire aims to gain views and feelings from patients and their families about the management of their care under the NFC Program.

Quality and safety indicator data collected at an organisational, divisional and/or unit level relevant to paediatric lung transplantation includes:

- Number and type of surgery
- Mortality rates
- Complications of surgery
- Wound infections
- Length of stay in ICU
- Length of stay in ward
- Adverse events

The following benchmarks have already been established for the lung transplant operation at AHM:

- Anaesthesia preparation time <60 minutes
- Surgical start time (from surgical start to knife to skin) <15 minutes
- Allograft implantation times: first lung < 150 minutes, second lung < 90 minutes.

The AHM maintains a cardiothoracic transplant database that is run by a dedicated database manager. This database is an extensive repository of clinical information on both the transplant recipient but also the organ donor, and includes details of over 2100 lung transplants performed at the AHM.

Outcome data following lung transplantation (both adult and paediatric cases) are reported to the Australia and New Zealand Cardiothoracic Organ Transplant Registry (ANZCOTR). This registry contains information on every heart, heart-lung and lung transplant performed in all six Australian and New Zealand Cardiothoracic Transplant Centres. The ANZCOTR publishes an annual report providing statistical information on the numbers of transplants performed, waiting list activity and survival outcomes. The registry also contributes its Australian de-identified information to the International Society of Heart and Lung Transplantation (ISHLT) who maintain a global registry of cardiothoracic transplant activity. Data is also forwarded to the Australia and New Zealand Organ Donation Registry (ANZOD) (www.anzdata.org.au) that records and reports on a wide range of statistics that relate to organ donation following death within Australia and New Zealand.

In addition, the Paediatric Lung Transplant Coordinator maintains a database tracking long-term outcomes of all patients undergoing paediatric lung transplantation across Australia.

The AHM pioneered, through an extensive pre-clinical research program, the establishment of donation after cardiac death (DCD) as an additional donor lung source in Australia. The use of DCD lungs has now been taken up and established in all of the Australian lung transplant programs and at AHM represents the donor source in over 25% of all lung transplants performed. Given that DCD lungs have only been used for the past eight years, AHM maintains a dedicated DCD database that

specifically monitors clinical outcomes following lung transplantation using both DCD and conventional brain dead donors.

2.6.2 COMPLICATIONS AND REASONS FOR READMISSION

AHM/RCH reported that in total, five patients from the NFC PLHLT Program (33.3%) have been readmitted early post-transplant for an average of 12 days (range two – 29 days). Data reported by the ISHLT indicate that internationally 58% of paediatric lung transplant patients (n=315) are re-hospitalised within 1 year of transplant. Table 2.10 below provides details regarding catastrophic events and reasons for readmission as reported in NFC Annual Reports covering the first three years of the program, however the actual number of patients readmitted and number of readmissions are unclear from these data (which were provided as per NFC reporting template).

**Recommendation:** It is recommended that the NFC reporting template be amended to require the number of patient readmissions to be reported.

*(Consolidated list of recommendations 11)*

Reasons for readmission given in Annual Reports include:

- Supraventricular tachycardia
- Hypotension
- Hypertension
- Bowel obstruction
- Pain
- Invasive aspergillus
- Pericardial effusion
- Shortness of breath.
<table>
<thead>
<tr>
<th>Year</th>
<th>No. transplants(a)</th>
<th>Catastrophic events</th>
<th>Unplanned readmissions to ICU</th>
<th>Readmissions post discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011-12</td>
<td>6</td>
<td>• Supraventricular tachycardia and hypotension (readmitted to ICU day 15 – reached full recovery) &lt;br&gt;• Hypertension crisis and transient cortical blindness (readmitted to ward – made full recovery) &lt;br&gt;• Invasive aspergillus - death</td>
<td>• Supraventricular tachycardia and hypotension (readmitted to ICU day 15 post-transplant – reached full recovery) &lt;br&gt;• Pain management (day 7) and asystolic arrest</td>
<td>• Small bowel obstruction, partial bowel obstruction, cytomegalovirus reactivation, complex social issues and C Diff toxin positive (three admissions to ward between 7-14 weeks post-transplant – resolved with medical management and psychosocial support)</td>
</tr>
<tr>
<td>2012-13</td>
<td>1</td>
<td>• Tachycardia and increased O₂ requirements (readmitted to ICU day 8 – full recovery) &lt;br&gt;• Semi elective pericardiocentesis of a large pericardial effusion (readmitted to ICU day 33 – successful procedure and full recovery)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2013-14</td>
<td>2</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>• Shortness of breath (month 2, overnight admission – resolved)</td>
</tr>
</tbody>
</table>

Source: NFC Annual Reports 2011-12 to 2013-14  
(a) All patients in this period received bilateral lung transplants with one patient having expected care pathway and clinical progress (2011-12) and all other patients having complicated care pathways and clinical progress.

Internationally, the most common morbidity at one year post transplant in over 40% of surviving children is hypertension, followed by diabetes mellitus (22%) and bronchiolitis obliterans syndrome (13%)\(^{25}\). One year post transplant morbidity data were not available in this review.

As discussed previously in section 2.4.3, to date the NFC PLHLT Program has transferred the entire care for interstate patients to the local transplant team at three months post discharge from hospital following transplantation. While the NFC site does maintain a cardiothoracic transplant database (refer section 2.6.1) that the NFC PLHLT Program has not routinely collected clinical outcomes data beyond survival. No clinical data on the incidence of hypertension, diabetes mellitus or bronchiolitis obliterans syndrome has been collected on the whole cohort by the NFC PLHLT Program, although these data were reported to be routinely collected for Victorian patients.

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Recommendation: It is recommended that the NFC site develop linkages to collect and document long-term complications (such as hypertension, diabetes mellitus or bronchiolitis obliterans syndrome).

(Consolidated list of recommendations 6)

2.6.3 Comments from Referring Clinicians and Other Stakeholders

Referring clinicians and clinicians responsible for post-transplant care in the local jurisdiction were asked to comment on the care provided by the NFC PLHLT Program and any issues arising for patients referred or accepted to the program from their jurisdictions. Of the three clinicians responsible for post-transplant care in local adult lung transplant services who participated in the consultations, and the seven referring clinicians, all but one had nothing but praise for the quality of care provided to patients. This is illustrated by the following comments:

“We have nothing but praise for the service. They were extremely responsive, handled a difficult family very sensitively, and both the family and us were extremely grateful.” (Referring clinician, outside Victoria)

“We went into this with the unknown [transporting a patient on ECMO], and realised that they [NFC PLHLT team] are a very good team and provide an excellent service. They were very proactive in getting everyone involved in the discussion, and we had a very successful and satisfying outcome.” (Key jurisdictional stakeholder, outside Victoria)

2.6.4 Comments from Patients and Families

Patients and families were asked to comment on their satisfaction with the quality of care provided by the NFC PLHLT Program in the NFC Patient and Family Questionnaires (n=3 completed) and during the focus group conducted for this review (n=5 participating families). All patients/families rated the quality of care provided by the NFC PLHLT Program very highly, in particular noting the teamwork and the care provided for paediatric patients within the adult hospital. A sample of comments is provided below:

“The Alfred transplant team were excellent with all help they gave us. My daughter went on life support two days after we had lungs. We could not have had a better team looking after us.” (Patient and Family Questionnaire respondent, 2011-12)

“The care pre, during and post-transplant for my daughter was exceptional. Doctors, nurses, specialists were so mindful of her young age and the impact on family, including younger sibling. We came from NSW, The Alfred is THE best facility and we will be forever grateful.” (Patient and Family Questionnaire respondent, 2011-12)

“RCH and AHM all work together as a team. We couldn’t ask for better care.” (Focus group family participant, 2015)

“During our first assessment [at RCH with visit to AHM], we were exposed to the most amazing teamwork between everyone including the surgeon, anaesthetist, dietitian, physio, ward clerk etc. This continued when we came again for assessment then transplant – the care was remarkable.” (Focus group family participant, 2015)

“The knowledge of the team has been very impressive particularly regarding Mycobacterium abscessus in our case. They are incredibly compassionate, well organised, committed and truly
multidisciplinary. The accommodation subsidy and emotional support provided are fantastic.” (Focus group family participant, 2015)

2.7 Teaching, training and research

Key personnel at both AHM and RCH were and continue to be identified in the areas of cardiothoracic surgery, anaesthesia, intensive care, respiratory medicine, perfusion services, general and intensive care nursing for further specialised training. Extending beyond exposure to local and national education opportunities, a number of the multi-disciplinary NFC PLHLT team at AHM have travelled to the major international paediatric lung transplant centres in the United States (St Louis Children’s Hospital, Texas Children’s Hospital) and Europe (Great Ormond Street, London), and established professional, education, training and research links between Victoria and the world’s leading paediatric lung transplant hospitals.

The PLHLT NFC encourages ongoing professional development to ensure the delivery of advanced care, clinical practice and improved patient outcomes. Key personnel at both the AHM and RCH, identified in the areas of cardiothoracic surgery, anaesthesia, intensive care, respiratory medicine, perfusion services, clinical technology, general and ICU care nursing, continue to be supported to maintain and develop their paediatric competency skills by attending specialist courses and national and international conferences. Two conferences that were attended by members of the NFC PLHLT Program in 2015 were the International Society for Heart and Lung Transplantation (ISHLT) annual scientific meeting and the International Paediatric Transplant Association (IPTA) conference.

The NFC PLHLT Program is a foundation member of the International Paediatric Lung Transplant Collaborative (IPLTC) that meets annually to promote multi-centre approaches to patient management. Meetings are held at the International Society of Heart and Lung Transplantation (ISHLT) Annual Conference each year. Members of the NFC PLHLT Program from the AHM have attended IPLTC meetings since 2006 and have represented AHM at every subsequent annual meeting. In addition, the NFC PLHLT team contributes to the IPLTC clinical database, which is run from the Children’s Hospital St Louis, USA. The database collects clinical data on paediatric lung transplants performed in the major paediatric lung transplant programs around the world. The aim of this database is to collect longitudinal data on paediatric lung transplant patients to advance understanding of lung transplantation in this population, with the ultimate aim of increasing life expectancy and improving the quality of life for these patients and their families.

The AHM has an established paediatric nursing education and competency framework. Education is specifically directed towards those nurses directly involved in the care of the paediatric lung transplant patient; for example, nurses from ICU, the respiratory and cardiothoracic wards, Hospital in the Home and Medical Day Unit. All key areas responsible for paediatric care have a designated Nurse Educator who continually liaises with the Paediatric Lung Transplant Coordinator. The Paediatric Lung Transplant Nurse Specialist group meet regularly and identify areas where education is best targeted. Depending on the staff demographic this may be directing the less experienced staff to paediatric on-line learning or more senior staff to paediatric advanced learning study days.

Across both AHM and RCH campuses, staff attended study days to maintain their specialised skills and knowledge in paediatric lung transplantation. In-house lung transplant paediatric education consists of one to two hour workshops and seminars that are attended by AHM nursing, medical and allied health staff, which run throughout the year. Topics include “Supporting the Paediatric Patient in the Adult Setting”; “Introduction to the Paediatric Lung Transplant Service”; “Paediatric Physiotherapy Education”; “The Child in Hospital”; “Paediatric Pharmacology”; “Paediatric Anatomy and Physiology”;
“Paediatric Nutrition”; “Needle Fears Versus Phobias”; “Care of the Deteriorating Child”; “Engagement of the Child”; and “Resus for Kids”.

A list of research publications and presentations given by members of the NFC PLHLT Program team is provided in Appendix C.

2.8 **Risk management**

The AHM reported working within established risk management frameworks and guidelines which provide the following:

- A systematic approach to the early identification and management of risks
- Consistent risk assessment criteria
- Accurate and concise risk information that informs decision making including direction of the service
- Risk treatment strategies that are cost effective and efficient in reducing risk to an acceptable level; and
- Monitoring and review of risk levels to ensure that risk exposure remains within an acceptable level.

The establishment and challenges of a paediatric lung transplant service operating within an adult environment (AHM) was reported as requiring continual risk assessment from the time of concept, through state-based funding to its current NFC status. Throughout all aspects of the treatment pathway, it was reported that team members from both the AHM and RCH have worked to ensure that the care of a child within an adult hospital is not in any way compromised. Approaches taken have been previously discussed in section 2.4.1 of this report. The NFC PLHLT Program Annual Report 2013-14 states that in order to address the risks posed by the small number of specialist doctors, nurses and allied health staff on the NFC PLHLT team, additional staff for each key appointment have been identified and have covered these roles as required.

2.9 **Summary of key findings**

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<tr>
<th>Review domain</th>
<th>Key findings</th>
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<tbody>
<tr>
<td>Access</td>
<td>1. A total of 31 patients were referred to the NFC PLHLT Program in the first three years, and 37 patients in total to Q1 2015/16. This represents an average of eight to nine referrals per year.</td>
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<td></td>
<td>2. Victorian patients were over-represented in referral numbers, possibly due to a higher proportion of patients with pulmonary hypertension being referred than in other states (61.5% vs 12.5% of total referrals respectively had diagnosis of pulmonary hypertension).</td>
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<td>3. Criteria for referral align with international practice, and NFC PLHLT team is very responsive to discussion regarding these criteria and particular patients with referring sites. Conditions that were previously considered as absolute contraindications are now considered on a case by case basis. The team will now consider acceptance of patients on ECMO, with <em>Mycobacterium abscessus</em> or <em>Burkholderia cenocepacia</em>. Psychosocial factors that may affect adherence to medical care are critical to success and considered in decision making.</td>
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### Key findings

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<th>Review domain</th>
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<tr>
<td>4.</td>
<td>Initial screening assessment conducted by members of the NFC PLHLT team, either at the NFC site or at the home jurisdiction if patients are too unwell to travel, to assess whether transplant is a feasible and appropriate option and whether/when the patient should proceed to formal assessment.</td>
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<td>5.</td>
<td>A total of 17 patients progressed to formal assessment conducted at ACH/RCM and were subsequently accepted to the Program in the first three years, and 22 patients in total to Q1 2015/16. This represents an average of five to six patients per year accepted to the NFC PLHLT Program (54.8-59.5% of those referred).</td>
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<td>6.</td>
<td>A total of nine patients underwent lung or heart-lung transplant in the first three years, and a total of 15 patients in total to Q1 2015/16. This represents an average of three to four patients per year undergoing lung or heart-lung transplant, with a range of one to six per year.</td>
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<td>7.</td>
<td>The majority of patients fell within the current target group for the program (children and adolescents aged six to 15 years typically weighing 20-40kg, noting that under the approved criteria it is stipulated that weight should not be an exclusion to transplant if the patient is in the right age range). One patient was five years old and one 16 years old, and one patient was under 20kg and five patients over 40kg. HOI’s international expert supports the NFC PLHLT site request that the program be expanded to include patients 4-15 years weighing ≥10kg. The NFC site for paediatric lung and heart-lung transplantation may also treat older adolescents (aged 15 years but less than 18 years) where they are smaller, of lower body weight, or have complex paediatric issues (including psychosocial issues).</td>
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<td>8.</td>
<td>Number of transplants is limited to some extent by donor organ availability, with majority of organs coming from Victoria. Median waitlist time is 57 days, ranging from 1-442 days. In an effort to counter the lack of organs, AHM/RCH are accepting more marginal organs (e.g. DCD) and conducting lobar transplants. Two children (9.1%) have died on the waitlist since 1 July 2011.</td>
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### Health outcomes

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<th>9.</th>
<th>Outcomes from the NFC PLHLT Program appear similar to international outcomes data collected by ISHLT. Since NFC status, four of the 15 children transplanted under the NFC PLHLT Program have died as a consequence of complications related to transplantation (non-adherence, a common problem in adolescent health, was an important contributor to poor outcomes in two of the transplanted children). Comparison of one-year survival rates with ISHLT data are as follows:</th>
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<td>6-10 year olds: NFC program 100% survival (three patients alive); ISHLT 95.2% (50 patients alive)</td>
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<tr>
<td></td>
<td>11-17 year olds: NFC program 75.0% survival (nine patients alive); ISHLT 81.1% (226 patients alive)</td>
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<tr>
<td>10.</td>
<td>The AHM reported in its submission to the review that since 2006, when the PLHLT service was first established (outside of the NFC Program), one year survival for the 29 transplant procedures has been 84% to September 2015, comparable to the global experience of 81.1% one year survival for 11-17 year olds reported by the ISHLT. The AHM commented that the more recent reduction on one year survival outcomes may be influenced by the acceptance of more marginal patients in recent years.</td>
</tr>
<tr>
<td>11.</td>
<td>A specific adolescent-focussed education program has now been</td>
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</table>
### Key findings

Developed and implemented to address issues with non-adherence in adolescence, in collaboration with the Adolescent Service at the RCH. The NFC PLHLT Program has also included a request and budget for a child psychologist to be added to the core NFC PLHLT team for the future.

12. Quality of life is an important outcome measure for children undergoing lung transplantation, and potential to improve quality of life was reported by AHM to be a key consideration in decisions regarding transplant. Formal assessment of quality of life outcomes was not conducted in the first year of the program, but an ongoing research project was initiated in 2012-13 and results will become available in the next two years.

### Model of care

13. A number of modifications and initiatives have been implemented to address limitations of running a paediatric service in an adult hospital. These include cross credentialing of staff, an ongoing education program, combined paediatric and lung transplant physician input at all stages of the care pathway, and broad paediatric and lung transplant expertise to allow continuation of a viable and functional program in the absence of care staff.

14. The NFC PLHLT Program offers a continuum of care that extends from the point of referral to three months post-transplant. The care continuum includes the following stages:

- **Initial referral**: This is generally from Paediatric Respiratory Physician or Paediatric Cardiologist in the home jurisdiction.

- **Screening assessment**: Conducted by NFC PLHLT team (or local team in some cases) in patient’s home jurisdiction following initial telephone consultation with referring clinician, with the aim of deciding whether to progress patient to formal transplant assessment or defer transplant with ongoing outpatient review as required.

- **Formal detailed transplant assessment**: Conducted over 5 days at RCH with two outpatient days at AHM (note that all patients proceeding to formal assessment to date have been accepted to the program).

- **Care on waiting list**: The average length of time on the waiting list is 119 days (median 57); during this time patients are able to live at home if they are within a four hour travel time to the NFC site, with care provided by the local paediatric team and reviewed NFC PLHLT team every six months; patients relocating to Melbourne receive care at RCH, and waiting list review conducted by NFC PLHLT team every six weeks.

- **Lung transplant procedure**: The lung transplant operation is performed following organ retrieval by senior surgeons from the AHM's Cardiothoracic Surgical Department, with attendance by RCH cardiothoracic surgeons if required; Mean ICU length of stay post-transplant is 12 days and mean total hospital stay is 27 days, with accommodation provided for families if required.

- **Post discharge care**: Provided for up to three months post discharge from hospital under the NFC PLHLT Program, and patients who do not live near Melbourne remain near AHM during this time; involves clinic visits and investigations, review by Paediatric Respiratory Specialist at RCH, allied health program, education sessions, Hospital in the Home.
<table>
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<th>Review domain</th>
<th>Key findings</th>
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<td></td>
<td>for antimicrobial therapy, and readmission if required.</td>
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<tr>
<td>15.</td>
<td>Ongoing care is provided by the AHM/RCH Paediatric Lung Transplant Service for local Victorian patients, with transition to AHM adult lung transplant program when patient reaches 18 years old. Interstate patients are referred back to local state-based adult lung transplant programs with review by the NFC PLHLT team as required. Established long term follow-up clinics exist with clinicians in NSW, Queensland, Tasmania, SA and WA.</td>
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<tr>
<td>16.</td>
<td>All jurisdictional stakeholders reported that the screening visit by NFC PLHLT team in the patients’ home jurisdiction and/or the subsequent formal assessment undertaken at the NFC site are extremely valuable components of the program and provides psychological support to patients and families, clinical assessment and upskilling of local practitioners.</td>
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<td>17.</td>
<td>Although the NFC PLHLT Program comprises key back up staff, and patient experiences support excellent transition between core and back up staff, some concerns have been raised regarding the ability to maintain services with the small number of key staff critical to the reputation of the program (noting that this issue was not raised by the NFC PLHLT team or patients).</td>
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<tr>
<td>Non-inpatient services</td>
<td>18. The NFC PLHLT Program provides non-inpatient services relevant to provision of initial assessment and care whilst on waitlist, as well as post discharge care for the first three months post discharge from hospital during which time it is anticipated that patients will remain close to the AHM/RCH.</td>
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<td></td>
<td>19. Following discharge from the NFC PLHLT Program, care is transferred either to the NFC PLHLT Program’s hospital-based clinic or local services interstate including life-long support by a local transplant team. For those patients who live outside of Melbourne, the PLHLT Unit Head and the Paediatric Lung Transplant Coordinator meet with each patient and their family to answer any questions prior to them returning home. Each child is then referred to a local physician attached to an adult transplant team, or a physician with experience in lung transplant wherever possible.</td>
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<td></td>
<td>20. Provision of post discharge care in the home jurisdiction between adult and paediatric services is organised on a case by case basis depending on patient need and local services and expertise available. Stakeholders reported that the NFC PLHLT Program has a key role in facilitating discussions for planning of post discharge care in home jurisdictions for provision of post-discharge, which may benefit from videoconference or other approaches to involve all stakeholders to ensure consistency of messages.</td>
</tr>
<tr>
<td>Quality and safety</td>
<td>21. Reflecting that paediatric lung transplant recipients are being predominantly cared for in an adult hospital (AHM), the NFC PLHLT Program reports initiatives implemented to ensure that paediatric care is not compromised.</td>
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<td></td>
<td>22. In total, five patients from the NFC PLHLT Program (33.3%) have been readmitted early post-transplant for an average of 12 days (range 2 – 29 days). Reasons for readmission include supraventricular tachycardia, hypotension, hypertension, bowel obstruction, pain, invasive aspergillus, pericardial effusion or shortness of breath.</td>
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</tbody>
</table>
|                        | 23. Patients, families and referring clinicians generally described the quality of
### Key findings

<table>
<thead>
<tr>
<th>Review domain</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>the service as excellent.</td>
</tr>
<tr>
<td>Teaching, training and research</td>
<td>24. The NFC PLHLT Program encourages ongoing professional development to ensure advanced care, clinical practice and improved patient outcomes. Key personnel at both the AHM and RCH, (identified in the areas of cardiothoracic surgery, anaesthesia, intensive care, respiratory medicine, perfusion services, clinical technology, general and ICU care nursing), continue to be supported to maintain and develop their paediatric competency skills by attending specialist courses and national and international conferences. 25. Members of the NFC PLHLT Program have published widely in national and international publications, and several research projects are currently underway (refer Appendix C)</td>
</tr>
<tr>
<td>Risk management</td>
<td>26. Key risks arising from the provision of a paediatric service in an adult hospital were identified early in the establishment of the service at AHM, and strategies developed and implemented to largely mitigate these risks. These strategies include cross credentialing of staff, and appointments dedicated to the program at both the AHM and RCH. An education program specific to the needs of adolescent patients has recently been developed to address the particular needs of this group. Stakeholders including patients, families, referring clinicians and other jurisdiction staff reported that the paediatric service was of a high standard at AHM.</td>
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</table>
ASSESSMENT OF THE FUTURE NFC PROGRAM

This chapter provides the assessment of factors required under this review to be considered in recommendations regarding the future of the NFC PLHLT Program. These factors include the following:

- New evidence in clinical practice and technology development
- Assessment of future demand and patient throughput
- Factors for consideration in recommendations regarding number of NFC sites.

At the conclusion of this chapter a summary of key findings are provided with respect to the above.

3.1 NEW EVIDENCE IN CLINICAL PRACTICE AND TECHNOLOGY DEVELOPMENT

The AHM/RCH reported that the model of care has not changed substantially since the establishment of the state-funded paediatric lung transplant program in 2006 and the NFC PLHLT Program in 2011. However, a number of changes to clinical practice have evolved or are evolving:

1. Extended target population
2. Previously contraindicated patients:
   - ECMO-bridge-to-transplant
   - patients colonised with *Mycobacterium abscessus* or *burkholderia cenocepacia*
3. Paracorporeal lung assist devices
4. ABO-incompatible lung transplantation for younger children (less than five year old)
5. Ex vivo lung perfusion

The NFC Guidance states that it is a requirement for established NFC’s to notify of changes to the approved NFC service as follows:

*Any proposed or potential change in the AHMAC-approved NFC service (e.g. patient pathway, patient selection criteria, model of care, etc.) must be brought to the attention of the relevant jurisdictional NFC Reference Group member before the NFC implements those changes otherwise the site may not be eligible for funding for all of its activity. The NFC Reference Group will give consideration to funding activity that varies from the AHMAC approved pathway or model of care under the NFC Program on a case by case basis or, if practicable, agree to defer consideration to the next scheduled review of the particular technology.’*

The review identified that this notification had not occurred in relation to patients less than 5 years of age, patients on ECMO-bridge-to-transplant; or patients colonised with *Mycobacterium abscessus* or *burkholderia cenocepacia*. As a consequence, these changes have not been approved by NFC Reference Group. It is the conclusion of this review that these changes significantly increase the risk
profile of patient transplanted in the NFC PLHLT Program. It is therefore considered that these changes should be formally considered by the NFC Reference Group. HOI's recommendations are presented in the sections that follow.

3.1.1 Extended Target Population

In their submission to the review, AHM/RCH have requested that the target population for the PLHLT NFC be amended to children aged 4 years up and weighing greater than 10 kg. The site reported that:

- the original NFC PLHLT Program identified the target population was children aged from 6 years and weighing greater than 20 kg.
- In 2014, the AHM/RCH were referred a 5 year old female weighing 14kg who was in advanced respiratory failure due to underlying pulmonary hypertension. After a detailed multi-disciplinary assessment that involved cardiothoracic surgeons, respiratory physicians, anaesthetists and intensivists from both AHM and RCHM, a consensus view was reached that AHM had sufficient expertise to offer heart-lung transplantation in this child who otherwise did not meet the target population for the NFC PLHLT Program.
- After consultation with and agreement from the NFC Reference Group, this child was listed for heart-lung transplantation and she subsequently underwent successful heart-lung transplantation in August 2014.
- More recently, the AHM/RCH have been referred a similarly sized 4-year old child with severe pulmonary hypertension. With agreement from the NFC Reference Group, this patient has been listed and remains on the waiting list for heart-lung transplantation.

The AHM/RCH consider that in Australia there is an unmet need for transplantation for younger children (less than five years old).

International Evidence

With respect to children under five years, there are relatively few transplants performed globally each year in this age group. Data from the ISHLT registry for the 12 months to 31 December 2014 indicted ten transplant recipients aged 1 to 5 years old, compared to 15 recipients aged 6 to 10 and 78 recipients aged 11 to 17 years of age. Only a small number of institutions with the capacity to offer lung transplantation down to this very young age and small size.

The most recent update from the Pulmonary Transplantation Council of ISHLT states that appropriate selection of paediatric candidates (<18 years) is critical to maximise the overall survival of children and adolescents (Weill, et al., 2015). In terms of lung transplant recipient age, Kirkby and Hayes (2014) found that whilst children aged 6-10 displayed improved earlier survival compared to other paediatric age groups, the difference in survival was not maintained long term. As presented in Figure 3.1, the outcomes for the 1-5 year old cohort are comparable to the other cohorts presented. Benden et al. (2013) also confirmed Kirby and Hayes’ (2014) finding for the same cohort when controlling for all indicating conditions. Magee et al., cited by Hayes Jr, et al., (2015) also state that children between one and ten have improved long-term outcomes than infants or adolescents, yet concluded that the reasons for poorer outcomes among specific age cohorts was unknown and required further research.
For heart-lung transplantation, Spahr & West, 2014 analysed the ISHLT data from 1982 to 2011 identifying pair-wise comparisons of the 1-5 year old cohort (n=104) with 6-10 years old and 11-17 were not significant, as presented in Figure 3.2.

CF is the leading indication for lung transplantation in paediatric patients but indications vary by age cohort. Idiopathic pulmonary arterial hypertension (IPAH) is mostly diagnosed in one to five year olds whereas surfactant protein B deficiency, CHD and idiopathic pulmonary arterial hypertension (IPAH) are more commonly diagnosed in those under the age of one (Benden, et al., 2013).

Weil et al (2015) acknowledge that assessments of paediatric candidates for lung transplants presents specific challenges including recognition of specific underlying lung disease; surgical approaches; effects of immunosuppressive treatment and infections on the developing immune system and on the child’s somatic growth (Schmid & Benden, 2016). The guidelines advise the transplant community to choose wisely and where experience and capability is demonstrated with high risk patients by individual centres – that good practice principles should ensure that overt extrapolation beyond sensible boundaries should not occur in less experienced centres Weil et al (2015).
FEEDBACK FROM CONSULTATIONS

Referring clinicians, clinicians responsible for post-transplant care in the local jurisdiction, and other jurisdiction stakeholders were invited to comment on the appropriateness of the current target group for the NFC PLHLT Program (children and adolescents six to 15 years typically weighing 20-40kg). All stakeholders reported that the upper age limit was appropriate, as long as there was flexibility to allow those on the cusp (i.e. 14-15 year olds) to be referred to local adult lung transplant services if more appropriate (e.g. based on assessment of clinical condition, weight, emotional maturity, psychosocial and family factors). It was reported that in several jurisdictions this had already occurred following discussion between the referring clinician, the local transplant service clinicians and executive (as these patients do not receive NFC funding) and the NFC site.

Almost all stakeholders considered that the service should be available to patients younger than six years in line with what is occurring internationally, as long as expertise was available to provide this procedure and care, it was clinically indicated, and that good outcomes were possible. Our international clinical expert has advised that internationally, most programs are now providing PLHLT in progressively younger patients with little impact on outcomes. Although surgically similar however, additional allied health support may be required to focus on neurodevelopmental outcomes. Data reported by ISHLT for the period 1 October 2010 to 30 September 2014 indicates that transplanted patients aged 1 to 4 years old represent 7.7% of all transplanted patients aged 1 to 17 years of age. Based on this transplantation rate, extension of target group to include four year olds is expected to result in an increase in the number of PLHLT patients of 0.3 per annum.

CONCLUSION

Based on the data above, and in consultation with our international clinical expert, it is the conclusion of the Review that PLHLT for children aged 4 years up and weighing greater than 10 kg is considered established clinical practice and is consistent with the NFC eligibility criteria.

Recommendation: It is recommended that the NFC Reference Group endorse the expansion of the target cohort of patients to include children and adolescents 4 to 15 years typically weighing ≥10kg.

(Consolidated list of recommendations 3)

3.1.2 PREVIOUSLY CONTRAINDICATED PATIENTS

As reported earlier in the United States, medical and surgical contraindications for those under age 18 can vary between transplantation centres with some centres recognising absolute contraindications as relative contraindications and vice versa. Further, contraindication in some centres may not be considered such in other centres if patients are selected carefully Weill et al. (2015). This view is supported by our international clinical associate.

The site submission to this review reported that there continues to be evolution as to what are regarded as contraindications to lung transplantation. The AHM advises that the following conditions that were previously considered as absolute contraindications are now considered on a case by case basis at AHM:

- PLHLT for patients on ECMO-bridge-to-transplant
- Patients colonised with Mycobacterium abscessus or Burkholderia cenocepacia.
Patients on ECMO as a Bridge to Transplant

The NFC site reported the following in relation to the ECMO-bridge-to-transplant:

- this approach reflects recent advances in the field of lung transplantation, and was not recognised as a viable pathway to transplantation in 2011 when the original submission for establishment of a NFC PLHLT Program was made
- the NFC site has pioneered ECMO-bridge-to-transplant in the paediatric population and staff have published and presented widely on this approach (see Appendix C)
- The AHM has an established protocol regarding ECMO use as a bridge to lung transplant and extensive experience transplanting children from ECMO (from 2009 which predates NFC) and have published experience in this field that is being cited internationally (Casswell, et al., 2013).
- The Lung Advisory Committee arm of TSANZ has recently updated ‘lung recipient suitability criteria’ in an as yet unpublished consensus statement, including statement on ECMO-bridge-to-transplant.

Two patients have now been accepted to the program on ECMO as a bridge to transplant, and the NFC PLHLT team is expecting that these patients are likely to comprise around 20% of new referrals in the future.

International evidence

Mechanical ventilation and ECLS as a bridge to transplantation in children is considered a relative contraindication for paediatric candidates who should be selected carefully as stated in the latest ISHLT consensus document (Weill, et al., 2015). The following guidelines for extracorporeal life support (ECLS) in adults can be seen in Table 3.1.

<table>
<thead>
<tr>
<th>ECLS recommended</th>
<th>ECLS not recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young age</td>
<td>Septic shock</td>
</tr>
<tr>
<td>Absence of multiple organ dysfunction</td>
<td>Multi-organ dysfunction</td>
</tr>
<tr>
<td>Good potential for rehabilitation</td>
<td>Sever arterial occlusive disease</td>
</tr>
<tr>
<td></td>
<td>Heparin-induced thrombocytopenia</td>
</tr>
<tr>
<td></td>
<td>Prior prolonged mechanical ventilation</td>
</tr>
<tr>
<td></td>
<td>Advanced age</td>
</tr>
<tr>
<td></td>
<td>Obesity</td>
</tr>
</tbody>
</table>

Patient selection for lung transplantation requires careful consideration. Weill et al. (2015) explains that contraindications are generally extrapolated from adult data and are hence similar. However, these authors (amongst others) also explain that in the United States, medical and surgical contraindications for those under age 18 can vary between transplantation centres with some centres recognising absolute contraindications as relative contraindications and vice versa. Mechanical ventilation and ECLS as a bridge to transplantation in children is considered a relative contraindication in some centres but recent literature indicates that this may not be the case if patients are selected prudently. Casswell et al. (2013) consider ECMO a relative contraindication in the paediatric setting – and treat the criteria more as a list of factors likely to identify a patient who may not benefit from ECMO with the understanding that as evidence accrues, the guidelines could change. Weiss et al (2015) also explains that the contraindications identified in relation to adult patients may not be as
relevant in a paediatric setting. A sample of absolute and relative contraindications in paediatric lung transplantation are presented in Table 3.2.

| Table 3.2: Absolute and relative contraindications (Conrad & Cornfield, 2014) |
|-----------------------------|-----------------------------|
| Absolute contraindications  | Relative contraindications  |
| • Active malignancy         | • Pleurodesis               |
| • Sepsis                    | • Renal insufficiency       |
| • Active tuberculosis       | • Markedly abnormal body mass index |
| • Severe neuromuscular disease | • Mechanical ventilation/tracheostomy |
| • Documented, refractory non-adherence | • Severe scoliosis |
| • Multiple organ dysfunction | • Poorly controlled diabetes mellitus |
| • Acquired Immunodeficiency Syndrome | • Osteoporosis |
| • Hepatitis C with histologic liver disease | • Chronic airway infection with multiple resistant organisms (*Burkholderia cenocepacia, Burkholderia dolosa or Mycobacterium abscessus*) |
| • ECMO                      | • Fungal infection/colonisation |
| • Cerebral dysfunction      | • Hepatitis B surface antigen positive |
| • Active hepatitis C infection | • Active collagen vascular disease |
|                             | • Congenital or acquired immunodeficiency syndromes |

Whilst the authors present some contemporary approaches to bridging children to transplant who would otherwise have been contraindicated and have obtained some positive results it is important to note, as did these authors, that further research is required in these areas and that the small sample size limits the studies to some extent (Hayes, et al., 2015). Also, longer term outcomes are not known given the recency of the research.

Hayes et al. (2013) explored the use of using active physical rehabilitation in a paediatric patient on venovenous ECMO as a bridge to transplant, through the placement of a single-site bicaual dual-lumen catheter. This approach facilitates respiratory support in a critically ill patient whilst avoiding sedation and the use of paralytics and allows for rehabilitation and nutrition methods to be applied. The authors explain that whilst this approach has been developing as a treatment option for some adult patients, there has been limited experience in this approach in a paediatric sample. Hayes et al. (2013) applied this approach in a 13-year-old patient and suggested that physicians who are also caring for paediatric patients in their centres should be made aware of this approach as a potential option in patients who would usually be contraindicated for transplant. The advantages of allowing patients to be lucid may include allowing them to actively participate in rehabilitation to minimise deconditioning (Hayes Jr, et al., 2015; Rheder, et al., 2013).

Wong et al. (2015) reported on the morbidity and mortality of children (less than 18 years) on ECMO awaiting lung transplantation. The report collected data from 9 centres (26 children) and concluded that children on ECMO awaiting lung transplantation had an 85% of surviving to transplantation and acceptable long term survival. Wong et al. (2015) suggested that this approach could be considered to bridge younger children to either heart-lung or lung transplantation.

Most of the literature cited above supports the use of ECMO in children but Orr (2014) explains that whilst contraindications for heart-lung transplant vary across centres and whilst the philosophy around
this approach is changing with respect to paediatric patients, most centres are reluctant to carry out the surgery on patients undergoing venoarterial (VA)-ECMO.

Schmidd & Benden (2016) consider cardiopulmonary support with extracorporeal life support (ECLS) systems - especially ECMO bridging strategies - valuable treatment options in highly selected cases (Chiumello, et al., 2015). This recommendation was based on favourable outcomes using ECMO on a small patient cohort in Zurich and successful short and mid-term outcomes in Australia on four children between the ages of 11 and 15 (Casswell, et al. 2013). In addition, the authors also cite a larger recent analysis of the United Network for Organ Sharing (UNOS) database by Hayes et al., (2015) who conclude that paediatric patients on ECMO at the time of lung transplantation appear not to have an increased mortality risk compared to patients not on ECMO. The authors designed their study to address the issue of no data on long-term survival after transplant for children requiring ECMO. Hayes et al (2015) suggest that ECMO be used on a case-by-case system reflecting availability of ECMO and surgical expertise yet acknowledge that further research is required to define patient selection and protocols to optimise short and long-term outcomes. Hayes et al (2015) acknowledges that although ECMO may allow extended time on the wait list to optimise organ allocation, it requires considerable resources such as increased need of blood products due to increased allosensitisation, and immediate post-operative mortality is high.

A recent systematic review involving 14 retrospective adult studies by Chiumello, et al., (2015) concluded that ECMO therapy is being used more frequently as a promising bridging strategy to mechanical ventilation but current clinical evidence does not allow any firm conclusions on efficacy of ECMO in addition to or as an alternative to mechanical ventilation. It should be noted that paediatric cases were screened out of this review so the applicability of this conclusion to the paediatric cohort should be reflected. Dorgan & Hadjiliadis (2014) also advise caution regarding publication bias based on the likelihood of publication of successful case studies which may not be truly representative of this low volume procedure. Cautious clinical judgement in selecting lung transplant candidates for use with ECMO as a bridge-to-transplant is suggested.

Conclusion

Based on the data above, and in consultation with our international clinical expert, it is the conclusion of the Review that the use of ECMO bridge to transplant is considered established clinical practice in centres with expertise in ECMO and is consistent with the NFC eligibility criteria.

**Recommendation:** It is recommended that the NFC Reference Group endorse the practice of the NFC site to accept ECMO-bridge-to-transplant patients on a case by case basis in accordance with existing protocols. Should the NFC Reference Group endorse these changes, it is recommended that the outcomes of higher risk patients be separately reported to the NFC Reference Group as part of the NFC annual reporting process.

*(Consolidated list of recommendations 4)*

**Patients colonised with Mycobacterium abscessus or Burkholderia cenocepacia**

The NFC site has reported the commencement of treatment for patients with M. abscessus and B.cenocepacia infections into the NFC PLHLT Program. The NFC site reports that their approach in assessing patients with these infections is consistent with the consensus guidelines (Weill, et al., 2015) given that the ‘infection with Burkholderia cenocepacia, Burkolderia gladiola, and multidrug resistant mycobacterium abscessus can be considered if the infection is sufficiently treated preoperatively and
there is reasonable expectation for adequate control postoperatively. For patients with these infections to be considered suitable transplant candidates, the patients should be evaluated by centres with significant experience managing these infections in the transplant setting, and patients should be aware of the increased risk of transplant because of these infections’.

AHM/RCH report that after considering their own experience of favourable outcomes in patients who develop *Mycobacterium abscessus* after transplantation and an anticipated increase in the number of paediatric patients with abscessus, they performed a systematic review of the literature on *Mycobacterium abscessus* and convened a series of meetings with acknowledged infectious disease experts to review local and global experience of abscessus and lung transplantation. Combining AHM data with the published literature the AHM report a 70% 1-year survival in this cohort.

A protocol was subsequently developed consisting of aggressive intravenous antimicrobial therapy that extends for several months before and after transplantation. Before being listed for patients must demonstrate that they can tolerate combinational intravenous antibiotics (for at least three months) and that the infection is controlled (smear negative). At the time of this review, AHM/RCH report that they are managing three children (one transplanted, one wait-listed, one mid-assessment) who otherwise historically would have been deemed unacceptable for lung transplantation. As these children are transplanted, the NFC PLHLT Program will audit their progress to ensure satisfactory post-transplant outcomes.

The Alfred Hospital is experienced in managing patients with *M. abscessus* and has recent published experience managing these patients (Smibert, et al., 2016) and one manuscript in preparation (Morrisey, et al., 2016).

**International evidence**

ISHLT guidelines list sepsis as an absolute contraindication but considers colonisation with highly resistant or highly virulent bacteria a relative contraindication without any further specificity (Dorgan & Hadjiliandis, 2014; Weill, et al., 2015). While formal guidelines do not consider *B. cenocepacia* an absolute contraindication to lung transplant – most transplant centres do not currently perform lung transplants in CF patients with this infection (Dorgan & Hadjiliandis, 2014). The presence of *B. cenocepacia* in particular is associated with early death and poor survival rates after lung transplantation. The presence of multi-resistant *P. aeruginosa* is also an absolute contraindication in some transplant centres (Williams, 2005; De Soyza, 2003). Dorgan & Hadjiliandis (2014) consider *B. cenocepacia* to be the main genomovar that leads to poor outcomes after lung transplantation, while other strains were not as bad. They consider *B. cenocepacia* to warrant a strong contraindication to lung transplant, noting that the potential for misidentification of *Burkholderia* subspecies is high.

*M. abscessus* colonisation is also considered a relative contraindication in some centres (Conrad & Cornfield, 2014), yet an absolute contraindication in others. The evidence surrounding *M. abscessus* is more controversial than *B. cenocepacia*, with mixed results in the adult lung transplant population (Cherneko, et al., 2006; Lobo, et al., 2013). Dorgan & Hadjiliandis (2014) do not consider there is enough evidence to recommend the safety of lung transplantation during an active *M. abscessus* infection and that treatment of this organism requires significant expertise given its aggressive nature. As no guidelines are available this paucity of data to guide treatment may be contributing to the current limited outcomes. Smibert et al., (2016) suggest that the current data indicates that pre-transplant treatment with intravenous and oral antimycobacterial agents with a 3-drug (minimum) regimen with the aim of reducing *M. abscessus* burden to smear negativity should be adopted as the centres that report better outcomes treated their patients in this fashion (Smibert, et al., 2016). It should be noted that these reviews are also not paediatric specific.
Two recent investigations have identified that favourable outcomes can be achieved for this cohort:

1. The University of North Carolina examined the post-lung transplantation outcomes of CF patients with M. abscessus pre-transplant. Lung transplantations from 1992 to 2012 were retrospectively examined. Patients with at least one respiratory sample positive for M. abscessus prior to transplantation were included (N=13, average age 24.6 years). The analysis identified survival post-transplant as 77% alive at one year, 64% at three year, and 50% at five year; none died of M. abscessus. The survival data showed no statistically significant difference (p = 0.8) compared with a contemporaneously transplanted population of CF patients without M. abscessus (n = 154). The study concluded that lung transplantation, with favourable survival, is possible in CF patients with M. abscessus. (Lobo, et al., 2013).

2. Data on 65 patients from 14 case reports/case series (is case series the correct nomenclature?) was added to that from nine patients identified at the AHM, resulting in a total of 74 patients. Median age was 29 years. In the 67 patients where outcomes were documented 1-year survival was 77.6% (52/67). The study concluded that 1-year survival rates are better than previously reported. Further research is required to elucidate risk factors and confirm outcomes. (O. Morrissey et. al. 2016)

**Conclusion**

Our international clinical expert, in consideration of these data, and recent developments in the field, advised that treatment of this cohort is not considered research. However, published studies for this cohort are limited. As reported above there are varying opinions on the treatment of the cohort and acceptance as clinical practice is centre-specific. Very few centres transplant patients with these organism, but it is reasonable to consider (based on the NFC site’s recent transplantation of the patients in this cohort) that the AHM is a centre with expertise in caring for these patients. Our clinical expert has advised that at the SickKids Toronto they do transplant patients with *B. cepacia*, but have had significantly lower survival rates compared to those without. They do not currently treat any patients with *M. abscessus*. Based on the data above, in consultation with or international clinical expert, and considering the AHM history and success in transplanting and treating patients with mycobacterium abscessus it is the conclusion of the review that inclusion of patients colonised with *Mycobacterium abscessus* or *Burkholderia cepacia* is consistent with the NFC eligibility criteria.

**Recommendation:** It is recommended that the NFC Reference Group endorse the practice of the NFC site to accept patients colonised with *Mycobacterium abscessus* or *Burkholderia cepacia* on a case by case basis in accordance with existing protocols. Should the NFC Reference Group endorse these changes, it is recommended that the outcomes of higher risk patients be separately reported to the NFC Reference Group as part of the NFC annual reporting process.

(Consolidated list of recommendations 5)

### 3.1.3 PARACORPOREAL LUNG ASSIST DEVICES

As an alternative to ECMO, Hoganson et al. (2014) explored the use of paracorporeal lung assist devices in neonates (one child aged 23 days) and young children (three, aged 2, 9 and 23 months) with decompensated respiratory failure as a bridge to recovery or lung transplantation. In this study, these patients who were placed on ECMO after decompensating were transitioned to a pumpless paracorporeal lung assist device with inflow from the pulmonary artery and return to the left atrium.
The device bridged one patient to transplant, one to recovery (with maximal medical therapy) and whilst the remaining two died waiting for a suitable donor, they were supported past the average wait time for paediatric donor lungs (27 days) at 54 and 72 days respectively. The authors theorised that given paediatric patients who bridge from ECMO to transplant tend to derive poorer outcomes, the approach used here could be considered to bridge children with decompensated respiratory failure to lung transplantation.

Our international expert has advised that paracorporeal lung assist devices have also been utilised in older aged children and adolescents.

3.1.4 ABO-INCOMPATIBLE LUNG TRANSPLANTATION

ABO-incompatible organs have been used in heart transplantation for younger children (less than five year old) with positive outcomes reported and recently the transplantation of ABO-incompatible lungs has been undertaken in a 4-week old infant where a size compatible and blood group compatible organ was not available, marking the first procedure in an infant known to the authors. Six months post-transplant, the infant was reported to have experienced no episodes of graft rejection, his anti-B isoheamagglutins remained negative with normal expiratory flows, weight and height and development (Grasemann, Perrot, Bendiaik, Cox, van Arsdell, Keshavjee & Solomon, 2012).

Our international expert has advised that a second ABO-incompatible lung transplant has subsequently been successfully completed in an infant at this same centre, and that at two years of age this patient is doing well (data not published). It is the view of our international associate that ABO-incompatible lung transplant should not currently be part of the NFC PLHLT Program.

3.1.5 EX VIVO LUNG PERFUSION

The introduction of EVLP to the lung transplantation program aims to increase the availability of suitable donor lungs for transplantation. Traditionally, a high percentage of offered donor lungs are rejected on the basis of uncertainty about their quality, with concern that implanting lungs that may fail would lead to recipient morbidity, mortality and increased health costs. Until the relatively recent advent of EVLP, lung quality was based on in vitro (in the donor) physiological function and the retrieving team’s experience and gestalt. Today, in greater than 30% of centres worldwide, and all three of Australia’s other Lung Transplant Units, ex vivo perfusion is available to assess the quality of ‘extended’ or questionable donor lungs.

A number of slightly different EVLP systems are being marketed worldwide namely Transmedics, XVIVO; Vivoline; and a generic Canadian made version. They vary on slight differences between the original Swedish and Canadian prototypes. Essentially the principle is the same whereby retrieved lungs are brought back to the recipient’s implanting centre in an ice chest as per current practice, the pulmonary artery and veins are connected to an ECMO type circuit, while the trachea is connected to a ventilator. The lungs are slowly warmed up and reperfused. After several hours if the assessment of the lungs is favourable, oxygenation and pulmonary pressures/resistance are normal and stable, then transplant can proceed.

As the NFC PLHLT Program supports all Australian children awaiting lung transplantation, with 10-15% of these patients dying whilst on waitlist (two patients to date) and others waiting up to 442 days for transplant, increased use of the lung donor pool is likely to save lives and improve quality of life for these patients. The ability to assess lungs carefully using EVLP may avoid morbidity, mortality and

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26 NFC PLHLT Site submission to the review, September 2015 p58
27 Ibid.
costs of complications for these patients, and may allow for the support of donor organs for some hours to improve the efficiency of lung transplant scheduling and matching.

With more than 80% of donor lungs potentially injured and not considered suitable for transplantation, the use of normothermic ex vivo lung perfusion has been explored in order to assess damaged donor lungs for function and in turn, suitability for transplantation (Cypel et al., 2011). In a study where injured lungs removed from DCD and DBD donors were subjected to four hours of EVLP and transplanted (although the age of recipients was not specified), similar outcomes for recipients were obtained compared to lungs selected through traditional approaches (Cypel et al., 2011).

These authors posited that this method could be useful to assist in identifying lungs not suitable for transplantation which may otherwise appear functional according to other in vivo testing procedures and to assess DCD lungs for function.

It should be noted that the NFC PLHLT site has not included the costs associated with EVLP.

Our international clinical expert advises that EVLP has already increased the number of transplants performed internationally (for both paediatric and adult recipients) utilising marginal or suboptimal donor organs, with a small number of centres worldwide using EVLP clinically. The future for EVLP was reported to be its use with uncontrolled DCD donor organs. A number of stakeholders, and both of our clinical associates, supported the use of EVLP. It is noted by HOI that organ retrieval and organ donation, and by extension the costs of EVLOP technology, are outside of the scope of the NFC Program. States and Territories are responsible for providing (and funding) deceased organ retrieval services.

3.2 ASSESSMENT OF FUTURE DEMAND AND PATIENT THROUGHPUT

Data provided by the NFC site Annual Reports and in the submission to the review demonstrates that the number of paediatric lung or heart-lung transplants varies by year, and has ranged from one to seven since 2006 (including one patient from New Zealand who received a transplant outside the NFC Program). As demonstrated in Table 3.3 below, an average of three to four patients per year have received a lung or heart-lung transplant since 2011-12, and prior to that an average of just under three patients per year.
Table 3.3: Number of paediatric lung or heart-lung transplants by year at AHM

<table>
<thead>
<tr>
<th>Year</th>
<th>No. transplants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-NFC</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>3</td>
</tr>
<tr>
<td>2007</td>
<td>2</td>
</tr>
<tr>
<td>2008</td>
<td>2</td>
</tr>
<tr>
<td>2009</td>
<td>4</td>
</tr>
<tr>
<td>2010</td>
<td>2</td>
</tr>
<tr>
<td>NFC PLHLT Program</td>
<td></td>
</tr>
<tr>
<td>2011/12(a)</td>
<td>7</td>
</tr>
<tr>
<td>2012/13</td>
<td>1</td>
</tr>
<tr>
<td>2013/14</td>
<td>2</td>
</tr>
<tr>
<td>2014/15</td>
<td>3</td>
</tr>
<tr>
<td>2015 Q1</td>
<td>3</td>
</tr>
</tbody>
</table>

Source: NFC Annual Reports and Submission to the review

(a) Includes one patient from NZ who underwent lung transplant outside NFC Program

The estimated demand for services in the next three to five years is likely to stay the same or increase slightly based on the following:

1. **Steady number of referrals.** All referring clinicians and jurisdictional stakeholders consulted were of the opinion that in the next five to 10 years the overall number of referrals to the program would be unlikely to change significantly, although the mix of diagnoses or patient ages may change slightly. It was considered that with improved outcomes for paediatric patients with cystic fibrosis, more of these patients were likely to reach adulthood before requiring lung transplantation. Data to model these impacts is not available.

2. **Increase in number of patients able to be transplanted.** AHM/RCH predict a slight increase in number of transplants per year in the next three years based on program acceptance of more marginal patients (e.g. patients on ECMO or with *Mycobacterium abscessus*) and more marginal donor organs.

During the site visit to SCHN, participating clinicians considered that for patients living in Sydney (and particularly in the western regions) demand for both paediatric heart and/or lung transplantation may increase if a local service were available at SCHN. Clinicians estimated that would involve approximately three to five additional patients per year for lung or heart-lung transplantation and that a commensurate increase would also be seen in number of local organ donors if a local transplant service were available. Subsequent consultation with referring clinicians in NSW did not identify any evidence to support this position. The review is unable to validate these estimations.

### 3.2.1 Comments from Referring Clinicians and Other Stakeholders

All stakeholders indicated that **demand for PLHLT was likely to remain relatively steady over the next three to five years, although the mix of patient diagnoses and ages may change.** Most clinicians commented that due to improved care of patients with cystic fibrosis in early years, these patients are now more likely to reach adulthood prior to requiring transplant, although there may still be patients including those born overseas who may need transplant prior to adulthood. As these patients currently comprise the majority of referrals, this will reduce program numbers, but this is likely
to be balanced by an increase in other areas. It was reported that there may be an increased number of referrals of children and adolescents with other conditions that would previously have been fatal in infancy but who are now staying alive long enough to require transplant. These patients are likely to include those with interstitial lung disease or congenital heart disease. In addition, it was viewed that there may be a slight increase in referral numbers as referring clinicians became more comfortable with the service, or based on service expansion to include younger ages.

### 3.3 ASSESSMENT OF NUMBER OF SITES

Khan et al. (2015) demonstrated that paediatric specific experience as well as centre volume can impact paediatric lung transplant outcomes, with paediatric specific experience particularly important in adolescence (13-17 year olds). Key findings from Khan et al include the following:

1. **In recipients aged ≤ 12 years**, who can present a more challenging transplant case compared to older children and adults for a variety of anatomical, physiological and neurodevelopmental reasons, there was a lower graft and patient survival rate in low volume paediatric lung transplantation centres (defined as performing median <4 lung transplants per year) compared to high volume paediatric centres (≥4 per year, and ≥50% of these being in paediatric patients). Adult centres (defined as having over 50% of lung transplants being in adults, and noting that the median number of paediatric lung transplants in these centres per year was one) demonstrated graft and patient survival rates that were significant clinically but not statistically better than low volume paediatric centres.

2. **In older children (13-17 years)**, survival in high volume paediatric centres was similar to low volume paediatric centres and better than in adult centres. However, these authors found that differences resulted from non-surgical factors such as higher non-adherence rates or other adolescent issues which may generally be better managed in paediatric centres.

Khan et al. conclude that there may be too many transplant centres performing lung transplants in paediatric patients and that with the majority of centres performing less than two procedures per annum, centres may not be developing the expertise required to support this age group appropriately and effectively. The authors recommend that paediatric lung transplantation should be performed at specialised centres with sufficient volume and specific expertise in paediatric patients, and that adult centres should carefully consider the issues which are presented by taking on paediatric patients. This is particularly so in adolescent patients who have a high non-adherence rate and require a sufficiently experienced team to support them. As previously noted, the current NFC PLHLT site at AHM is well aware of these factors and has implemented and continues to improve strategies to address specific requirements of adolescent patient management within the adult centre.

With the exception of clinicians from SCHN in NSW, all referring clinicians consulted during the review process considered that a single site was appropriate to conduct the NFC PLHLT Program over the next three to five years (noting previous comments that some flexibility is required for patients at the top end of the age range to allow transplant at local adult transplant services if more appropriate). It was viewed that this was a very specialised service for a low volume of patients, and that the numbers did not support an increase in the number of centres.

Arguments put forward by SCHN clinicians and executive to increase the number of sites funded to provide PLHLT (and/or heart transplant) included the following:

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• Availability of another site would increase awareness and increase not only referrals to the program but also the number of organ donations available at the host jurisdiction
• Reduce donor organ ischaemic time
• Competitive pressure between units would lead to continued improvements in service delivery
• Retain key staff who are trained to deliver these services, as per the following comment:
  “Staff involved in provision of transplant services are those who want to do this. If we don’t allow these specialists to provide this service, they will be snapped up overseas.”
  This was also supported by another stakeholder outside NSW and Victoria, who stated that NSW had “arguably the best trained paediatric cardiothoracic surgeon in Australia”.
• Pre-emptive planning to ensure that Australia has the ongoing capacity to provide these services into the future.

SCHN clinicians reported that a particular benefit of providing the NFC PLHLT Program from SCHN would be that it would be provided wholly in a paediatric hospital. Further the commissioning of a single cardiothoracic (i.e. heart and lung) transplantation NFC Program would address the issue of ‘sufficient volume’ (however, consideration of a paediatric cardiothoracic (i.e. heart and lung) transplantation NFC Program is outside the scope of this review).

In addition, it was noted separately by one clinician from SCHN that although it was recognised that increased volume improves expertise in conducting the procedure and managing these patients, almost all centres worldwide are providing the procedure to less than five patients per year. The most important criteria was viewed to be centre experience in solid organ transplant and ability to provide comprehensive post-operative care to patients.

Based on our review of the evidence base and in consultation with our international clinical expert it is considered that the NFC Reference Group should continue to approve the delivery of PLHLT services at a single site.

**Recommendation:** It is recommended that the NFC Reference Group endorse continuation of the delivery of NFC PLHLT Program for an additional three years at a single site and based on performance, that site should be the exiting AHM/RCH site, with a further review to be conducted at the end of that period.

(Consolidated list of recommendations 1)
3.4 **Summary of key findings**

<table>
<thead>
<tr>
<th>Review domain</th>
<th>Key findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>New evidence in clinical practice and technology</td>
<td>1. AHM/RCH are currently requesting an expansion of the NFC PLHLT Program to include <strong>patients four to 15 years with a minimum weight of 10kg</strong>, and are exploring the possibility of providing a service to younger children (less than five year old) at the RCH with input from the AHM transplant team in the future.</td>
</tr>
<tr>
<td></td>
<td>2. There is broad stakeholder support for lowering the minimum age limit for the NFC PLHLT Program based on international experience, as long as expertise is available to provide this care. All stakeholders reported that the upper age limit was appropriate but that flexibility was required for some patients aged 14-15 years who may be better managed under the local adult transplant service (i.e. based on psychosocial circumstances, emotional maturity, and size). This has already occurred in several jurisdictions.</td>
</tr>
<tr>
<td></td>
<td>3. Following risk assessment and the development of clinical protocols, AHM/RCH are now accepting <strong>patients on ECMO-bridge-to-transplant and/or patients colonised with Mycobacterium abscessus or Burkholderia cenocepacia</strong> who would previously have been contraindicated for transplant. The NFC PLHLT team is expecting that these patients are likely to comprise around 20-25% of new referrals in the future.</td>
</tr>
<tr>
<td></td>
<td>4. The NFC Program site commented that children undergoing life-saving transplant surgery are likely to face significant long-term psychological challenges related to the chronic need to take life-saving immunosuppressant medications, and have included a request and budget for a <strong>child psychologist</strong> to be added to the core NFC PLHLT team for the future.</td>
</tr>
<tr>
<td></td>
<td>5. AHM reported that they are in the process of considering purchase of <strong>EVLP technology</strong>. It is noted by HOI that organ retrieval and organ donation, and by extension the costs of EVLOP technology, are outside of the scope of the NFC Program. States and Territories are responsible for providing (and funding) deceased organ retrieval services.</td>
</tr>
<tr>
<td>Projected demand</td>
<td>6. The estimated demand for services in the next three to five years is likely to stay the same or increase slightly to three to five lung or heart-lung transplants per year based on the following:</td>
</tr>
<tr>
<td></td>
<td>‒ Little overall change in the number of referrals, with decrease in the number of patients with cystic fibrosis requiring transplant before adulthood but increase in number of referrals of patients with other diagnoses (e.g. interstitial lung disease) or younger ages.</td>
</tr>
<tr>
<td></td>
<td>‒ Increase in the number able to be transplanted, based on program acceptance of more marginal patients (e.g. patients on ECMO or with Mycobacterium abscessus) and more marginal donor organs.</td>
</tr>
<tr>
<td></td>
<td>7. Clinicians from Children’s Hospital Westmead were of the view that for patients living in NSW (and particularly in the western regions of Sydney), the number of referrals for paediatric heart and/or lung transplantation may increase by an additional three to five per year if a local service were available at SCHN, with a commensurate increase in the number of local organ donations.</td>
</tr>
</tbody>
</table>
### Review domain | Key findings
--- | ---
Number of NFC sites | 8. With the exception of clinicians from SCHO in NSW, all referring clinicians consulted during the review process considered that a single site was appropriate to conduct the PLHLT Program over the next three to five years with a further review to be conducted at the end of that period.
This chapter presents the analysis of the costs and pricing structure associated with the NFC PLHLT Program and is based on information provided by the NFC site, the views of our clinical advisers and the literature review.

4.1 NFC PROGRAM COSTING AND FUNDING

The funding of each NFC site is calculated based on the payment of an agreed price of the procedure performed by the NFC site, multiplied by the anticipated number of procedures per annum. The NFC funding provided should be reasonably commensurate with costs of the NFC part of a service.

Funding for the NFC Program is provided by state and territory jurisdictions according to their population share of the total NFC Program budget. This includes funding for individual NFCs, the cost of the NFC Secretariat and the cost of any planned assessments and reviews in a given financial year. The price for the NFC PLHLT procedure is indexed annually in accordance with Australian Institute of Health and Welfare’s health-specific cost index and the Productivity Commission’s derived index of technology growth, as used for the National Healthcare Agreement growth factor.

The NFC PLHLT Program was established from 1 July 2011 establishing a price of $314,266, (noting that there was no distinction made between type of transplant). A summary of the price per procedure funded by the NFC since 2011 is presented in Table 4.1.

| Table 4.1: Funded price per procedure by financial year |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | 2011/12         | 2012/13         | 2013/14         | 2014/15         | 2015/16         |
| Price per procedure | $314,266  | $327,905  | $339,480  | $350,513  | $361,975  |
| Indexation rate(a) | -  | 4.3%  | 3.5%  | 3.3%  | 3.3%  |

(a) Indexed annually by an amount reflecting the Australian Institute of Health and Welfare health-specific cost index and the Productivity Commission derived index of technology growth.

The established 2011-12 price per procedure included funding for costs related to: screening of referrals ($13,354); pre-acceptance work-up and assessment ($52,358); and the decision to accept ($5,468). In total, 22.6% ($71,180) of the price per procedure funded items. As a consequence of the release of updated NFC Guidance, these costs are now not considered part of the defined NFC-funded episode of care. This is discussed further in section 4.3.7 below.
4.1.1 NFC Guidance Costing Proforma

The NFC Guidance provides a costing pro forma that specifies the data elements to be reported by NFC sites to support the assessment of individual procedures for consideration of NFC status and to support the ongoing review process for existing NFCs. Costs are reported on the basis of the defined care pathways.

A clear definition of the start and end point for an episode of care for an individual NFC procedure is required. In general, the jurisdictions are required to pay for patients until the patient is admitted for the definitive NFC treatment or procedure. NFC Program funding is provided from that point until three months post discharge. Following this period jurisdictions resume responsibility for providing funding. There may be exceptions to this general scope depending on the type of procedure funded under the program, subject to AHMAC approval.

Total costs include all inputs associated with admitted pre-care activities and the inputs and costs associated with any post treatment and follow up care. To ensure equity of access to the NFC sites, total costs include travel and accommodation for interstate patients and a parent/carer.

4.1.2 Costing Methodology

Consistent with the NFC Guidance, the cost reporting approach is based on the ‘average cost of the patient care pathway’ and the identification of all cost inputs for each care pathway for direct and indirect patient care costs as follows:

1. **Direct patient costs for each phase of patient care.** It is assumed that for each care pathway there are a number of phases of care that comprise different cost drivers including:
   - Acceptance for NFC treatment
   - Inpatient pre NFC treatment/monitoring
   - Theatre/surgery admission for NFC procedures
   - Intensive care / high dependency unit admission
   - General ward admission
   - Outpatient care prior to discharge from the NFC program
   - Other direct patient costs (including transport and accommodation).

2. **Indirect patient costs.** These costs relate to administrative and operational support costs that cannot be directly attributed to the delivery of patient care in terms of:
   - NFC Program management costs which require an allocation of costs based on time spent or bed days covered by various personnel on the NFC Program
   - Health service and hospital administration and overhead costs that are generally calculated as a percentage of the direct patient care costs.

The NFC costing methodology is not a full cost recovery model but that in accordance with the NFC Guidance, the price per procedure should be reasonably commensurate with the costs of delivering the agreed component of the services (i.e. from admission for the definitive treatment to three months post discharge). HOI supports the view of the NFC Reference Group that it is essential to balance the

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29 Nationally Funded Centres Program Guidance Document (Part 1) Guidance for Established NFCs (Governance, Management, Funding, and Review (October 2015))
need to establish an appropriate price for each procedure with the need to ensure the ongoing sustainability of the NFC Program.

The costing protocol is based on the utilisation of three main methods:

1. **NFC standard costs** - NFC standard costs were to be used for where there is no significant variability across large metropolitan specialist hospitals and applies to the following cost components:
   - single discipline outpatient clinics (to be applied to Tier 2 Non-Admitted Services classification weightings) and
   - travel and accommodation
   - indirect patient costs (expressed as a % of direct costs)

   Specified NFC standard costs are provided in the guidance materials.

2. **Costs derived from clinical costing systems** - This method is used when direct patient utilisation data from clinical costing systems are sufficiently accurate to estimate that patient level costs for the NFC episode of care.

3. **Cost build-up methodology** - This method is recommended in cases where standard costs cannot be derived and clinical costing systems are unlikely to adequately account for inputs or amount of resources used. As with the clinical costing method, the cost build-up should be based on the inputs and costs of previous NFC patients.

### 4.2 Cost analysis

In contrast to the 2015/16 funded price per procedure of $361,975, the 2015 Review Submission of AHM reported a cost per procedure of $533,573 ($171,598 higher (47%) than the current price (refer Table 4.2 below)). However, the Review identified a number of errors in the costings, and following a request to the NFC site for supplementary information, a revised costing was submitted to the Review on 7 December 2015, reporting a cost per patient of $412,303 ($50,328 higher (14%) than the current price (refer Table 4.2 below)). **Noting this revised costing, the balance of this report provides analysis against the AHM-revised costing only.**

<table>
<thead>
<tr>
<th>Item</th>
<th>Original submission</th>
<th>AHM-revised costing</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost per procedure submitted in AHM submission (2015/16)</td>
<td>$533,573</td>
<td>$412,303</td>
<td>($121,270)</td>
</tr>
<tr>
<td>Current funded price per procedure</td>
<td>$361,975</td>
<td>$361,975</td>
<td>-</td>
</tr>
<tr>
<td>Change ($)</td>
<td>$171,598</td>
<td>$50,328</td>
<td></td>
</tr>
<tr>
<td>Change (%)</td>
<td>47%</td>
<td>14%</td>
<td></td>
</tr>
</tbody>
</table>
4.2.1 Benchmark cost data

The review was unable to identify any recently published literature (since 2010) on the costs associated with paediatric lung and heart-lung transplantation, and the note that the previous review was only able to cite cost data in respect to adult lung transplantation from the US and UK.

Adult cost data on lung transplantation is submitted to the IHPA as part of the National Hospital Cost Data Collection (NHCDC) annual reporting process. These data indicate that Australian hospitals provided adult lung or heart-lung transplants involving 153 separations at an average cost of $135,520, with an associated average length of stay of 30.5 days (refer Table 4.3 below).

<table>
<thead>
<tr>
<th>DRG</th>
<th>Round 17 (FY1213)</th>
<th>Round 16 (FY1112)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRG Description</td>
<td>LUNG OR HEART-LUNG TRANSPLANT</td>
<td>LUNG OR HEART-LUNG TRANSPLANT</td>
</tr>
<tr>
<td>Number of hospitals submitting data</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Separations</td>
<td>153</td>
<td>136</td>
</tr>
<tr>
<td>ALOS (days)</td>
<td>30.5</td>
<td>28.8</td>
</tr>
<tr>
<td>Inlier boundary (a) (days)</td>
<td>10 to 98</td>
<td></td>
</tr>
<tr>
<td>Paediatric adjustment</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Average Cost per DRG ($)</td>
<td>$135,520</td>
<td>$132,260</td>
</tr>
</tbody>
</table>

Notes: (a) L3H3 method was used by IHPA to identify inlier boundary outside of which are short-stay and long-stay outliers

While a paediatric cost for A03Z is not available, IHPA recognises that there are higher costs associated with treating paediatric patients. IHPA has identified key paediatric patient characteristics impacting on higher costs included age and the presence of co-morbidities, as well as supervision, children needing more support for interventions, family support, increased medication administration costs and lower economies of scale.

The Round 17 NHCDC cost report also provides a breakdown of the component costs for DRG A03Z (refer Table 4.4 below) reporting that:

- Direct costs were reported as 88% of total costs

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The largest cost component related to critical care\textsuperscript{35} services representing 30\% of total reported costs, followed by operating rooms\textsuperscript{36} and pharmacy\textsuperscript{37}, both representing 14\% of total reported costs.

### Table 4.4: Costs components on A03Z, NHCDC Round 17

<table>
<thead>
<tr>
<th>Cost component</th>
<th>Direct costs</th>
<th>Overhead costs</th>
<th>Total costs</th>
<th>% of total costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ward Medical</td>
<td>$8,369</td>
<td>$787</td>
<td>$9,156</td>
<td>7%</td>
</tr>
<tr>
<td>Ward Nursing</td>
<td>$10,036</td>
<td>$509</td>
<td>$10,545</td>
<td>8%</td>
</tr>
<tr>
<td>Non Clinical Salaries</td>
<td>$3,149</td>
<td>-</td>
<td>$3,149</td>
<td>2%</td>
</tr>
<tr>
<td>Pathology</td>
<td>$5,820</td>
<td>$637</td>
<td>$6,457</td>
<td>5%</td>
</tr>
<tr>
<td>Imaging</td>
<td>$1,972</td>
<td>$401</td>
<td>$2,373</td>
<td>2%</td>
</tr>
<tr>
<td>Allied</td>
<td>$4,214</td>
<td>$744</td>
<td>$4,958</td>
<td>4%</td>
</tr>
<tr>
<td>Pharmacy</td>
<td>$18,023</td>
<td>$441</td>
<td>$18,464</td>
<td>14%</td>
</tr>
<tr>
<td>Critical Care</td>
<td>$37,057</td>
<td>$3,603</td>
<td>$40,660</td>
<td>30%</td>
</tr>
<tr>
<td>Operating Rooms</td>
<td>$16,978</td>
<td>$2,007</td>
<td>$18,985</td>
<td>14%</td>
</tr>
<tr>
<td>Supplies</td>
<td>$4,140</td>
<td>$1,413</td>
<td>$5,553</td>
<td>4%</td>
</tr>
<tr>
<td>Prostheses</td>
<td>$1,322</td>
<td>-</td>
<td>$1,322</td>
<td>1%</td>
</tr>
<tr>
<td>On-Costs</td>
<td>$7,492</td>
<td>-</td>
<td>$7,492</td>
<td>6%</td>
</tr>
<tr>
<td>Hotel</td>
<td>-</td>
<td>$3,894</td>
<td>$3,894</td>
<td>3%</td>
</tr>
<tr>
<td>Depreciation</td>
<td>-</td>
<td>$2,047</td>
<td>$2,047</td>
<td>2%</td>
</tr>
<tr>
<td>Other</td>
<td>$414</td>
<td>$51</td>
<td>$465</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Average A03Z cost</strong></td>
<td><strong>$118,986</strong></td>
<td><strong>$16,534</strong></td>
<td><strong>$135,520</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

| % of total           | 88\%         | 12\%           | 100\%       |
| Overhead as % of direct | 14\%        |                |             |
4.3 Analysis of NFC PLHLT Procedure Costs

A comparison of AHM reported costs, to the costs submitted in the previous review (adjusted for inflation) is presented by care pathway in Table 4.5 below. While the detailed review of costs is provided later in this chapter, the key variances are identified as follows:

1. **Work up and assessment costs have decreased.** This cost reduction is principally due to a decrease in the assumed number of assessments each year (reduced from 12 assessments per year to 8 per year).

2. **Inclusion of organ retrieval costs.** The AHM utilise their own retrieval team to retrieve and transport organs for the NFC PLHLT Program. It has been noted that these costs were excluded in the 2010 review; however, have been reinstated in this review (notwithstanding the NFC Guidance document specifically excludes these costs). Existing transplant providers receive funding from respective jurisdictional health departments to undertake donor organ retrieval, although this is not specifically for NFC activity.

3. **Inclusion of inpatient pre-treatment monitoring costs related to ECMO-bridge-to-transplant.** The AHM/RCH provides ambulatory ECMO to patients as a bridge to lung transplant. In total since 2009, five children have bridged to and through transplantation utilising ECMO technology.

4. **Decrease in general ward admission costs.** General ward admission costs have reduced, due to a decrease in length of stay, though these savings are partially offset by the increased costs of treating Mycobacterium/HITH patients. The incidence of *Mycobacterium abscessus* colonisation in CF children appears to be increasing and the AHM predicts that 25% of future referrals will include patients colonised with *Mycobacterium abscessus*. The current submission includes a budget of $23,222 for 20% of patients to include intensive antimicrobial therapy, typically using three intravenous antibiotics via a hospital-in-the-home (HITH) program (assumed 91 days in HITH).

5. **Increased program management costs.** There has been a reported cost increase due to the Head of Unit and the Paediatric Lung Transplant Coordinator being entirely allocated to this cost category. In the 2010 review these costs were spread across multiple cost components.

6. **Indirect costs** were not separately reported in the 2010 review, but were included in the respective care pathway line items.
Table 4.5: Cost comparison of AHM submission to the prior review costs, by care pathway

<table>
<thead>
<tr>
<th>Cost by care pathway</th>
<th>AHM-revised costing</th>
<th>2010 accepted costs (adjusted for inflation)</th>
<th>Variance ($)</th>
<th>Variance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outside defined pathway</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Referral &amp; screening</td>
<td>$6,844</td>
<td>$15,381</td>
<td>($8,537)</td>
<td>-56%</td>
</tr>
<tr>
<td>Work-up and assessment (incl. travel)</td>
<td>$31,016</td>
<td>$60,307</td>
<td>($29,291)</td>
<td>-49%</td>
</tr>
<tr>
<td>Outpatient pre NFC treatment/monitoring</td>
<td>$6,012</td>
<td>$10,972</td>
<td>($4,960)</td>
<td>-45%</td>
</tr>
<tr>
<td>Organ retrieval</td>
<td>$12,803</td>
<td>-</td>
<td>$12,803</td>
<td>NA</td>
</tr>
<tr>
<td>Part A: Direct patient costs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A.1. Acceptance to NFC program</td>
<td>$2,824</td>
<td>$6,298</td>
<td>($3,474)</td>
<td>-55%</td>
</tr>
<tr>
<td>A.2. Inpatient pre NFC treatment/monitoring</td>
<td>$9,683</td>
<td>-</td>
<td>$9,683</td>
<td>NA</td>
</tr>
<tr>
<td>A.3. Theatre/surgery admission for NFC procedures</td>
<td>$28,565</td>
<td>$23,613</td>
<td>$4,952</td>
<td>21%</td>
</tr>
<tr>
<td>A.4. Other procedures (non-surgical)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>A.5. Intensive care / high dependency unit admission</td>
<td>$52,735</td>
<td>$83,300</td>
<td>($30,565)</td>
<td>-37%</td>
</tr>
<tr>
<td>A.6. General ward admission</td>
<td>$35,065</td>
<td>$61,312</td>
<td>($26,247)</td>
<td>-43%</td>
</tr>
<tr>
<td>A.7. Outpatient care prior to discharge</td>
<td>$46,148</td>
<td>$38,587</td>
<td>$7,561</td>
<td>20%</td>
</tr>
<tr>
<td>A.8. Other direct patient costs</td>
<td>$19,113</td>
<td>$35,434</td>
<td>($16,321)</td>
<td>-46%</td>
</tr>
<tr>
<td>Part B: Program management costs</td>
<td>$69,141</td>
<td>$26,770</td>
<td>$42,371</td>
<td>158%</td>
</tr>
<tr>
<td>Part C: Indirect costs</td>
<td>$92,355</td>
<td>-</td>
<td>$92,355</td>
<td>NA</td>
</tr>
<tr>
<td>Total</td>
<td>$412,304</td>
<td>$361,975</td>
<td>$50,329</td>
<td>14%</td>
</tr>
<tr>
<td>Component analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Direct Costs</td>
<td>$250,808</td>
<td>$335,205</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indirect Costs (Part B and C)</td>
<td>$161,496</td>
<td>$26,770</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Direct Costs (%)</td>
<td>61%</td>
<td>93%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indirect Costs (%)</td>
<td>39%</td>
<td>7%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4.3.1 UNDERLYING ASSUMPTIONS AND COST DRIVERS

To provide a more detailed break-down of the key cost drivers since the 2010 review, Table 4.6 below presents a comparison of the underlying assumptions as follows:

1. **Interstate patients.** The assumed ratio of interstate patients has generally decreased (from 67% to 50%), but is reasonable given recent experiences and referral patterns.
2. **ECMO-bridge-to-transplant.** As noted earlier, costs related to ECMO as a bridge to lung transplant have been included for the first time.
3. **ECMO patient transfer.** The AHM have included costs of transferring patients on ECMO from RCHM to AHM immediately prior to transplantation.
4. **Reduced length of stay.** The length of stay in both ICU and the ward have been reduced to reflect the current median (both from 14 days to 10 days).

5. **Mycobacterium/HITH.** As noted earlier, the costs for intensive antimicrobial therapy have been included for the first time.

6. **Child Psychologist.** The submission includes a budget for a child psychologist to be added the core PLHLT NFC team to support non-adherence efforts and adolescent-focussed education.

7. **Overhead and on-cost rates.** Amendments to the rates used to calculate salary on-costs (reduced from 30% to 13.5%) and overheads (increased from 13% (on salary costs only) to 20% on all costs). These revised rates are consistent with the NFC Guidance.

### Table 4.6: Cost assumptions and drivers of cost

<table>
<thead>
<tr>
<th>Items</th>
<th>AHM-revised costing</th>
<th>2010 costing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Referral</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients per year</td>
<td>12</td>
<td>18</td>
</tr>
<tr>
<td>% from interstate</td>
<td>50%</td>
<td>67%</td>
</tr>
<tr>
<td>Workup</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients per year</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>% from interstate</td>
<td>50%</td>
<td>67%</td>
</tr>
<tr>
<td>Bed days</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>ECMO-bridge-to-transplant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECMO bridge (patients per year)</td>
<td>1</td>
<td>NA</td>
</tr>
<tr>
<td>Days on ECMO bridge</td>
<td>21</td>
<td>NA</td>
</tr>
<tr>
<td>Patients treated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients transplanted per year</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>% from interstate or more than 4 hours</td>
<td>60%</td>
<td>67%</td>
</tr>
<tr>
<td>Retrievals per year</td>
<td>6</td>
<td>Excluded</td>
</tr>
<tr>
<td>Retrievals by AHM team</td>
<td>100%</td>
<td>Excluded</td>
</tr>
<tr>
<td>Percentage of interstate organ retrievals</td>
<td>50%</td>
<td>Excluded</td>
</tr>
<tr>
<td>Theatre time (hours)</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>ECMO patient transfer (% of patients)</td>
<td>20%</td>
<td>NA</td>
</tr>
<tr>
<td>ICU stay (days)</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>Ward stay (days)</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>Mycobacterium (% of patients)</td>
<td>20%</td>
<td>NA</td>
</tr>
<tr>
<td>HITH bed days for Mycobacterium Patients</td>
<td>91</td>
<td>NA</td>
</tr>
<tr>
<td>Readmission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Readmission rate</td>
<td>33%</td>
<td>100%</td>
</tr>
<tr>
<td>ICU stay (days)</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
### 4.3.2 Costs Categories Outside of the Defined Pathway

The NFC recently released updated guidance document to govern the pricing for the NFC program\(^\text{38}\). The guidance includes statements that specifically exclude elements of the costs submitted by AHM as follows: ‘... the referring jurisdiction will pay for the patient until the patient is admitted for the definitive NFC treatment or procedure. The NFC Program will then pay for the patient costs until three months post discharge.’ As a consequence, outpatient costs prior to the admission for transplant are excluded from the NFC funded price.

In addition, it is established practice that organ retrieval costs are not funded by the NFC program.

As a consequence, the Review has proposed an amendment (proposed cost adjustment 1) to exclude the following costs included in the AHM-revised costing (noting that items (A) to (C) are currently included in the funded price per procedure, as they were accepted in the 2010 Assessment).

**Table 4.7: Cost categories excluded by the Review based on the NFC defined pathway**

<table>
<thead>
<tr>
<th>Cost description</th>
<th>Direct costs</th>
<th>Associated on-costs</th>
<th>Associated overhead</th>
<th>Total costs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Referral and screening</strong></td>
<td>$6,844</td>
<td>$308</td>
<td>$1,430</td>
<td>$8,582</td>
</tr>
<tr>
<td>Costs of referral receipt and assessment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(includes travel to referring hospitals)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excluded as prior to 'admission for the definitive NFC treatment’.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>B. Work-up and assessment (incl. travel)</strong></td>
<td>$31,016</td>
<td>$1,335</td>
<td>$6,470</td>
<td>$38,821</td>
</tr>
<tr>
<td>Costs of investigations and work out as outpatient, or as inpatient (brief 2 day visit).</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excluded as prior to 'admission for the definitive NFC treatment’.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>C. Outpatient pre NFC treatment/monitoring</strong></td>
<td>$6,012</td>
<td>$264</td>
<td>$871</td>
<td>$7,147</td>
</tr>
<tr>
<td>Costs of review of listed patients prior to admission (includes interstate travel).</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excluded as prior to 'admission for the definitive NFC treatment’.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^{38}\) Nationally Funded Centres (NFC) Program Guidance Document (part 3): Guidance for Pricing NFC Episodes of Care and the NFC Costing Pro Forma (October 2015)
Cost description | Costs per procedure
--- | ---
| Direct costs | Associated on-costs | Associated overhead | Total costs |
D. Organ retrieval | $12,803 | $1,664 | $2,893 | $17,360 |
*Costs of staff for organ retrieval (NB private jet funded by DonateLife). Organ retrieval costs are not funded by the NFC Program.*

Total | $56,675 | $3,571 | $11,664 | $71,910 |

While the Review has excluded these costs in the recommendation for the NFC PLHLT price per procedure, HOI is of the view that these costs are both necessary costs of delivering the program, and material in value. The AHM has stated that these costs are included as they are ‘...integral to ensuring optimal transplant outcomes ...’ for patients. In these circumstances, the NFC sites should seek to utilise existing mechanisms (ABF/cross-border agreements) to recover costs with respect to interstate patients. An alternative approach would to seek AHMAC approval to include these costs in the care pathway (refer consolidated list of recommendations 8).

### 4.3.3 Direct Patient Costs

This section presents analysis for each of the defined NFC direct-cost pathways

**Acceptance to NFC Program**

The NFC site has reported total costs per annum of $14,120 (excluding on-costs and overhead allocations) in respect to the costs of completing a joint expert multidisciplinary review to assess patients for inclusion on the wait list of the NFC PLHLT Program. Costs have been based on the inclusion of eight patients per year on to the program (noting that costs have not been included for those patients who are not added to the wait list (assumed to be four patients per annum)). On a ‘cost per procedure’ basis, these costs were allocated across the forecast transplant activity of five transplants per year, resulting in $2,824 per patient (refer Table 4.5 above). Inclusion of these costs is consistent with the requirements of the NFC Guidance.

However, data presented earlier indicates that on average 5.2 patients are assessed per year for inclusion on the waitlist, and it is forecast that five patients per annum will be transplanted. Accordingly, the Review has proposed (**cost adjustment 2**) that these costs be reduced by $1,059 per procedure (excluding on-costs and overhead allocations) or $1,442 (inclusive of all costs). This activity should be funded through existing cross border funding agreements.

**Table 4.8: NFC program acceptance costs (2015/16)**

<table>
<thead>
<tr>
<th>Item</th>
<th>Direct costs</th>
<th>On costs</th>
<th>Overhead</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost per review</td>
<td>$1,765</td>
<td>$238</td>
<td>$401</td>
<td>$2,404</td>
</tr>
<tr>
<td>At AHM assumed volume 8 reviews/ year</td>
<td>$14,120</td>
<td>$1,904</td>
<td>$3,208</td>
<td>$19,232</td>
</tr>
<tr>
<td>Allocated across patient transplant volume (cost per transplant)</td>
<td>$2,824</td>
<td>$381</td>
<td>$642</td>
<td>$3,846</td>
</tr>
<tr>
<td>Restated to 5 reviews per annum/five transplants per annum</td>
<td>$1,765</td>
<td>$238</td>
<td>$401</td>
<td>$2,404</td>
</tr>
<tr>
<td>Reduction required</td>
<td>$1,059</td>
<td>$143</td>
<td>$240</td>
<td>$1,442</td>
</tr>
</tbody>
</table>
INPATIENT PRE NFC TREATMENT/MONITORING

The NFC site has reported total costs per annum of $48,417 (excluding on-costs and overhead allocations) in respect to the costs for ECMO-bridge-to-transplant for one patient per annum. On a cost per procedure basis this equates to $9,683 per procedure (refer Table 4.5 above). The costing assumes a 21 day period on ECMO, valued as a base bed-day rate in ICU of $2,072, with additional costs key clinical staff at relevant hourly rates. Inclusion of these costs is consistent with the requirements of the NFC Guidance.

However, two issues were considered by the review:

1. To what extent should the ECMO admission be included on the NFC-funded care pathway? That is, should the ECMO treatment be considered a separate (and earlier) admission/separation funded under jurisdictional activity based funding arrangements?
2. If considered part of the NFC-funded care pathway, to what extent does this reflect an alternative care pathway, requiring AHMAC-approval?

It is the conclusion of the review that ECMO-bridge-to-transplant occurs at a point prior to the ‘definitive admission’ for the NFC procedure, and is therefore outside of the NFC funded care-pathway. These costs should be funded by jurisdictions through the appropriate activity based funding DRG. Accordingly, the Review has proposed (proposed cost adjustment 3) these costs be removed, reducing the costs by $9,683 per procedure (excluding on-costs and overhead allocations) or $12,740 (inclusive of all costs).

Recommendation: It is noted that the NFC Reference Group has an AHMAC approved review cycle for the NFC Guidance (every three years) and it is recommended that this include definitions of the ‘care pathway’ and the circumstances where deviations from that care pathway require AHMAC approval.

(Consolidated list of recommendations 8)

Further, given the evolving nature of clinical practice in the high cost, low volume procedures that are established under the NFC Program, we note that the NFC Guidance is reviewed on a three-year cycle. To support the revision process; the NFC Reference Group should invite jurisdictions to provide regular feedback on the NFC Guidance documents. Submissions received should be reviewed for urgency and criticality on an ongoing basis and if not immediately actioned to be recorded in a change-register and reviewed during the next scheduled revision.

Recommendation: It is noted that the NFC Reference Group has an AHMAC approved review cycle for the NFC Guidance (every three years) and it is recommended that the review process should incorporate invitations to jurisdictions to provide regular feedback to ensure urgent or critical matters are addressed in an appropriate timeframe.

(Consolidated list of recommendations 9)

THEATRE/SURGERY ADMISSION FOR NFC PROCEDURES

The NFC site has reported total costs per annum of $142,823 (excluding on-costs and overhead allocations) for theatre and surgical costs (including Immunosuppression and diagnostic investigations). This equates to $28,565 per procedure (refer Table 4.5 above) excluding on-costs and overhead allocations.
overhead allocations, or $36,520 per procedure (inclusive of all costs). Costs included are summarised in the table below.

**Table 4.9: Theatre and surgery costs (2015/16)**

<table>
<thead>
<tr>
<th>Item</th>
<th>Timeframe</th>
<th>Per annum</th>
<th>Per procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transport of interstate patients via air ambulance (two/year)</td>
<td></td>
<td>$27,292</td>
<td>$5,458</td>
</tr>
<tr>
<td>ECMO patient transfer (one/year)</td>
<td></td>
<td>$6,600</td>
<td>$1,320</td>
</tr>
<tr>
<td>Diagnostic investigations</td>
<td></td>
<td>$8,112</td>
<td>$1,622</td>
</tr>
<tr>
<td>Pre theatre admission</td>
<td>0.5 day</td>
<td>$1,397</td>
<td>$279</td>
</tr>
<tr>
<td>Pre-transplant induction immunosuppression &amp; antibiotics</td>
<td></td>
<td>$2,778</td>
<td>$556</td>
</tr>
<tr>
<td>Theatre</td>
<td>10 hours</td>
<td>$96,645</td>
<td>$19,330</td>
</tr>
<tr>
<td>Total (excluding on-costs)</td>
<td></td>
<td>$142,823</td>
<td>$28,565</td>
</tr>
<tr>
<td>On-costs (applied to salary and wages only)</td>
<td></td>
<td>$11,617</td>
<td>$2,323</td>
</tr>
<tr>
<td>Overheads</td>
<td></td>
<td>$28,159</td>
<td>$5,632</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>$182,599</td>
<td>$36,520</td>
</tr>
<tr>
<td>2010 Assessment (indexed)</td>
<td>10 hours</td>
<td></td>
<td>$23,613</td>
</tr>
</tbody>
</table>

Of note is the inclusion, for the first time, of ECMO patient transfer costs. The NFC site considers that inclusion of this cost at the rate of 1 in 5 patients is conservative, and the review has accepted this based on the site’s recent experience and the relatively immaterial value. However, it is the conclusion of the review that ‘transport of interstate patients’ and the ‘ECMO patient transfer’ occur at a point prior to the ‘definitive admission’ for the NFC procedure, and is therefore outside of the NFC funded care-pathway. Accordingly, the Review has proposed (proposed cost adjustment 4) these costs be removed, reducing the costs by $6,778 per procedure (excluding on-costs and overhead allocations) or $8,134 (inclusive of all costs).

Inclusion of the remainder of these costs is consistent with the requirements of the NFC Guidance and the assumptions are consistent with the NFC site experience.

After proposed adjustment 4, the revised cost per procedure is $28,386, an increase of $4,773 relative to the 2010 indexed cost. This increase is explained as follows:

- Additional Cardiology transoesophageal echocardiogram cost in 2015/16 ($221), blood cross match double in price from $450 to $900 per patient ($450) due to price increase and complexity of patients resulting in average cost per test to increase.
- Higher paid Cardiothoracic Anaesthetist consultant used in 2015/16 (Impact estimated as $2663). Theatre hours remain the same at 10hrs per patient.
- additional 0.5 day ward stay required before theatre.
INTENSIVE CARE / HIGH DEPENDENCY UNIT ADMISSION

The NFC site has reported total costs per annum of $263,676 (excluding on-costs and overhead allocations) for intensive care costs (including immunosuppression and diagnostic investigations). This equates to an average cost of $52,735 per procedure excluding on-costs and overhead allocations, or $68,639 per procedure (inclusive of all costs). Costs included are summarised in the table below.

Table 4.10: Intensive care costs (2015/16)

<table>
<thead>
<tr>
<th>Item</th>
<th>Timeframe</th>
<th>Per annum</th>
<th>Per procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU stay (clinical staff and bed costs)</td>
<td>10 days</td>
<td>$184,997</td>
<td>$36,999</td>
</tr>
<tr>
<td>Investigations</td>
<td></td>
<td>$39,988</td>
<td>$7,998</td>
</tr>
<tr>
<td>Drugs</td>
<td></td>
<td>$38,156</td>
<td>$7,631</td>
</tr>
<tr>
<td>Nutrition &amp; special supplements</td>
<td></td>
<td>$535</td>
<td>$107</td>
</tr>
<tr>
<td><strong>Total (excluding on-costs)</strong></td>
<td></td>
<td><strong>$263,676</strong></td>
<td><strong>$52,735</strong></td>
</tr>
<tr>
<td>On-costs</td>
<td></td>
<td>$22,322</td>
<td>$4,464</td>
</tr>
<tr>
<td>Overheads</td>
<td></td>
<td>$57,200</td>
<td>$11,440</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>$343,198</strong></td>
<td><strong>$68,639</strong></td>
</tr>
<tr>
<td>2010 Assessment (indexed)</td>
<td>14 days</td>
<td></td>
<td>$83,300</td>
</tr>
</tbody>
</table>

Inclusion of these costs is consistent with the requirements of the NFC Guidance and the assumptions are consistent with the NFC site experience (median ICU stay of 10 days, noting that average ICU LOS is 12 days). The underlying bed day rate for the ICU stay was $2,043 per day, with an additional $373 per day included for consumables. The overall rate used by AHM is lower than the national ICU rate (inclusive of overheads) of $200 per hour ($4,800 per day) determined by IHPA as part of 2015-16 National Pricing Model (a linear regression by state/territory was used to derive state/territory hourly ICU costs).

The ICU costs reported are significantly less than the 2010 Assessment, principally a result of a reduction in the underlying bed days from 14 days, to 10 days.

GENERAL WARD ADMISSION

The NFC site has reported total costs per annum of $175,326 (excluding on-costs and overhead allocations) for ward stay costs (including readmissions). On a cost per procedure basis this equates to $35,065 per procedure excluding on-costs and overhead allocations, or $44,115 per procedure (inclusive of all costs). Costs included are summarised in the table below.
<table>
<thead>
<tr>
<th>Item</th>
<th>Timeframe</th>
<th>Per annum</th>
<th>Per procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ward stay (clinical staff and bed costs)</td>
<td>10 days</td>
<td>$77,286</td>
<td>$15,457</td>
</tr>
<tr>
<td>Investigations</td>
<td></td>
<td>$18,785</td>
<td>$3,757</td>
</tr>
<tr>
<td>Drugs</td>
<td></td>
<td>$17,867</td>
<td>$3,573</td>
</tr>
<tr>
<td>Nutrition &amp; Special supplements</td>
<td></td>
<td>$535</td>
<td>$107</td>
</tr>
<tr>
<td>HITH for Mycobacterium patients</td>
<td>1 patient (91 days)</td>
<td>$23,222</td>
<td>$4,644</td>
</tr>
<tr>
<td>Readmission</td>
<td>33% of patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICU</td>
<td>1 day</td>
<td>$9,668</td>
<td>$1,934</td>
</tr>
<tr>
<td>Ward</td>
<td>8 days</td>
<td>$27,963</td>
<td>$5,593</td>
</tr>
</tbody>
</table>

**Total (excluding on-costs)** $175,326 $35,065

**On-costs** $8,487 $1,697

**Overheads** $36,762 $7,352

**Total** $220,575 $44,115

2010 Assessment (indexed) $61,312

Inclusion of these costs is consistent with the requirements of the NFC Guidelines and the assumptions are consistent with the NFC site experience (median ward stay of 10 days, noting that average ward LOS is 15 days). The underlying bed day rate for the ward stay was $445 per day (noting this excludes the salary costs of the specialist clinical team which are included at hourly rates). In addition, costs include:

- Hospital in the home costs related to *Mycobacterium* patients. An underlying daily rate of $242 was used to cost this care.
- Readmission included at rates consistent with the recent experience of the NFC site

The ward stay costs reported are significantly less than the 2010 Assessment, principally a result of:

- A reduction in the ward length of stay from 14 days to 10 days
- A reduction in the assumed readmission rate from 100% of patients to 33% of patients
- Partially offset by the inclusion, for the first time, of the hospital-in-the-home costs for *Mycobacterium* patients.

**Outpatient care prior to discharge**

The NFC site has reported total costs per annum of $230,738 (excluding on-costs and overhead allocations) for outpatient costs prior to discharge from the NFC Program. This equates to an average cost of $46,148 per patient excluding on-costs and overhead allocations, or $59,385 per patient inclusive of all costs. Costs included are summarised in the table below.
Table 4.12: Outpatient costs prior to discharge (2015/16)

<table>
<thead>
<tr>
<th>Item</th>
<th>Per annum</th>
<th>Per procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient staff costs</td>
<td>$123,702</td>
<td>$24,740</td>
</tr>
<tr>
<td>Investigations</td>
<td>$46,594</td>
<td>$9,319</td>
</tr>
<tr>
<td>Drugs</td>
<td>$57,762</td>
<td>$11,552</td>
</tr>
<tr>
<td>Consumables</td>
<td>$1,000</td>
<td>$200</td>
</tr>
<tr>
<td>Local transport for interstate patients</td>
<td>$1,680</td>
<td>$336</td>
</tr>
<tr>
<td><strong>Total (excluding on-costs)</strong></td>
<td><strong>$230,738</strong></td>
<td><strong>$46,148</strong></td>
</tr>
<tr>
<td>On-costs</td>
<td>$16,700</td>
<td>$3,340</td>
</tr>
<tr>
<td>Overheads</td>
<td>$49,488</td>
<td>$9,898</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$296,926</strong></td>
<td><strong>$59,385</strong></td>
</tr>
<tr>
<td>2010 Assessment (indexed)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The review has made the following observations:

- Outpatient clinical costs are included based on hourly rates on the program's intended outpatient follow-up schedule.
- Investigation costs include bronchoscopy, bronchoalveolar lavage and biopsy (conducted monthly, over a three month period) totalling $28,145 per annum (excluding on-costs and overheads).
- Drug costs include immunosuppressant’s (Tacrolimus ($100), Azathioprine/Mycophenolate mofetil, Prednisolone) daily, for 90 days, totalling $37,633 per annum (excluding on-costs and overheads).

‘Local transport for interstate patients’ (proposed adjustment 5), the WEIS-funded bronchoscopy costs within ‘investigations’ (proposed adjustment 6), and PBS-funded outpatient drug costs (Tacrolimus and oral valganciclovir) (proposed adjustment 7) have been removed as alternative funding sources existing for these items. After adjustment the restated outpatient costs are $42,886 with the increase reflective of increases in the price of drugs.

**Other direct patient costs**

The NFC site has reported total costs per annum of $114,325 (excluding on-costs and overhead allocations) for other direct patient costs. Costs included are summarised in the table below.
Table 4.13: Other direct patient costs (2015/16)

<table>
<thead>
<tr>
<th>Item</th>
<th>Per annum</th>
<th>Per procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transition</td>
<td>$13,326</td>
<td>$2,665</td>
</tr>
<tr>
<td>Accommodation and parent/carer flights</td>
<td>$82,240</td>
<td>$16,448</td>
</tr>
<tr>
<td><strong>Total (excluding on-costs)</strong></td>
<td><strong>$95,566</strong></td>
<td><strong>$19,113</strong></td>
</tr>
<tr>
<td>On-costs</td>
<td>$638</td>
<td>$128</td>
</tr>
<tr>
<td>Overheads</td>
<td>$18,121</td>
<td>$3,624</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$114,325</strong></td>
<td><strong>$22,865</strong></td>
</tr>
<tr>
<td>2010 Assessment (indexed)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. **Transition costs** relate to the costs of providing transition support back to local care after the three month education and rehabilitation. These costs included clinical staff time as well as flights interstate to meet with the referring respiratory specialist and local adult lung transplant service for interstate patients. As these costs are outside of the defined NFC-funded pathway, and the review has proposed these be removed from the costing in full (refer proposed cost adjustment 8).

2. **Accommodation and parent/carer flights** have been costed in relation to:
   - Flights for parent/carer of interstate patients to relocate to Melbourne at $1,500 per family (three per annum)
   - Pre-transplant accommodation (one month) in Melbourne for relocated families at $160 per night (3 families per annum). These costs have been determined as being outside of the defined NFC-funded pathway, and the review has proposed these be removed from the costing in full ($4,080 before overhead, and $4,896 per patient inclusive of overhead; proposed cost adjustment 9).
   - Post-transplant accommodation in Melbourne to cover 28 days in-patient stay plus 90 days rehab/education at $160 per night (three families per annum)
   - Other sundry costs (such as local transport and wheelchair hire). These costs total less than $100 per patient and have been accepted as immaterial.

These costs are consistent with the recent experience of the NFC. However, we noted that the recently released NFC Guidance includes standard costs for air travel ($1,308.60) and accommodation ($123.21 per night) which are less than the costs applied in the AHM revised costing. Reducing the costs to these NFC standard costs results in a cost reduction per patient (excluding on-costs and overhead) of $2,720 (refer proposed cost adjustment 10). Inclusive on on-costs and overhead the reduction is $3,536 per patient.

### 4.3.4 Program management costs

The NFC site has reported program management costs as follows:
Program management costs have increased significantly from the 2010 Assessment, however this is principally attributed to the allocation of the Head of Paediatric Lung Transplant Program (0.6 FTE) and Paediatric Lung Transplant Coordinator (1.0 FTE) entirely to this cost category, whereas in the prior review, while the total FTE was the same (i.e. 1.6 FTE in total) the costs were spread across multiple cost categories, with only 0.38 allocated to 'program management'.

Staff education costs related to attendance at the Paediatric Advanced Life Support (PALS) course, and in-service education through clinical placement at ECH and education days. These costs have been determined as being outside of the defined NFC-funded pathway, and the review has proposed these be removed from the costing in full ($11,659 before overhead, and $13,991 per patient inclusive of overhead; proposed cost adjustment 11).

### 4.3.5 INDIRECT COSTS

Indirect costs have been included in the costing as follows:

- Salary on-costs, determined as 13.5% of base salaries. Total on-costs are $131,331 per annum ($26,265 per patient)
- Overheads determined as 20% of costs, in accordance with the NFC Guidance standard costs. Total overheads are $337,964 per annum ($67,593 per patient)

The review considers these costs have been appropriately calculated.

### 4.3.6 SALARY RATES

A large proportion of costs included in the AHM-revised costing relate to salary costs. As part of the review HOI compared a sample of the rates used to the Victorian Public Health Sector Enterprise Agreement, and through this process it was identified that a number of ‘loadings’ have been applied to base rates used in the costing calculations as follows:
Table 4.15: Combined impact of salary loadings

<table>
<thead>
<tr>
<th>Item</th>
<th>Effective multiplier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base rate</td>
<td>1.00</td>
</tr>
<tr>
<td>Initial loading of 30%</td>
<td>1.30</td>
</tr>
<tr>
<td>Application of on-costs of 13.5%</td>
<td>1.47</td>
</tr>
<tr>
<td>Application of 20% overhead rate</td>
<td>1.77</td>
</tr>
</tbody>
</table>

As a consequence, the combined effect is that salary costs have a 77% loading in the costing. While the review has accepted the application of the 13.5% on-cost rate and the 20% overhead rate, it is considered that the 30% initial loading is an error in the site’s calculations. This view is supported by the review of the 2010 Assessment report which identified, that at that time, AHM applied a 30% loading to base rates to account for salary overhead. Based on our analysis it appears that the site has erroneously continued to apply this rate, as well as, applying the new on-cost and overhead rates. It is our determination that this has overstated costs by $17,307 per patient (excluding on-costs and overhead) and $23,494 per patient (inclusive of all costs) (proposed cost adjustment 12). However, we note that the NFC site considers that the 30% loading is necessary to account for ‘shift penalties, allowances and overtime’.

4.3.7 Summary of adjusted costs and price recommendation

The review of submitted costs has identified a number of proposed cost adjustments. The impact of these adjustments on the submitted NFC site costs are presented in Table 4.16 below. It should be noted that the adjusted comparative price column provides the adjusted 2015/16 price for items that were endorsed in 2010, but now determined to be outside the defined NFC-funded care pathway. As a consequence of the proposed adjustments, the revised cost is:

1. $101,088 (28%) less than the existing 2015/16 price per procedure, principally as a result of the removal of cost components currently included in the price that are now outside of the defined NFC-funded care pathway.
2. $11,738 (5%) more than the ‘adjusted comparative price’ per procedure.
### Table 4.16: Summary of proposed adjustments to costs (2015/16) per procedure

<table>
<thead>
<tr>
<th>Item</th>
<th>AHM revised cost 2015/16</th>
<th>Adjusted comparative price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Submitted costs per procedure</td>
<td>$319,950</td>
<td>$361,975</td>
</tr>
<tr>
<td><strong>Adjustments:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Cost categories outside NFC pathway</td>
<td>($56,675)</td>
<td>($86,660)</td>
</tr>
<tr>
<td>2. Program acceptance costs (volume adjustment)</td>
<td>($1,059)</td>
<td>-</td>
</tr>
<tr>
<td>3. Remove ECMO-bridge-to-transplant</td>
<td>($9,683)</td>
<td>-</td>
</tr>
<tr>
<td>4. Remove transport costs prior to admission</td>
<td>($6,778)</td>
<td>($7,187)</td>
</tr>
<tr>
<td>5. Remove local transport in outpatient pathway</td>
<td>($336)</td>
<td>-</td>
</tr>
<tr>
<td>6. Remove WEIS funded investigations from outpatient pathway</td>
<td>($5,148)</td>
<td>-</td>
</tr>
<tr>
<td>7. Remove PBS funded ‘drug costs’ from outpatient pathway</td>
<td>($8,265)</td>
<td>($8,763)</td>
</tr>
<tr>
<td>8. Remove ‘transition’ costs</td>
<td>($2,665)</td>
<td>($7,784)</td>
</tr>
<tr>
<td>9. Remove pre-transplant travel</td>
<td>($4,080)</td>
<td>($4,326)</td>
</tr>
<tr>
<td>10. Revised travel and accommodation rates</td>
<td>($3,497)</td>
<td>-</td>
</tr>
<tr>
<td>11. Remove education costs</td>
<td>($11,659)</td>
<td>($6,758)</td>
</tr>
<tr>
<td>12. Correction to salary loadings</td>
<td>($12,279)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Revised cost per procedure</strong></td>
<td>$198,603</td>
<td>$249,149</td>
</tr>
<tr>
<td>Adj. to existing 2015/16 price</td>
<td>($101,088)</td>
<td></td>
</tr>
<tr>
<td>% of existing price</td>
<td>-28%</td>
<td></td>
</tr>
<tr>
<td>Adj. to comparative 2015/16 price</td>
<td>$11,738(^{(a)})</td>
<td></td>
</tr>
<tr>
<td>% of comparative price</td>
<td>4.7%(^{(a)})</td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**
(a) This increase effectively represents the impact of the changed methodology for on-cost and overhead charges. In the prior review on-costs (30%) and overheads (13%) were applied only to salary-based items in the costing. In the current costing, on-costs (13.5%) are applied to salary-based cost elements, and overheads (20%) applied to all costs. HOI has estimated the impact of this change, based on the accepted cost-items identified above, is an increase is costs per patient of approximately $28,800. The balance of the increase predominantly relates to costs associated with Mycobacterium patients.
**Recommendation:** It is recommended that the NFC Reference Group endorse the revised pricing structure from 1 July 2015 for the delivery of the NFC PLHLT Program of **$260,887 per procedure**. The price should be indexed in subsequent financial years in accordance with the NFC Guidance.

*(Consolidated list of recommendations 2)*
CONCLUSION

This chapter presents a summary of the review findings and recommendations for the future NFC status of the NFC PLHLT Program.

5.1 SUMMARY OF KEY REVIEW FINDINGS

Based on our assessment of the NFC PLHLT Program delivered at AHM in collaboration with the RCH, it has been demonstrated that the program provides high quality services and delivers excellent patient outcomes that are comparable to international standards.

Based on the evidence analysed against the NFC Guidance criteria and with assessment of contemporary evidence base in providing this procedure, it is recommended that the NFC PLHLT Program continues as a concentrated service at a single site as part of the NFC Program, with modifications to amend the target group for the NFC PLHLT Program to children and adolescents four to 15 years typically weighing ≥10kg.

5.1.1 ASSESSMENT AGAINST NFC GUIDANCE CRITERIA

The key findings of the assessment the NFC PLHLT Program in accordance with the NFC Guidance criteria are summarised below.

1. Access. A total of 37 patients were referred to the NFC PLHLT Program between 1 July 2011 and 25 September 2015, representing an average referral rate of 8-9 patients per year. A total of 15 patients have undergone PLHLT between 1 July 2011 and 25 September 2015 under the program representing an average of three to four patients per year. Referrals and transplant rates broadly reflect birth populations across Australia, however, Victoria appears over-represented NSW appears under-represented (the annual transplant rate per million population in Victoria was four times that for NSW (2.03 per million compared with 0.51 per million)). As a comparison, HOI has determined the equivalent rate in North America is 0.71 per million (for children aged 6 to 17).

2. Health outcomes. Outcomes from the NFC PLHLT Program appear similar to international outcomes data collected by ISHLT. Since NFC status, four of the 15 children transplanted under the NFC PLHLT Program have died as a consequence of complications related to transplantation (non-adherence, a common problem in adolescent health, was an important contributor to poor outcomes in two of the transplanted children). Comparison of one-year survival rates with ISHLT data are as follows:
   - 6 to 10 year olds: NFC program 100% survival (three patients alive); ISHLT 95.2% (50 patients alive)
   - 11 to 17 year olds: NFC program 75.0% survival (nine patients alive); ISHLT 81.1% (226 patients alive)

3. Model of care and service delivery. The NFC PLHLT Program offers a continuum of care that extends from the point of admission for the definitive treatment to three months post discharge from hospital following that treatment.
A number of modifications and initiatives have been implemented to address limitations of delivering a paediatric service in an adult hospital.

The current model of care includes screening assessment prior to acceptance to the program that includes a visit by the NFC PLHLT team to the patient’s home jurisdiction, as well as a five day inpatient stay in Melbourne for detailed assessment (costs are material and outside of the costed pathway included under the NFC Guidance). Referring clinicians considered these visits to be extremely valuable components of the Program.

Referring clinicians also reported high levels of satisfaction with the NFC PLHLT Program, having excellent working relationships with the NFC site and were supportive of the model of care provided by the Program.

SCHN clinicians have expressed the view that that the model of care (paediatric transplantation in an adult setting at only one national site) is inappropriate, and that the NFC PLHLT Program should reside in a paediatric hospital, and/or be supplemented with an additional site to better support the Australian population.

4. **Non-inpatient services.** Following discharge from the program, care is transferred either to the PLHLT Program’s hospital-based clinic or local services interstate including life-long support by a local transplant team.

5. **Quality and safety.** The NFC site has well established plans, protocols and clinical guidelines to deliver the Program to a high standard of quality and safety. Adverse events have been documented and appropriately managed by the sites and referring practitioners.

6. **Teaching, training and research.** Members of the program’s multidisciplinary team at the NFC site actively contributed to teaching, training and research both locally and internationally.

7. **Emerging clinical practice.** The AHM/RCH are now accepting appropriate patients on ECMO-bridge-to-transplant and/or patients colonised with *Mycobacterium abscessus* or *Burkholderia cenocepacia* who would previously have been contraindicated for transplant. The NFC PLHLT team is expecting that these patients are likely to comprise around 20-25% of new referrals in the future.

The NFC site has proposed the program should be expanded to include patients 4-15 years with a minimum weight of 10kg, and are exploring the possibility of providing a service to younger children (less than five year old) at the RCH with input from the AHM transplant team in the future. There was broad stakeholder support for lowering the minimum age limit for the Program, and this is supported by our international expert in line with international best practice.

In an effort to counter the lack of organs, the program is accepting more marginal organs (e.g. donation after cardiac death, with the majority of these organs from Victoria) and conducting lobar transplants.

AHM reported that they are in the process of considering the purchase of EVLP technology but that this was not included in the costs of services. It is noted by HOI that organ retrieval and organ donation, and by extension the costs of EVLOP technology, are outside of the scope of the NFC Program. States and Territories are responsible for providing (and funding) deceased organ retrieval services.

Our international expert has advised that ABO-incompatible lung transplant should not currently be part of the NFC PLHLT Program.

8. **Service demand.** The estimated demand for services in the next three to five years is likely to stay the same or increase slightly based on the following:
- **Steady number of referrals.** All referring clinicians and jurisdictional stakeholders consulted were of the opinion that in the next five to 10 years the overall number of referrals to the program would be unlikely to change significantly

- **Increase in number of patients able to be transplanted.** AHM/RCH predict a slight increase in number of transplants per year in the next three years based on program acceptance of more marginal patients (e.g. patients on ECMO or with *Mycobacterium abscessus*) and more marginal donor organs.

Based on our review of the evidence base and in consultation with our international clinical expert it is considered that the NFC Reference Group should continue to approve the delivery of PLHLT services at a single site.

9. **Risk Management.** AHM reported working within established risk management frameworks and guidelines. Key risks arising from the provision of a paediatric service in an adult hospital were identified early in the establishment of the service at AHM, and strategies developed and implemented to largely mitigate these risks.

10. **NFC PLHLT Program costs.** The program was established from 1 July 2011 based a price of $314,266 and included funding for: screening of referrals ($13,354); pre-acceptance work-up and assessment ($52,358); and the decision to accept ($5,468). In total, 22.6% ($71,180). The price per procedure funded items that were not considered part of the current definition of the NFC-funded episode of care. Consistent with the NFC Guidelines, the Review has made cost adjustments to remove these items from the cost per procedure.

HOI’s analysis of the costs data that were reported by the NFC site identified a number of potential adjustments. As a consequence, the Review determined a price per procedure (2015/16) of $260,887.

### 5.2 OPPORTUNITIES FOR IMPROVEMENT

This Review identified the following opportunities for improvement to be considered by the NFC Reference Group:

1. **Expanded target cohort.** It is recommended that the NFC Reference Group endorse the expansion of the target cohort of patients to include children and adolescents 4 to 15 years typically weighing ≥10kg. (Consolidated list of recommendations 3)

2. **Inclusion of previously contraindicated patients.** It is recommended that the NFC Reference Group endorse the practice of the NFC site to accept certain previously contraindicated patients (ECMO-bridge-to-transplant and/or patients colonised with *Mycobacterium abscessus* or *burkholderia cenocepacia*) on a case by case basis. Should the NFC Reference Group endorse these changes, it is recommended that the outcomes of higher risk patients be separately reported to the NFC Reference Group as part of the NFC annual reporting process. (Consolidated list of recommendations 4 and 5)

3. **Build linkages to collect longer term complications data.** It is recommended that the NFC PLHLT site develop linkages to collect and document long-term complications such as diabetes, hypertension etc. (Consolidated list of recommendations 6)

4. **Definition of the NFC care pathway.** It is noted that the NFC Reference Group has an AHMAC approved review cycle for the NFC Guidance (every three years) and it is recommended that this include definitions of the ‘care pathway’ and the circumstances where deviations from that care pathway require AHMAC approval. (Consolidated list of recommendations 7)
5. **Regular review of NFC Guidance.** It is noted that the NFC Reference Group has an AHMAC approved review cycle for the NFC Guidance (every three years) and it is recommended that the review process should incorporate invitations to jurisdictions to provide regular feedback to ensure urgent or critical matters are addressed in an appropriate timeframe. (Consolidated list of recommendations 8)

6. **Improved communication to referrers.** It is recommended that NFC site reviews communication processes with referrers to provide information on contemporary treatment and outcomes data to referrers, explain referral, patient support and discharge protocols, and provide opportunities for referrers to provide feedback and recommendations for the future. (Consolidated list of recommendations 9)

7. **Improved post-discharge support.** It is recommended that as part of the standard discharge protocols for the NFC program that the NFC site facilitates as post-discharge develop videoconference or similar involving all stakeholders (including the patient/family) to ensure consistency in the post-discharge support provided by the NFC PLHLT Program and consistency in the care provided by local services. (Consolidated list of recommendations 10)

8. **Reporting of readmissions.** It is recommended that the NFC reporting template be amended to specifically require the number of patient readmissions to be reported. (Consolidated list of recommendations 11)

**5.3 Future review of the NFC PLHLT Program**

In accordance with the NFC Guidance, the next evaluation of the NFC PLHLT Program should be conducted under the NFC Program in three years.
APPENDIX A: LITERATURE REVIEW

The objectives of the literature review were to establish a comprehensive evidence base of the published literature since the conduct of the initial 2010 NFC Paediatric Lung and Heart-Lung Transplantation assessment to form the basis of the current review as to whether the clinical practice/technology still warrants NFC status and whether the current NFC service is satisfactory. From this perspective, the key focus of the literature review was on the following:

- Clinical activity and service demand
- Transplantation indicators and demographics
- Waitlist acceptance and organ allocation processes
- The transplantation process
- Contemporary developments in clinical practice and procedure
- Health outcomes and variations.

A detailed methodology for the literature review is presented below.

LITERATURE REVIEW SEARCH STRATEGY

LITERATURE REVIEW OBJECTIVES

The objectives of the literature review are to establish a comprehensive evidence base of the published literature since the conduct of the initial 2010 NFC Paediatric Lung and Heart-Lung Transplantation assessment to form the basis of the current review as to whether the clinical practice/technology still warrants NFC status and whether the current NFC service is satisfactory. From this perspective, the key focus of the literature review will be to address the research questions to assess the safety and effectiveness of the program by describing the relevant population, intervention and outcomes.

SEARCH QUESTIONS

Review questions have been based on the objectives of the literature review and the requirements of the NFC Review Criteria, and are outlined below. Note that data from sites provided during the project and obtained during the consultation process will also provide additional information to address some of these questions.

Access

1) What is the demographic profile of children undergoing lung or heart-lung transplantation internationally and in Australia? Consider age, weight, diagnoses, and location.

2) What are the international and Australian clinical indicators for paediatric lung or heart-lung transplantation, and how do these vary by age group?

3) What are the international best practice clinical acceptance criteria for patient inclusion or exclusion for paediatric lung or heart-lung transplantation, including absolute and relative contraindications for the procedure?
4) How do these acceptance criteria compare with clinical acceptance criteria at the NFC Paediatric Lung and Heart-Lung Transplantation site?

5) To what extent do patients undergoing NFC Paediatric Lung and Heart-Lung Transplantation meet the clinical acceptance criteria and what are the reasons for any deviation?

6) How do Australian allocation criteria for determining priority or allocation of available donor organs compare with international allocation criteria for paediatric lung and heart-lung transplantation?

**Health outcomes**

7) What health outcomes are being achieved with paediatric lung and heart-lung transplantation in terms of perioperative and postoperative morbidity and mortality, both internationally and for the Australian NFC site?

8) Do outcomes vary by the type of transplant received? For example:

   - Bilateral lung deceased donor transplant
   - Single lung deceased donor transplant
   - Heart-lung transplant
   - Living donor lung transplant?

9) What other factors, if any, contribute to differences in health outcomes for each of the above procedures (e.g. patient demographic variables, clinical acceptance criteria, timing of procedure, surgeon/hospital volumes, post-operative in hospital care, outpatient care)?

10) What is the optimal throughput and critical mass of patients required to deliver acceptable outcomes for these procedures? Consider both surgeon and hospital volumes.

11) How are data collected to assess health and quality of life outcomes over time?

12) What are the complications and readmission rates internationally and in Australia for paediatric lung and heart-lung transplantation?

**Service demand**

13) What is the existing and forecast future demand for the procedure taking into account any changes in clinical practice?

**Models of care and service delivery (including non-inpatient services)**

14) What is the current best practice model of care for paediatric lung and heart-lung transplantation in terms of service scope, continuum of care, workforce, clinical infrastructure, equipment and facilities, relationship between paediatric and adult programs, and relationship with and role of referring practitioners?

15) What clinical guidelines, treatment protocols and care pathways exist for the provision of paediatric lung and heart-lung transplantation?

**Changes to clinical practice**

16) What recent or foreseeable changes, if any, exist in the clinical indications, patient population or management of patients requiring paediatric lung or heart-lung transplantation?
Teaching, training and research
17) To what extent has the Australian NFC site been involved in research and clinical trials regarding paediatric lung and heart-lung transplantation?

Proposed review search terms
The review criteria and proposed review search terms with respect to the relevant population, intervention, comparators and outcomes (PICO) for the literature scan are presented in Table below. Note that identification of comparators is not relevant to this review. It is anticipated that the search terms will include (but not be limited to) those presented in Table, and will use Boolean operators (e.g. AND, OR) as required.

Table A.1: Primary and secondary search terms

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Primary search term</th>
<th>Secondary search terms used to narrow or broaden search as required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>Paediatric</td>
<td>Age, Weight, Diagnosis</td>
</tr>
<tr>
<td>Intervention</td>
<td>Lung transplantation, Heart-lung transplantation</td>
<td>Indicators, Acceptance criteria, Inclusion, Exclusion, Contraindications, Allocation criteria, Model of care</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Outcomes, Morbidity, Mortality, Survival, Volume-outcome relationship, Quality of life</td>
<td>Perioperative, Postoperative, Long term Measures</td>
</tr>
</tbody>
</table>

Literature review strategy
The proposed strategy has been designed to reflect the objectives of the research project and the subject content. HOI will apply a systematic approach to the conduct of the literature review applying frameworks informed by the Cochrane Handbook for Systematic Reviews of Interventions. This scan will seek to collate all evidence that fits pre-specified eligibility criteria in order to address the project objectives. Critical appraisal is an integral process in the review of research and other material and HOI will endeavour to identify methodological flaws within the literature and make informed decisions on the reliability, validity and quality of the research evidence obtained.

Material relevant to paediatric lung or heart-lung transplantation will be obtained through a range of methods such as:
- preliminary Internet scan
- targeted electronic database search using key terms and set parameters
- reference to specific government or non-government organisations relevant to the topic
• text, reference or academic hard copy materials (where applicable)
• material recommended by specialists and relevant stakeholders
• material referenced in NFC site submissions
• ‘snowballing’ or identifying relevant author and research through reference lists of primary materials
• citation tracking or ‘forward searching’ which involves reviewing materials that have used the primary material as a reference in more recent material.

The literature garnered through this review is generally categorised as a primary, secondary or tertiary source:
1. Primary source- original research from journals, articles or conferences.
2. Secondary source- evaluations, meta-reviews or syntheses of original work.
3. Tertiary source- formal overview material such as an academic text or reference book.

All material that will be included in the literature review discussion paper will be appropriately referenced within the concluding bibliography. Table below presents key criteria for the present literature review strategy.

<table>
<thead>
<tr>
<th>Search characteristics</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review Scope</td>
<td>• Primary source- original research from journals, articles or conferences.</td>
</tr>
<tr>
<td></td>
<td>• Secondary source- evaluations, meta-reviews or syntheses of original work.</td>
</tr>
<tr>
<td>Data Sources – general databases</td>
<td>The following databases will be accessed during this review. However, the list is not exhaustive and additional journal search databases will be utilised by the project team.</td>
</tr>
<tr>
<td></td>
<td>• Cochrane – <a href="http://www.cochrane.org">www.cochrane.org</a></td>
</tr>
<tr>
<td></td>
<td>• Pubmed, PubMed Central, Medline</td>
</tr>
<tr>
<td></td>
<td>• Google</td>
</tr>
<tr>
<td></td>
<td>• Ovidsp</td>
</tr>
<tr>
<td>Data Sources – systematic review databases</td>
<td>• Cochrane Database of Systematic Reviews and the Centre for Reviews and Dissemination DARE database (Database of Abstracts of Reviews of Effects)</td>
</tr>
<tr>
<td></td>
<td>• Centre for Reviews and Dissemination DARE database (Database of Abstracts of Reviews of Effects) including the accompanying HTA database and NHS EED (NHS Economic Evaluation Database)</td>
</tr>
<tr>
<td>Search timeframes</td>
<td>The scan will be limited to literature published from the year 2010 on (except for seminal or formative work preceding this year) and will include material published in English only.</td>
</tr>
</tbody>
</table>

**CRITICAL APPRAISAL OF THE RESEARCH LITERATURE**

A key consideration for this project is that the literature review produces findings that will inform and add to the present evidence base relating to the NFC Paediatric Lung or Heart-Lung Transplantation procedure. Robust research outcomes will in turn facilitate the development of evidence based hospital reform. The literature review methodology will encompass the search strategy design, data
extraction and synthesis for quality assurance purposes. Modifications to the standard systematic review process have been proposed to reflect better the topic of study and to reduce the length of time taken to conduct the review while not compromising on the effectiveness and applicability of the findings.

Critical appraisal aims to identify the quality of the material identified through the literature search. HOI will undertake critical appraisal of the research through application of Critical Appraisal Tools. The relevant criteria for this review are presented in the table below:

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Elements considered</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bibliographic details</strong></td>
<td>• Author</td>
</tr>
<tr>
<td></td>
<td>• Source</td>
</tr>
<tr>
<td></td>
<td>• Year of research and publication</td>
</tr>
<tr>
<td><strong>Study design</strong></td>
<td>• Randomised control</td>
</tr>
<tr>
<td></td>
<td>• Cohort</td>
</tr>
<tr>
<td></td>
<td>• Pre and post hoc study</td>
</tr>
<tr>
<td></td>
<td>• Observational</td>
</tr>
<tr>
<td></td>
<td>• Case-control</td>
</tr>
<tr>
<td></td>
<td>• Population based or cross-sectional</td>
</tr>
<tr>
<td></td>
<td>• Case study</td>
</tr>
<tr>
<td></td>
<td>• Evaluation</td>
</tr>
<tr>
<td><strong>Aims and study methodology</strong></td>
<td>• Were the aims clearly identified and reflected in the study design?</td>
</tr>
<tr>
<td></td>
<td>• Quality of research design and methodology including data collection</td>
</tr>
<tr>
<td></td>
<td>• Quality of tools used within study (if relevant)</td>
</tr>
<tr>
<td></td>
<td>• Sufficient description regarding study methodology</td>
</tr>
<tr>
<td></td>
<td>• Study setting and context</td>
</tr>
<tr>
<td></td>
<td>• Potential study biases</td>
</tr>
<tr>
<td>Criteria</td>
<td>Elements considered</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Ethical conduct                | • Was the study undertaken ethically?  
• Was the methodology independently approved?  
• Was informed consent obtained?  |
| Sample and population          | • Participant number  
• Study population (sampling processes if applicable)  
• Participant selection processes (inclusion and exclusion criteria)  
• Generalisability of findings |
| Study findings                 | • Were the defined and measured outcomes appropriate?  
• Were the findings statistically significant?  
• Will these findings have relevance to current research aims?  
• To what extent are the study findings generalizable?  
• What did the authors conclude based on the findings? How were the findings interpreted? |
| Outcomes available             | • Quantitative data only  
• Qualitative data only  
• Quantitative and qualitative data |
| Quality of source              | • Credibility of the material source  
• Currency of the material |
| Study overview                 | • Strengths and weaknesses of the study, theory, policy and practice implications?  
• Implications of finding to present project  
• General comments or key reference identified |

Not all criteria will apply to all research material such as secondary sources and grey literature. However, the critical analysis of this type of literature focuses on the quality of the information, the credibility of the source, currency, relevance and applicability to the current project.

**A BRIEF HISTORY OF PAEDIATRIC LUNG AND HEART-LUNG TRANSPLANTATION**

Since lung transplantation was pioneered in 1963, over 43,000 transplantations have been undertaken in adults across the globe. The first paediatric patient to undergo lung transplantation was a 16 year old boy presenting with familial pulmonary fibrosis in 1987 and between this year and 2014, 1,875 children (of all ages, including infants) have since received a lung transplant (Kirkby & Hayes, 2014). As a slightly newer procedure, the first adult heart-lung transplant was performed in 1981 followed by a paediatric heart-lung transplantation conducted in 1986 in 15 year old girl (Orr, 2014).

Since 1986, significant developments in surgical procedures, perioperative and postoperative management, recipient selection and organ allocation processes, have resulted in steady improvements in short term survival of transplantation, amongst other outcomes.
CLINICAL ACTIVITY AND SERVICE DEMAND

In 2011, 43 transplant centres across the globe reported undertaking paediatric lung transplantation procedures with the majority of centres located in the United States and Europe (where ‘paediatric’ is defined as under 18 years of age). Between 2006 and 2011, although just over 100 children received a lung transplant each year, it is evident that most paediatric centres have very low procedure volumes compared with adult programs (Kirkby & Hayes, 2014). Only five paediatric centres worldwide reported performing over five paediatric lung transplants annually in 2010 (Khan et al, 2015). Internationally the number of paediatric heart-lung transplantation procedures undertaken has steadily decreased over the years (Benden et al., 2012).

Australia represents <3% of all PLHLTs conducted internationally. According to the International Society for Heart and Lung Transplantation (ISHLT) Registry, there were five paediatric lung or heart-lung transplants performed in Australia during the period 1 January 2013 through to 30 September 2014, one of which was a heart-lung transplant. These transplants represented 2.4% of all paediatric lung and heart-lung transplant activity reported through the ISHLT Registry during this time (refer table below).

| Table A.3: Paediatric lung and heart-lung transplant activity in Australasia, 17 years and younger, 1 January 2013 - 30 September 2014 (ISHLT, 2014) |
|-------------------------------|--------------------------|-----------------------------|---------------------------------|
| Transplant and recipient age group | Australasia | Entire ISHLT Registry | Proportion of international activity |
| Lung Transplant |
| <1 year | - | 6 | - |
| 1-5 years | - | 17 | - |
| 6-10 years | - | 30 | - |
| 11-17 years | 4 | 137 | 2.9% |
| Heart-Lung Transplant |
| <1 year | - | - | - |
| 1-5 years | - | 3 | - |
| 6-10 years | 1 | 5 | 20.0% |
| 11-17 years | - | 8 | - |
| Combined total | 5 | 206 | 2.4% |

The timing of transplantation is heavily influenced by the availability of donor organs. Keeshan, et al (2015) report that the number of lung transplants undertaken per year has risen in both paediatric and adult cohorts, and posit that improvements in donor matching and allocation have resulted in this increase in volume in an environment where supply (donor pool) has not simultaneously increased. In 2011, the Scientific Registry of Transplant Recipients (SRTR) in the United States reported in 2011 that of those paediatric candidates removed from the waiting list:

- 38.8% were removed from due to transplant
- 26.5% were removed due to death
- 12.2% were removed after their condition improved
6.1% were removed due to being too unwell to undergo the procedure.

Whilst there remains a significant demand for transplant, waitlist mortality in the United States has reduced from 28.3% per 100 wait-list years in the 1998/99 cohort to 11.2% in 2002/03 with the figure remaining relatively stable since this time (15% per 100 wait-list years in 2010/11) (SRTR, 2011). Data obtained through the Australia and New Zealand Organ Donation (ANZOD) Registry indicates that very few donor organs were retrieved from donors under the age of 14 between 2004 and 2013 (noting that these data, presented in Table, groups older paediatric patients with younger adults, meaning that data for ages 15 to 18 alone, were not available). This limited supply of paediatric organs has important clinical implications, as lung and heart-lung transplant from adults to younger children in particular, is not generally feasible due to the physical size differences in donor organs and recipient organ and chest cavity. As such, size matching is critical to this type of transplant (S. C. Sweet & Barr, 2014).

### Table A.4: Lung and heart-lung donor age of transplanted organs in Australia between 2004-2013 (ANZOD, 2015)

<table>
<thead>
<tr>
<th>Organ</th>
<th>Age 0-4</th>
<th>Age 5-14</th>
<th>Age 15-24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lungs</td>
<td>0</td>
<td>30</td>
<td>203</td>
</tr>
<tr>
<td>Left Lung</td>
<td>0</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>Right Lung</td>
<td>0</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Heart Lung</td>
<td>0</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>0</td>
<td>38</td>
<td>237</td>
</tr>
</tbody>
</table>

Whilst Australia is currently challenged by a limited supply of younger donor organs, the distribution of organs by donor age is also variable across different geographic regions internationally. Figure A.1 indicates that between 2000 and 2012, 75% of donors for paediatric lung transplant in the United States and 43% of donors in Europe were aged under 18 years. European figures were similar to that obtained for ‘other’ countries (which may include Australia) however, divergence can be seen in the number of donors aged between 0-10, with the United States having substantially more availability for this age group compared to countries outside of Europe and America (Benden et al., 2013).
In response to national shortages of paediatric lung donors, the Alfred Hospital has developed strategies to support young children awaiting lung transplantations. One approach is to use lungs donated after cardiac death (DCD) in lieu of the use of lungs donated after brain death (DBD) which have historically been relied upon for transplantation. This practice has been increasing since 2006 in response to donor shortage and to increase the donor organ pool. The figure illustrates this trend in Australia based on data from the ANZOD Registry, although use in paediatric patients is not specified:

Figure A.2: Recipients of lung transplants by organ donor type – Australia (ANZOD, 2015)

The changing nature and improvements in surgical and post-surgical management over the past number of years has reduced the demand for heart-lung transplantation. Orr (2014) reported that the increasing demand for a scarce number of donor heart-lungs and the requirement for fair organ distribution and allocation led to an initial shift towards lung transplantation in patients whose hearts were structurally sound and functioning normally. More specifically, lung transplantation has also more recently become a viable option for patients with end stage pulmonary hypertension related to Eisenmenger’s syndrome (ES). Such patients, who once required a heart-lung transplant, are now able to undergo lung transplantation and concurrent intra-cardiac repair of congenital heart disease (CHD). Similarly, treatment for pulmonary hypertension has also improved such that the need for heart-lung
transplant in children with end-stage idiopathic pulmonary hypertension can often be delayed (Orr, 2014; Spahr & West, 2014). Our international clinical expert has also advised that even in patients with severe idiopathic pulmonary hypertension with right ventricular hypertrophy/dilation, in most cases a lung rather than heart-lung transplant can be undertaken as the heart will usually improve functionally post lung transplant.

However, despite these improvements and the flow on effect on the demand for heart-lung transplant in paediatric populations, Spahr and West (2014) consider that the procedure will not become obsolete. These authors reason principally that centres have started to become more inclined to perform this more complex procedure for congenital heart disease and that centres will also need to offer this option when other surgical and medical options are insufficient to address the increasingly complex cases which are presented.

**TRANSPANTATION INDICATORS AND DEMOGRAPHICS**

Clinical presentation for lung or heart-lung transplantation is usually dependent on primary diagnosis. Children may present with respiratory insufficiency or respiratory failure, exercise intolerance, poor growth, hypoxemia, carbon dioxide retention, abnormal pulmonary function test findings, and frequent respiratory exacerbations that require antibiotics and/or anti-inflammatory medications. Children with underlying pulmonary vascular disorders may present with syncope, exercise intolerance, poor growth, cyanosis, and impaired quality of life (Faro & Visner, 2013).

Across all paediatric age groups combined, cystic fibrosis (CF) is the most common indication for lung transplantation worldwide, followed by idiopathic pulmonary arterial hypertension (IPAH). Other less common indications include idiopathic pulmonary fibrosis (IPF), surfactant protein deficiencies and other diseases now more uniformly classified as childhood interstitial lung diseases, congenital heart disease (CHD), and re-transplantation (Faro & Visner, 2013). Table A.4 below presents international data on common indications for paediatric lung transplantation during 2012 for young people under 18 years of age. These data demonstrate the variance in the indication for lung transplants between the age groups. For older children and adolescents aged 11-17 years, CF is the indication for the majority of cases. However, for younger children this is less likely to be the case.

**Table A.4: Most common indications for paediatric lung transplantation, ISHLT (Kirkby & Hayes, 2014)**

<table>
<thead>
<tr>
<th>Age group</th>
<th>Indication for transplant</th>
<th>Proportion of total transplanted in age group</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year infants</td>
<td>Surfactant protein b deficiency</td>
<td>17%</td>
</tr>
<tr>
<td></td>
<td>Congenital heart disease</td>
<td>17%</td>
</tr>
<tr>
<td></td>
<td>IPAH</td>
<td>13%</td>
</tr>
<tr>
<td>1-5 years</td>
<td>IPAH</td>
<td>22%</td>
</tr>
<tr>
<td></td>
<td>IPF</td>
<td>17%</td>
</tr>
<tr>
<td></td>
<td>Pulmonary fibrosis (other)</td>
<td>9%</td>
</tr>
<tr>
<td></td>
<td>Retransplant</td>
<td>9%</td>
</tr>
<tr>
<td>6-10 years</td>
<td>CF</td>
<td>53%</td>
</tr>
<tr>
<td></td>
<td>IPAH</td>
<td>9%</td>
</tr>
<tr>
<td></td>
<td>BOS (non-retransplant)</td>
<td>7%</td>
</tr>
</tbody>
</table>
### Analysis of the ISHLT dataset in 2013 indicates that the majority of lung transplants between 1986 and 2011 have been carried out in older children (ages 11 to 17). As presented in Figure A.3, 73% of lung recipients were between these ages, up slightly from 70% in 2010, and age distribution has remained fairly consistent over this time period (Benden et al., 2013). Age distribution can however vary between geographical area internationally; Benden et al. (2013) report that across this time, 84% of transplants were performed in children above age 11 in North America, whilst 68% of transplants in Europe were performed for this age group. Nonetheless, whilst it would appear that there is some divergence by geographical location, the majority of paediatric lung transplant activity occurs between the ages of 11 and 17 across the globe.

**Figure A.3: Paediatric lung recipient age distribution by transplant year, ISHLT (Benden et al., 2013)**

The majority of paediatric lung transplants have been carried out in low volume centres and this distribution has remained steady since 1990 (refer Figure A.4). In 2011, 38 out of the 43 reporting centres conducted between 1 and 4 paediatric lung transplants each year and only two conducted between 10-19 procedures (Benden et al., 2013). Centres have not reported conducting more than 20 procedures per years since 1998 and the number of centres which did report this activity was small.
As previously discussed, the majority of paediatric lung transplants occur in centres in North America and Europe (18 and 20 centres reported in 2011 respectively) with very few centres outside these locations reporting the procedure (refer Figure A.5 below).

There is a higher proportion of lung transplants undertaken for patients with CF in Europe (73%) compared to North America and elsewhere (Benden et al., 2013) (Zafar et al., 2011).

In cases where patients have end-stage lung disease associated with or causing, cardiac dysfunction or CHD associated with pulmonary artery/vein abnormalities, heart-lung transplantation may be indicated (Orr, 2014) (Spahr & West, 2014). Heart-lung transplantation may also be considered following a previous transplantation. Evaluation for a heart-lung transplant will often occur when a patient has an underlying disease which is compromising cardiac and pulmonary function and has a predicted survival of less than two years as a result. For patients with a predicted survival to be greater than two years it has been suggested that the outcome benefit does not warrant the heart-lung transplant process at present (Benden et al., 2013).
Table A.5 below presents United States’ data on indications for paediatric heart-lung transplant by year of age from 1988-2013. Based on this data, paediatric heart-lung procedures during this time period were most likely due to a diagnosis of primary pulmonary hypertension (approximately 29.3% of all patients), followed by congenital heart disease and ES (19.7% and 16.0% respectively). Spahr and West (2014) analysed diagnosis data obtained from the Organ Transplant and Procurement Network and found that heart-lung transplants in response to ES as an indication have steadily decreased over the years and there had not been such a case from 2002 performed in the United States paediatric transplant population.

Table A.5: Indications for heart-lung transplant by age in the United States (1988-2013) (Spahr & West, 2014)

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>Age &lt;1</th>
<th>Age 1-5</th>
<th>Age 6-10</th>
<th>Age 11-17</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary pulmonary hypertension</td>
<td>1</td>
<td>13</td>
<td>11</td>
<td>30</td>
<td>55</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>5</td>
<td>13</td>
<td>4</td>
<td>15</td>
<td>37</td>
</tr>
<tr>
<td>Eisenmenger’s</td>
<td>2</td>
<td>6</td>
<td>2</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>Congenital</td>
<td>1</td>
<td>10</td>
<td>2</td>
<td>7</td>
<td>20</td>
</tr>
<tr>
<td>CF</td>
<td>-</td>
<td>1</td>
<td>4</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Lung re-transplant</td>
<td>-</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Restrictive cardiomyopathy</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Pulmonary vascular disease</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td>Heart re-transplant</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Alpha 1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Alveolar proteinosis</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>7</td>
<td>18</td>
</tr>
<tr>
<td><strong>All diagnoses</strong></td>
<td><strong>16</strong></td>
<td><strong>52</strong></td>
<td><strong>28</strong></td>
<td><strong>92</strong></td>
<td><strong>188</strong></td>
</tr>
</tbody>
</table>

As with lung transplantations, the majority of heart-lung transplants were undertaken in older children. The number of heart-lung transplants carried out in total has been steadily decreasing across the globe over the years. This figure has also changed over time such that no heart-lung transplantations have been reported in infants between 2007 and 2010 (Benden et al., 2012). These data are presented in Figure A.6.
Similar to the findings in relation to paediatric lung transplantation, there are some divergences in heart-lung transplantation when analysing by age and geographic region. In Europe, 72% of heart-lung transplants were undertaken in children aged between 6 and 17 with the United States reporting more transplants in the 0-5 age group between 2007 and 2010 (refer Figure A.7) (Benden et al., 2012). Again, despite the differences by region, the majority of heart-lung transplants are carried out in older children and adolescents.

**Comments from our international expert.** Our international expert has indicated that in terms of foreseeable changes to clinical indicators or patient populations, patients are presenting with increasing complexities and co-morbidities to transplant centres. Also, ABO-incompatible infant lung transplants have now been successfully completed (Grasemann et al, 2012) and this has increased, and will continue to increase, the organ donor pool for infants specifically.

**WAITLIST ACCEPTANCE AND ORGAN ALLOCATION**
Careful patient selection and timing of transplantation are important to ensure that the opportunities for positive outcomes are maximised. Timing of surgery can significantly influence the survival benefit,
which entails an understanding of the stage and course of the primary disease to balance out the need to delay the transplantation to maximise survival potential, while endeavouring to provide a necessary transplant before death while on a waiting list (Sweet et al., 2008); (Liou, Adler, Cox, & Cahill, 2007).

There are a range of clinical and medical guidelines available to assist practitioners in this complex decision at the point of identification for referral to a transplantation centre and at waitlisting for transplantation post acceptance to a centre.

According to the American Society of Transplantation consensus statement, regardless of diagnosis, all lung transplant candidates should possess (Weill et al., 2015):

1. A clear diagnosis or adequately delineated trajectory of illness despite optimal medical therapy that puts the individual child at risk of dying without a lung transplant.
2. An adequate array of family support personnel.
3. Adequate access to transplant services and medications after transplantation.
4. Adequate evidence of willingness and ability on the part of patient and parent to adhere to the rigorous therapy, daily monitoring, and re-evaluation schedule after transplant.

In addition, there are several important anatomical, physiological, psychosocial and epidemiologic factors that are unique to paediatric lung transplantation such as:

- size of both paediatric lung donor and recipient and matching of lung size and bronchial and vascular anastomoses
- maturity of immune systems (in particular for infants)
- risk of certain infections issues such as seasonal respiratory tract viruses following transplant
- nutrition, gastroesophageal reflux disease and risk of aspiration
- adherence to prescribed therapies for adolescents.

In Australia, the Transplantation Society of Australia and New Zealand (TSANZ), *Organ transplantation from deceased donors: Consensus statement on eligibility criteria and allocation protocols (Version 1.4 — 15 April 2015)* outlines lung recipient inclusion and exclusion criteria (across all age groups) without specific reference to paediatric criteria. The 2010 NFC Assessment Review recommended (recommendation 4) the ‘development of clinical protocols and acceptance criteria, drawing on best practice in the linked adult program and the best international paediatric programs’.

Although indications for lung transplantation in children have expanded over time, the decision to undergo such a procedure should take into account the trajectory of the underlying illness and psychosocial factors such as the emotional readiness of the patient to the associated demands of daily therapy and frequent procedures (Faro & Visner, 2013). The literature suggests that there are cognitive, academic and behavioural concerns that may arise for children who have undergone thoracic transplantation. Therefore, appropriate psychosocial evaluation and counselling in the pre-and post-transplant period is important for young people (Brosig, Hintermeyer, Zlotocha, Behrens, & Mao, 2006).

The ISHLT has recently released a 3rd edition to their Consensus Report for the Selection of Lung Transplant Candidates, a component of which covers relevant inclusion and exclusion criteria and considerations for paediatric lung transplantation candidate selection. The ISHLT confirms that similar to adults, children should be referred to a centre when they present with a progressive lung disease on maximal medical therapy, a short predicted life expectancy and a poor quality of life. Particular considerations in a paediatric context are that potential candidates for transplantation should be referred as soon as possible particularly for smaller patients as the waiting times for transplantation...
tend to be longer. Whilst appropriate family support should be in place, it is also critical that the child themselves commits to the procedure and the follow up medical regimen (Weill et al., 2015).

The full range of testing that can be undertaken to assist in the determination of suitability for lung transplantation and the purpose for these tests are presented in Table A.6 below.

Table A.6: Testing to determine appropriateness for paediatric lung transplant (Faro & Visner, 2013)

<table>
<thead>
<tr>
<th>Test</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory testing</td>
<td></td>
</tr>
<tr>
<td>Complete blood count with differential</td>
<td>Determine baseline values and screen for underlying immunodeficiency</td>
</tr>
<tr>
<td>Prothrombin time and/or activated partial thromboplastin time</td>
<td>Detect abnormalities that may complicate surgery if untreated</td>
</tr>
<tr>
<td>Blood typing and screening</td>
<td>Donor and recipient matching</td>
</tr>
<tr>
<td>Renal disease battery</td>
<td>Detect adverse effects of calcineurin inhibitors and certain antimicrobial agents</td>
</tr>
<tr>
<td>Liver function tests and/or hepatitis battery</td>
<td>Assess for abnormal results which could contraindicate lung transplantation</td>
</tr>
<tr>
<td>Preformed reactive antibody panel</td>
<td>Assess the risk of developing antibody-mediated rejection</td>
</tr>
<tr>
<td>Lipid profile</td>
<td>Detect adverse effects of certain immunosuppressant agents</td>
</tr>
<tr>
<td>Human immunodeficiency virus (HIV) venereal disease research laboratory test</td>
<td>Assess for abnormal results which could contraindicate lung transplantation</td>
</tr>
<tr>
<td>Immunoglobulin G serologic tests for rubeola, rubella, herpes, Epstein-Barr virus, varicella, toxoplasmosis, and cytomegalovirus (CMV)</td>
<td>Screen for previous exposure and the need for vaccination</td>
</tr>
<tr>
<td>Autoimmune screening</td>
<td>Screen for antinuclear antibodies, antinuclear cytoplasmic antibodies, rheumatoid factor, and quantitative immunoglobulins (in specific patients)</td>
</tr>
<tr>
<td>Arterial blood gas tests</td>
<td>Measure of lung function</td>
</tr>
<tr>
<td>Thyroid profile</td>
<td><em>(No reason provided by author.)</em></td>
</tr>
</tbody>
</table>

# References

- Weill et al., 2015
### Imaging

<table>
<thead>
<tr>
<th>Test</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest radiography</td>
<td>Determine the extent of disease</td>
</tr>
<tr>
<td>Chest computed tomography (CT) scanning</td>
<td>Determine the extent of disease and the size of the thorax and vessels</td>
</tr>
<tr>
<td>Ventilation-perfusion scanning</td>
<td>Assist in determining the function of both lungs and, in a bilateral sequential procedure, to determine which lung should be replaced first</td>
</tr>
<tr>
<td>Echocardiography</td>
<td>Evaluate for pulmonary hypertension</td>
</tr>
<tr>
<td>Sinus CT scanning</td>
<td>Determine the need for surgical intervention in patients with CF before transplantation</td>
</tr>
<tr>
<td>Bone densitometry</td>
<td>Assess risk for fractures in patients with end-stage lung disease</td>
</tr>
</tbody>
</table>

### Other tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary function testing</td>
<td>Assist in determining the need for lung transplantation</td>
</tr>
<tr>
<td>Six-minute walk test</td>
<td>Assist in determining the need for lung transplantation</td>
</tr>
<tr>
<td>Sputum culture and susceptibilities</td>
<td>Inform choice of antimicrobial agents after transplantation</td>
</tr>
<tr>
<td>Purified protein derivative of tuberculin skin test</td>
<td>Rule out active tuberculosis (absolute contraindication)</td>
</tr>
<tr>
<td>Electrocardiography</td>
<td>Screen for right ventricular hypertrophy or other cardiac dysfunction</td>
</tr>
<tr>
<td>Cardiac catheterization</td>
<td>Measure degree of pulmonary hypertension or to assess benefits of vasodilator therapy (select cases)</td>
</tr>
</tbody>
</table>

### CONTRAINDICATIONS FOR TRANSPLANTATION

Contraindications for transplantation must also be considered in the process. In terms of contraindications for lung transplantation, Weill et al. (2015) explains that these are generally extrapolated from adult data and are therefore similar. However, these authors (amongst others) also explain that in the United States, medical and surgical contraindications for those under age 18 can vary between transplantation centres with some centres recognising absolute contraindications as relative contraindications and vice versa. Mechanical ventilation and extra corporeal life support (ECLS) as a bridge to transplantation in children is considered a relative contraindication in some centres but recent literature indicates that this may not be the case if patients are selected carefully. Weiss also explains that the contraindications identified in relation to adult patients may not be as relevant in a paediatric setting. Absolute and relative contraindications in paediatric lung transplantation are presented in Table A.7.
Table A.7: Absolute and relative contraindications (Conrad & Cornfield, 2014) Faro & Visner, 2013

<table>
<thead>
<tr>
<th>Absolute contraindications</th>
<th>Relative contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Active malignancy</td>
<td>• Pleurodesis</td>
</tr>
<tr>
<td>• Sepsis</td>
<td>• Renal insufficiency</td>
</tr>
<tr>
<td>• Active tuberculosis</td>
<td>• Markedly abnormal body mass index</td>
</tr>
<tr>
<td>• Severe neuromuscular disease</td>
<td>• Mechanical ventilation/tracheostomy</td>
</tr>
<tr>
<td>• Documented, refractory non-adherence</td>
<td>• Severe scoliosis</td>
</tr>
<tr>
<td>• Multiple organ dysfunction</td>
<td>• Poorly controlled diabetes mellitus</td>
</tr>
<tr>
<td>• Acquired Immunodeficiency Syndrome</td>
<td>• Osteoporosis</td>
</tr>
<tr>
<td>• Hepatitis C with histologic liver disease</td>
<td>• Chronic airway infection with multiply resistant organisms (Burkholderia cenocepacia, Burkholderia dolosa or Mycobacterium abscessus)</td>
</tr>
<tr>
<td>• ECMO</td>
<td>• Fungal infection/colonization</td>
</tr>
<tr>
<td>• Cerebral dysfunction</td>
<td>• Hepatitis B surface antigen positive</td>
</tr>
<tr>
<td>• Active hepatitis C infection</td>
<td>• Active collagen vascular disease</td>
</tr>
<tr>
<td></td>
<td>• Congenital or acquired immunodeficiency syndromes</td>
</tr>
</tbody>
</table>

Contraindications for lung transplant are also relevant when considering heart-lung transplantation. However, contraindications specific to heart-lung transplantation include extra cardiac disease such as severe end-organ disease (including renal or hepatic disease), human immunosufficiency virus (HIV) infection, other infection which is either active or treatment-resistant, significant aortopulmonary collaterals, allosensitisation as well as other psychosocial factors such as a psychiatric condition, severe depression and a history of poor adherence to medical regimes. Any previous thoracic surgery will also need to be considered (Spahr & West, 2014). Orr (2014) also explains that whilst contraindications for heart-lung transplant vary across centres and whilst the philosophy around this approach is changing with respect to paediatric patients, most centres are reluctant to carry out the surgery on patients undergoing venoarterial (VA)-ECMO.

**Priority allocation of donor organs**

Determination of priority allocation of available donor organs varies between countries at present. Allocation criteria can be based on length of waiting time (in itself problematic for lung and heart-lung transplantation) or urgency of need. Within Australia and the United Kingdom patients who are most ill are those who are prioritised for transplantation procedures (Morton, Malouf, Plit, Spratt, & Glanville, 2007). According to data from the Australia and New Zealand Cardiothoracic Organ Transplant Registry, there were 180 people (all ages) in Australia and New Zealand in 2013 waiting for lung transplantation with a mean wait time of 161 days (Keogh, Williams & Pettersson, 2013).

In Australia, the Transplantation Society of Australia and New Zealand (TSANZ) *Organ transplantation from deceased donors: Consensus statement on eligibility criteria and allocation protocols (Version 1.4 — 15 April 2015)* (TSANZ, 2015) sets out the current lung allocation protocols as follows (noting that there is no separate allocation process for paediatric lungs):
The recognised lung transplant unit in the home state is offered the donation as detailed below and given 30 minutes to respond to the offer.

If the home state declines the offer, the lung donation offer is made on to the non-home state recognised lung transplant units, with a 30-minute response time, based on a rotation kept by each state donor coordination team. If all recognised lung transplant units refuse the offer, it is then rotated through any units that have non-nationals awaiting transplantation.

<table>
<thead>
<tr>
<th>State of donor</th>
<th>Lung Transplant Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSW, ACT</td>
<td>NSW</td>
</tr>
<tr>
<td>VIC, TAS</td>
<td>VIC</td>
</tr>
<tr>
<td>QLD</td>
<td>QLD</td>
</tr>
<tr>
<td>WA</td>
<td>WA</td>
</tr>
<tr>
<td>SA, NT</td>
<td>On rotation through above states</td>
</tr>
</tbody>
</table>

The allocation of donor lungs is complicated by considerable issues of logistics and the permutations/combinations of the different options of potential lung (and or heart) transplant that a cardiothoracic transplant unit need to consider when donor organs are offered.

Donor lungs are allocated by the accepting lung transplant unit considering the following criteria.

1. ABO compatibility
2. Size compatibility
3. Absence of a positive T-cell cross-match
4. Where more than one potential recipient meets the above criteria the first choice will be determined by the following process:
   - Clinical urgency (Logistics, Long-term outcome benefit)
   - Recipient waiting time, all other factors being equal

Based on Organ Procurement and Transplantation Policies in the United States, if a patient listed for lung transplantation is aged 12 years or older the timing of the transplantation is dependent on their ‘lung allocation score’ which considers the risk of mortality while on the waiting list and potential transplantation benefit. In addition, the United States based United Network for Organ Sharing implemented an allocation system for children younger than 12 years of age. It prioritises allocation of lungs to the sickest child as determined through two distinct priority levels:

- **Priority 1:** Candidates that meet one of the following criteria:
  - Respiratory failure as defined by one or more of the following: continuous mechanical ventilation, forced inspiration of oxygen more than 50% to maintain saturation levels of more than 90%, an arterial or capillary PCO₂ more than 50 mm Hg or a venous PCO₂ of more than 56 mm Hg
  - Pulmonary hypertension as defined by any of the following: pulmonary vein stenosis involving 3 or more vessels, or has any of the following in spite of medical therapy - suprasystemic PA pressures, cardiac index > 2 L/min/M², syncope, haemoptysis

- **Priority 2:** all other patients under 12 years are priority 2 candidates.
Donor lungs are allocated first to the child with the most waiting time as a priority 1 candidate, who is also a suitable donor blood type and size match. If a suitable priority 1 candidate is not able to be identified, the donor lungs are offered to the child with the most waiting time on the priority 2 list.

**THE TRANSPLANTATION PROCESS**

Once allocation of donor organs is made, the transplantation process occurs over three distinct phases: (1) pre-operative assessment and management; (2) perioperative management and transplantation; and, (3) postoperative management of the patient. The ISHLT have released a number of clinical guidelines and protocols to guide some of these processes, the following of which are of relevance to paediatric lung and heart-lung transplantation:

- An International ISHLT/ATS/ERS Clinical Practice Guidelines: Diagnosis and Management of Bronchiolitis Obliterans Syndrome
- SHLT Monograph Volume 7: Pediatric Lung Transplantation
- ISHLT Monograph Volume 9: Pulmonary Hypertension and Right Heart Failure

The American College of Chest Physicians have also released evidence based clinical practice guidelines: Monitoring of Non-steroidal Immunosuppressive Drugs in Patients with Lung Disease and Lung Transplant Recipients.

**PREOPERATIVE MANAGEMENT**

Whilst patients remain on the waiting list a range of preoperative management strategies can be put in place to optimise their medical care and promote optimal health in order to undergo transplantation and to address any medical issues arising through the evaluation discussed above. Preoperative approaches or bridges to transplant can include the following where considered appropriate (Faro & Visner, 2013):

- improving the patient’s nutritional status
- providing pulmonary rehabilitation
- decrease the number of pulmonary exacerbations for which intravenous antibiotics are required
- apply medical therapies with epoprostenol or other pulmonary vasodilators, such as sildenafil and bosentan to patients with IPH
- use of the Novalung® Interventional Lung Assist device in patients with acute respiratory distress syndrome

Some surgical options are also available such as the placement of gastrostomy tube for nutritional resuscitation (Faro & Visner, 2013). However, as discussed previously at Section 3.4.1, thoracic surgeries can be a relative contraindication for heart-lung transplantation (Spahr & West, 2014).

**PERIOPERATIVE MANAGEMENT**

The application of an induction regime of immunosuppressive drugs to inhibit rejection of the lung allograft and in turn the development of bronchiolitis obliterans syndrome (BOS) can also be applied although this approach, and the drugs applied varies by transplant centre (Faro & Visner, 2013). Conrad and Cornfield (2014) indicate that around 60% of paediatric lung transplant recipients reported to the ISHLT received some form of induction therapy during the perioperative period.
Comments from our international expert. Our international expert has advised the following:

- Antibiotics are administered during the perioperative phase.
- Induction therapy is most commonly an interleukin-2 receptor antagonist and a minority receive anti-lymphocyte globulin or antithymocyte globulin (ref: ISHLT registry).
- Maintenance immunosuppression consists of triple immunosuppression, most commonly tacrolimus, mycophenolate mofetil/mycophenolic acid and prednisone in paediatric lung transplant recipients, although cyclosporine, azathioprine and prednisone is still used in a few centres.

Transplantation procedure

Currently, the most frequently performed procedure is a bilateral sequential lung transplant via median sternotomy. In this procedure, Conrad and Cornfield (2014) explain that the mainstem bronchi and left and right pulmonary arteries are connected via end-to-end anastomoses following which two pulmonary veins with intact atrial connections are harvested from each donor lung and each left atrial patch is connected to the recipient heart. The benefits of this particular approach are that cardiopulmonary bypass time is minimised which in turn can reduce the risk of surgical and postsurgical complications (Conrad & Cornfield, 2014).

Mancini (2014) described the contemporary heart-lung transplantation procedure to include the following steps although any relevant paediatric considerations were not identified. The procedure is undertaken using cardiopulmonary bypass. The heart and lungs are removed with care taken to preserve the phrenic nerves and to address bronchial artery circulation so as to prevent postoperative bleeding complications. Following this the donor organs are inserted and a tracheal anastomosis is performed, followed by the right atrial anastomosis and then the aortic anastomosis. Care must also be taken to ensure that the donor trachea is as short as possible given the limited vascularity of the area.

Postoperative management

Where surgical complications have not arisen, most patients will expect to remain in hospital for two weeks post-surgery. Whilst they remain intubated, frequent bronchoscopy may be required in order to evaluate the anastomotic site and to clear the airway from debris and secretions. Chest tubes will then be removed once they are draining less than the specified volume of fluid per day (dependent on size of recipient) and when no air leak is present. Ideally, patients will be extubated with 24-28 hours in order to minimise barotrauma and further oxidant injury and at this point the patient should be transferable from the intensive care unit (Faro & Visner, 2013). However, mechanical ventilation will be prolonged if there is evidence of graft dysfunction and inspired oxygen will be maintained at less than 60% while systemic arterial saturation is set at 94% or greater, to further minimise any damage (Conrad & Cornfield, 2014).

Intravenous antibiotics and other antimicrobials will be administered for two weeks and physical therapy including physiotherapy will also be initiated and intensified as necessary. At this point the patient should then be discharged to a post-transplantation centre close to the transplant centre’s grounds, although this can vary by centre (with some centres preferring for patients to remain within the hospital) (Faro & Visner, 2013). According to the transplant centre’s protocol patients will undergo a surveillance bronchoscopy with transbronchial biopsy (Faro & Visner, 2013). Furthermore, patients will also undergo maintenance immunosuppression. Faro and Visner (2013) explain that the majority of centres prefer to apply tacrolimus-based regimes as the side effects are more manageable for
paediatric patients which can in turn have a positive impact on adherence to the overall post-surgical regime.

Once discharged from the post-transplantation centre, patients require a suite of outpatient based care. Supports include (Faro & Visner, 2013):

- routine monitoring which can include pulmonary rehabilitation sessions and multiple visits per week to the centre to conduct laboratory and imaging testing
- therapeutic drug monitoring whereby patients are instructed to monitor vital indicators including their lung function, blood pressure, temperature, and weight on a daily basis
- daily spirometry (for children old enough to do so) which monitors forced expiratory volume in 1 second and oximetry for younger children
- bronchoscopy (noting the disparity in approaches by centre with some only conducting the procedure when clinically indicated and others more routinely doing so)

**CONTEMPORARY DEVELOPMENTS IN CLINICAL PRACTICE**

With the variation in the supply and demand of donor organs in paediatric patients, the most recent developments in clinical practice relate to developing or improving bridges to transplantation to either improve chances of survival whilst on the waiting list or improve outcomes post-transplant. Studies have focused in particular on paediatric patients who are contraindicated for transplant due to requiring ECMO.

Whilst the authors present some contemporary approaches to bridging children to transplant who would otherwise have been contraindicated and have obtained some positive results it is important to note, as did these authors, that further research is required in these areas and that the small sample size limits the studies to some extent. Also, longer term outcomes are not known given the recency of the research. However, this body of research does present centres with options to consider in their future service delivery.

**Patients on ECMO**

Hayes et al. (2013) explored the use of using active physical rehabilitation in a paediatric patient on venovenous ECMO as a bridge to transplant, through the placement of a single-site bicalval dual-lumen catheter. This approach facilitates respiratory support in a critically ill patient whilst avoiding sedation and the use of paralytics and allows for rehabilitation and nutrition methods to be applied. The authors explain that whilst this approach has been developing as a treatment option for some adult patients, there has been limited experience in this approach in a paediatric sample. Hayes et al. (2013) applied this approach in a 13 year old patient and suggested that physicians who are also caring for paediatric patients in their centres should be made aware of this approach as a potential option in patients who would usually be contraindicated for transplant.

Wong et al. (2015) also reported on a four year old child who was successfully bridged to heart-lung transplant using ambulatory veno-arterial ECMO and indicated that success had never been previously reported. Despite a number of post-surgical complications which occurred, including cardiac arrest and grade 3 primary graft dysfunction, the patient made a full recovery without any neurological issues. Wong et al. (2015) suggested that this approach could be considered to bridge younger children to either heart-lung or lung transplantation.
PARACORPOREAL LUNG ASSIST DEVICES

As an alternative to ECMO, Hoganson et al. (2014) explored the use of paracorporeal lung assist devices in neonates (one child aged 23 days) and young children (three, aged 2, 9 and 23 months) with decompensated respiratory failure as a bridge to recovery or lung transplantation. In this study, these patients who were placed on ECMO after decompensating were transitioned to a pumpless paracorporeal lung assist device with inflow from the pulmonary artery and return to the left atrium. The device bridged one patient to transplant, one to recovery (with maximal medical therapy) and whilst the remaining two died waiting for a suitable donor, they were supported past the average wait time for paediatric donor lungs (27 days) at 54 and 72 days respectively. The authors theorised that given paediatric patients who bridge from ECMO to transplant tend to derive poorer outcomes, the approach used here could be considered to bridge children with decompensated respiratory failure to lung transplantation.

Our international expert has advised that paracorporeal lung assist devices have also been in older aged children and adolescents.

ABO-INCOMPATIBLE LUNG TRANSPLANTATION

ABO-incompatible organs have been used in paediatric heart transplantation with positive outcomes reported and recently the transplantation of ABO-incompatible lungs has been undertaken in a 4-week old infant where a size compatible and blood group compatible organ was not available, marking the first procedure in an infant known to the authors. Six months post-transplant, the infant was reported to have experienced no episodes of graft rejection, his anti-B isohemagglutins remained negative with normal expiratory flows, weight and height and development (Grasemann, Perrot, Bendiak, Cox, van Arsdell, Keshavjee & Solomon, 2012).

Our international expert has advised that a second ABO-incompatible lung transplant has subsequently been successfully completed in an infant at this same centre, and that at two years of age this patient is doing well (data not published).

EX-VIVO LUNG PERFUSION

With more than 80% of donor lungs potentially injured and not considered suitable for transplantation, the use of normothermic ex vivo lung perfusion (EVLP) has been explored in order to assess damaged donor lungs for function and in turn, suitability for transplantation (Cypel et al., 2011). In a study where injured lungs removed from DCD and DBD donors were subjected to 4 hours of EVLP and transplanted (although the age of recipients was not specified), similar outcomes for recipients were obtained compared to lungs selected through traditional approaches (Cypel et al., 2011).

These authors posited that this method could be useful to assist in identifying lungs not suitable for transplantation which may otherwise appear functional according to other in vivo testing procedures and to assess DCD lungs for function.

It was reported by our international clinical expert that EVLP has already increased the number of transplants performed internationally utilising marginal or suboptimal donor organs, with a small number of centres worldwide using EVLP clinically. The future for EVLP was reported to be its use with uncontrolled DCD donor organs.

HEALTH OUTCOMES AND VARIATIONS

This section presents findings in relation to the health outcomes which are currently being achieved for transplant recipients and the changes which have occurred over time in outcomes achieved. Short and...
long term survival, variation in outcomes by procedure type, common complications and other factors which have implications on health outcomes are discussed.

**SHORT AND LONG TERM SURVIVAL**

Although long term outcomes for children receiving lung transplants remain moderate, there is clear evidence that survival after paediatric lung transplant has improved steadily over the years. Figure A.8 shows that patients who received a transplant in the most recent era (2002-2010) had a five year survival of 54% (and a 7 year survival of 44%), an improvement from 46% in children who received a transplant in the previous five years (Benden et al., 2012).

**Figure A.8: Kaplan-Meier survival in paediatric lung transplant recipients by era, ISHLT (Benden et al., 2012)**

Paediatric survival has also become somewhat level with adult survival, with median survival years reported at 4.9 and 5.4 respectively for transplants conducted between 1990 and 2011 (Kirkby & Hayes, 2014). These data are presented in Figure A.9.

**Figure A.9: Median survival in paediatric lung transplant recipients compared to adults (Kirkby & Hayes, 2014)**

The steady improvement in survival is mainly due to advances made in surgical procedure, anaesthetic management, post-transplant critical care management, organ preservation, infection prevention and control and treatment strategies to combat early graft rejection, as well as the refinement of recipient selection and allocation (Zafar et al., 2011). However, whilst initial survival rates have increased over the past two decades, long term survival rates have not changed during this time (Zafar et al., 2011).
Survival rates for heart-lung transplants have also increased over the years with five year survival rates similar to those recorded for lung transplantation (50%) using ISHLT data obtained from 2004-2010. This figure has increased from 45% between 1997 and 2003 (Benden et al., 2012; Spahr & West, 2014). These data are presented in Figure A.10.

**Figure A.10: Paediatric heart-lung transplants Kaplan-Meier survival by era (January 1982-June 2011), ISHLT (Spahr & West, 2014)**

![Survival Curve](image)

However, Spahr and West (2014) explain that whilst improvement in survival is evident and mainly due to an increased ability to respond to events such as surgical complications, early graft failure, infection and thromboembolism, a slow progressive decline in survival remains for heart-lung transplant recipients (as it does for lung recipients, discussed above) and that this steady decline usually results from chronic lung rejection.

**FUNCTIONING AND QUALITY OF LIFE**

Beyond short and long term survival, when considering health outcomes, consideration must also be given to the achievement of improved functioning and quality of life. In 2011, more than 80% of surviving recipients received a functional status (Lansky score/scale) of greater than or equal to 80 (of 100) at one and three years post transplantation (Benden et al., 2013). The Lansky scale is a specific measure for paediatric cohorts measuring from 10: ‘completely disabled, not even passive play’, to 100: ‘fully active’. A measure of 80 on the scale is equivalent to ‘restricted in strenuous play, tires more easily, otherwise active’. In terms of functioning, Gruber et al. (2012) specified further that for surviving lung recipients:

- improvements in their quality of life are evident
- a relatively normal life is achieved including attending school and participating in sports unless their lung function is impacted by BOS
- psychological symptoms (e.g. panic attacks or depression) which are common in the first weeks post transplantation generally reduce

For heart-lung recipients, in terms of functional ability in those who survive the transplant, an increased ability to engage in daily activities including sport/exercise has been reported, as has a general satisfaction in undergoing the transplant. However cognitive, academic and behavioural issues have arisen in some children (Spahr & West, 2014). The literature suggests that there are a number of challenges with respect to obtaining data around quality of life in paediatric transplant patients and these are discussed further on at Section 0).
Complications causing mortality and morbidity

A number of complications can arise post-transplant which can impact on quality of life, function and in the end, survival of both lung and heart-lung transplantation. Between 2008-2011, rehospitalisation of just over half of paediatric lung transplant patients occurred by one year post-surgery (Valapour et al., 2014). Kirkby and Hayes (2014) explain that the most common causes of death in first 30 days following lung transplantation for paediatric patients is graft failure which accounts for 30% of mortality within this timeframe. However, from one month to one year following transplantation, non-CMV infection and graft failure account for 50% of recipient deaths. Beyond this time, BOS becomes the most common cause of death and accounts for 40% of mortality rates at 1 to 3 and 3 to 5 years post-transplantation. Beyond five years, BOS still accounts for 47% of deaths and as such, remains the principal barrier to long term survival in paediatric patients (as it does for adult patients). Benden et al. (2012) provide a more detailed breakdown of causes of death in lung recipients at each post-surgical stage using ISHLT data from 1992 to 2011 (refer Table 5.1 below).

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>0-30 days</th>
<th>31 days – 1 year</th>
<th>&gt;1 – 3 years</th>
<th>&gt;3 – 5 years</th>
<th>&gt; 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchiolitis Obliterans</td>
<td>10.1%</td>
<td>38.3%</td>
<td>39.1%</td>
<td>45.2%</td>
<td></td>
</tr>
<tr>
<td>Acute rejection</td>
<td>2.6%</td>
<td>1.9%</td>
<td>1.0%</td>
<td>2.2%</td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>5.0%</td>
<td>3.3%</td>
<td>4.3%</td>
<td>6.0%</td>
<td></td>
</tr>
<tr>
<td>Non-lymphoma malignancy</td>
<td>0.6%</td>
<td>0.5%</td>
<td>3.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>3.1%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>13.2%</td>
<td>33.3%</td>
<td>15.3%</td>
<td>19.6%</td>
<td>10.7%</td>
</tr>
<tr>
<td>Non-cytomegalovirus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graft failure</td>
<td>30.7%</td>
<td>19.5%</td>
<td>23.4%</td>
<td>21.7%</td>
<td>20.2%</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>15.8%</td>
<td>3.8%</td>
<td>1.4%</td>
<td>1.1%</td>
<td></td>
</tr>
<tr>
<td>Technical</td>
<td>11.4%</td>
<td>3.1%</td>
<td>2.9%</td>
<td>3.3%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Multiple organ failure</td>
<td>9.6%</td>
<td>11.9%</td>
<td>4.8%</td>
<td>3.3%</td>
<td>7.1%</td>
</tr>
<tr>
<td>Other</td>
<td>16.7%</td>
<td>7.5%</td>
<td>9.1%</td>
<td>5.4%</td>
<td>6.0%</td>
</tr>
</tbody>
</table>

In terms of other comorbidity factors, using IHSLT data from 1994 to 2011, Benden et al. (2012) reported the following at one year and five years post-transplant for lung recipients (refer Table A.9):

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Within 1 year</th>
<th>Within 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>41.7%</td>
<td>69.8%</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>10.0%</td>
<td>32.8%</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>5.1%</td>
<td>15.8%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>23.5%</td>
<td>36.8%</td>
</tr>
<tr>
<td>BOS</td>
<td>13.2%</td>
<td>35.9%</td>
</tr>
</tbody>
</table>
Most common causes of death in heart-lung recipients and relative comorbidities are similar to those in lung transplant recipients, with graft failure the leading cause of death post-transplant within the first month and BOS steadily increasing as cause of death beyond one year post-transplant (Spahr & West, 2014). Causes of death in heart-lung recipients are presented in Figure A.11:

**Figure A.11: Leading causes of death for paediatric heart-lung transplant recipients from 0 to 15 years post-transplant (April 1994–June 2012), ISHLT (Spahr & West, 2014)**

![Diagram showing leading causes of death for heart-lung transplant recipients](image)

**Factors influencing outcomes achieved**

A range of demographic and medical factors can have implications on health outcomes post-surgery for both lung and heart-lung recipients. The impacts of procedure type, recipient age and centre volume are discussed below.

**Procedure type**

Although single lung transplantation is a relatively common option in adult lung transplantation, bilateral lung transplantation has become the preferred option for several end stage pulmonary diseases in paediatric patients (Orr, 2014). For children undergoing surgery, survival is reported to be significantly better with double rather than single lung transplantation, with median year survival recorded at 5.4 compared to 1.9 years (Benden et al., 2013).
Another alternative, or rather last resort option, is living related donor lobe lung transplant (LDLLT) which has been used in the past to increase the donor pool, in particular for those patients who would not survive the waiting list for cadaveric organs. However, very few procedures are now carried out internationally as the procedure is often unsuccessful (Oto, Miyoshi, Sugimoto, & Yamane, 2015) and reports are almost exclusively from centres in Japan.

In another study (Date et al., 2012), this time using a sample of 14 patients, 10 of which were paediatric, a single (as opposed to double) donor LDLLT was found to generate some positive results for patients who would otherwise have died very soon. However, survival among these 14 patients was significantly worse than the survival in a group of 78 patients undergoing bilateral LLDLT during the same period (P = .044). Yamane et al. (2012) (whose sample included 10 children out of a sample of 59 patients) have confirmed that this option is a limited but final option with satisfactory outcomes able to be achieved in pulmonary function when full transplant is not an option.

Indication

As can be seen a range of indications for transplantation exist. As discussed previously CF is the principal indicator for lung transplantation although Kirkby and Hayes (2014), Benden et al. (2013) and Conrad and Cornfield (2014) found that patients with or without the condition display similar post-operative outcomes in terms of median survival. Interestingly, whilst poorly controlled diabetes mellitus can be a relative contraindication for lung transplantation, Gruber et al. (2012) found that the presence of pre-transplant diabetes mellitus has been associated with improved health outcomes post-transplant including survival. These authors posited that the beneficial effects of insulin treatment and the less severe impact of developing diabetes pre as opposed to post transplant as potential explanations for this occurrence and noted that other authors were unsure of the reasons for their similar findings.

For recipients of a heart-lung transplant, patients presenting with ES or CHD tend to display worse health outcomes than for those who have received a transplant for primary pulmonary hypertension (PPH) (presented in Figure A.13), with median survival years recorded at 2.6 and 1.9 years compared to 4.7 years for those presenting with IPAH (Spahr & West, 2014). Spahr and West (2014) reason that this may be due to the fact that patients with PPH have less chronic disease and as a result may experience less deconditioning than in patients with ES or CHD.
Recipient age

In terms of lung transplant recipient age, Kirkby and Hayes (2014) found that whilst children aged 6-10 displayed improved earlier survival compared to other paediatric age groups, the difference in survival is not maintained long term, as presented in Figure A.14. Benden et al. (2013) also confirmed this finding when controlling for all indicating conditions.

For heart-lung transplantation, it has been debated whether infancy can predispose patients to poorer health outcomes including reduced chances of survival, compared to older children. There are challenges in making determinations around the impact on infancy at the time of transplant given so few are undertaken in this age group across centres, limiting the data to inform analysis (Spahr & West, 2014). However, these authors did find when analysing the ISHLT data from 1982 to 2011 that outcomes were worse in heart-lung recipients aged under one year, as presented in Figure A.15.
Centre volume

Khan et al. (2015) demonstrated that paediatric specific experience as well as centre volume impact on paediatric lung transplant outcomes, with paediatric specific experience particularly important in adolescence (13-17 year olds). Key findings from Khan et al include the following:

1. **In recipients aged ≤ 12 years**, who can present a more challenging transplant case compared to older children and adults for a variety of anatomical, physiological and neurodevelopmental reasons, there was a lower graft and patient survival rate in the low volume paediatric lung transplantation centres (defined as performing median <4 lung transplants per year) compared to high volume paediatric centres (≥4 per year, and ≥50% of these being in paediatric patients) (graft survival: half-life = 5.7 versus 2.2 years; patient survival: half-life = 7.6 versus 3.9 years). However, despite a tendency to improved patient and graft survival in high volume paediatric centres over adult centres (where over 50% of lung transplants are in adults, and noting that the median number of paediatric lung transplants in these centres per year was one), this did not reach statistical significance. Adult centres demonstrated graft and patient survival rates that were clinically significant but not statistically better than low volume paediatric centres.

2. **In older children (13-17 years)**, survival in high volume paediatric centres was better than in adult centres and was similar between low volume paediatric and high volume paediatric centres. These authors found that surgical issues were less important than non-surgical factors in explaining poorer survival outcomes for older children and adolescents in adult centres than in paediatric centres (even low volume paediatric centres), and propose that differences can be explained by superior effectiveness of paediatric centres in adolescent management following recovery from surgery. Issues in adolescent management relate particularly to a high non-adherence rate in this age group.

These authors continued that there may be too many transplant centres performing lung transplants in paediatric patients and that with the majority of centres performing less than 2 procedures per annum, centres may not be developing the expertise required to support this age group appropriately and effectively. This has particular implications for centres where pay for performance funding models have been implemented. In light of this, Khan et al. (2015) made the following commentary and recommendations:

- Paediatric lung transplantation should be performed at specialised centres with sufficient volume and specific expertise in paediatric patients.
However, decommissioning low volume centres could increase logistical issues for the patient and their families in receiving care and there is the potential that low volume centres who are in fact achieving comparably positive outcomes to higher volume centres could also be closed down as a result.

Low volume centres could consider engaging the more experienced or high volume centres in performance improvement (examples included comparing surgical and medical protocols and recipient selection criteria) in order to increase skills and in turn improve outcomes.

Adult centres should carefully consider the issues which are presented by taking on paediatric patients. This is particularly so in adolescent patients who have a high non-adherence rate and will require a sufficiently experienced team to support them.

Other factors impacting on health outcomes

Other factors which have been found to either improve or limit health outcomes post-transplantation have been identified:

- Collaboration between medical and surgical teams for lung transplant improve outcomes (Zafar et al., 2011)
- Pre-lung transplant admission to hospital is associated with poorer health outcomes including decreased early survival (Gruber et al., 2012)
- In terms of pre-heart-lung transplant interventions, those who require inotropic support, mechanical ventilation, and/or mechanical circulatory support have lower chance of survival post-transplant (Spahr & West, 2014)

Outcomes data collection and associated challenges

At an international level, data related to paediatric lung and heart-lung transplantation is collected through a number of databases. These include the ISHLT, Scientific Registry of Transplant Recipients (United States), Organ Procurement and Transplantation Network (United States) and more locally, ANZOD and the Australia and New Zealand Cardiothoracic Organ Transplant Registry.

The majority of the data referred to in the literature reviewed here has been obtained through the ISHLT who have established an international registry of these transplantation types. The benefits of using this particular data registry are twofold. First, the ISHLT compiles data from across the globe and is therefore not restricted to one geographic region and secondly, the database is specific to paediatric lung and paediatric heart-lung transplants as opposed to a general transplant data registry which tend not to provide more in depth details and data around paediatric samples.

Data has been collected on the ISHLT registry since 1983 and tracks both morbidity and mortality data post-transplant. Presently, 223 centres from 18 countries submit data to the registry. Whilst participation is voluntary and not all centres contribute their data, it is generally believed that the majority of centres do in fact do so (Kirkby & Hayes, 2014). The following key outcomes data are collected for use in analyses.

- Primary and contributory cause of death
- Hospitalisations and reasons for admission/s
- Functional status
- Academic progress and activity level
- Cognitive and motor development
- Height and weight
- Graft functioning and causes of failure
- Presence of BOS, CAD and other clinically significant events including viruses, malignancy, diabetes
- Rejection episodes
- Maintenance of medications

A number of challenges to collecting outcomes data have been identified in the literature. First, it may be difficult to assess the functional status and quality of life in paediatric patients who are not able to communicate and secondary reporting of quality of life and functional status by parents or attending physicians may be impacted by bias (Kirkby & Hayes, 2014). Secondly, whilst the data on the ISHLT registry is comprehensive, disease specific outcomes are not accessible through annual reports and access to data is based on application and prioritised according to most urgent need for the data (Sweet, 2013). The registry itself is also limited in terms of the level of detail with respect to infection and rejection (Sweet, 2013). Gruber et al. (2012) also argue that paediatric specific outcomes data is scarce and reliance must be made on organ function data.

SUMMARY OF KEY FINDINGS FROM THE LITERATURE REVIEW

Table A.10 provides a summary of the findings emerging from the analysis of contemporary developments in PLHLT that have been categorised in accordance with the six review domains.

<table>
<thead>
<tr>
<th>Review domain</th>
<th>Key findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical activity and service demand</td>
<td>1. The supply of organs is not currently meeting demand either in Australia or internationally in paediatric populations. With a limited supply of paediatric-sized organs (38 available from donors aged under 15 from 2004-13), Australian centres have implemented other options to support those who remain on the waiting list.</td>
</tr>
<tr>
<td></td>
<td>2. Significantly more paediatric lung than heart-lung transplants are undertaken both internationally and in Australasia. Internationally in 2011, 43 centres reported paediatric lung transplants (around 100 per year in total) whilst five transplants were reported in Australasia (including one heart-lung).</td>
</tr>
<tr>
<td></td>
<td>3. This difference in activity between transplant types is due to medical and surgical improvements mitigating the requirement for heart-lung transplant in some patients.</td>
</tr>
<tr>
<td>Indicators and demographics</td>
<td>4. Across all paediatric age groups, CF is the most common indication for lung transplantation in paediatric patients followed by IPAH.</td>
</tr>
<tr>
<td></td>
<td>5. Whilst there are some differences by geographical location internationally, the majority of paediatric lung transplant activity occurs between the ages of 11 and 17.</td>
</tr>
<tr>
<td></td>
<td>6. The overwhelming majority of procedures are conducted in low volume centres (1-4 transplants per year) in the United States and Europe.</td>
</tr>
<tr>
<td></td>
<td>7. The most common indication for paediatric heart-lung transplant is primary pulmonary hypertension (approximately 29.3% of all patients), followed by CHD and ES (19.7% and 16.0% respectively), although over the past years transplants for ES have declined significantly.</td>
</tr>
<tr>
<td></td>
<td>8. Whilst there are some geographic differences, the majority of heart-lung transplants have been undertaken in older children.</td>
</tr>
</tbody>
</table>
### Review domain: Waitlist acceptance and organ allocation

9. The decision to refer a patient to a transplant centre and to place them on the waitlist for transplantation is complex and both points and is guided by a range of clinical guidelines and protocols in each region or country internationally.

10. In general, children should be referred to a centre when they present with a progressive lung disease on maximal medical therapy, a short predicted life expectancy and a poor quality of life.

11. Potential paediatric candidates for transplantation should be referred as soon as possible particularly for smaller patients and whilst appropriate family support should be in place, it is also critical for the child themselves to commit to the procedure and the follow up medical regimen.

12. Contraindications for transplantation are generally similar to that in adults; however, classification of absolute and relative contraindication can vary between centres.

13. In terms of allocating organs to recipients, in Australia this process is guided by the TSANZ’s Organ transplantation from deceased donors: Consensus statement on eligibility criteria and allocation protocols which considers ABO compatibility, size compatibility, absence of positive T-cell cross-match at first and if multiple recipients meet these criteria, clinical urgency and recipient waiting time will be considered.

### The transplantation process

14. The transplantation process occurs over three distinct phases; pre-operative assessment and management, perioperative and transplantation and postoperative management of the patient.

15. Whilst patients remain on the waiting list preoperative management strategies are put in place to optimise their medical care and promote optimal health in order to undergo transplantation and to address any medical issues.

16. Perioperatively, an induction immunosuppression drugs to inhibit rejection of the lung allograft and in turn the development of BOS is applied in the majority of paediatric transplant centres.

17. The most frequently performed lung transplant procedure conducted is a bilateral sequential lung transplant via median sternotomy. Heart-lung transplants are undertaken using cardiopulmonary bypass.

18. Immediately postoperatively, patients will remain intubated and bronchoscopy may be undertaken to evaluate the anastomotic site and to clear the airway from debris and secretions. Patients will often be extubated within 24-28 hours and intravenous antibiotics and other antimicrobials may be applied for two weeks, along with physiotherapy therapy.

19. According to the transplant centre’s protocol patients will undergo a surveillance bronchoscopy with transbronchial biopsy and maintenance immunosuppression. Beyond this point, the patient will have multiple assessments on an outpatient basis to monitor progress.

### Contemporary developments in clinical practice

20. The most recent developments in clinical practice have been around developing or improving bridges to transplantation to either improve chances of survival whilst on the waiting list or improve outcomes post-transplant. These approaches have been developed in response to lack of organ availability. Studies have focused in particular on paediatric patients who have previously been contraindicated for transplant with ECMO or paracorporeal
### Review domain

<table>
<thead>
<tr>
<th>Key findings</th>
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<tbody>
<tr>
<td>lung assist devices as a bridge to transplant.</td>
</tr>
<tr>
<td>21. Other recent developments include successful transplant using ABO incompatible organs in infants, and increasing use of EVLP to increase the number of transplants able to be conducted using marginal or suboptimal donor organs.</td>
</tr>
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</table>

### Health outcomes

| 22. Whilst initial survival of paediatric lung and heart-lung transplantation has increased over the years (at around 50% survival at 5 years post-transplant for both procedures), long term survival has not changed in this time. |
| 23. More than 80% of lung recipient survivors obtained a functioning status of greater than 80% in 2011 three years post-transplant and many reported a good quality of life (including attending school and engaging in physical activity). Similar findings have been made for heart-lung recipients although cognitive and behavioural issues can arise. |
| 24. The most common causes of death in first 30 days post lung transplant is graft failure (accounting for 30% of deaths). However, from one month to one year following transplantation, non-CMV infection and graft failure account for 50% of deaths. BOS becomes the most common cause of death at 1-3 and 3-5 years post-transplantation (causing 40% of deaths) and continues to account for 47% of deaths beyond 5 years. For heart-lung recipients graft failure is the leading cause of death post-transplant within the first month and BOS steadily increasing as cause of death beyond one year post-transplant. |
| 25. Survival is reported to be significantly better with double rather than single lung transplantation, with median year survival recorded at 5.4 compared to 1.9 years for paediatric patients undergoing transplantation between 1990-2011. |
| 26. Indication for lung transplantation does not influence survival whilst heart-lung recipients presenting with ES or CHD tend to display worse health outcomes than for those who have received a transplant for primary pulmonary hypertension (PPH) with median survival years recorded at 2.6 and 1.9 years compared to 4.7 years for those presenting with IPAH. |
| 27. Whilst children aged 6-10 can display improved earlier survival post lung transplant compared to other paediatric age groups, the difference in survival is not maintained long term. For heart-lung transplant, outcomes are worse in recipients aged less than one year. |
| 28. In recipients aged less than 13, patient and graft survival was poorer in paediatric centres performing less than 4 lung transplants per year compared to paediatric centres performing ≥4 per year. However, there is no difference in survival rates for these patients between high volume paediatric centres and adult transplant centres (where median number of paediatric lung transplants was one per year). Delivering at least 4 lung transplants per annum in paediatric centres can improve outcomes, and those delivering less than this amount may not be developing the skills sufficient to achieve desired outcomes in this complex cohort. |
| 29. In recipients aged 13-17 years, patient and graft survival was poorer in adult centres compared with paediatric centres, particularly where paediatric centres conduct ≥4 lung transplants per year. This is primarily due to issues of non-adherence in adolescents. Adult centres performing lung transplantation in these patients must ensure than non-adherence and other psychosocial
### Review domain | Key findings
---|---
| | issues are adequately planned for and addressed.
30. There are a number of databases available but the ISHLT has been relied upon most for providing paediatric specific data on lung and heart-lung transplants. Despite a number of outcomes data being reported through the ISHLT, barriers remain in accessing data around quality of life in paediatric lung and heart-lung recipients.
APPENDIX B: LITERATURE REVIEW REFERENCES


Morrissey, O. Snell G., Lевvey B., Westall G., Cheng A, Bills H.. Department of Infectious Diseases, The Alfred Hospital, Melbourne, Australia, Lung Transplant Service, The Alfred Hospital, Melbourne, Australia, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Australia) Abstract presented ISHLT Annual meeting 2016


APPENDIX C: LUNG TRANSPLANT PUBLICATIONS AND PRESENTATIONS INVOLVING NFC STAFF

PAEDIATRIC LUNG TRANSPLANT PUBLICATIONS


Snell GI, Paraskeva M, Westall G. Managing bronchiolitis obliterans syndrome (BOS) and chronic lung allograft dysfunction (CLAD) in children: What does the future hold. 2013. Pediatric Drugs 15;


Westall GW, Burton JH, Marasco SF, Robertson CF, Snell GI; Lobar Lung Transplantation: a Novel Approach to Reduce Waiting list Mortality in Children Requiring Lung Transplantation; Respirology; March 2008; V13; S2


Westall GP, Merry C, Burton J, Robertson C, Snell GI; The Child with Advanced Lung Disease: Addressing an Unmet Need; Respirology 2007; 12: S1

Merry CJ, Negri JC, Rowland MA, Marasco SF, Esmore D, Snell G; Paediatric Lung Transplantation: Establishment and Early Experience in a Non-Paediatric Hospital. Heart, Lung and Circulation 2007; 16:S49


**Paediatric Lung Transplant Presentations**

July 2015 – New Zealand Thoracic Society, Rotarua
Oral presentation by Glen Westall – Transplantation in Children

April 2015 – International Society of Heart and Lung Transplantation, Nice, France
Poster presentation by Jenny Maree Marshall – Recovering and coping with new lungs in a big, big world: strategies to maximize paediatric lung transplant recovery and coping in the acute adult hospital setting

March 2015 - 19th Congress of the International Society for Human and Animal Mycology, Melbourne
Oral presentation by Glen Westall – Fungal Infection in Paediatric Lung Transplantation

September 2014 – CF Nurses Association Annual Meeting, Melbourne
Oral presentation by Glen Westall – Paediatric Lung Transplantation and Cystic Fibrosis

July 2014 – Transplantation Society of Australia & New Zealand, Canberra
Oral presentation by Greg Snell – Paediatric Lung Transplantation in Australia

July 2014 – World Congress of Cardiology, Melbourne
Oral presentation by Glen Westall – Paediatric Lung Transplantation and Pulmonary Hypertension

July 2013 – International Paediatric Transplant association, Warsaw, Poland
Poster presentation by Jenny Maree Marshall – The complexities of client centered practice for the core allied health respiratory clinician in Paediatric Lung Transplantation – Strategies for preserving human integrity and longevity in the field

April 2013 – International Society of Heart and Lung Transplantation, Montreal
Oral presentation by Glen Westall – The Presensitized Patient and Antibody-mediated Rejection

June 2012 – Transplantation Society of Australia and New Zealand, Canberra
Oral presentation by Glen Westall – Lung Transplantation and DCD

June 2011 – Transplant Coordinator’s Advanced Course, Canberra
Oral presentation by Glen Westall – Donation issues in Lung Transplantation
March 2010 – Cystic Fibrosis Tasmania, Launceston
Oral presentation by Glen Westall – Paediatric Lung Transplantation

August 2009 – 8th Australasian Cystic Fibrosis Conference, Sydney
Oral presentation by Glen Westall – Paediatric Lung Transplantation

July 2009 – Roche National Transplant Symposium, Melbourne
Oral presentation by Glen Westall – Paediatric Lung Transplantation

April 2009 – International Paediatric Transplant Association, Istanbul
Poster presentation by Jacquie Burton and Jenny-Maree Marshall – Education and Rehabilitation Programme following Lung Transplantation in Children
Oral presentation by Jacquie Burton – Cadaveric Lobar Lung Transplantation an Option for Paediatric patients Awaiting Lung Transplant
Oral presentation by Colleen Jackson – Body Composition and Bone Mineral Density Changes Post Lung Transplantation

August 2008 – International Society of Transplantation, Sydney
Poster presentation by Jacquie Burton and Jenny-Maree Marshall - Rehabilitation and Transition after Lung Transplantation in Children

May 2008 – International Paediatric and Child Health Nurses Conference, Darwin
Oral presentation by Jacquie Burton – Lung Transplantation in Children

March 2008 – Thoracic Society of Australia New Zealand & Australia and New Zealand Society of Respiratory Science Annual Scientific Meeting, Melbourne
Poster presentation by Jacquie Burton - Lobar Lung Transplantation: a Novel Approach to Reduce Waiting list Mortality in Children Requiring Lung Transplantation

November 2007 - Australian Transplant Coordinators Association and Transplant Nurses Association Conference, Melbourne
Poster presentation by Jacquie Burton - The Child with Advanced Lung Disease: Addressing an Unmet Need

August 2007 – Cystic Fibrosis Australia Conference, Sydney
Plenary presentation by Glen Westall – Paediatric Lung Transplantation
Poster presentation by Jacquie Burton - The Child with Advanced Lung Disease: Addressing an Unmet Need

March 2007 - Thoracic Society of Australia New Zealand & Australia and New Zealand Society of Respiratory Science Annual Scientific Meeting, Auckland
Poster presentation by Glen Westall - The Child with Advanced Lung Disease: Addressing an Unmet Need


