

Paediatric Liver Transplantation (PLT)

Review of Nationally Funded Centre Status

A report by the
Medical Services Advisory Committee
to the Australian Health Ministers' Advisory Council

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Mail Drop 106
GPO Box 9848
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The Medical Services Advisory Committee (MSAC) is an independent committee which has been established to provide advice to the Minister for Health and Ageing on the strength of evidence available on new and existing medical technologies and procedures in terms of their safety, effectiveness and cost-effectiveness. The MSAC also undertakes health technology assessment work referred by the Australian Health Ministers' Advisory Council (AHMAC), and reports its findings to AHMAC.
MSAC recommendations do not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

This report was prepared by the Medical Services Advisory Committee. The systematic review of the literature and the data analyses were conducted with the assistance of Ms Silke Wallerer and Dr Sally Lord from the NHMRC Clinical Trials Centre, University of Sydney. The report was edited by Matthew Stevens, ScienceScape Editing, Sydney.

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Executive summary

Paediatric liver transplantation in Australia

Paediatric liver transplantation (PLT) is the only treatment available for children with irretrievable acute liver failure or chronic end-stage liver disease. Untreated, these conditions lead to impaired growth and untimely death.

In Australia, 3 Nationally Funded Centres (NFCs) provide PLT services: the Royal Children's Hospital, Brisbane (RCHB); the Royal Children's Hospital, Melbourne (RCHM); and the Children's Hospital at Westmead, Sydney (CHWS). PLT is generally performed as whole liver transplantation (WLT), reduced-size liver transplantation (RLT) or split liver transplantation (SLT). Living-donor liver transplantation (LDLT) and liver cell transplantation (LCT) have also been performed in Australia.

Background to this review

The Medical Services Advisory Committee (MSAC) was established by the Australian Government to strengthen the role of evidence in health financing decisions in Australia. MSAC's fourth term of reference is to undertake health technology assessment work on behalf of the Australian Health Ministers' Advisory Council (AHMAC).

The NFC Program provides a national policy for public sector provision of high-cost, highly specialised clinical practices and technologies with limited demand.

The objectives of the NFC Program are to ensure that:

- there is maximal 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; and
- health and cost outcomes of these technologies are monitored and evaluated.

The NFC Program requires that a formal review be undertaken after the initial establishment of an NFC, to determine whether this status is still warranted.

PLT services at RCHB, RCHM and CHWS were approved for NFC status in 1993. AHMAC published a review of these sites in 2002 that concluded that the sites continued to meet the criteria for NFC funding. Other significant recommendations were:

- that the age for PLT be raised to include all children under 14 years;
- that all sites develop the capacity to perform SLT; and
- that a prescribed format for data collection, including costs, be established to ensure uniformity in reporting.

The present review was undertaken to update the 2002 review. It has been prepared by the MSAC at the request of AHMAC. The MSAC engaged a team from the NHMRC Clinical Trials Centre to support this work. The review was conducted in accordance with AHMAC guidelines and considered access; health outcomes; service delivery; quality and safety; teaching, training and research; the need for continued service concentration; cost; and cost estimates, as outlined in the *NFC Guidance for Management, Governance, Funding, Establishment and Review—April 2006*. This report provides MSAC's advice to the NFC Reference Group of AHMAC.

Review objectives and approach

Consistent with the guidelines for the review of existing NFCs, the objectives of this review were:

- to determine whether or not existing NFC sites and their activities should continue at a reduced, equal, or increased level for a further defined period; and
- to make appropriate recommendations.

The review considered each of the elements for review of existing NFC sites and used information from scientific literature, data provided by the 3 NFC sites as part of the annual statistical return data, information obtained through the Australia and New Zealand Liver Transplant Registry (ANZLTR) and information from the advisory panel's visit to each of the centres. In addition, a literature review of health technology assessment (HTA) reports and systematic reviews on PLT published since 2002 was conducted.

Existing systematic reviews

A search of the International Network of Agencies for Health Technology Assessment (INAHTA) database identified 2 systematic reviews of PLT published since 2002. One systematic review reported recent evidence that health-related quality of life (QoL) of children and adolescents receiving a PLT improved significantly after transplantation compared to before transplantation. A second systematic review investigated LDLT and found limited evidence from observational studies to suggest that LDLT was superior to other types of PLT in children younger than 2 years of age, but was less safe and effective than WLT and SLT in older children.

Review of the NFC PLT program against NFC review criteria

Access to the Nationally Funded Centres

Over the 7 years from July 1999 (CHWS: July 2002) to 2005–06 (RCHB: July 2005; RCHM: March 2006; CHWS: May 2006), 241 patients have been referred for treatment at the NFC PLT sites, of whom 206 (85%) were accepted onto a transplant program. Interstate referrals comprised between 10 per cent (RCHM) and 31 per cent (RCHB) of patients assessed at each site. An additional 31 per cent of patients assessed at RCHB were overseas referrals.

Between 1999 and July–October 2006, 172 PLTs were performed, at an average rate of 22 per year (between 1999 and 2005, range: 15–27). The average number of liver transplants undertaken per year varied between the 3 NFC sites: 10 at the CHWS, 7 at the RCHB and 5 at the RCHM.

Overall patient numbers treated at the 3 NFC sites have decreased since 1999 from the numbers in the 10 years to 1999, when on average 32 transplants were performed per year. This decrease is mainly attributable to a reduction in referrals of children from overseas since the early 1990s. A slight increase in patient numbers has been observed at the RCHM and CHWS sites since 2000–2001.

WLT, RLT, SLT, LDLT and LCT have been performed in Australia. The proportions of PLTs performed as RLT or WLT have decreased with increasing use of SLT, which now accounts for almost half of all PLTs performed. In the last 5 years, SLTs as a proportion of all PLTs ranged between 24 per cent (RCHM) and 70 per cent (CHWS). Since 1990, 13 LDLTs have been performed in Australia and New Zealand. One LCT has been undertaken at RCHM in 2004.

Since 2002, the number of children awaiting transplants at the 3 NFC sites has been relatively constant, ranging between 14 and 17 per year. Waiting times varied widely between patients at all sites. From the information available, no difference in waiting time between interstate and local patients or between different age groups could be identified.

The rate of transplants performed in children by state of residence per 100,000 population < 18 years of age in each state ranged between 0 and 4.23. The figures do not allow conclusions about whether access to the PLT services is different for patients residing in a state with or without a PLT NFC site. However, the data available to this review did not reveal any difficulties of access to the PLT services for particular patient groups.

Health outcomes

One-year survival was similar at the 3 sites, and ranged between 83 and 88 per cent; these data compare well with data from the United Kingdom (93%, 2001–2004; 90%, 1995–2000) and the United States (Studies of pediatric liver transplantation [SPLIT] registry: 88%; Cincinnati children's hospital medical centre [CCHMC] paediatric liver care centre: 92%). The perioperative mortality rate at RCHM was 13 per cent (6/47) from 1988 to 2000. Perioperative mortality was not reported by CHWS or RCHB.

There were no statistically significant differences in the percentages of unplanned readmissions to ICU or nosocomial infections between CHWS and RCHM sites (these outcomes were not reported for RCHB), nor in the rates of incidence of retransplantation and biliary leak requiring intervention between all 3 sites. CHWS reported a significantly higher rate of thrombosis (portal vein thrombosis, hepatic artery thrombosis [HAT]) than the other 2 sites. Ten of the 16 cases of thrombosis reported by CHWS in the period 1999 to 2006 involved patients who received SLT.

Service delivery

At RCHB and RCHM, surgical personnel are based at the cooperating adult transplant unit, whereas the program at CHWS is a stand-alone PLT unit. RCHB and RCHM have adopted a strict protocol-driven approach to service delivery.

RCHM and RCHB had good-quality long-stay accommodation facilities, but the panel felt that there is scope for improvement at CHWS.

Strong ties between paediatric and adult liver transplant units are desirable; however, potentially increased stress on services in association with SLT may be of particular relevance in combined units.

Quality and safety

RCHM uses a published protocol for preoperative to postoperative care until discharge. Both RCHM and RCHB have adopted procedures to increase the safety of PLT, especially to minimise the risks associated with SLT. The development of agreed treatment and management guidelines for PLT across all sites is considered important in order to ensure high quality and consistent patient care across Australia.

All sites have provided data to the Commonwealth as a requirement for funding under the NFC Program. Data collection methods differed between the sites. Data on QoL and consumer satisfaction of children and their families after PLT have not been collected; however, reporting requirements have recently been amended to include collection of QoL data. Development and implementation of a protocol for data collection would ensure that a common dataset across Australia is established. This would also allow closer monitoring of complications, such as biliary strictures and hepatic artery thrombosis.

At RCHM and CHWS, rates of unplanned readmissions to ICU and nosocomial infection of 10 to 24 per cent and 30 to 50 per cent were considered acceptable and indicate a safe and high-quality provision of the PLT service. However, the high rate of HAT (23%) at CHWS has raised concerns about the safety of the current treatment protocol that need to be addressed.

Teaching, training and research

Teaching and training arrangements are in place at RCHM and CHWS (this information was not available from RCHB). All NFC sites have published papers in peer-reviewed journals and are currently conducting research projects.

Need for continued service concentration

After a decrease in the number of PLTs from a peak in the early 1990, numbers have been relative constant since 1999 and averaged 22 per year between 1999 and 2005. Although RCHM and CHWS have reported a slight recent increase in patient numbers, advisory panel expert opinion suggests that patient numbers are likely to remain constant. However, increased survival of PLT patients and an increase in the proportion of transplants performed as SLT may contribute to an increased demand for PLT services, especially post-transplantation care and patient follow-up services.

PLT requires a highly specialised, multidisciplinary team for pre-, peri- and post-transplantation paediatric care, including liver and biliary surgeons, hepatologists and gastroenterologists, paediatric anaesthetists, radiologists, paediatric ICU specialists, dieticians, nurse educators, social workers, donor technicians and transplant recipient coordinators. These requirements apply to all types of PLT, but are particularly relevant in the more recently developed and complex techniques such as SLT and LDLT.

Concentration of PLT services is important for maintenance of the multidisciplinary team, especially the surgical skills involved in conducting PLT; however, the minimum annual patient throughput required is difficult to determine.

A current demand estimate of 22 transplants/year indicates that 1 NFC PLT unit would suffice, but 2 units would be adequate considering both demand and access issues. Combined adult–paediatric transplant units and a protocol-driven approach to service delivery may provide advantages in terms of feasibility to maintain critical patient throughput.

Cost

PLT is a complicated surgical procedure incurring high costs associated with ICU stay during and after transplantation and requires lifelong follow-up and immunosuppressive therapy. However, the episode of care considered under NFC funding for PLT does not consider lifelong follow-up and drug costs that are usually carried by referring jurisdictions or by the Highly Specialised Drugs program.

Cost estimates

PLT-type specific cost estimates provided by the 3 NFC sites were available for WLT and SLT. For WLT, cost estimates were \$195,812 at CHWS, \$195,092 at RCHM and \$167,007 at RCHB. For SLT, estimates were \$288,095, \$195,469 and \$170,590, respectively. However, the quality and extent of costing information provided vary, particularly with regards to the episode of care assumed, which limits the comparability of cost estimates.

Recommendations

MSAC has considered the provision of paediatric liver transplantation services in Australia and recommends that the procedure should continue to be funded under NFC arrangements with a further review in three years.

Based on estimated national demand of around 20 patients per year, the Committee considers that one NFC unit would be sufficient, but that two units would be appropriate having regard to access issues.

The outcomes of all three sites compare well with international data in relation to one year survival. The Committee found that combined adult-paediatric units appear to function at least as well, if not better, than stand-alone paediatric surgical units. It is the Committee's opinion that combined adult-paediatric transplant units and a protocol driven approach to service delivery are likely to be a more viable approach in the future.

The MSAC recommends the following to enhance the operation of the PLT NFC program:

- development of PLT treatment and management guidelines to achieve reduction of morbidity and complications, especially those associated with split liver transplantation;
- that living-donor liver transplantation be performed in accordance with agreed selection and treatment guidelines;
- improved and consistent data collection, with a stronger emphasis on health outcomes, including quality of life; and
- that surgical workforce succession planning be addressed in a coordinated plan for training and workforce management.

Background

The Medical Services Advisory Committee (MSAC) was established by the Australian Government to strengthen the role of evidence in health financing decisions in Australia. It was established in 1998 to replace the Australian Health Technology Committee. MSAC's fourth term of reference is to undertake health technology assessment (HTA) work on behalf of the Australian Health Ministers' Advisory Council (AHMAC).

The Nationally Funded Centres Program

The Nationally Funded Centres (NFC) Program provides a national policy for public sector provision of high-cost, highly specialised clinical practices and technologies with limited demand.

The objectives of the NFC Program are to ensure that:

- there is maximal 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; and
- health and cost outcomes of these technologies are monitored and evaluated.

The types of technologies considered for NFC status are those for which the provision of services at one or a small number of designated centres is appropriate and for which it is important to ensure access to high-quality and affordable services.

Funding decisions are driven by evaluation and evidence-based assessment. The NFC Program requires that a formal review process be undertaken after the initial establishment of an NFC, to determine whether this status is still warranted. Accordingly, this report reviews NFC status for paediatric liver transplantation (PLT). It has been prepared at the request of the AHMAC by a team from the National Health and Medical Research Council (NHMRC) Clinical Trials Centre that has been engaged by MSAC to support this work.

NFC reviews—paediatric liver transplantation

Reviews of liver transplantation were conducted in 1991 and 1993. The 1991 review recommended that NFC units for liver transplantation should be established. The 1993 review found that adult liver transplantation no longer met the criteria applying to NFCs, but recommended that liver transplantation should continue to be funded by this program for children under 3 years of age to ensure high quality of care for these patients.

The 1993 NFC assessment resulted in 3 sites being approved for NFC status for the provision of PLT:

- the Royal Children’s Hospital, Brisbane (RCHB)
- the Royal Children’s Hospital, Melbourne (RCHM), and
- the New Children’s Hospital, Westmead, Sydney (CHWS).

AHMAC requested a review of these sites in 1997, the results of which were published in 2002. The review concluded that the sites continued to meet the criteria for NFC funding. Other significant recommendations were:

- that the age for PLT be raised to include all children up to and including 14 years, with children at the age of 14 to be assessed on an individual basis;
- that all sites develop the capacity to perform split liver transplantation (SLT); and
- that a prescribed format for data collection, including costs, be established to ensure uniformity in reporting.

In 2006, sites providing the PLT service were again scheduled for review to determine the need for continued NFC status. The review was conducted in accordance with AHMAC guidelines and considered access; health outcomes; service delivery; quality and safety; teaching, training and research; the need for continued service concentration; cost; and cost estimates. These criteria for the review of established NFCs are defined in the *NFC Guidance for Management, Governance, Funding, Establishment and Review—April 2006*. This report provides MSAC’s advice to the NFC Reference Group of AHMAC.

Methodology

Objectives

Consistent with the NFC guidelines for the review of existing NFCs, the objectives of this review were:

- to determine whether or not existing NFC sites and their activities should continue at a reduced, equal, or increased level for a further defined period; and
- to make appropriate recommendations.

Approach

The MSAC considered a number of information sources in conducting this review. These included scientific literature, data provided by currently funded sites, information obtained through the Australia and New Zealand Liver Transplant Registry (ANZLTR) and information from the advisory panel's visit to each of the centres. Recent HTA reports and systematic reviews on PLT were also reviewed.

Literature review

The literature review included a search of the International Network of Agencies for Health Technology Assessment (INAHTA) database for HTA reports and systematic reviews on PLT published since 2002 (refer to section 'Existing systematic reviews', page 7, and Appendix C).

Site data

The review considered data provided by the 3 transplant units. Site visits were also made. Comprehensive data on issues of cost, throughput, waiting lists and outcomes were requested from each unit, and provided as part of the annual statistical returns required under the terms of NFC funding.

To address the objectives of the review, the following criteria from the NFC Guidance document were examined:

- access to the NFCs
- health outcomes
- service delivery
- quality and safety
- teaching, training and research
- need for continued service concentration
- cost
- cost estimates.

Paediatric liver transplantation in Australia

The history and evolution of PLT has been well-documented in previous NFC reports. The first paediatric liver transplant in Australia was performed at RCHB in 1985. CHWS followed in 1986, and RCHM in 1995. More recently, the liver transplant unit at Sir Charles Gairdner Hospital in Perth, Western Australia, has begun to perform PLT in children over 30 kg, which roughly relates to children older than 10 years of age.

PLT is widely accepted as an effective therapy for infants and children with end-stage liver disease, an illness leading to impaired growth, poor quality of life (QoL) and untimely death.

Surgical techniques

Whole liver transplantation

Whole liver transplantation (WLT) has become increasingly uncommon owing to the shortage of small, size-matched donor organs for paediatric recipients. This has led to the development and increasing use of more innovative methods of procurement (MSAC 2002). These include reduced-size liver transplantation (RLT), SLT, living-donor liver transplantation (LDLT) and liver cell transplantation (LCT).

Reduced-size liver transplantation

The Brisbane unit began its reduced-size grafts program in 1987 (Lynch et al. 1992). In reduced-size liver transplantation (RLT), the left or right lobe of an adult liver is used for transplantation in a child, and the remaining lobe is discarded. Reduced-size grafts have now been used for several years, with results as good as, or better than, those of size-matched transplants (MSAC 2002). Murcia et al. (1996) found similar complication rates in both techniques. De Ville de Goyet et al. (1993) found a significantly lower incidence of arterial thrombosis in reduced-size transplants.

The use of reduced-size grafts, however, reduces the adult liver pool, and it is argued that the technique makes inefficient use of adult donor livers. This concern has led to the development of other methods to increase the donor pool.

Split-liver transplantation

Split-liver transplantation (SLT) is a complex and time-consuming procedure that uses 1 liver for 2 recipients. It is becoming a more routine medical practice and is now undertaken at all 3 NFC sites. Restrictions are placed on the size, age, anatomical type and health of livers eligible for splitting. Donor selection is crucial, and marginal donors are not considered.

Living-donor liver transplantation

Advances in hepatic resection techniques have made it relatively safe to remove the left lateral segments of the liver of a live donor and transplant this lobe into another person. Emond and Lieb (1996), Renz et al. (1995) and Jurim et al. (1995) cite the following advantages of LDLT: the increase in the overall supply of livers; the provision of a graft of high functional quality; the procurement of a graft as an elective procedure, which provides flexibility of medical timing, thereby permitting optimal transplantation into the recipient; and the possibility of 2 types of immunological advantage. In emergency circumstances, LDLT may be the only option of providing PLT.

Liver cell transplantation

Liver cell transplantation (LCT) involves the infusion of mature adult hepatocytes into the portal system of the recipient. The technique addresses the needs of patients with inborn errors of metabolism, whose health is unstable but who are not sick enough for orthotopic transplantation. LCT is currently an experimental procedure and has been performed only once in Australia, at the Melbourne NFC site in 2004. As the technology develops, the use of this procedure can be expected to increase.

Current service provision

Royal Children's Hospital, Brisbane

The RCHB provides PLT service in conjunction with the adult program at Princess Alexandra Hospital. RCHB performed its first PLT in 1985.

Precise staff numbers were not provided in the data, but the team comprises staff in the following fields:

- surgery
- gastroenterology
- liver transplant coordinator
- social work
- dietetics
- physiotherapy
- chaplaincy
- pharmacy
- play therapy
- occupational therapy
- psychology
- nursing

RCHB provides PLT to patients from both Queensland and interstate.

Royal Children's Hospital, Melbourne

The RCHM is located in Parkville, Victoria, and operates the Victorian Liver Transplant Unit (VLTU) in conjunction with Austin Health, at Heidelberg, which performs adult liver transplant services. Surgeons from the Austin campus perform the transplant surgery at both sites.

The VLTU transplant team comprises:

- surgeons and theatre staff
- hepatologist/gastroenterologist
- liver transplant coordinator
- social worker
- dietician
- physiotherapists
- chaplain
- pharmacist
- play therapist
- nursing unit manager & nursing staff
- administration

The RCHM provides transplant services to patients throughout Victoria and interstate. The facility performed its first paediatric transplant in 1995.

Children's Hospital, Westmead, Sydney

The New South Wales (NSW) NFC performed its first paediatric liver transplant in 1986. CHWS operates in collaboration with Royal Prince Alfred Hospital, but the surgeons at CHWS perform transplants only at Westmead.

The liver transplant staff forms part of the gastroenterology team, and comprises:

- liver transplant surgeon
- hepatologists/gastroenterologists
- junior staff (hepatology/gastroenterology)
- nurse (liver transplant, chronic liver disease)
- allied health—including dietetics, occupational therapy, play therapy, social work, and psychology
- administration

CHWS takes patients from interstate and has treated patients from NSW, the Australian Capital Territory (ACT), South Australia and Western Australia.

Existing systematic reviews

A search of the INAHTA database for systematic reviews and HTA reports on PLT published since 2002 is summarised in Appendix C. This search identified 2 systematic reviews of PLT (Scott 2004; Taylor et al. 2005); the characteristics and results of these studies are presented in Appendix C (Table 15) and summarised below.

Taylor et al. (2005) assessed the overall health-related QoL in children and adolescents after liver transplantation. They found that various aspects of health-related QoL improved significantly after transplantation compared to before transplant (1 study); improvements were also found in children after transplantation compared to a healthy population and children with other chronic illnesses, but these differences were not statistically significant.

Scott (2004) systematically reviewed postoperative complications and long-term patient outcomes of recipients of LDLT. They identified 8 primary comparative studies and 2 registry studies that reported data from a comparison of LDLT with cadaveric liver transplants. No randomised controlled trials were identified in this review, and the observational studies included may be subject to bias and provide only limited evidence to allow conclusions on the safety and effectiveness of LDLT. A summary of these studies suggests that LDLT is superior to all forms of cadaveric liver transplantation in children younger than 2 years of age, but it may be inferior in safety and efficacy to WLT and SLT in older children.

Review of the NFC PLT Program

Access to the Nationally Funded Centres

Number of patients referred to and treated at the NFC sites

A total of 241 patients have been referred for treatment at PLT NFC sites from July 1999 (CHWS: July 2002) to date (June 2005 RCHB), March 2006 RCHM, May 2006 CHWS). Of these referrals, 206 patients (85%) were accepted onto a transplant program. Table 1 displays the number and referral sources of children assessed at the 3 NFC sites and the number accepted for treatment.

The RCHM reported the highest number of new patients referred and accepted per year during this period (mean number of patients accepted per year: RCHM 16; CHWS 14; RCHB 6). Between 10 per cent (RCHM) and 31 per cent (RCHB) of patients assessed at each site were interstate referrals. An additional 31 per cent of patients assessed at RCHB were overseas referrals (Table 1) (Royal Children's Hospital Brisbane 2006; Royal Children's Hospital Melbourne 2006; The Children's Hospital at Westmead 2006).

Table 1 Number and referral sources of new patients assessed and accepted at paediatric liver transplant NFCs July 1999 to June 2005; March–May 2006^a

NFC site	Patients accepted <i>N</i> (total assessed)	Interstate referrals <i>N</i> (%) [total assessed]	Referral source								
			NSW	Vic	Qld	SA	WA	NT	ACT	TAS	Over-seas
CHWS, NSW	54 (65)	13 (24%) [15 (23%)]	41 (50)	1 (1)		7 (7)	4 (5)		1 (2)		
RCHM, Vic	110 (114)	11 (10%) [12 (11%)]		98 (101)		7 (7)			2 (3)	2 (2)	1 (1)
RCHB, Qld	42 (62)	13 (31%) [19(31%)] ^b	2 (4)		16 (28)	2 (3)	8 (11)	1 (1)			13 (15) ^c
Total	206 (241)	37 [46]	43 (54)	99 (102)	16 (28)	16 (17)	12 (16)	1 (1)	3 (5)	2 (2)	14 (16)

Abbreviations: NFC = Nationally Funded Centre; CHWS = New Children's Hospital, Westmead, Sydney; RCHM = Royal Children's Hospital, Melbourne; RCHB = Royal Children's Hospital, Brisbane; NSW = New South Wales; Vic = Victoria; Qld = Queensland; SA = South Australia; WA = Western Australia; NT = Northern Territory; ACT = Australian Capital Territory; TAS = Tasmania.

a Data from NSW refer to 7/2002–3/2006, as data from 7/1999 to 6/2002 were not available; data from QLD were available only until June 2005.

b Overseas referrals: 13 (31%) (15 (24%))

c 13 international patients accepted onto transplant program (15 referrals) included 8 patients from New Zealand (9 referrals), 3 from Japan (4 referrals) and 1 each from Malaysia and Nauru.

Figure 1 displays the number of children receiving liver transplants at the NFC sites between 1999 and July–October 2006. The most recent information from the 3 sites shows that in this period, the number of paediatric liver transplants in Australia per year ranged between 15 and 27 (Figure 1). Overall, 172 PLTs were performed in Australia between 1999 and 2006, made up of 81 at CHWS, 51 at RCHB and 40 at RCHM. Between 1999 and 2005, an average of **22 PLTs per year** were undertaken (CHWS: 10;

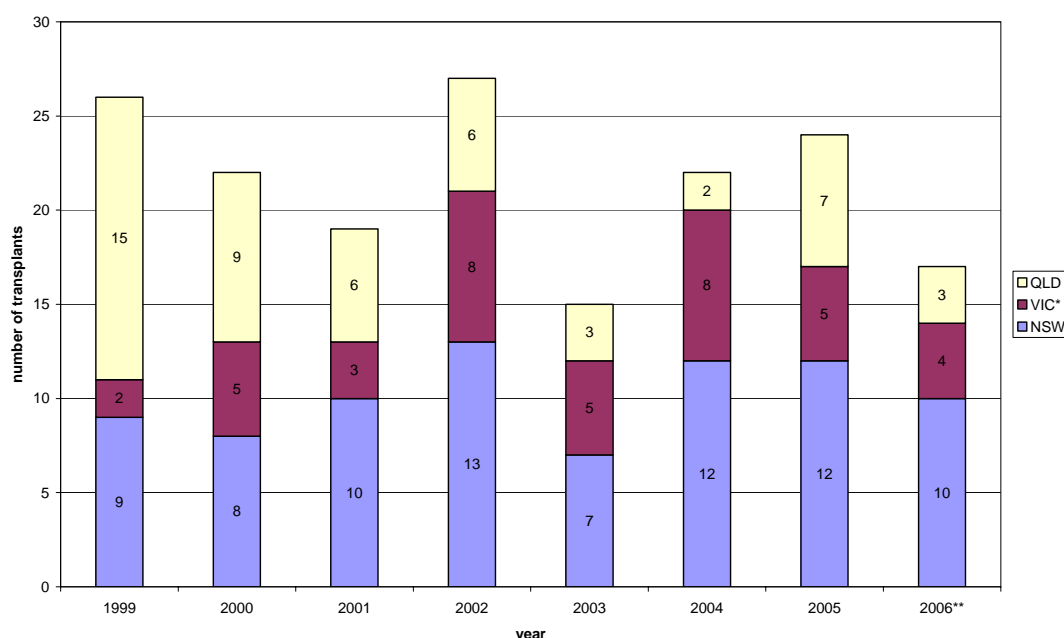
RCHB: 7; RCHM: 5) (Hardikar 2006; Hardikar et al. 2006; Lynch 2006; The Children's Hospital at Westmead et al. 2006).

The number of PLTs performed before 1999 (1985–1998) was reported in the MSAC 2002 report (Medical Services Advisory Committee 2002). In the 10 years from 1989 to 1998, 324 transplants were undertaken, giving a yearly average of 32 transplants. These figures indicate a decrease in annual patient numbers at the 3 NFC sites since 1999.

Data from the recent ANZLTR report indicate that the number of paediatric transplants performed on Australian and New Zealand patients over the last 10 years has been constant. An average number of 27 transplants per year was reported for the period between 1999 and 2005, and an average of 26 for the 5 years to 1999 (Australian and New Zealand Liver Transplant Registry 2005). The registry data indicate that these numbers are lower than for the 5 years prior (1989–1993), when an average of 36 patients per year received transplants. The ANZLTR documents the number of liver transplants performed in children each year at the 3 Australian NFC sites and at liver transplant centres in Perth, Western Australia, and Auckland, New Zealand.

Trends in the number of transplants over time differ at the 3 NFC sites. At RCHB, the number of transplants ranged between 15 and 29 per year between 1988 and 1996, but the numbers declined in the following years, as shown by ANZLTR data. This site used to treat patients referred from New Zealand and Asia (50 per cent of patients treated between 1985 and 1998 were overseas referrals (Medical Services Advisory Committee 2002)). PLT centres have since been established in New Zealand and Asia, and thus the numbers of both patients and transplants performed at RCHB have been reduced (mean of 6/year [range: 2–9] from 2000 to 2005 (Lynch 2006)).

Figure 1 Number of liver transplants in children at NFC sites 1999–2006, by year and site



Abbreviations: NFC = Nationally Funded Centre; NSW = New South Wales; VIC = Victoria; QLD = Queensland.

* Data for Victoria represent number of patients ($n = 40$), not number of transplants. From information indicating that there were 2 retransplants in this period (Royal Children's Hospital Melbourne 2006), the number of transplants would be 42. This could not be presented in this figure, as it is not clear when these occurred.

** Data to July 2006 (RCHM) or October 2006 (CHWS/RCHB).

In contrast, at RCHM, the number of patients receiving PLT increased between July 2001 and July 2006 (mean of 7 patients/year) compared to the 6-year period between 1995 and 2001 (3 patients/year) (Hardikar 2006). The CHWS also reports an increase in the number of transplants, from an average of 7 per year between 1992 and 1999 to 10 per year between 2000 and 2006 (The Children's Hospital at Westmead et al. 2006).

Thus, the decrease in overall patient numbers at the 3 NFC sites since 1999 appears to be attributable to a reduction in referrals of children from overseas owing to the availability of transplant services provided in their own jurisdictions.

Types of paediatric liver grafts transplanted

The shortage of small, size-matched donor organs for paediatric recipients has led to the development of new methods of procurement. These include reduced-size liver transplantation (RLT), split-liver transplantation (SLT), living-donor liver transplantation (LDLT) and liver cell transplantation (LCT).

The information reported on numbers of PLT by type of graft differed between sites and did not suffice to provide total numbers. The following paragraphs summarise the available information.

The proportion of PLTs performed as WLTs was 34 per cent from 1985 to 2005, according to data from the ANZLTR report, but the proportion appears to have decreased to 28 per cent in the 5 years from 2001 to 2005 (Australian and New Zealand Liver Transplant Registry 2005). At RCHB, WLTs comprised 46 per cent of all transplants performed between 2001 and 2005 (Lynch 2006).

CHWS was the first PLT NFC site to introduce RLT, in 1986, and it has since been performed at all three PLT NFC sites. According to data from the ANZLTR report, the proportion of transplants performed as RLT appears to have decreased with the increasing use of SLT (Australian and New Zealand Liver Transplant Registry 2005). These data indicate that in the 5 years from 2001 to 2005, up to a third of all transplants were RLTs. However, an accurate estimate can not be provided from the information in the ANZLTR report, as the data on RLT include patients undergoing LDLT (13 LDLTs since 1990). At RCHB, RLT comprised 29 per cent of all transplants performed between 2001 and 2005 (Lynch 2006).

RCHB was the first NFC site to introduce SLT, in 1989. SLT was introduced at RCHM in 2000 and at CHWS in 2002. The ANZLTR report indicates that since then, 18 per cent of all transplants have been performed as SLTs. In the 5 years from 2001 to 2005, 47 per cent of all PLTs were SLTs (Australian and New Zealand Liver Transplant Registry 2005).

CHWS performs the highest proportion of SLTs: 70 per cent of all transplants performed between 2002 and 2006. In comparison, SLT accounted for 24 per cent of all transplants performed at RCHM and 33 per cent at RCHB (from information available up to 2005) (Lynch 2006; Royal Children's Hospital Melbourne 2006; The Children's Hospital at Westmead et al. 2006).

RCHB performed the first LDLT in the world in 1990. As reported in the ANZLTR report, 13 LDLTs have so far been performed in Australia and New Zealand (Australian

and New Zealand Liver Transplant Registry 2005). CHWS has performed 5 LDLTs, 4 of these since 2002 (The Children’s Hospital at Westmead et al. 2006). The total number of LDLTs undertaken at RCHB and RCHM has not been reported.

RCHM is the first and so far the only Australian site to perform an LCT, in 2004 (Hardikar et al. 2006).

Patients awaiting treatment

Table 2 shows the numbers of children awaiting a liver transplant annually from 1999 to date at the 3 NFC sites. Nationally, these figures have been relatively constant since 2002 (14–17 each year), although the data from the RCHM indicate an increase in waiting times at this site. CHWS reported the highest number of patients on the waiting list each year until 2005–2006, when RCHM reported a higher number (Royal Children’s Hospital Brisbane 2006; Royal Children’s Hospital Melbourne 2006; The Children’s Hospital at Westmead 2006).

Table 2 Number of patients awaiting treatment at PLT NFCs, 1999–2006^a

NFC site	Number of children awaiting PLT (on waiting list)						
	1999–2000	2000–01	2001–02	2002–03	2003–04	2004–05	2005–06
CHWS, NSW	–	–	–	7	10	6	6
RCHM, VIC	2	1	3	4	4	5	8
RCHB, QLD	1	2	1	3	3	3	1 ^b
Total ^c	3	3	4	14	17	14	15

Abbreviations: PLT = paediatric liver transplantation; NFC = Nationally Funded Centre; CHWS = New Children’s Hospital, Westmead, Sydney; RCHM = Royal Children’s Hospital, Melbourne; RCHB = Royal Children’s Hospital, Brisbane; NSW = New South Wales; VIC = Victoria; QLD = Queensland.

- a Data from NSW refers to 2002 to 3/2006, as data from 1999 to 2002 were not available; data from QLD are available only until June 2005
- b Current number of children on waiting list. Information from presentation at site visit.
- c Total numbers are not comparable over time as they refer to 2 centres for 1999–2002 and to 3 centres from 2002 to date.

The waiting times from the time of listing to the time of transplantation varied widely between patients at all sites (Table 3). The data were broken down by jurisdiction of residence of recipients, but no differences in waiting times between interstate and local patients or by age group could be identified. No differences in waiting periods over time were found (Royal Children’s Hospital Brisbane 2006; Royal Children’s Hospital Melbourne 2006; The Children’s Hospital at Westmead 2006).

Table 3 Waiting times for transplant from time of listing at 3 NFC PLT sites, 1999–2000 to 2005–06, by age

NFC site	n children (0–3/4–15)	Waiting times (median and range)	
		0–3 years	4–15 years
CHWS, NSW	44/36 ^a	1 to 695 days ^b	1 to 1467 days ^b
RCHM, VIC	21/17 ^a	43 (1 to 445) days	166 (1 to 610) days
RCHB, QLD	n.r.	1 to 987 days ^b	1 to 189 days ^b

Abbreviations: PLT = paediatric liver transplantation; NFC = Nationally Funded Centre; CHWS = New Children’s Hospital, Westmead, Sydney; RCHM = Royal Children’s Hospital, Melbourne; RCHB = Royal Children’s Hospital, Brisbane; NSW = New South Wales; VIC = Victoria; QLD = Queensland.

a These numbers do not seem to reflect patient numbers on waiting lists as displayed in Table 2.

b Data to calculate median were not available.

Patient deaths on waiting list

Table 4 displays the number of patients who died while waiting for a paediatric liver transplant at the 3 NFC sites. These figures are small and do not show any differences between sites (Royal Children’s Hospital Brisbane 2006; Royal Children’s Hospital Melbourne 2006; The Children’s Hospital at Westmead 2006).

Table 4 Number of patients who died on the waiting list for PLT at 3 PLT NFC sites, 1999–2000 to 2005–06

NFC site	Number of patients who died on the waiting list						
	1999–2000	2000–01	2001–02	2002–03	2003–04	2004–05	2005–06
CHWS, NSW	1	1	4	0	1	0	0
RCHM, Victoria	2	1	1	2	0	0	0
RCHB, Queensland	0	0	1	0	1	0	n/a

Abbreviations: PLT = paediatric liver transplantation; NFC = Nationally Funded Centre; CHWS = New Children’s Hospital, Westmead, Sydney; RCHM = Royal Children’s Hospital, Melbourne; RCHB = Royal Children’s Hospital, Brisbane; NSW = New South Wales; VIC = Victoria; QLD = Queensland

Patient demographic information

Table 5 shows the characteristics of the children treated at the NFC sites. Information about patient characteristics was not consistently reported between sites. The available information indicates that patient characteristics are similar across the 3 sites, with the exception that RCHM treated a larger proportion of patients older than 3 years than the other sites (Hardikar et al. 2002; Lynch 2006; The Children’s Hospital at Westmead et al. 2006; The Children’s Hospital Westmead Liver Transplant Service 2006).

Table 5 Profile of patients treated at 3 NFC PLT sites

NFC site	n children	Age	Sex	Ethnicity or origin	Most common indications for PLT ^a
CHWS, NSW	47	Mean: 3.4 y (of 42 children)	Male: 50% (of 46 children)	1 Aboriginal, 2 non-English-speaking, 1 NZ	Extrahepatic biliary atresia: 51% Metabolic disease: 29% Acute liver failure: 10%
RCHM, VIC ^b	50	24% ≤ 3 y; 68% > 3 y	Male: 54%	All Australian	Extrahepatic biliary atresia: 32% Metabolic disease: 26% Acute liver failure: 26%
RCHB, QLD	233 ^c	Median: 2.06 y (23 d – 14.9 y)	Male: 43%	Other (not AUS/NZ): n = 97 transplants	Extrahepatic biliary atresia: 68% Metabolic disease: 8% Acute liver failure: 8%

Abbreviations: PLT = paediatric liver transplantation; NFC = Nationally Funded Centre; CHWS = New Children's Hospital, Westmead, Sydney; RCHM = Royal Children's Hospital, Melbourne; RCHB = Royal Children's Hospital, Brisbane; NSW = New South Wales; VIC = Victoria; QLD = Queensland; NZ = New Zealand; AUS = Australia

- a For NSW and QLD it is not clear from the information available whether these numbers refer to indications of patients referred to the service or of patients who received a transplant.
b Data available from Hardikar et al. (2002) (patients treated until 2000).
c All patients treated between 1985 and 12/2005.

Access to paediatric liver transplant sites

As an indicative measure of access to PLT services in Australia, the rate of transplants performed in children by state of residence per 100,000 population under 18 years of age in each state was calculated. Information about the number of transplants performed in the 3-year period 2002–2005 was available from all sites; population data were available from Census 2001 information (Table 6). Among the 3 states with PLT NFC sites, Queensland had a relatively low proportion of children receiving a liver transplant (0.66 per 100,000), compared with the 2 more populous states (NSW 2.09, VIC 2.02). In the states without PLT NFC sites, PLT was performed at rates of between 1.27 (ACT) and 4.23 (Tasmania) per 100,000 population. No PLT was performed in children residing in the Northern Territory, which has a population of 57,064 children under the age of 18 years. Without further information about the incidence of paediatric liver disease in Australia and factors associated with PLT need that may vary by state (eg, age distribution of the population under 18 years, risk factors for liver disease), these figures do not allow conclusions about whether access to the PLT services differs for patients residing in a state with or without a PLT NFC site. However, the data available to this review did not reveal any difficulties of access to the PLT services for particular patient groups.

Table 6 Use of PLT service by state of residence of children and per 100,000 of total population 0–17 years of age in each state

	NSW	VIC	QLD	SA	WA	NT	ACT	TAS
Total patients 2002–03 – 2004–05 ^a	33	23	6	11	7	0	1	5
Total population 0–17 years of age ^b	1,579,365	1,139,739	914,244	349,238	475,910	57,064	78,608	118,181
Number of patients receiving transplant per 100,000 population	2.09	2.02	0.66	3.15	1.47	0.0	1.27	4.23

Abbreviations: PLT = paediatric liver transplantation; NSW = New South Wales; VIC = Victoria; QLD = Queensland; SA = South Australia; WA = Western Australia; NT = Northern Territory; ACT = Australian capital territory; TAS = Tasmania.

- a Data provided in annual statistical return pro forma.
b Australian Bureau of Statistics, Population Census 2001.

Health outcomes

Mortality

The RCHM reported a perioperative mortality rate of 13 per cent (6/47) for the period from 1988 to 2000; this includes patients operated on at Austin Hospital (until 1995). These deaths occurred in the first week after transplant and were due to vascular causes (3), HAT (1), infection (2) or post-transplantation lymphoproliferative disease (1) (Hardikar et al. 2002). CHWS and RCHB reported an overall mortality of 10 per cent (6/61) and 18 per cent (5/28) for patients treated from 1999 to date, respectively, but did not specify the time period to which these rates refer, or the cause of death (Royal Children's Hospital Brisbane 2006; The Children's Hospital at Westmead 2006).

Long-term survival

Table 7 summarises long-term survival associated with PLT performed at each of the NFC sites, as reported by the 3 sites (Hardikar 2006; Hardikar et al. 2006; Hardikar et al. 2002; Lynch 2006; Royal Children's Hospital Brisbane 2006; The Children's Hospital at Westmead 2006; The Children's Hospital at Westmead et al. 2006).

One-year survival was similar at the 3 sites and ranged between 83 and 88 per cent. At RCHB and CHWS, the data refer to all patients treated at the site until 2005–06; at RCHM, the 1-year survival rate applies to patients treated until 2000.

One-year survival data compare well with data from the United Kingdom (93% 2001–2004; 90% 1995–2000) and the United States (Studies of pediatric liver transplantation [SPLIT] registry: 88%; Cincinnati Children's Hospital Medical Centre [CCHMC] paediatric liver care centre: 92%) (NHS Blood and Transplant 2006; Tiao et al. 2006).

Table 7 Long-term survival associated with PLT at the NFC sites

	Long-term survival ^a			Long-term survival in SLT patients
	1-year	5-year	10-year	
CHWS, NSW	84% ^b	81% ^b	76% ^b	89% at 3 years No significant difference in patient or graft survival by type of graft (2002–2005)
RCHM, VIC	88% ^c		85% ^c	88% (8/9 patients receiving SLT since 2000)
RCHB, QLD	83% ^d	78% ^d	73% ^d	No significant difference in patient or graft survival by type of graft (1985–2005)

Abbreviations: PLT = paediatric liver transplantation; NFC = Nationally Funded Centre; CHWS = New Children's Hospital, Westmead, Sydney; RCHM = Royal Children's Hospital, Melbourne; RCHB = Royal Children's Hospital, Brisbane; NSW = New South Wales; VIC = Victoria; QLD = Queensland; SLT = Split liver transplantation.

a No information available on median follow-up time or numbers of patients at different follow-up time points.

b Data on patients treated between 1986 and 2006; data on children treated between 2004 and 2005: 1- & 2-year survival of 92 per cent.

c Data on patients treated between 1988 and 2000 (published in Hardikar et al. [2002]).

d Data from 1/1985 to 12/2005 (presentation), *n* = 233; unclear how many patients follow-up is based on.

Morbidity

There was no statistically significant difference in the rate of unplanned readmissions to ICU or the rate of nosocomial infection reported by RCHM and CHWS. RCHB did not report detailed information about these outcomes for this comparison (Table 8).

(Hardikar 2006; Hardikar et al. 2006; Royal Children's Hospital Brisbane 2006; The Children's Hospital at Westmead 2006; The Children's Hospital at Westmead et al. 2006).

The rates of incidence of retransplantation and biliary leak requiring intervention were similar across the 3 sites (11%–15% and 7%–11% respectively). CHWS reported a higher rate of thrombosis (PVT, HAT) than the other 2 sites (23% v. 4%, Fisher's exact test, $P = 0.004$). Of the 16 cases of thrombosis reported by CHWS in the period 1999–2006, 10 occurred in patients who received SLT (the number of SLTs performed in this period was not reported).

CHWS also separately reported complications arising in patients receiving SLT: 40 per cent of children receiving SLT had biliary strictures and 39 per cent had sepsis/cholangitis.

Table 8 Morbidity associated with PLT at the NFC sites from 1999 to 2006

	Unplanned readmissions to ICU <i>n/N</i> (% of transplants)	Retransplantation <i>n/N</i> (% of patients)	Thrombosis (PVT, HAT) <i>n/N</i> (% of transplants)	Biliary leak requiring intervention <i>n/N</i> (% of transplants)	Nosocomial infections <i>n/N</i> (% of transplants)
CHWS, NSW	5/50 (10%) ^a	9/61 (15%)	16/70 (23%) ^b [HAT 16, PVT nr]	8/70 (11%)	25/50 (50%) ^c
RCHM, VIC	8/43 (19%) ^d	6/47 (13%) ^e	2/53 (4%) ^e [PVT 1, HAT 1]	3/43 (7%)	10/33 (30%) ^f
RCHB, QLD	n.r. ^g	5/46 (11%)	2/51 (4%) [HAT 2, PVT nr]	4/51 (8%)	n.r. ^h

Abbreviations: PLT = paediatric liver transplantation; NFC = Nationally Funded Centre; CHWS = New Children's Hospital, Westmead, Sydney; RCHM = Royal Children's Hospital, Melbourne; RCHB = Royal Children's Hospital, Brisbane; NSW = New South Wales; VIC = Victoria; QLD = Queensland; ICU = intensive care unit; PVT = portal vein thrombosis; HAT = hepatic artery thrombosis; n.r. = not reported.

a Data from 2002 to 2006.

b Overall vascular complications reported in annual stats return under adverse events since 2002 = 8 of 50 transplants (16%) performed in the same time period; HAT rate for SLTs since introduction of SLT program in 2002 reported as 18.7 per cent.

c Includes 14 cases of viral infection and 11 cases of bacterial infection.

d Number of transplants based on reported number of patients receiving transplants and retransplant rates. It is further reported that 13 cases (28% of patients) have had to return to ICU since 1995.

e Data from 1995 to 2006.

f Data from 2002 to 2006. Includes 1 patient with 2 diagnoses of urinary tract infection during 1 transplant admission.

g NFC site information indicated that these complications occurred, but no details were provided.

h Since 1995, infections reported in 9 patients (19%).

No information on the QoL of children undergoing PLT was provided by the 3 NFC sites, although research in this area is being conducted (RCHB) or planned (CHWS) (see section 'Teaching, training and research', page 19).

The CHWS found that all children who underwent a liver transplant and survived returned to school. It further recorded 'medical fitness' and whether children attended school full-time in an appropriate class, a lower class than the appropriate age or a school

for the developmentally handicapped (The Children’s Hospital Westmead Liver Transplant Service 2006).

Hardikar et al. (2002) reported that all survivors of PLT treated at RCHM between 1988 and 2000 were able to attend ‘age-appropriate activities including kindergarten, school and employment.’

Service delivery

Information about inpatient service staffing and other services provided as part of the PLT service at the 3 NFC sites is summarised in Table 9 and Table 10 (Hardikar et al. 2006; Lynch 2006; The Children’s Hospital Westmead Liver Transplant Service 2006).

Table 9 Staffing for inpatient PLT service at the 3 NFC sites

NFC site	Staffing				
	Senior medical	Junior	Nursing	Allied health	Administrative
CHWS, NSW ^a	3 FTE 1 PLT surgeon 2 hepatologists/gastroenterologists	2 FTE (cover liver and gastro patients)	1 FTE 1 CNC ^b	1 dietician ^c (since July 06)	1.6 FTE
RCHM, VIC	1.5 FTE paediatric hepatologist (plus call backup through consultants of gastro department) surgeons (and theatre personnel) based at Austin Hospital (4–5 surgeons, 1–2 lead surgeons)	n.r.	1 FTE liver transplant coordinator ^d		n.r.
RCHB, QLD (detailed information not provided—info from site visit)	liver transplant surgeons service both adult and children LT services paediatric hepatologists/gastroenterologists (referral to gastroenterologist) 2 radiologists	1 registrar ICU, 1 emergency, general	liver transplant coordinator	n.r.	n.r.

Abbreviations: PLT = paediatric liver transplantation; NFC = Nationally Funded Centre; CHWS = New Children’s Hospital, Westmead, Sydney; RCHM = Royal Children’s Hospital, Melbourne; RCHB = Royal Children’s Hospital, Brisbane; NSW = New South Wales; VIC = Victoria; QLD = Queensland; FTE = full-time equivalent; LT = liver transplant; ICU = intensive care unit; CNC = clinical nurse consultant; n.r. = not reported.

- a Only liver transplant surgeon, liver transplant physician and CNC nurse are dedicated to PLT service. All other services are provided to all patients on the ward areas.
- b Dedicated to PLT service, ‘manages care across all service settings (inpatient, liver transplant clinic, facilitates transfer back to referring service and to adult service (as part of Adolescent Transition Programs).
- c Other allied health services, including physiotherapy, occupational therapy, psychology and social work, are provided as part of ward cohort.
- d Other allied health staff (dietitians, social workers, physiotherapists) are allocated through gastroenterology department.

The following plans for staffing were reported by the 3 sites:

- CHWS reported having difficulty recruiting a second liver transplant surgeon. However, more recently (March 2007) an additional liver transplant surgeon has been employed, with an imminent start date (approximately May 2007). Other new positions considered include 1 additional full-time equivalent (FTE) staff specialist in

hepatology, a medical fellowship position, additional clinical nurse consultant (CNC) support to manage the increasing post-transplantation caseload; and data management and administrative support.

- RCHB reported that 2 wards (1 high-dependency unit) are to open soon, which could lead to a shortage of ICU nurses, as these staff are difficult to recruit.
- RCHM reported to have advertised for a 0.5 FTE hepatologist.

Table 10 Other services provided as part of the PLT service at the 3 NFC sites

NFC site	Services provided
CHWS, NSW	Local outpatient service: 1 liver disease/liver transplant outpatient clinic per week (~80–100 patients/month) 80 liver transplant recipients, followed-up at least every 3 months Other services: Occasional attendance at Sydney Children's Hospital Randwick Consultation service by phone to all Area Health Services in NSW, and interstate liver service Information to referring practitioners: via formal outpatient letters, computer-generated discharge summaries, informal communications
RCHM, VIC	Local outpatient service: Weekly, dedicated liver transplant clinic Other services: Biliary atresia support group (including ongoing educational sessions) Information to referring practitioners: n.r.
RCHB, QLD	n.r.

Abbreviations: PLT = paediatric liver transplantation; NFC = Nationally Funded Centre; CHWS = New Children's Hospital, Westmead, Sydney; RCHM = Royal Children's Hospital, Melbourne; RCHB = Royal Children's Hospital, Brisbane; NSW = New South Wales; VIC = Victoria; QLD = Queensland; n.r. = not reported.

In addition to in- and outpatient services, the NFC sites provide long-stay accommodation facilities where patients and their families from interstate can reside while the child is on the waiting list or after surgery. Facilities at all sites were visited. It was found that RCHM and RCHB offered good-quality facilities for long-stay accommodation, but the panel felt that there is scope for improvement at CHWS.

Generally, the NFC sites vary in the broad approach to service delivery, particularly in how the PLT program is integrated into the gastroenterology/hepatology and adult transplant services. All PLT NFC sites cooperate with the adult liver transplant units in their cities, but the level of cooperation differs between NFC sites. The PLT services at RCHB and RCHM are set up in strong cooperation with the adult transplant units, in particular with regards to the surgical aspects of the service. At these sites, surgeons operate at both paediatric and adult sites; at RCHM, surgeons also participate in patient selection and work-up. The service at CHWS operates as a stand-alone PLT unit.

The RCHB unit is more surgically based, giving the surgeon responsibility for the postoperative care of the child. At CHWS and at RCHM, postoperative care is part of the gastroenterologist's role, and at RCHM, surgical staff are involved as well. RCHB and RCHM also appear to have a strong protocol-driven approach to service delivery (RCHM even more so than RCHB).

The increased use of SLT has reportedly led to increased demand and stress on hospital services, as SLT is associated with increased graft procurement time and increased surgical time and difficulty. In particular, SLT has been associated with a higher complication rate (HAT, biliary strictures, cholangitis, sepsis) and higher rates of admissions (interventional radiology, anaesthetics) (The Children's Hospital at Westmead et al. 2006). Increased stress on services in association with SLT may be of particular relevance where the surgical aspects of the service are shared between paediatric and adult transplant units.

Quality and safety

Treatment protocols

Adherence to treatment protocols was not formally assessed in the statistical return and other information provided by the NFC sites and was reported only by RCHM.

RCHM reported that their PLT service uses a published protocol that is updated regularly and that 'covers care of the liver transplant patient from preoperative work-up through activation, immediate postoperative care and ward care until discharge.' Furthermore, an ICU clinical pathway and post-transplantation ward observation sheets are used.

RCHM and RCHB have adopted approaches to increase the safety of the procedure, especially to minimise the risks associated with SLT. At RCHM, specific protocols to reverse coagulation problems (Kyoto protocol) are used. RCHM has not recorded any HAT since the adoption of this protocol, although they report that a few cases of bleeding have occurred. At RCHB, the hepatic artery anastomosis is performed by microvascular surgeons to minimise the risk of hepatic artery damage.

The development of agreed treatment and management guidelines for PLT across all sites is considered important in order to ensure high-quality and consistent patient care across Australia.

Data collection

All sites have provided data to the Commonwealth as a requirement for funding under the NFC program. Data collection methods differed between the sites. At RCHM, data on PLT patients are transferred manually to the Victorian liver transplant unit (VLTU) on a weekly basis, and outpatient data are collected prospectively with a standardised post-transplant assessment tool. The site is currently awaiting an upgrade of the VLTU database and anticipates entering data 'live' at the RCHM site. RCHB collects data using electronic health records. Data collection methods at CHWS were not reported.

Although hospitals may provide general feedback and complaints processes, none of the PLT sites has collected data on the QoL or consumer satisfaction specifically of children and their families after PLT. Reporting requirements have been amended in 2006 to allow the routine collection of comparable QoL data in the future. Development and implementation of a national protocol for all data collection would ensure that a

common dataset across Australia is established. This would also allow closer monitoring of complications, eg, biliary strictures and hepatic artery thrombosis.

Quality- and safety-related outcomes

Complications related to PLT occurring at the 3 NFC sites are summarised in Table 8 (page 15). The incidence of unplanned readmissions to ICU, thrombosis and nosocomial infections can be used as indicators for the quality and safety of the provided PLT services. This information was not available from RCHB. At RCHM and CHWS, rates of unplanned readmissions to ICU rates and nosocomial infection of 10 to 24 per cent and 30 to 50 per cent were considered acceptable and indicate a safe and high-quality provision of the PLT service. The high rate of HAT (23%) at CHWS has raised concerns about the safety of the current treatment protocol, which need to be addressed.

Satisfaction of patients and parents/carers with the PLT service was not formally assessed by any of the NFC sites.

RCHM provides extensive information to parents/carers before the transplantation and after discharge. Information provided after discharge contains various documents 'to improve and measure both understanding and compliance with the complex medication regime,' including a quiz to test knowledge of medications, a laminated sheet with information regarding medications, and a daily or weekly medication dispensing sheet that is reviewed regularly at each clinic visit. This may contribute to the quality of post-transplantation care of patients at this site.

Teaching, training and research

Teaching and training

RCHM and CHWS reported convening weekly meetings to review transplant patients. At CHWS, these meetings are held at the adult liver transplant site at Royal Prince Alfred Hospital. At RCHM, meetings are usually held on site, although complex cases are discussed at the adult transplant site (Austin Hospital).

CHWS also reported maintaining educational and clinical links with other hospitals in Sydney (Sydney Children's Hospital Randwick, Royal Prince Alfred Hospital, Royal North Shore Hospital) and holding a weekly teaching ward round and individual teaching groups with students.

RCHM stated that senior medical staff attend one or more liver and transplant conferences per year.

RCHM and CHWS also reported on long-term training plans. RCHM has identified the need to train additional specialist nurses, and CHWS is seeking to appoint a medical fellowship position.

RCHB did not report information about teaching and training programs.

Research achievements

All NFC sites have published their research in peer-reviewed journals.

RCHB was the first site to undertake a PLT in Australia (in 1985). It also performed the first SLT in Australia (1989) and the first LDLT in the world (1990).

RCHM reported the first transjugular intrahepatic portosystemic shunt in a child in Australia, the first LCT in the Southern Hemisphere and the first REX shunt procedure performed in Australia.

Current research

Table 11 lists current research projects at the 3 NFC sites.

Table 11 Current research conducted at the 3 NFC PLT sites

NFC site	Clinical research	Quality-of-life research
CHWS, NSW	Review of renal function (glomerular filtration rate) before and after transplant Cross-sectional study of nutritional status after transplantation	Planned involvement in multicentre international QoL study (Canada, UK)—pending ethics
RCHM, VIC	Toll-like receptors—ontogeny and responses in children with hepatitis B and C Urotension II and its role in chronic liver disease and portal hypertension Immunological aspects of LCT Changes in haemostatic factors during and after liver transplantation in children A randomised controlled trial comparing the use of parenteral and oral antibiotics for cholangitis in patients with biliary atresia	QoL only informally assessed
RCHB, QLD	Antithrombin supplementation after liver transplantation (review) Long-term medical outcomes after PLT Anthropometry and active cell mass in long-term survivors of PLT Long-term cognitive, academic and psychosocial outcomes after liver transplant (start 9/2006)	Long-term cognitive, academic and psychosocial outcomes after liver transplant (start 2006) Development and validation of a disease-specific health-related QoL questionnaire for children after liver transplantation (international, multicentre)

Abbreviations: PLT = paediatric liver transplantation; NFC = Nationally Funded Centre; CHWS = New Children's Hospital, Westmead, Sydney; RCHM = Royal Children's Hospital, Melbourne; RCHB = Royal Children's Hospital, Brisbane; NSW = New South Wales; VIC = Victoria; QLD = Queensland; LCT = liver cell transplant; QoL = quality of life.

Need for continued service concentration

Demand for PLT service

Information provided in the section 'Number of patients referred to and treated at the NFC sites' (page 8) indicates that the annual number of liver transplants performed nationally between 1999 and 2005 was relatively constant and averaged 22 per year. This number represents a decrease from the early 1990s, which can be attributed mainly to a decrease in overseas referrals with the establishment of PLT centres in Asia and New Zealand.

RCHM and CHWS reported that clinical indications for PLT have expanded in recent years. Patients with conditions such as hepatic malignancies, viral hepatitis and some rare metabolic conditions, which were previously regarded as contraindications for PLT, are now offered a liver transplant as curative treatment (Hardikar et al. 2006; The Children's Hospital Westmead Liver Transplant Service 2006). As a result of these new indications, NFC sites have suggested that demand for PLT is likely to increase in the future (Hardikar et al. 2006; The Children's Hospital Westmead Liver Transplant Service 2006). The observed increase in the number of transplants at RCHM and CHWS in the last 5 years may be an indication of this anticipated trend (see section 'Number of patients referred to and treated at the NFC sites' pages 8-10), as may be the slight increase in children waiting for transplants at RCHM (see Table 2). RCHM anticipates an additional 5 or 6 referrals annually owing to the expansion of indications for PLT, and an overall increase in referrals of 50 to 75 per cent in the medium to short term (Hardikar et al. 2006; The Children's Hospital Westmead Liver Transplant Service 2006).

Although indications for PLT may have expanded, expert opinion from the advisory panel suggests that the number of transplants is likely to remain constant.

More broadly, the demand for liver transplant services overall, including post-transplantation care and long-term follow-up services, has been increasing. During 2005, CHWS's liver transplant unit averaged 12 to 15 inpatients at any one time, compared to approximately 5 to 10 patients before 2001 (Hardikar et al. 2006; The Children's Hospital Westmead Liver Transplant Service 2006). Based on average patient numbers from the last 5 years, RCHM expects a 34 per cent increase in the number of post-transplantation patients by 2011 (Hardikar 2006). The following factors may contribute to an increased demand for PLT services:

- An increase in survival of PLT patients.
- An increase in the proportion of PLT performed as SLT. SLT is generally more complex and thus associated with more complications (biliary strictures, hepatic vein obstructions), which require additional post-transplantation services such as interventional radiology services (eg, biliary tract stricture dilatation, hepatic vein dilatations, cholangiography, ultrasound-guided needle liver biopsy), imaging (eg, MRI, CT) and anaesthetics (eg, for oesophageal variceal banding) (The Children's Hospital Westmead Liver Transplant Service 2006).

Technology

PLT requires a specialised, multidisciplinary team for pre-, peri- and post-transplantation paediatric care, including liver and biliary surgeons, hepatologists and gastroenterologists, paediatric anaesthetists, radiologists, paediatric intensive care unit (ICU) specialists, dietitians, nurse educators, social workers, donor technicians and transplant recipient coordinators. The PLT team at RCHB also includes microvascular surgeons.

These requirements apply to all types of PLT, but are particularly relevant in the more recently developed techniques such as SLT and LDLT. SLT is much more time-consuming and complex than whole-liver graft transplantation, and extensive experience is necessary to ensure high-quality and safe service provision.

Special requirements for service provision of LDLT have been emphasised by a recent Canadian HTA report that finds that ‘programs performing LDLT must adhere to an extremely high standard of care that includes standard protocols for preoperative evaluation of potential donors and postoperative follow-up of donors and recipients, as well as strong psychosocial evaluation and support programs’ (Scott 2004).

Continuing developments in immunosuppressive therapies further contribute to the specialised expertise requirements of PLT.

Demonstrated evidence of effectiveness of service

The previous MSAC review found that in the long term, ‘some of the genetic enzyme deficiency diseases may be treated by methods other than transplantation, for example cell therapy and gene therapy’ (MSAC 2002). However, to date no alternative treatment is available for children with an indication for liver transplantation (Hardikar et al. 2006) and PLT remains the treatment of choice.

All 3 sites have achieved 1-year patient survival rates of between 83 and 88 per cent (see Table 7, page 14), which compare well with data from the United Kingdom (93% 2001–2004; 90% 1995–2000) and the United States (SPLIT registry: 88%; CCHMC paediatric liver care centre: 92%) (NHS Blood and Transplant 2006; Tiao et al. 2006). Complication rates are generally acceptable as well, although the rate of HAT (23%) at CHWS was considered high.

Minimum required patient throughput

The previous MSAC review found ‘evidence of an association between transplant program volume and patient survival’, although the minimum annual throughput required for maintenance of skills was difficult to determine (MSAC 2002). Current expert advice is that international data on minimum throughput in PLT are not consistent. Expert opinion from the advisory panel suggests that maintenance of surgical skills may be facilitated if the surgeon conducting liver transplants in children also undertakes adult liver transplants. In this regard, close cooperation of a PLT service with an adult transplant unit may be advantageous. Furthermore, if a site had high patient throughput in the past, relatively lower patient throughput may suffice for maintenance of skill.

In the United Kingdom, 3 centres (Birmingham, King's College, Leeds) perform PLTs in children and adolescents aged 0 to 17 years. Between April 2005 and March 2006, 86 patients received a liver transplant at these sites (NHS Blood and Transplant 2006).

Equity of access

Ensuring equity of access is an important criterion of the NFC Program and is particularly relevant in PLT. Special considerations for PLT patients include the uncertain waiting period for a donor organ; the speed with which the patient needs to be mobilised when a donor organ becomes available; the logistics of getting to the hospital that has the transplantation unit; the possibility of extended hospitalisation if complications occur; and the need for frequent outpatient visits during the first year after transplantation (MSAC 2002).

Travel and accommodation are included in the NFC episode of care, which ensures equity of access of patients being referred to an NFC PLT site from interstate. However, differences across states and territories in assistance schemes for travel and accommodation for patients and their families within the state or territory may result in differences in access to the PLT service in patients from remote areas.

The data available do not indicate any differences in survival, waiting times or deaths on the waiting list by state of referral.

Cost

PLT is a complicated surgical procedure, and the item incurring the highest cost is likely to be the ICU stay during and after transplant. PLT patients also require a lifelong period of follow-up and immunosuppressive therapy at high cost. However, the episode of care considered under NFC funding for PLT does not consider lifelong follow-up costs. Outpatient follow-up and the cost of immunosuppressive therapy provided to admitted public hospital patients are usually carried by referring jurisdictions. Immunosuppressive drugs for non-admitted patients are funded through the Highly Specialised Drugs program.

No equipment with a high capital cost is needed to perform PLT, and there are no equipment or construction requirements associated with a high capital cost that would make concentration of services more cost-effective.

Although the limited demand and the specialised expertise and infrastructure involved suggest that concentration of services to a high-volume program may be more efficient than provision of PLT at more than 1 centre, there is no evidence that a high-volume program will have superior outcomes at lower costs (MSAC 2002).

Cost estimates

All 3 current NFC sites provided cost estimates for their PLT service. Cost estimates were \$254,357 for CHWS, \$198,900 for RCHM and \$170,590 for RCHB. The CHWS estimate is an average cost of 14 actual patients undergoing WLT (1), SLT (10), LDLT

(1) or RLT (2). RCHB and RCHM cost estimates were derived by using an average episode of care scenario.

However, cost estimates provided by RCHB and RCHM are not indicative of average costs, as they include costs associated with SLT (additional costs of surgical and theatre staff) and with LDLT (additional cost of diagnostic work-up and review [RCHM only]). Thus, for RCHB and RCHM, total costs for each type of liver transplant—WLT, SLT and LDLT—were calculated separately, including only the costs specific to the liver transplant type. For CHWS, type-specific transplant costs are available that are based on different numbers of actual patients (between 1 and 10, see previous paragraph). The type-specific total PLT costs are displayed in Table 13 (page 31).

The cost estimates were broken down into pretransplant assessment costs, transplant admission costs, other direct patient costs (patient/supporter travel and accommodation) and indirect costs. These components are summarised for each site in Table 12. The costings provided by each site are discussed separately in the sections below, and differences between the sites are discussed on page 28. Detailed applicant cost tables are provided in Appendix D.

CHWS—New South Wales costing

CHWS has estimated a cost per patient for PLT of \$254,357. This is an average cost of 14 actual patients undergoing WLT (1), SLT (10), LDLT (1) and RLT (2). Average total costs by type of transplant were \$195,812 for WLT, \$288,095 for SLT, \$136,965 for LDLT and \$173,635 for RLT.

These estimates include direct and indirect costs associated with PLT, considering costs of staff, ICU and general ward stay, pharmacy, imaging, pathology, allied health, post-transplantation follow-up, and patient travel and accommodation.

CHWS provided cost details from their patient reporting systems, with actual costs where available. The reporting categories differ from the template provided to the applicants. Thus, some costs were provided in greater detail and others were collated; and some were included in a different section; eg, it was reported to be difficult to separate costs of diagnostics, labs and overheads for ICU, and thus these were included in the inpatient ward costs. From the information available, it appears that the patient data provided apply to patients receiving PLT in 2005–06.

Latest cost information provided by CHWS included detailed costings of individual patients. A detailed analysis of this information was not provided by CHWS and was beyond the scope of this review. A summary of the individual costing information by type of liver transplant is included in Appendix D.

The cost estimates provided did not report indirect costs separately. Indirect costs were included under various cost categories, such as medical, allied health staff, diagnostic imaging and pathology tests, and ICU and general ward stay. The cost estimates considered costs of post-transplantation follow-up up to 16 years.

The sections below comment on details of these patient-level costings by type of transplant, particularly where costs vary widely between individual patients.

Whole liver transplant

The cost estimate for a patient undergoing WLT was \$195,812, as based on 1 patient treated at CHWS. Costing tables are provided in Appendix D (detailed costing in Table 17 and summary in Table 16). The following main cost remarks should be considered.

- Costs of referral to the PLT service were not included. It is reported that this patient was already admitted to hospital at the time the possibility of a liver transplant arose.
- The episode of care for this patient included 5.5 days ICU stay, 22 days in ward, and follow-up after admission from 3 months to 16 years. Follow-up costs up to 12 months are reported to be based on actual patient episodes; costs from 12 months onwards were estimated on the basis of an assumed 4 visits per year plus pathology and pharmacy costs. It is not clear from the information available how long this patient was monitored before transplant, ie, how long the patient was on the waiting list before receiving a transplant.
- In addition to the costs of post-transplantation follow-up, 'other direct patient costs' of \$92,725 include resource use associated with travel (4 cab charge vouchers) and accommodation (27 days at \$20/day).
- Indirect costs were not reported separately. However, they are reported to be included in costs of staff, diagnostic imaging, pathology tests, ICU and ward stay.

Split liver transplant

An average cost estimate for SLT at CHWS was provided, based on 10 patients. A summary of the costs incurred by each patient is given in Appendix D (Table 16). The following section discusses the main aspects of the individual costing data provided, in particular where costs varied widely:

- Costs for referral to the service were not included for any of the 10 patients.
- The average work-up cost was \$5,135; this cost generally ranged between \$0 and \$4,159, but 1 patient incurred work-up costs of \$38,825. It appears that the major cost component of these high work-up costs was pharmacy (89 dispensed drugs, \$31,856; no further details provided).
- The average cost of pretransplant monitoring was \$51,995, generally ranging from \$0 to \$58,340, but 1 patient incurred costs of \$378,341. It appears that the major components of the high resource use associated with pretransplant monitoring in this patient were pharmacy (43 dispensed drugs, \$316,279; no further details provided) and medical and nursing staff monitoring (\$46,623).
- Costs incurred with intensive care admission were \$36,291 on average, ranging mainly between 0\$ and \$42,277; there was 1 outlier incurring an ICU admission cost of \$189,413. Cost of ICU stay was associated with length of stay and the medical and nursing monitoring and diagnostic investigations required. The patient incurring the highest cost during ICU admission appears to have had an ICU stay of 93 days, incurring ICU ward stay costs of \$63,049 (direct and indirect) and diagnostic investigation costs totalling \$81,791.
- Costs associated with general ward admission were \$111,777 on average, ranging between \$0 and \$150,876, with the exception of 1 patient incurring a cost of \$321,146. For this patient, ward stay costs were \$184,516 (direct and indirect costs)

for 132 days, incurring another \$50,668 for medical monitoring by a gastroenterology specialist (3174 hours, 'based on service weight').

- The costing data provided included costs of follow-up after transplantation from 3 months to 16 years. Follow-up costs up to 12 months are based on actual patient episodes; costs of outpatient transplant review from 12 months onwards were estimated on the basis of an assumed 4 visits per year plus pathology and pharmacy costs.
- In addition to the costs of post-admission follow-up, resource use associated with travel (4 cab charge vouchers) and accommodation (at \$20 per day) was costed.

Living-donor liver transplant

The cost estimate for a patient undergoing LDLT was \$136,965, based on 1 patient. A summary of this costing is provided in Appendix D (Table 16). The following main cost remarks should be considered:

- For this patient, no resource use associated with referral to service, work-up, acceptance on list and pretransplant monitoring was costed.
- The costs for stay in ICU and general ward were based on 9 days in ICU and 45 days in general ward. Costs of follow-up after transplantation were also considered. Follow-up costs up to 3 months included 2 inpatient visits (costed with average cost of DRG H02A major biliary tract procedures and DRG K63Z inborn errors of metabolism), and costs for follow-up from 3 to 6 months were based on 4 outpatient visits. Costs of follow-up from 12 months to 16 years were estimated on the basis of an assumed 4 visits per year plus pathology and pharmacy costs.
- Besides costs of post-transplantation follow-up, 'other direct patient costs' of \$41,398 include resource use associated with travel (4 cab charge vouchers) and accommodation (54 days at \$20/day).
- Indirect costs were not reported separately, but were reported to be included in costs of diagnostic imaging and pathology tests, ICU and ward stay.

Cut-down liver transplant

The cost estimate for RLT at CHWS was \$113,842, the average of 2 actual patients treated at CHWS. The individual costings are summarised in Appendix D (Table 16).

RCHM Victoria costing

RCHM has estimated a cost per patient for PLT of \$198,900. This estimate includes costs associated with SLT (additional costs of surgical and theatre staff) and with LDLT (additional cost of diagnostic work-up and review). Total costs for each type of liver transplant—whole liver, split liver and living-donor liver transplant— were calculated to include only the specific cost of the liver transplant type.

The cost analysis provided by RCHM has been broken down into pretransplant assessment costs, transplant admission costs, other direct patient costs (patient/supporter travel and accommodation) and indirect costs. These cost components are summarised in Table 12. Details of the costings are provided in Appendix D (Tables 20 to 23).

Cost estimates include direct and indirect costs associated with PLT and consider staff, ICU, ward, pharmacy, imaging, pathology, allied health, patient travel and accommodation, and indirect costs.

This costing was based on a combination of information from the hospital's clinical costing system and from actual caseload experience and data. The exact steps in the clinical pathway (including the staff involved and the actual length of stay in ICU, high-dependency unit and general ward) were identified based on the 10-year experience of the PLT team. This represents an average cost scenario; high and low outlier patients were excluded from the costing.

The cost analysis included costs accrued at Austin Hospital, which hosts the adult liver transplant service and cooperates with RCHM in the PLT program. Costs to Austin Hospital are associated with LDLT work-up, expert review after acceptance on the list, surgical staff (not theatre usage or staff), postoperative surgical review, postoperative immunosuppressive tests and staff on-call costs (indirect costs) (see details in Appendix D, Tables 20 to 23).

Main cost remarks

- The episode of care assumed in this analysis includes a 12-week pretransplant monitoring period (waiting time) and a 45-day postoperative period in hospital (10 days ICU, 35 days general ward). No post-admission follow-up consultation or testing has been included in the costing.
- RCHM has provided an estimate of the resource use associated with travel and accommodation, of \$760, that considers that only 20 per cent of patients receiving liver transplant at RCHM are interstate patients and thus provides an average estimate for these costs. For each interstate patient, accommodation costs of \$2,800 (14 days @ \$200) and the cost of 2 interstate trips of \$1,000 (2 trips @ \$500) were considered. Applying total costs for travel and accommodation results in a total cost for 1 interstate patient of \$205,057 (this estimate also takes into account higher indirect costs, calculated as 15 per cent of direct costs).
- Indirect costs included the costs of program management (including clinical nurse coordinator) and overheads. Staff overheads were included in staff rates. Other overheads (infrastructure, depreciation, maintenance, etc.) were calculated by applying a 15 per cent rate to the overall direct costs.
- Costs from S100 revenue (\$8,086) were subtracted from admission costs.

RCHB Queensland costing

RCHB estimated a cost per patient of \$170,590. This estimate includes costs associated with SLT (additional costs of surgical and theatre staff). Total costs for WLT were calculated by subtracting the SLT-specific costs of the total estimate. No costs associated with LDLT were considered.

The cost analysis provided by RCHB has been broken down into pretransplant assessment costs, transplant admission costs, other direct patient costs (patient/supporter travel and accommodation) and indirect costs. These cost components are summarised in Table 12. Details of the costings are provided in Appendix D (Tables 24 to 27).

Cost estimates include direct and indirect costs associated with PLT and consider staff, ICU, ward, pharmacy, imaging, pathology, allied health, patient travel and accommodation, and indirect costs.

This costing was provided using a combination of costing approaches. The clinical costing system Transition II has been used 'where possible'; from the information available, this was the case for estimation of indirect overhead costs. Travel and accommodation costs were based on actual expenditure for the only interstate patient treated in 2005–06. Staff costs were based on actual labour costs for staff identified in the program, and other items were based on an average episode of care scenario.

Main cost remarks

- The episode of care assumed in this analysis included a 12-month pretransplant monitoring period (waiting time) and a 7-week postoperative period in hospital (7 days ICU, 30 days general ward). No post-admission follow-up consultation or testing was included.
- The resource use associated with travel and accommodation for an interstate patient was included in the cost estimate and considered accommodation costs of \$6,600 and the cost of 2 interstate trips of \$3,200 (no further detail provided).
- Indirect costs included the costs of program management (CNC nurse coordinator) and overheads. It appears that staff overheads were included in staff rates. Other overhead costs (infrastructure, depreciation, maintenance, etc.) were based on average cost per liver transplant patient treated at RCHB from the clinical costing system (Transition II).

Appraisal of differences between costings

Tables 12 and 13 display cost components and total costs by type of liver transplant for all 3 PLT NFC sites. However, the comparability of cost estimates is limited owing to differences between the sites in the quality and extent of costing information provided, particularly with regards to the episode of care assumed. The average cost estimate reported by CHWS was higher than those from RCHB and RCHM. Considering that 10 of the 14 patients included in the average estimate at CHWS received SLT, it appears that the difference in average cost estimates between CHWS and the 2 other sites may be driven by the high SLT costs at CHWS, which are 33 per cent higher than at the other sites (see Table 13).

Specific costs associated with SLT provided by RCHM and RCHB only consider the additional costs of surgical and theatre staff and do not assume any other additional resources, such as those associated with treatment of complications and postoperative care that may occur with this type of PLT. The CHWS estimate for cost of SLTs is based on 10 actual patients. This may render the estimate more likely to accurately capture any additional costs of SLT. On the other hand, there were extreme cost outliers that resulted from high resource use associated with dispensed drugs during pretransplant monitoring (\$316,279 in 1 patient), and long ICU and general ward stays of 93 and 132 days, respectively, in 2 other patients. As average costs may be inflated by these extreme outlier costs, they may not be an accurate representation of an average scenario. Furthermore, costs of post-transplantation follow-up to 16 years were considered only by CHWS, resulting in a much higher estimate of 'other direct patient costs' than at RCHM or RCHB for all types of PLT, including SLT. This may overestimate NFC program costs if the episode of care did not extend to post-transplantation follow-up to 16 years.

Table 12 Summary of cost components of cost estimates provided by 3 NFC PLT sites

	NSW ^a	VIC ^b	QLD
COST ESTIMATES PROVIDED			
Pretransplant costs			
Referral to service	\$0	\$772	\$420
Work-up	\$3,761	\$3,810	\$1,463
(Work-up LDLT)	n.a.	(\$7,243) ^{c,d}	n.r.
Acceptance on list	\$977	\$2,038 ^c	\$3,713
Pretransplant monitoring	\$38,046	\$6,112	\$12,435
<i>Total pretransplant costs</i>	<i>\$42,784</i>	<i>\$12,732</i>	<i>\$18,032</i>
<i>Total pretransplant costs including LDLT costs^d</i>	<i>n.r.</i>	<i>\$16,165</i>	<i>n.r.</i>
Transplant admission costs			
Theatre/surgery	\$8,868	\$17,300 ^c	\$28,995
(Theatre/surgery split liver)		(\$17,676) ^{c,e}	\$32,578
Intensive care admission	\$31,709	\$41,806 ^c	\$39,556
General ward admission	\$100,705	\$48,959 ^c	\$30,996
<i>Total transplant admission costs</i>	<i>\$141,282</i>	<i>\$108,065</i>	<i>\$117,578</i>
<i>Total transplant admission costs including split liver costs^e</i>	<i>n.r.</i>	<i>\$108,441</i>	<i>\$121,161</i>
<i>Other direct patient costs</i>	<i>\$70,291</i>	<i>\$3,800 (\$760)^f</i>	<i>\$9,800</i>
Items included:			
Accommodation for interstate patients	Variable (at \$20/day)	14 d at \$200/day \$2,800 (\$560) ^f	\$6,600 (actual expenses)
Patient transport		2 interstate trips \$1,000 (\$200) ^f	2 interstate trips \$3,200
Post-transplantation follow-up	First 3–6 months: actual patient episodes 12 mo – 16 y: 4 visits/year+ tests & pharmacy	Not included	Not included
<i>Overheads/indirect costs</i>	<i>\$0</i>	<i>\$73,534</i>	<i>\$39,628</i>
Items included:	(not reported separately; included in cost items above)	\$52,262: CNC nurse coordinator 1 h/day for length of stay (\$2,430), staff on-call costs (\$36,745) ^c admin. (\$13,087)	CNC nurse coordinator 1.5 FTE \$21,523
Program management			
Overheads	n.r.	\$21,273 ^g	18,105 ^h

Abbreviations: NFC = Nationally Funded Centre; PLT = paediatric liver transplantation; NSW= New South Wales; VIC = Victoria; QLD = Queensland; LDLT = living-donor liver transplantation; FTE = full-time equivalent; CNC = clinical nurse consultant.

- a Based on overall average of costs reported (14 patients: 1 living donor, 2 whole grafts, 2 cut down, 9 split). Costs by type of liver transplant are provided in Appendix D.
- b Costs for Victoria include costs incurred by the Royal Children's Hospital and Austin Hospital.
- c These cost items include costs incurred by Austin Hospital.
- d 'Work-up LDLT costs' and not 'Work-up costs' are used for calculation of total pretransplant costs including LDLT costs.
- e 'Theatre/surgery split liver' costs and not 'Theatre/surgery' costs are used to calculate total transplant admission costs including split liver costs.
- f Only 20 per cent of patients come from interstate, and cost of travel and accommodation was applied only to these patients to calculate average costs. Cost in parentheses refers to total costs for 1 interstate patient.
- g Staff overheads are included in staff costs.
- h Derived from clinical costing system (Transition II). Staff overheads are included in staff costs.

CHWS average estimates were higher for all cost components than those at RCHM and RCHB (see Table 12). Pretransplant and transplant admission costs were comparable at RCHB and RCHM despite differences in certain aspects of the episode of care (eg, waiting time and length of ICU and general ward stays), but CHWS costs were higher.

Costs of travel and accommodation were considered by all sites, but CHWS did not consider interstate travel costs.

Indirect costs were not costed out separately by the CHWS, but were included in relevant cost categories for staff, test, and ICU and ward stay costs. Indirect costs varied at RCHB and RCHM, mainly because of high staff on-call costs that were included as program management costs by RCHM.

Table 13 Summary of cost estimates provided by 3 NFC PLT sites by type of transplant

	CHWS ^a	RCHM ^b	RCHB
Whole liver transplant	\$195,812	\$195,092	\$167,007
Split liver transplant	\$288,095	\$195,469	\$170,590
Living-donor liver transplant	\$136,965	\$198,525	n.r.
Reduced liver transplant	\$173,635	n.r.	n.r.

Abbreviations: NFC = Nationally Funded Centre; PLT = paediatric liver transplantation; CHWS = New Children's Hospital, Westmead, Sydney; RCHM = Royal Children's Hospital, Melbourne; RCHB = Royal Children's Hospital, Brisbane.

a The average NSW cost estimate was \$254,357 (based on 14 patients).

b These are costs for an average patient (travel and accommodation cost applied to 20%). Applying total costs for travel and accommodation results in total costs for 1 interstate patient of \$201,249 for WLT, \$201,625 for SLT and \$204,681 for LDLT (these estimates also take into account higher indirect costs, calculated as 15% of direct costs at RCHM).

Summary and discussion

PLT is the only treatment available for children with irretrievable acute liver failure or chronic end-stage liver disease. Between 1999 and 2006, 172 PLTs were performed in Australia (CHWS: 81; RCHB: 51; RCHM: 40), at an average rate of 22 per year (1999–2005). No accurate figures on total numbers of PLT by type of graft at the 3 NFC PLT sites were available, but PLT data from the ANZLTR that include PLT patients in Western Australia and New Zealand indicate that between 2001 and 2005, close to half of PLTs were performed as SLT, and the remainder as either RLT or WLT.

The 3 NFC sites reported similar 1-year survival rates, ranging between 83 and 88 per cent. These compare well with data from the United Kingdom (93% 2001–2004; 90% 1995–2000) and the United States (SPLIT registry: 88%; CCHMC paediatric liver care centre: 92%) (NHS Blood and Transplant 2006; Tiao et al. 2006). RCHM reported a perioperative mortality rate of 13 per cent (6/47) from 1988 to 2000 (figures were not reported by CHWS or RCHB). Rates of unplanned readmissions to ICU and nosocomial infections were not significantly different between sites, and ranged from 10 to 19 per cent and 30 to 50 per cent respectively (figures were not reported by RCHB). The 3 NFC sites reported similar rates of incidence of retransplantation (11%–15%) and biliary leak requiring intervention (7%–11%). CHWS reported a significantly higher rate of thrombosis (PVT, HAT) than the other 2 sites. Ten of the 16 cases of thrombosis (63%) reported by CHWS in the period 1999 to 2006 occurred in patients who received a split liver graft, indicating the need for additional preventive measures at CHWS.

The 3 NFC PLT sites differ in their approach to service delivery. The services at RCHB and RCHM are set up as combined units that share surgical personnel with the adult transplant unit in their cities, whereas the service at CHWS is a stand-alone PLT unit. Given the outcomes of PLT observed at the 3 sites, the advisory panel found that combined units appear to function at least as well as if not better than stand-alone paediatric surgical units. The advisory panel further suggested that generally, a broad approach to service delivery and strong ties between the PLT unit and the adult transplant unit would be desirable. However, it has also been acknowledged that increased stress on services in association with SLT may be of particular relevance in combined units. At RCHM, where there are only 2 anaesthetists for both the adult and children transplant services and capacities would be stretched if there were transplant operations being conducted at both units at the same time. This is of relevance especially for the provision of SLT. At RCHM, of 19 split livers, 9 had to be discarded, possibly owing to a lack of capacity to perform concurrent adult and paediatric liver transplantation. The panel advised that capacities need to be maximised to ensure that both segments resulting from splitting the liver are used. This may involve the consideration of graft transport to other transplant sites if necessary.

A lack of succession planning for PLT staff, in particular surgical staff, was identified by the advisory panel at all sites. In particular, the advisory panel felt that at CHWS, the sustainability of the service was jeopardised given that its PLT service has been based on only 1 PLT surgeon for 20 years. How problems with resource management are approached depends on the number of sites chosen to provide the PLT NFC service in the future. If the service continues to be funded at 3 sites, resource planning of paediatric surgical skills may be difficult, and service provision in combined units is likely to be the more viable approach. If PLT services are provided in combined units, options for

succession planning may include the establishment of different career structures (eg, PLT surgery plus other surgery, such as adult transplants). It is recommended that a coordinated plan for training and workforce management be implemented within the NFC PLT program.

The advisory panel further suggested that having a full-time transplant recipient coordinator based at the site is an advantage. Problems may arise at CHWS, where the recipient coordinator is based at the adult liver transplant service at Royal Prince Alfred Hospital.

The provision of long-stay accommodation facilities is considered important given the long waiting times and potentially long episode of hospitalised care associated with PLT. It was found that the facilities in NSW did not meet an acceptable standard and need improvement.

For effective provision of PLT services, appropriate coordination of paediatric liver grafts is necessary. The advisory panel suggested that issues around organ procurement, recipient coordination, donor harvesting and transportation need to be discussed on a national level and be appropriately resourced.

The advisory panel considered a protocol-driven approach to service delivery to be an important aspect of quality assurance of the PLT service. In particular, the protocol-based approaches to minimising the risks associated with SLTs have been welcomed. The advisory panel suggested that agreed treatment and management guidelines for PLT across all sites be developed in order to ensure high-quality and consistent patient care across Australia.

Although the previous MSAC report (2002, p 16) 'noted the need for more rigorous outcome data on mortality, morbidity and quality of life', the advisory panel found that gaps still exist in data collection at the NFC sites. Reporting requirements should be amended to include information on QoL or consumer satisfaction of children and their families. Furthermore, development and implementation of a protocol for data collection would ensure that a common dataset across Australia is established and allow closer monitoring of complications, such as biliary strictures and HAT.

PLT is a highly specialised, multidisciplinary procedure requiring extensive experience to ensure high-quality and safe service provision. These aspects are particularly relevant in more recently developed and complex techniques such as SLT and LDLT. Concentration of PLT services is important for maintenance of the skilled multidisciplinary team, and especially of the surgical skills involved in conducting PLT; however, an estimate of minimum annual patient throughput is difficult to determine.

Patient numbers are not expected to change to a large extent in the long term, and so to remain around the current average of 22 transplants per year. However, increased survival and an increase in the proportion of transplants performed as SLTs may contribute to an increased demand for PLT services, especially post-transplantation care and follow-up services. Still, a current demand estimate of 22 transplants per year indicates that 1 NFC PLT unit would suffice, but 2 units would be adequate considering both demand and access issues. Combined adult–paediatric transplant units and a protocol-driven approach to service delivery may provide advantages in terms of feasibility to maintain critical patient throughput.

Cost estimates by the 3 NFC sites ranged from \$167,007 (RCHB) to \$195,812 (CHWS) for WLT and from \$170,590 (RCHB) to \$288,095 (CHWS) for SLT. However, variability in the quality and extent of the costing information provided limits the comparability of these cost estimates.

Recommendations

MSAC has considered the provision of paediatric liver transplantation services in Australia and recommends that the procedure should continue to be funded under NFC arrangements with a further review in three years.

Based on estimated national demand of around 20 patients per year, the Committee considers that one NFC unit would be sufficient, but that two units would be appropriate having regard to access issues.

The outcomes of all three sites compare well with international data in relation to one year survival. The Committee found that combined adult-paediatric units appear to function at least as well, if not better, than stand-alone paediatric surgical units. It is the Committee's opinion that combined adult-paediatric transplant units and a protocol driven approach to service delivery is likely to be a more viable approach into the future.

The MSAC recommends the following to enhance the operation of the PLT NFC program:

- development of PLT treatment and management guidelines to achieve reduction of morbidity and complications, especially those associated with split liver transplantation;
- that living-donor liver transplantation be performed in accordance with agreed selection and treatment guidelines;
- improved and consistent data collection, with a stronger emphasis on health outcomes, including quality of life; and
- that surgical workforce succession planning be addressed in a coordinated plan for training and workforce management.

Appendix A MSAC terms of reference and membership

MSAC's terms of reference are to:

- advise the Minister for Health and Ageing on the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost-effectiveness and under what circumstances public funding should be supported;
- advise the Minister for Health and Ageing on which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost-effectiveness;
- advise the Minister for Health and Ageing on references related either to new and/or existing medical technologies and procedures; and
- undertake health technology assessment work referred by the Australian Health Ministers' Advisory Council (AHMAC) and report its findings to AHMAC.

The membership of MSAC comprises a mix of expertise covering pathology, nuclear medicine, surgery, specialist medicine, general practice, clinical epidemiology, clinical trials, health economics, consumers, and health administration and planning:

Member	Expertise or affiliation
Dr Stephen Blamey (Chair)	general surgery
Associate Professor John Atherton	cardiology
Professor Syd Bell	pathology
Dr Michael Cleary	emergency medicine
Dr Paul Craft	clinical epidemiology and oncology
Dr Kwun Fong	thoracic medicine
Dr Debra Graves	medical administration
Dr David Gillespie	gastroenterology
Professor Jane Hall	health economics
Professor John Horvath	Chief Medical Officer, Department of Health and Ageing
Dr Terri Jackson	health economics
Professor Brendon Kearney	health administration and planning
Associate Professor Frederick Khafagi	nuclear medicine
Associate Professor Donald Perry-Keene	endocrinology
Dr Ray Kirk	health research
Dr Ewa Piejko	general practice
Ms Sheila Rimmer	consumer health issues
Ms Samantha Robertson	Acting Assistant Secretary, Department of Health and Ageing

Professor Ken Thomson	radiology
Dr Douglas Travis	urology
Dr Mary Turner	Australian Health Ministers' Advisory Council representative
Dr David Wood	orthopaedics

Appendix B Advisory panel

Advisory panel

Professor Brendon Kearney (Chair) MBBS FRACP FRACMA Executive Director Clinical Systems Department of Human Services South Australia	Member of MSAC
Mr Stephen Blamey BSc MBBS FRACS Consultant General and Gastrointestinal Surgeon Monash Medical Centre Victoria	Member of MSAC
Dr Mary Turner MBBS DCCH MHA MBA FRACP FRACMA Senior Medical Adviser Funding, Health and Information Policy Branch Metropolitan Health and Aged Care Services Victoria	Member of MSAC
Dr Jane Cook Senior Medical Adviser Health Technology Section Medicare Benefits Branch Medical and Pharmaceutical Services Division Department of Health and Ageing ACT	Department of Health and Ageing
Dr Doug Travis MBBS FRACS Head of Urology Western Health Victoria	Member of MSAC
Ms Barbara Renton BA GradDipEd GradDipApplPsych GradCertHealthEcon MBA Director Intergovernment Relations SA Department of Health South Australia	NFC Reference Group representative

Dr Robert Padbury

Division of Surgical and Specialty Services
Flinders Medical Centre
South Australia

Dr David Moore

Women's and Children's Hospital
South Australia

Appendix C Identification of existing systematic reviews

The INAHTA database (<http://www.crd.york.ac.uk/crdweb/>) was searched for HTA reports and systematic reviews on PLT published since 2002.

The search strategy combined the terms ‘pediatric’, ‘paediatric’ and ‘child’ with the term ‘liver transplant’ and yielded 32 results (Table 14).

Table 14 Search terms used to identify HTA reports, INAHTA database, 2002 – November 2006

Search terms	Number of articles identified
P(a)ediatric liver transplant*	6
child* liver transplant*	26

Two of these 32 papers (1 HTA, 1 published systematic review) addressed the purpose of this review—liver transplantation in children—and were thus included in the review. Table 15 provides a summary of methods, results and quality of these studies.

Table 15 Summary of existing systematic reviews and HTA reports published since 2002

Author, place & year	Objective	Methods	Quality assessment of review
Alberta Heritage Foundation for Medical Research Alberta, Canada 2004 Information paper	To evaluate the published evidence on the safety, efficacy, and current status of LDLT for the treatment of end-stage liver disease in children	Literature review: <i>Databases:</i> EBM reviews—ACP Journal Club, EMBASE, Medline, Cochrane Library, HealthSTAR, CINAHL, Science Citation Index, NHS CRD (UK), Biological Abstracts, HTA agencies (as per CCOHTA HTA checklist) <i>Time period:</i> January 1995 – June 2000 <i>Inclusion/exclusion criteria:</i> <i>Study types/design:</i> included systematic reviews, comparative studies with $n \geq 10$, in English <i>Population:</i> children (<18 y of age) undergoing liver transplantation for any indication; living donors whose donated liver graft was transplanted into a child (<18 y of age) <i>Intervention:</i> any type of liver transplant where graft is harvested from living donor <i>Comparator:</i> any type of liver transplant where graft is harvested from cadaveric donor, if results are presented by graft type <i>Outcomes:</i> at least 1 of following for both intervention and comparator: perioperative and postoperative mortality or morbidity, graft survival, convalescence interval, QoL, liver function <i>Quality:</i> Search strategy described; no details on number of reviewers and quality assessment of studies; standardised data extraction	FAIR QUALITY Was the research question clearly defined? YES Were inclusion/exclusion criteria reported that addressed the review question? YES Was the search adequate? YES Was the quality of the included studies assessed? NO Are sufficient details about the individual included studies presented? YES
Results: <u>Included studies:</u> <ul style="list-style-type: none"> 25 studies were included in the review: 11 non-randomised comparative studies reported recipient outcomes; 14 case series reported donor outcomes. No studies were reported as prospective. <u>Outcomes reported</u> <ul style="list-style-type: none"> Of 14 studies reporting donor outcomes, 14 reported on postoperative mortality or complications, 7 on operative outcomes and 8 on length of hospital stay. Of 11 studies of recipient outcomes, 9 reported on effectiveness outcomes, including patient outcomes (8) or graft survival (1 study reported on graft survival alone), and 6 reported on postoperative complications, including primary graft non-function (4), acute graft rejection (3), retransplantation rate (1) and reoperation rate (1). Donor outcomes <i>Study characteristics</i> <ul style="list-style-type: none"> 14 studies: 712 patients; median study period 5.5 years (13/14 studies) Length of follow-up reported by 5 studies; 2 studies reported > 1 year follow-up 			

Safety outcomes

- Mean duration of graft procurement procedure ~4–6 hours
- Average hospital stay = 5–14 days (8 studies)
- Postoperative deaths = 1/35(2.9%) (reported by 1 of 10 studies)
- Blood transfusion rare (<4%) except in 1 study where >50% donors received transfusion (6 studies)
- Postoperative complications included bile leak, incisional hernia, gastroduodenal ulcer and wound infection; 1 study reported 4% reoperation rates (10 studies)
- Recuperation period poorly reported: 1 study reported that ~72% of patients attained pre-donor status <3 months after procedure
- Quality of life: 1 study reported no donor regretted participation; 67% reported being regarded as non-patients with inadequate postoperative pain and follow-up; family relationships generally strengthened but most donors experienced financial strain

Recipient outcomes1. LDLT v. cadaveric whole organ transplant*Study characteristics*

- 8 comparative studies, median study period 11.5 years
- 2 registry studies:
 - (a) Roberts et al. 2004, US Organ Procurement & Transplantation Network registry, $N = 3800$ (primary transplants)
 - (b) Sindhi et al. 1999, United Network for Organ Sharing Scientific Registry Data (1990–1996), $N = 3400$ (some overlap with study (a), included wider age range and repeat transplants)

Safety

Reoperation: No difference LDLT v. cadaveric

Vascular complications: Conflicting results or no difference in other complications such as hepatic outflow or portal vein, biliary vein or hepatic vein complications

*Effectiveness**Survival*

Primary studies

- At 6 months—similar survival rates
- 12 months and up to 5 years LDLT higher than cadaveric, median 5-year survival LDLT 92% v. cadaveric 81%

Registry data

- Roberts et al. (2004) registry study: no difference in mortality of children 0–2 years and >10 years; higher risk of mortality in children 2–10 years ($P = 0.02$) for LDLT v. cadaveric.
- Sindhi et al. (1999) registry study: no difference in patient survival rates at 12 months; in patients <1 year improved patient outcomes for LDLT versus cadaveric

Graft survival rates

Primary studies

- Median 5-year graft survival LDLT 92% v. cadaveric 73%

Registry data

- Roberts et al. (2004) registry study: 30% lower risk of graft failure for LDLT v. cadaveric for children 0–2 years, higher risk of graft failure for LDLT v. cadaveric for children 2–10 years ($P = 0.02$); age 11–16 years ($P = 0.0001$)
- Sindhi et al. (1999) registry study: no difference in graft survival rates at 12 months; in patients <1 year improved graft outcomes for LDLT versus cadaveric

Primary graft non-function

No difference LDLT v. cadaveric

2. LDLT v. RSLT***Study characteristics***

- 5 comparative studies, median study period 11.6 years
- 1 registry study: Sindhi et al. (1999), $N = 3400$

Safety

Reoperation: NR

Vascular complications: lower rates of vascular complications for LDLT v. RSLT

Acute graft rejection: no difference detected

Effectiveness***Survival*****Primary studies**

- At 3 months—similar survival rates
- 12 months and up to 5 years LDLT higher survival than RSLT, median 5-year patient survival LDLT 92% v. RSLT 65%

Registry study

- 1-year patient survival rates higher for LDLT v. RSLT ($P = 0.001$); no difference if patients undergoing retransplantation or in ICU at time of transplant were excluded (>50% of patients receiving retransplant or in ICU at the time of transplant received RSLT)
- Similar results for children < 1 year ($P = 0.001$)

Graft survival rates**Primary studies**

- At 3 months: higher for LDLT v. RSLT
- At 12 months and up to 5 years: Higher for LDLT than RSLT, median 5-year graft survival LDLT 81% v. RSLT 63%

Registry study

- 1-year patient graft survival rates higher for LDLT v. RSLT ($P = 0.007$)
- Similar results for children < 1 year ($P = 0.001$)

3. LDLT v. SLT

Study characteristics

- 5 comparative studies, median study period ~14 years
- 1 registry study: Sindhi et al. (1999), $N = 3400$

Safety

Reoperation: no difference detected

Vascular complications: no difference detected

Acute graft rejection: no difference detected

Effectiveness:

Survival

Primary studies

- at 6 months—similar survival rates
- up to 5 years LDLT similar to SLT, median 5-year patient survival LDLT 92% v. RSLT 88%

Registry study

- 1-year patient survival rates similar for LDLT v. SLT

Graft survival rates

Primary studies

- At 6 months: similar graft survival rates
- up to 5 years LDLT similar to SLT, median 5-year graft survival LDLT 81% v. SLT 79%

Registry study

- 1-year patient graft survival rates higher for LDLT v. SLT ($P = 0.001$); not affected if patients undergoing retransplantation or in ICU at time of transplant were excluded

Conclusions

'The evidence base for LDLT is incomplete.

The current limited evidence suggests LDLT is superior to all forms of cadaveric liver transplantation in children younger than two years of age.

However the safety and efficacy of LDLT was equivalent to and in some cases worse than SLT and whole liver cadaveric donation in older children.

...The expansion of SLT is likely to diminish the need for LDLT and increase scrutiny about the ethics of LDLT in paediatric liver transplantation.

Despite its limitations, LDLT is a life saving procedure for some individuals where alternative transplant options are not available, such as very small children or for elective patients whose condition is likely to deteriorate before a cadaveric graft becomes available.

Future initiatives in LDLT must aim to achieve minimal morbidity and zero mortality for donors. Programs performing LDLT must adhere to an extremely high standard of care that includes standard protocols for preoperative evaluation of potential donors and postoperative follow-up of donors and recipients, as well as strong psychosocial evaluation and support programs.'

Author, place & year	Objective	Methods	Quality assessment of review
Taylor et al Institute of Liver Studies, Kings College Hospital, London, UK 2005 Information paper	To estimate overall health-related quality of life (HRQL) in children & adolescents after liver transplantation	<p>Literature review:</p> <p><i>Databases:</i> Medline, Cumulative Index to Nursing and the Allied Health Literature, PsycINFO, EMBASE, Allied and Complementary Medicine, Institute for Scientific Information, Web of Science, and Applied Social Sciences Index and Abstracts. Related web sites and proceedings of transplantation and associated conferences were also searched.</p> <p><i>Time period:</i> January 1990 – December 2003</p> <p><i>Inclusion/Exclusion criteria:</i></p> <p><i>Study types/design:</i> included studies in English</p> <p><i>Population:</i> children (< 18 y of age) undergoing liver transplantation</p> <p><i>Intervention:</i> isolated orthoptic, auxiliary, or living donor transplant</p> <p><i>Comparator:</i> participants as their own control (before and after transplant), age-appropriate healthy or ill population reference groups, or age-appropriate prospective healthy or ill samples. Adult population reference groups were excluded.</p> <p><i>Outcomes:</i> > 1 HRQL domains assessed from child, adolescent or parent.</p> <p><i>Quality:</i> Search strategy and quality assessment methods fully reported. Two independent reviewers appraised included studies.</p>	<p>HIGH QUALITY</p> <p>Was the research question clearly defined? YES</p> <p>Were inclusion/exclusion criteria reported that addressed the review question? YES</p> <p>Was the search adequate? YES</p> <p>Was the quality of the included studies assessed? YES</p> <p>Are sufficient details about the individual included studies presented? YES</p>
<p>Results:</p> <p><i>Included studies</i></p> <ul style="list-style-type: none"> • 11 studies were included in the review (10 cross-sectional, 1 longitudinal study). • Studies reported on a total of 395 children & adolescents who received liver transplants between 1981–2002. <p><i>Study characteristics</i></p> <ul style="list-style-type: none"> • Study instruments: specific HRQL instruments (8 studies), structured interviews (1) or both methods (1). One study used separate questionnaires to assess each domain of HRQL. • Study respondents: children (3 studies), adolescents (2), both children & adolescents (1), infants based on parental responses (1), parent report with mixed samples of children & adolescents (5) • Study quality: 9 studies included a comparison group; 1 of these compared before and after transplantation; 5 were assessed as using acceptable methodology. • Overall weak sampling methods and potential for selection bias; some HRQL instruments used were not validated for age group of interest; some studies relied on parental assessment, which may not be as relevant as the child's perspective. <p><i>Data synthesis</i></p> <ul style="list-style-type: none"> • Liver transplantation produces a worse HRQL than that of a healthy population (finding not statistically significant) • Liver transplantation produces no significant difference in HRQL v. other chronic illness 			

- Pre–post-transplantation comparisons: global health, physical health, psychosocial function improved significantly 6 months after transplant; family function improved after 1 year compared to pretransplant function (1 study)
- 5 studies investigated factors influencing HRQL, including time since transplant

Conclusion: 'liver transplantation impacts negatively in some areas of physical, psychological, social and family function and general wellbeing compared with general population. However this is a tentative conclusion because of lack of rigour adopted by some of the studies.'

Abbreviations: HTA = health technology assessment; LDLT = living-donor liver transplantation; RSLT = reduced-size liver transplantation; ICU = intensive care unit; SLT = split liver transplant; HRQL = health-related quality of life.

Appendix D Detailed cost tables

Detailed costing by CHWS, New South Wales

Table 16 displays a summary of cost components for individual patients as well as overall average costs for each type of liver transplant, as provided in the original cost information.

Table 16 Summary of individual cost estimates provided by CHWS, by type of transplant and cost components

	WLT	SLT											LDLT	RLT		
Total cost	Total cost	Cost patient 1	Cost patient 2	Cost patient 3	Cost patient 4	Cost patient 5	Cost patient 6	Cost patient 7	Cost patient 8	Cost patient 9	Cost patient 10	Average cost	Total cost	Cost patient 1	Cost patient 2	Average cost
Pretransplant costs																
Referral to service	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Work-up	1,302	38,825	4,146	415	1,662	0	0	1,153	120	4,159	870	5,135	0	0	0	0
Acceptance on list	960	8,160	1,800	0	360	0	0	0	0	2,400	0	1,272	0	0	0	0
Pretransplant monitoring	12,693	23,241	378,341	7,145	9,561	0	0	20,300	0	58,340	23,025	51,995	0	0	0	0
Total pretransplant costs	14,955	70,226	384,287	7,560	11,583	0	0	21,453	120	64,899	23,895	58,402	0	0	0	0
Transplant admission costs																
Theatre & surgery	8,553	6,399	8,385	4,531	5,678	17,760	13,850	18,851	0	5,053	5,367	8,587	9,681	10,368	9,671	10,020
Intensive care admission	14,885	9,099	14,298	34,295	28,526	189,413	42,277	19,922	0	20,334	4,750	36,291	32,766	16,685	16,679	16,682
General ward admission	64,694	87,742	143,546	79,441	73,224	150,876	321,146	78,104	0	135,078	48,618	111,777	53,121	109,248	65,032	87,140
Total transplant admission costs	88,132	103,240	166,229	118,267	107,428	358,049	377,273	116,876	0	160,465	58,736	156,656	95,567	136,302	91,381	113,842

	WLT	SLT											LDLT	RLT		
Total cost	Total cost	Cost patient 1	Cost patient 2	Cost patient 3	Cost patient 4	Cost patient 5	Cost patient 6	Cost patient 7	Cost patient 8	Cost patient 9	Cost patient 10	Average cost	Total cost	Cost patient 1	Cost patient 2	Average cost
Other direct patient costs	92,725	45,069	113,262	75,242	44,715	5,392	99,182	41,037	120,180	136,383	49,897	73,036	41,398	44,980	74,608	59,794
Overheads & indirect costs	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total direct and indirect cost	195,812	218,535	663,778	201,069	163,726	363,441	476,455	179,366	120,300	361,747	132,529	288,095	136,965	181,282	165,989	173,635

Abbreviation: WLT = whole liver transplantation; SLT = split liver transplant; LDLT = living-donor liver transplantation; RLT = reduced-size liver transplantation (= 'cut-down liver transplant' in original costing sheets).

Detailed costing by CHWS, New South Wales—whole liver transplant

Tables 17 to 19 display the details of the CHWS's original cost analysis of 1 WLT patient.

Table 17 Costs for pretransplant assessment of WLT patient, CHWS, New South Wales

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
REFERRAL TO SERVICE				\$0
WORK-UP				
Medical consultation and review	multiple medical consultation discussions with patient and family (rate per 30 min)			\$600
Allied health consultation				
Allied health consult. (social work) 10 h	award rates health allied professionals including overheads and other award payments (rate per min)	90		\$180
Allied health consult. (occ therapy)		60		\$120
Pathology/diagnostics				
Immunology		2		\$93
Biology	based on actuals; includes direct and indirect costs	5		\$131
Pharmacy (dispensed drugs)		4		\$178
SUB-TOTAL WORK-UP				\$1,302
ACCEPTANCE ON LIST				
Joint expert multidisciplinary review (team meeting to discuss patient's continued suitability for PLT)	8 h (1 h/week for 8 weeks); average salary cost for all staff	8	120.00	\$960
SUB-TOTAL ACCEPTANCE ON LIST				\$960
PRETRANSPLANT MONITORING				
Medical/nursing monitoring				
Under care of specialist	inclusive of overheads	148		\$1,500
In general ward	inclusive of overheads	148		\$4,721
General pathology/diagnostic testing				
Regular tests to monitor patient's continued suitability	inclusive of overheads	54		\$832
Imaging				
Incl. ultrasound and nuclear medicine	inclusive of overheads	6		\$1,327
Allied health monitoring/review				
Allied health monitoring (psychology)	service weight, inclusive of overheads			\$600
Allied health monitoring (physio.)	inclusive of overheads	375		\$483
Allied health monitoring (social work)	inclusive of overheads	360		\$608
Allied health monitoring (occ therapy)	inclusive of overheads	15		\$29
Allied health monitoring (dietetics)	inclusive of overheads	90		\$201
Pharmacy		10		\$983
Theatre	includes anaesthetist, nurses and other theatre costs per min	50		\$739
Recovery ward	minutes	140		\$670
SUB-TOTAL PRETRANSPLANT MONITORING				\$12,693
TOTAL PRETRANSPLANT COSTS				\$14,955

Abbreviations: WLT = whole liver transplantation; CHWS = New Children's Hospital Westmead, Sydney; NFC = Nationally Funded Centre; PLT = paediatric liver transplantation; occ = occupational

Table 18 Costs of admission for PLT procedure per patient, CHWS, New South Wales—WLT

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
THEATRE/SURGERY				
Transplantation				
Anaesthetist	incl. theatre cost and salaries of surgeons for theatre episode; assumes 1 sub-	376		
Nurse	sequent visit to theatre after transplant in same episode (min in theatre; No. nurses)	5		
Post-transplantation				
Anaesthetist	incl. theatre cost and salaries of surgeons for theatre episode; assumes 1 sub-	90		
Nurse	sequent visit to theatre after transplant in same episode (min in theatre; No. nurses)	3		\$8,553
Transplantation salaries	included in theatre costs			
SUB-TOTAL THEATRE/SURGERY				\$8,553
INTENSIVE CARE ADMISSION				
ICU stay (5.5 days) transplant & postop	includes total direct and indirect costs	132		\$3,468
Medical/nursing monitoring				
Surgeon monitoring 5.5 days	hours	132		\$1,885
Allied health monitoring/review	included in general ward admission figure			
Drugs/pharmacy	volume dispensed	17		\$3,090
Investigations/diagnostic				
Radiology	general radiology/ultrasound	11		\$1,580
Nuclear medicine		1		\$303
Biochemistry		948		\$2,331
Haematology		68		\$1,131
Microbiology		27		\$1,097
SUB-TOTAL INTENSIVE CARE				\$14,885
GENERAL WARD ADMISSION				
Ward stay (22 days)	incl. total direct and indirect costs; hours	529		\$33,134
Medical monitoring				
Gastro specialist (22 days)	hours	529		\$9,479
Allied health monitoring/review				
Allied health mon./review (psychology)	based on service weight			\$962
Allied health mon./review (physio.)	minutes	3745		\$5,702
Allied health mon./review (social work)		915		\$978
Allied health mon./rev. (occup. therapy)		510		\$988
Allied health mon./rev. (dietetics) (4 h)		135		\$248
Drugs/pharmacy (immunosuppressive & antibiotics)				
		74		\$6,666
Investigations/diagnostic				
Radiology	tests	11		\$1,415
Nuclear medicine	tests	1		\$303
Biochemistry tests	tests	531		\$1,291
Haematology	tests	123		\$2,008
Immunology	tests	1		\$36

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
Histopathology	tests	1		\$664
Microbiology	tests	24		\$819
SUB-TOTAL WARD ADMISSION				\$64,693
TOTAL PROCEDURE ADMISSION COSTS				\$88,131

Abbreviations: WLT = whole liver transplantation; CHWS = New Children's Hospital Westmead, Sydney; NFC = Nationally Funded Centre; PLT = paediatric liver transplantation; ICU = intensive care unit; mon = monitoring.

Table 19 Other direct costs for PLT per patient, CHWS, New South Wales—WLT

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
OTHER DIRECT PATIENT COSTS				
Accommodation of interstate patients	per day	27	20.00	\$540
Transport & ambulance	cab charges	4	100.00	\$400
Post-transplantation weeks 0 to 12 (first 3 months)				\$20,699
Post-transplantation weeks 13 to 24 (3–6 months)	based on actual patient episodes			\$29,533
Post-transplantation weeks 25 to 52 weeks (6–12 months)	based on actual patient episodes to 1/7/06			\$35,173
Post-transplantation outpatient review (12 months onwards)	estimate based on 4 visits/y, with labs \$259/visit; pharmacy \$60/visit for every year until age 16			\$6,380
TOTAL OTHER DIRECT COSTS				\$92,725

Abbreviations: WLT = whole liver transplantation; CHWS = New Children's Hospital Westmead, Sydney; NFC = Nationally Funded Centre; PLT = paediatric liver transplantation.

Detailed costing by RCHM, Victoria

Tables 20 to 23 display the details of the RCHM's original cost analysis.

Table 20 Costs per patient for pretransplant assessment, RCHM, Victoria

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
REFERRAL TO SERVICE				
Medical history investigation/consultation/review (consultant A attendance including 25% overheads) (4.5 h) ^a	SM41 LR85 rate (per min)	270	\$2.57	\$695
Assessment of family ability to undergo procedure and rehabilitation by social worker (90 min)	unit cost per min	90	\$0.86	\$78
SUB-TOTAL REFERRAL TO SERVICE				\$772
WORK-UP				
Medical consultations and review (multiple) w. patient and family (consultant A attendance) (5 h)	consultant A (SM41 LR85 rate) including 25% overheads (incl. recall/ on-call)	300	\$2.57	\$772
Allied health consultation				
Allied health consultation (psychology) 1 h	award rates health allied professionals including 20% overheads and other award payments (per min)	60	\$0.86	\$52
Allied health consultation (physiotherapy) 1 h		60	\$0.89	\$53
Allied health consultation (social work) 1 h		60	\$0.86	\$52
Allied health consultation (dietetics) 1 h		60	\$0.87	\$52
Allied health consultation (chaplain) 1 h		60	\$0.65	\$39
Joint expert multidisciplinary review 2 h	includes medical, nursing and allied health team, av. salary cost for all staff	120	\$6.05	\$726
Pathology/diagnostic				
Biochemistry (other)		1	\$10.00	\$10
Haematology (full blood count)		1	\$25.00	\$25
Immunology (other)		1	\$10.00	\$10
Microbiology (antibiotic cover)		2	\$20.00	\$40
Virology		10	\$15.00	\$150
Blood products (other)		1	\$15.00	\$15
Ultrasound		1	\$180.00	\$180
Miscellaneous pathology (haematology, blood & history, vaccination, serology, biochemistry)		10	\$25.00	\$250
Other medical consultations^b				
Immunology (1 h)	SM 41 base rate sessional award, incl. 20% overheads	60	\$2.31	\$138
Infectious disease (1 h)		60	\$2.31	\$138
Haematology (1 h)		60	\$2.31	\$138
Anaesthetic assessment (1 h)		60	\$2.31	\$138
Dental (1 h)		60	\$2.31	\$138
Mental health (1 h)		60	\$2.31	\$138
Respiratory (1 h)		60	\$2.31	\$138
Psychiatry (1 h)		60	\$2.31	\$138

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
Endocrinology (1 h)		60	\$2.31	\$138
Cardiology (1 h)		60	\$2.31	\$138
Non-salary cost for various supplies/consumables	disposables	10	\$25.00	\$250
LDLT SPECIFIC WORK-UP^c				
Surgical review (adult and child) (2 h)		120	\$1.58	\$190
Physician review (adult) (1 h)		60	\$1.58	\$95
Diagnostic tests/ work-up				
Chest x-ray	tests	1	\$47.15	\$47
Computed tomography	tests	1	\$480.50	\$481
Magnetic resonance imaging adult	tests	1	\$985.60	\$986
Magnetic resonance cholangiopancreatography	tests	1	\$403.20	\$403
Electrocardiogram	tests	1	\$42.50	\$43
Haematology	tests	1	\$73.45	\$73
Full blood count/clotting	tests	1	\$165.80	\$166
Viral serology	tests	1	\$295.70	\$296
Biochemistry	tests	1	\$119.16	\$119
Allied health consultation/ review				
Social work (1 h)	grade 5	60	\$0.94	\$56
Dietician (1 h)	grade 4	60	\$0.89	\$53
Physiotherapist (1 h)	grade 4	60	\$0.79	\$47
Psychiatrist (1 h)	senior specialist	60	\$1.41	\$85
Transplant coordinator (1 h)		60	\$0.72	\$43
SUB-TOTAL WORK-UP (including LDLT consideration)				\$7,243
SUB-TOTAL WORK-UP (excluding LDLT consideration)				\$4,060
ACCEPTANCE ON LIST				
Joint expert multidisciplinary review (regular team meetings [medical, CNC nursing, allied health staff] to discuss patient's continued suitability for PLT) (3 h)	average salary cost for all staff, per minute	180	\$6.05	\$1,089
Joint expert multidisciplinary review at Austin Hospital ^c	n.r.	2	\$474.33	\$949
SUB-TOTAL ACCEPTANCE ON LIST				\$2,038
PRETRANSPLANT MONITORING				
Medical/nursing monitoring				
Consultant (15 h) (incl. to other units)	n.r. (per min)	900	\$2.57	\$2,316
Senior registrar (2 h)	n.r. (per min)	120	\$1.10	\$132
Hospital medical officer (3 h)	n.r. (per min)	180	\$0.90	\$162
Nurse coordinator CNC (daily)	8 patients/year; rate/min	2,400	\$0.90	\$2,160
General pathology/diagnostic testing				
Regular testing to monitor patient's continued suitability	n.r.	10	\$25.00	\$250
Allied health monitoring/review				
Allied health monitoring (psychology) (2 h over 12 weeks on av. on waiting list)	average time on waiting list (12 weeks), rate/min	120	\$0.86	\$103

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
Allied health monitoring (physiotherapy) (1 h over 12 weeks on average on waiting list)		60	\$0.89	\$53
Allied health mon. (social work) (8 h over 12 weeks)		480	\$0.86	\$413
Allied health mon. (occ ther.) (1 h over 12 weeks)		60	\$0.87	\$52
Allied health mon. (dietetics) (2 h over 12 weeks)		120	\$0.87	\$104
Allied health mon. (play therapy) (4 h over 12 wks)		240	\$0.48	\$116
General pathology/diagnostic testing				
Ultrasound, imaging & radiology, haematology, blood & history, vaccination, serology, biochemistry	no details provided	10	\$25.00	\$250
SUB-TOTAL PRETRANSPLANT MONITORING				\$6,112
TOTAL PRETRANSPLANT COSTS (including LDLT costs)^d				\$16,165
TOTAL PRETRANSPLANT COSTS (excluding LDLT costs)^d				\$12,982

Abbreviations: WLT = whole liver transplantation; RCHM = Royal Children's Hospital Melbourne; NFC = Nationally Funded Centre; PLT = paediatric liver transplantation; mon = monitoring; LDLT = living-donor liver transplantation; n.r. = not reported; occ = occupational; av. = average.

a Includes 25% overheads (9% super, 1.5% Workcover, 1% long service leave, 8% staff replacement and 5% on-call/recall and other costs).

b Average 1 test from various medical consultants to determine or prepare patient's suitability.

c These are costs accrued to Austin Hospital (adult liver transplant service) and not the RCHM.

d These costs include costs to Austin Hospital. If only the costs to RCHM are considered, total pretransplant costs are \$12,034.

Table 21 Costs of admission for PLT procedure per patient, RCHM, Victoria

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
THEATRE/SURGERY				
Theatre salaries & wages				
Perfusionist (12 h)	perfusionist award grade 2y7	720	\$1.14	\$823
Anaesthetist (12 h)	SM41 classification	720	\$2.57	\$1,853
Theatre nursing scout (12 h)		720	\$0.70	\$504
Theatre utilisation				
Theatre usage (1 bed day)	infrastructure costs	1	\$2,000.00	\$2,000
Theatre recovery postop (0.3 bed-days)		0.3	\$750.00	\$225
Theatre appliances and consumables				
Medical gases and other consumables	no details provided	20	\$25.00	\$500
Anatomical pathology—tests performed on livers	no details provided	120	\$2.31	\$277
Split liver—salaries—Austin^a				
Senior surgeon (2 h)	per minute	120	\$1.58	\$190
Surgical assistant (2 h)	per minute	120	\$0.61	\$73
Theatre technician (2 h)	per minute	120	\$0.42	\$51
Scrub nurse (2 h)	per minute	120	\$0.53	\$63
Transplant salaries—Austin^a				
Senior surgeon to start, hepatectomy, portal artery, hepatic vein	per transplant	1	\$1,703	\$1,703
Senior surgeon to assist, backbench	per transplant	1	\$1,703	\$1,703
Surgical assistant	per transplant	1	\$56	\$568

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
Senior surgeon to do bile duct and close	per transplant	1	\$1,135	\$1,135
Anaesthetists ×2	per transplant	2	\$1,986	\$3,973
Scrub nurses ×2 (6 h each)	YS9 1st 2 h at time and a	720	\$0.53	\$728
Anaesthetic nurse (6 h each)	half, then double time	720	\$0.53	\$728
Theatre tech ×2 (6 h each)	HH5 1st 2 h at time and a	720	\$0.42	\$582
	half, then double time			
SUB-TOTAL THEATRE/SURGERY (considering SLT-specific costs)				\$17,676
SUB-TOTAL THEATRE/SURGERY (excluding SLT-specific costs)				\$17,300
INTENSIVE CARE ADMISSION				
ICU stay				
ICU stay transplant & postoperative (10 bed-days)	includes nursing cost ^b	10	\$2,379.00	\$23,790
Dressing & bandages changes (daily, 10 days)		10	\$25.00	\$250
Medical/nursing monitoring				
Consultant (incl. to other units) (2 h/day for 15 days)	minutes	1,800	\$2.57	\$4,631
Snr registrar (30 min per day for 10 days)	minutes	300	\$1.10	\$330
Hospital medical officer (30 min/day for 10 days)	minutes	300	\$0.90	\$270
Nurse coordinator CNC (2 h/day for 10 days)	bed days	1,200	\$0.90	\$1,080
Surgical review postoperative visits^a				
Senior surgeon review daily (3 visits @ 2 h each)		360	\$1.58	\$569
Recipient immunosuppressive assay (daily whilst inpatient—10 assays)	tests	10	\$34.35	\$344
Allied health monitoring/review		240	\$0.86	\$207
Allied health monitoring/review (psychology) (15 h)		900	\$0.89	\$801
Allied health monitoring (physiotherapy) (10 h)		600	\$0.86	\$517
Allied health monitoring (social work) (10 h)		600	\$0.87	\$519
Allied health monitoring (occupational therapy) (10 h)		600	\$0.87	\$519
Allied health monitoring (dietetics) (5 h)		300	\$0.77	\$232
Allied health monitoring (play therapy) (20 h)		1,200	\$0.48	\$582
Pharmacy/supplements				
Nutrition & special supplements (3 meals per day for 10 days)		30	\$35.00	\$1,050
Immunosuppressives (scripted/impressed)	not S100/PBS	10	\$50.00	\$500
Antibiotics and other	not S100/PBS	10	\$25.00	\$250
Investigations/diagnostics				
Radiology				
Chest x-ray (10)	requests	10	\$60.00	\$600
Electrocardiogram (2)	requests	2	\$120.00	\$240
Electroencephalogram	requests	1	\$50.00	\$50
Computed tomography	requests	1	\$150.00	\$150
Magnetic resonance imaging	requests	1	\$250.00	\$250
Ultrasound	requests	1	\$180.00	\$180
Vascular variation	requests	1	\$75.00	\$75
Biochemistry				
Urea and electrolytes		20	\$15.00	\$300

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
Lactate		20	\$15.00	\$300
Liver function test		20	\$15.00	\$300
Other		6	\$10.00	\$60
Haematology				
Full blood count		6	\$25.00	\$150
Clotting		10	\$25.00	\$250
Cross match		10	\$15.00	\$150
Other		6	\$10.00	\$60
Immunology				
Other		6	\$10.00	\$60
Microbiology				
Blood cultures		10	\$45.00	\$450
C-reactive protein		10	\$60.00	\$600
Antibiotic cover		10	\$25.00	\$250
Bronchioalveolar lavage		2	\$25.00	\$50
Other		6	\$10.00	\$60
Virology (viral investigation)		8	\$45.00	\$360
Blood products				
Blood		2	\$120.00	\$240
Cryoprecipitate		2	\$60.00	\$120
Other		6	\$10.00	\$60
SUB-TOTAL INTENSIVE CARE				\$41,806
GENERAL WARD ADMISSION				
General ward stay				
Ward stay (35 days after ICU discharge) ^c	ward costs include nursing salaries/wages	35	\$543.00	\$19,005
Dressing & bandages (daily changes for 35 days)		35	\$25.00	\$875
Patient meals (3/day for 35 days)		105	\$25.00	\$2,625
Medical/nursing monitoring				
Consultant (incl. to other units) (70 h)	includes ICU medical staff	4,200	\$2.57	\$10,806
Senior registrar (30 min for 35 days)		1,050	\$1.10	\$1,155
Hospital medical officer (30 min for 35 days)		1,050	\$0.90	\$945
Allied health monitoring/review				
Allied health monitoring (psychology) (6 h)		360	\$0.86	\$310
Allied health monitoring (physiotherapy) (32.5 h)		1,950	\$0.89	\$1,736
Allied health monitoring (social work) (70 h)		4,200	\$0.86	\$3,617
Allied health monitoring (occup. therapy) (5 h)		300	\$0.87	\$260
Allied health monitoring (dietetics) (7 h)		480	\$0.87	\$415
Allied health monitoring (music therapy) (15 h)		900	\$0.77	\$695
Allied health monitoring (play therapy) (35 h)		2,100	\$0.48	\$1,018
Drugs/pharmacy (scripted/impressed) (immunosuppressives & antibiotics)	av. cost per patient from PCM/clinical costing system			\$8,086
Drugs/pharmacy (\$100 revenue)	recognition of \$100 revenue			-\$8,086
Investigations/diagnostic				

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
Radiology (ultrasound)	tests	5	\$180.00	\$900
Biochemistry				
Urea and electrolytes		40	\$15.00	\$600
Lactate		40	\$15.00	\$600
Liver function test		40	\$15.00	\$600
Other		3	\$10.00	\$30
Haematology				
Full blood count	tests	3	\$25.00	\$75
Clotting	tests	20	\$25.00	\$500
Other	tests	3	\$10.00	\$30
Immunology (other)	tests	3	\$10.00	\$30
Microbiology				
Blood cultures		5	\$45.00	\$225
C-reactive protein	tests	10	\$60.00	\$600
Antibiotic cover	tests	3	\$25.00	\$75
Other	tests	3	\$10.00	\$30
Recipient immunosuppressive assay daily whilst inpatient (for 35 days) ^a	tests	35	\$34.35	\$1,202
SUB-TOTAL WARD ADMISSION				\$48,959
TOTAL TRANSPLANT ADMISSION COSTS (including split liver)^d				\$108,441
TOTAL TRANSPLANT ADMISSION COSTS (excluding split liver)^d				\$108,065

Abbreviations: RCHM = Royal Children's Hospital Melbourne; NFC = Nationally Funded Centre; PLT = paediatric liver transplantation; SLT = split liver transplantation; ICU = intensive care unit; PBS = Pharmaceutical Benefits Schedule; CNC = clinical nurse consultant; n.r. = not reported.

a These are costs accrued to Austin Hospital (adult liver transplant service) and not the RCHM.

b 21 patients total \$649,616; av. per patient is \$30,934. Av. length-of-stay ICU days is based on 6,682 hours = 278 days = 13 days for 21 patients; \$30,934/13 days = \$2,379 per day.

c Cost is \$362 but increased by 50% as patients are in high-dependency unit and 1:2 staff:patient ratio in ward.

d These costs include costs to Austin Hospital. If only the costs to RCHM are considered, total transplant admission costs are \$94,832.

Table 22 Other direct costs for PLT per patient, RCHM, Victoria

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
ACCOMMODATION				
Accommodation for interstate patients ^a	n.r.	14	\$200.00	\$2,800
Transport & ambulance				
2× interstate trips		2	\$500.00	\$1,000
TOTAL OTHER DIRECT COSTS^b				\$3,800

Abbreviations: PLT = paediatric liver transplantation; RCHM = Royal Children's Hospital Melbourne; NFC = Nationally Funded Centre.

a number of nights not reported, but quantity assumed to refer to 14 nights of accommodation

b In original costing, travel and accommodation cost was applied only to the 20% of patients that are interstate referrals. Using this approach, accommodation costs are \$560 and transport costs are \$200, resulting in an overall average for other direct costs of \$760.

Table 23 Indirect costs associated with PLT per patient, RCHM, Victoria

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
PROGRAM MANAGEMENT				
Unit head Administrative	Based on gastro patient bed-days. Total liver bed-days / total gastro bed-days = 338/4,232 = 9% applied to non-salaries and wages costs			
Secretarial & clerical				\$3,087
Program management at Austin Hospital (unit head, admin., secretarial & clerical) ^a				\$10,000
CNC nurse coordinator (60 min per day for total length of stay (45 days))		2,700	\$0.90	\$2,430
Staff on-call costs ^a				\$36,745
TOTAL PROGRAM MANAGEMENT				\$52,262
OTHER COSTS & OVERHEADS				
Overhead costs (infrastructure, depreciation, maintenance etc. [not staff])	15% of total direct costs			\$19,261
Overhead costs (infrastructure, depreciation, maintenance etc. [not staff]) at Austin ^a				\$5,129
TOTAL OTHER COSTS/OVERHEADS				\$24,390
TOTAL INDIRECT COSTS^b				\$76,651

Abbreviations: PLT = paediatric liver transplantation; RCHM = Royal Children's Hospital Melbourne; NFC = Nationally Funded Centre; CNC = clinical nurse consultant; SLT = split liver transplantation; LDLT = living-donor liver transplantation.

a These are costs accrued to Austin Hospital (adult liver transplant service) and not the RCHM.

b These costs include costs to Austin Hospital. If only the costs to RCHM are considered, total indirect costs are \$22,116. Indirect costs were calculated as 15% of all direct costs, including costs related to SLT and LDLT, and may thus be an overestimate of costs related to SLT, LDLT or WLT only.

Detailed costing by RCHB, Queensland

Tables 24 to 27 display the details of the RCHB's original cost analyses.

Table 24 Costs per patient for pretransplant assessment, RCHB, Queensland

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
REFERRAL TO SERVICE				
Medical consultation/review (consultant attendance including recall/on-call/other overheads)		1	\$420.00	\$420
SUB-TOTAL REFERRAL TO SERVICE				\$420
WORK-UP				
Allied health consultation				
Allied health consultation (psychology) 10 h	award rates health allied	600	\$0.72	\$432
Allied health consultation (social work) 10 h	professionals incl. overheads and other award payments (per min)	600	\$0.72	\$432
Allied health consultation (dietetics) 2 h		120	\$0.72	\$86
Other medical consultations^a				
Haematology (1 h)	award plus overheads (rate/min)	60	\$2.85	\$171
Dental (1/2 h)	award plus overheads (rate/min)	30	\$2.85	\$86
Respiratory (1/2 h)	award plus overheads (rate/min)	30	\$2.85	\$86
Endocrinology (1/2 h)	award plus overheads (rate/min)	30	\$2.85	\$86
Cardiology (1/2 h)	award plus overheads (rate/min)	30	\$2.85	\$86
SUB-TOTAL WORK-UP				\$1,463
ACCEPTANCE ON LIST				
Joint expert multidisciplinary review (regular team meetings [medical, CNC nursing, allied health staff] to discuss patient's continued suitability for PLT)	average salary cost for all staff (excl. CNC liaison nurses)	1	\$3,713.00	\$3,713
SUB-TOTAL ACCEPTANCE ON LIST				\$3,713
PRETRANSPLANT MONITORING				
Medical/nursing monitoring				
Consultant (1 h/month over 12 months)	n.r. (rate/min)	720	\$2.50	\$1,800
Senior registrar (1 h/month over 12 months)	n.r. (rate/min)	720	\$1.05	\$756
Hospital medical officer (1/month over 12 months)	n.r. (rate/min)	720	\$0.70	\$504
CNC nurse coordinator (daily) (no more details provided)	n.r.			\$5,600
Allied health monitoring/review				
Allied health mon. (psychology) (12 h over 12 months)	n.r. (rate/min)	720	\$0.72	\$518
Allied health mon. (social work) (12 h over 12 months)	n.r. (rate/min)	720	\$0.72	\$518
Allied health mon. (dietetics) (12 h over 12 months)	n.r. (rate/min)	720	\$0.72	\$518
General pathology/diagnostic testing				
Ultrasound/pathology tests (1/month over 12 mo)	n.r.	12	\$185.00	\$2,220
SUB-TOTAL PRETRANSPLANT MONITORING				\$12,435
TOTAL PRETRANSPLANT COSTS				\$18,032

Abbreviations: RCHB = Royal Children's Hospital Brisbane; NFC = Nationally Funded Centre; CNC = clinical nurse consultant; PLT = paediatric liver transplantation; mon. = monitoring, n.r. = not reported.

a Average 1 test from various medical consultants to determine and prepare patient's suitability.

Table 25 Costs of admission for PLT procedure per patient, RCHB, Queensland

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
THEATRE/SURGERY				
Theatre salaries & wages				
Anaesthetist (minutes in theatre)	relevant award	900	\$4.38	\$3,938
Theatre nursing scout	relevant award	900	\$1.05	\$945
Theatre appliances & consumables				
Medical gases and other consumables				\$2,470
Transplant salaries				
Senior surgeon to start, hepatectomy, portal artery, hepatic vein (10 h)	liver transplantation procedures are performed after-hours,	600	\$4.38	\$2,628
Senior surgeon to assist, backbench (10 h)	so salaries are calculated at overtime rates	600	\$4.38	\$2,628
Surgical assistant (10 h)		600	\$1.84	\$1,104
Senior surgeon to do bile duct and close (10 h)		600	\$4.38	\$2,628
Anaesthetists ×2 (15 h each)		1800	\$4.38	\$7,884
Scrub nurses ×2 (15 h each)		1800	\$1.05	\$1,890
Anaesthetic nurse (15 h)		900	\$1.10	\$990
Theatre tech ×2 (15 h each)		1800	\$1.05	\$1,890
Split liver—additional salaries				
Senior surgeon (8 h)	liver transplantation procedures are performed after-hours, so salaries are calculated at overtime rates	480	\$4.38	\$2,102
Surgical assistant (2 h)		120	\$1.84	\$221
Theatre technician (10 h)		600	\$1.05	\$630
Scrub nurse (10 h)		600	\$1.05	\$630
SUB-TOTAL THEATRE/SURGERY without extra SLT costs				\$28,995
SUB-TOTAL THEATRE/SURGERY with extra SLT costs				\$32,578
INTENSIVE CARE ADMISSION				
ICU stay (7 bed-days transplant & postoperative) (includes nursing cost)		7	\$2,956.00	\$20,692
Daily bandage/dressing changes (7 days)		7	\$115.00	\$805
Medical/nursing monitoring^a				
Consultant monitoring, 2 h/day for 7 days	(rate/min)	840	\$2.50	\$2,100
Senior registrar monitoring, 2 h/day for 7 days	(rate/min)	840	\$1.05	\$882
Hospital medical officer mon., 2 h/day for 7 days	(rate/min)	840	\$0.60	\$504
Nurse coordinator CNC mon., 2 h/day for 7 days		840	\$1.02	\$857
Surgical review postoperative visits				
Senior surgeon review daily postoperative (3 h costed in total, although 3 visits @ 2 h mentioned)	(rate/min)	180	\$2.50	\$450
Allied health monitoring/review				
Allied health mon./review (physiotherapy) (3.5 h)	(rate/min)	210	\$0.72	\$151
Allied health mon./review (social work) (3.5 h)	(rate/min)	210	\$0.72	\$151
Nutrition & special supplements				
cost per day (3× meals), unclear for how many days, nutrition special supplements (incl. total parenteral nutrition)				\$2,760
Drugs/pharmacy (scripted/impressed)				
Immunosuppressive (not S100/PBS)	n.r.			\$4,150
Antibiotics and other (not S100/PBS)	n.r.			\$3,810
Investigations/diagnostic				

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
Radiology				
Chest x-ray		1	\$48.00	\$48
Electrocardiogram		1	\$86.00	\$86
Ultrasound		7	\$111.00	\$777
Biochemistry				
Urea and electrolytes		14	\$21.00	\$294
Other		17	\$8.00	\$136
Haematology				
Full blood count		14	\$11.00	\$154
Other		12	\$9.45	\$113
Immunology		7	\$58.50	\$410
Microbiology (blood cultures)		7	\$32.30	\$226
SUB-TOTAL INTENSIVE CARE				\$39,556
GENERAL WARD ADMISSION				
Ward stay (30 days after ICU discharge)	ward costs include nursing salaries/wages	30	\$512.00	\$15,360
Dressing & bandages (daily changes)	n.r.			\$3,400
Medical/nursing monitoring				
Consultant monitoring, 1 h/day for 30 days		1800	\$2.50	\$4,500
Senior registrar monitoring, 1 h/day for 30 days		1800	\$1.05	\$1,890
Hospital medical officer mon., 1 h/day for 30 days		1800	\$0.70	\$1,260
Allied health monitoring/review				
Allied health mon./review (physiotherapy) (4 h)		240	\$0.72	\$173
Allied health mon./review (social work) (1 h)		60	\$0.72	\$43
Allied health monitoring/review (dietetics) (4 h)		240	\$0.72	\$173
Patient meals				
Cost per day (3× meals) for 30 days		30	\$4.20	\$126
Drugs/pharmacy (scripted/impressed)				
Immunosuppressive & antibiotics (assume for 30 days)		30	\$84.60	\$2,538
Investigations/diagnostic				
Radiology (ultrasound)		1	\$110.00	\$110
Biochemistry tests				
Urea and electrolytes		13	\$21.00	\$273
Lactate		13	\$13.10	\$170
Haematology				
Full blood count		13	\$11.00	\$143
Clotting		13	\$24.80	\$322
Other		10	\$9.45	\$95
Microbiology (blood cultures)		13	\$32.30	\$420
SUB-TOTAL WARD ADMISSION				\$30,996
TOTAL DIRECT COSTS OF PLT ADMISSION without extra SLT costs				\$117,578
TOTAL DIRECT COSTS OF PLT ADMISSION with extra SLT costs				\$121,161

Abbreviations: PLT = paediatric liver transplantation; RCHB = Royal Children's Hospital Brisbane; NFC = Nationally Funded Centre; SLT = split liver transplantation; ICU = intensive care unit; CNC = clinical nurse consultant; mon. = monitoring; PBS = Pharmaceutical Benefits Scheme; n.r. = not reported.

a Consultant/nursing 120 min/day monitoring patient (including ICU medical staffing) and 30 min/day senior registrar and hospital medical officer.

Table 26 Other direct costs of PLT per patient, RCHB, Queensland

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
OTHER DIRECT PATIENT COSTS				
Accommodation interstate patients				
Accommodation of interstate patient	based on actual accommodation expenses of only interstate patient in 2005–06	1	\$6,600.00	\$6,600
Transport & ambulance				
2× interstate trips	majority of interstate patients treated at RCHB reside in WA	1	\$3,200.00	\$3,200
TOTAL OTHER DIRECT COSTS				\$9,800

Abbreviations: PLT = paediatric liver transplantation; RCHB = Royal Children’s Hospital Brisbane; NFC = Nationally Funded Centre; WA = Western Australia.

Table 27 Indirect costs associated with PLT per patient, RCHB, Queensland

NFC resource use	Cost reference/details	Quantity	Unit cost	Total cost
PROGRAM MANAGEMENT				
CNC nurse coordinator	currently 1.5 FTE CNC nurse coordinators for liver transplant program (fixed cost) to coordinate approximately 6 patients (transplanted and waiting) per annum			\$21,523
TOTAL PROGRAM MANAGEMENT				\$21,523
OTHER COSTS & OVERHEADS				
Overhead costs (infrastructure, depreciation etc.)	based on average cost per liver transplant patient treated at RCHB from clinical costing system (transition)			\$18,105
TOTAL INDIRECT COSTS				\$39,628

Abbreviations: PLT = paediatric liver transplantation; RCHB = Royal Children’s Hospital, Brisbane; FTE = full-time equivalent; CNC = clinical nurse consultant.

Abbreviations

AHMAC	Australian Health Ministers' Advisory Council
ANZLTR	Australian and New Zealand liver transplant registry
CCHMC	Cincinnati Children's Hospital medical centre
CHWS	New Children's Hospital, Westmead, Sydney
CNC	Clinical nurse consultant
CT	Computed tomography
DRG	Diagnosis Related Group
DVT	Deep vein thrombosis
HAT	Hepatic artery thrombosis
HTA	Health Technology Assessment
ICU	Intensive care unit
INAHTA	International network of agencies for health technology assessment
LCT	Liver cell transplantation
LDLT	Living-donor liver transplantation
MBS	Medicare Benefits Schedule
MRI	Magnetic resonance imaging
MSAC	Medical Services Advisory Committee
NHMRC	National Health and Medical Research Council
NFC	Nationally Funded Centre
NSW	New South Wales
NYHA	New York Heart Association
PLT	Paediatric liver transplantation
PVT	Portal vein thrombosis
QoL	Quality of life
QUOROM	Quality of reporting of Meta-analyses

RCHB	Royal Children's Hospital Brisbane
RCHM	Royal Children's Hospital Melbourne
RLT	Reduced-size liver transplantation
SPLIT	Studies of pediatric liver transplantation
SLT	Split liver transplantation
VLTU	Victorian Liver Transplant Unit
WLT	Whole liver transplantation

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