

**SELECTED SPECIALTY  
AND STATEWIDE  
SERVICE PLANS**

**Number Three**

**Liver  
Transplantation**

**January 2002**

## **NSW HEALTH DEPARTMENT**

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This Selected Specialty and Statewide Service Plan was developed by the Statewide Services Development Branch between 1998 and 2000 with considerable contribution by the specialist clinicians in the field. The Selected Specialty Services Steering Committee provided significant direction to this process.

The Greater Metropolitan Services Implementation Group, under the auspices of the Government Action Plan for Health, then reviewed and ratified this Plan.

The considerable effort of all involved is acknowledged.

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## **EXECUTIVE SUMMARY**

In recognition of the need to plan a number of the more highly specialised health services on a statewide level, NSW Health has undertaken a series of service planning reviews. The services considered in this series are characterised by one, or a combination of factors, which include:

- a demonstration of a relationship between volume and quality
- the treatment of conditions that are not common
- the need for specialised skills of individual clinicians or team
- the need for highly specialised equipment and/or support services
- the early stage of development of the specialty
- shortages in supply or distribution of the workforce
- high cost infrastructure.

Liver transplantation is regarded as one of these Selected Specialty and Statewide Services in NSW, and is the third in a series to be released by NSW Health.

Liver transplantation is now an accepted part of the management of end-stage liver failure for a large number of irreversible acute and chronic liver diseases. More than 20,000 patients worldwide have undergone liver transplantation and survival rates achieved by world standard units are greater than 85% at one year and 70% at five years. Outcomes of liver transplantation depend upon the primary cause of the recipient's liver disease, and the clinical status of the recipient.

The standard criteria for donor organs are those from heart beating, brain dead donors who are less than 65 years old, human immunodeficiency virus (HIV) and Hepatitis B negative and with no underlying malignancy. Donor organs are matched for blood group compatibility but not usually for other immunological markers. Organs are transported in University of Wisconsin solution, which allows preservation for up to 12 hours. The recipient surgical procedure is a complex operation taking from 8-12 hours. In order to achieve good outcomes a high degree of expertise and coordination is required between many hospital staff and departments. A number of studies have demonstrated that the majority of patients overall attain a very good quality of life following successful liver transplantation.

In addition to the NSW based Australian National Liver Transplantation Unit (ANLTU) at Royal Prince Alfred Hospital, other adult liver transplantation units are located in Victoria, Queensland, South Australia and Western Australia. In 2000 148 liver transplants were performed in Australia, 51 of these in NSW.

In NSW, the most common indications for adult liver transplantation are chronic viral hepatitis, cholestatic liver diseases, and fulminant hepatic failure in addition to a wide range of other less common liver diseases. Outcomes at the ANLTU are equivalent to above average world results with one year patient and graft survival rates quoted at 82% and 78% respectively.

Paediatric liver transplantation accounts for approximately 20% of all transplants across Australia and is performed in Queensland, Victoria and at The Children's Hospital at Westmead (TCHW) in NSW. In children, the most common indications are biliary atresia and in-born errors of metabolism. About half of paediatric transplants are to infants under three years of age. In these very young patients, the procedure is technically more difficult due to the smaller size of recipients, the need for reduced sized grafts and the presence of scarring from previous surgery.

Demand for adult liver transplantation is growing due to an increase in the incidence of liver disease particularly chronic viral hepatitis, as well as an improvement in the effectiveness of transplantation for many liver diseases. It is estimated that NSW will reach a demand of approximately 15 transplants per million population over the next 3-5 years.

The supply of available donor organs is the most limiting factor on the ability to meet increasing demand. Organ donation rates in Australia remain at one the lowest levels in the industrialised world at 10.3 donors per million population. Currently approximately 16% of patients die on the waiting list while waiting a donor organ. Donation rates would need to increase to approximately 18-20 donors per million population in order to meet demand estimates over the next 3-5 years. The availability of donor organs for paediatric patients is likely to improve through the use of split liver donation techniques.

The use of living relatives as donors is undertaken in some centres. Living Related Liver Transplantation (LRLT) is more commonly performed for paediatric recipients. Indications are that there has been less than ten LRLTs performed in Australia, the significant proportion on children. St George Hospital expressed interest in developing this service for adults. In 2001, the Liver Transplant Standing Committee of the Transplant Society of Australia and New Zealand recommended that LRLT for elective cases awaiting cadaveric liver transplantation in Australia was not indicated at this stage.

Liver transplantation is a resource intensive procedure. Costing studies have estimated the average cost to range from \$95,500 to \$177,000 per procedure. The higher costs in this range reflect the inclusion of all components of care. In particular, the costs of long term follow up. Funding is centrally allocated to Central Sydney Area Health Service and TCHW. The exception is liver transplantation in under three year olds which is funded through the Nationally Funded Centre (NFC) Program.

South Australia has the highest rate of organ donation within Australia at 17 donors per million population. The South Australian system follows a model of organ donation used in Spain which has one of the highest donation rates in the world. The NSW Coordination Centre for Organ and Tissue Donation are implementing a system similar to that in South Australia. A key part of this system is the funding of organ donor coordinators based within each Area Health Service.

Another Liver Transplant Unit is unlikely to be required in NSW for at least the next 3-5 years and only if an increase in organ donation rates is achieved. Hepatologists at Westmead Hospital have expressed an interest in establishing a second adult Liver Transplant Unit in NSW if demand were sufficient.

The Selected Specialty and Statewide Service Plans will be reviewed on a regular basis. It is expected that the Liver Transplantation Plan will be reviewed in three years time. However, changes in donor rates and technological change will be monitored in order to determine whether a shorter timeframe for review is required.

## 1.0 INTRODUCTION

In considering the number and location of highly specialised services, many factors are taken into account. NSW Health considers access, quality of care and service efficiency in these decisions. There are a number of considerations that favour the decision to restrict health care provision to a limited number of sites, or to promote an integrated service network of sites and/or provider groups. These include:

- When there is reasonable evidence that, up to a certain level, patient outcomes improve as caseloads increase and that care needs to be concentrated to reach this level. This most often occurs with interventions that involve:
  - skills that require substantial training, practice and experience to develop and maintain;
  - large teams, in which the different specialised skills provided by separate team members (including doctors, nurses, technicians and allied health staff) are important, as is the way the team works together;
  - extensive infrastructure requirements, for example diagnostic services with highly specialised equipment and staff skills; and
  - treatment of conditions that are uncommon.
- When there are large infrastructure costs, with unnecessary duplication of services leading to inefficient use of resources. This is especially relevant when attempting to ensure value for money for the public and may occur with interventions that involve:
  - expensive equipment and/or buildings; and
  - substantial investment in staff training and/or recruitment.
- When the medical technologies involved require further research, development and evaluation, and there is an associated need to enhance the diffusion of knowledge in the area. This may include:
  - new or rapidly evolving medical technologies;
  - the need for substantial research infrastructure;
  - the need for research activity to reach "critical mass";
  - widespread enrolment of patients into clinical trials and the associated use of clinical protocols; and
  - a tendency for a lag between scientific knowledge and clinical practice.

As a result, a series of service planning reviews have been undertaken where a number of these criteria have been met.

Liver transplantation is regarded as one of these Selected Specialty and Statewide Services in NSW, and is the third in a series to be released by NSW Health.

## 2.0 CLINICAL TECHNOLOGY REVIEW

### 2.1 Introduction

The world's first human liver transplantation was performed in Colorado US in 1963.<sup>1</sup> Up until the early 1980s, results from liver transplantation were very poor with one year survival rates around 30%. Significant advances have occurred since then, most notably in immunosuppression and organ preservation as well as improvements in surgical techniques and peri-operative care.

More than 20,000 patients worldwide have undergone liver transplantation and survival rates achieved by world standard units are greater than 85% at one year and 70% at five years.<sup>2</sup> Liver transplantation is now an accepted part of the management of end-stage liver failure. It is the only treatment option for many patients with end-stage chronic liver disease that offers the prospect of long term survival.

Liver transplantation is a resource intensive procedure and one which requires the coordination of a large number of specialised staff and support services. In Australia approximately 140 transplants are performed annually, of these about 20% are to paediatric recipients. In most cases the number of transplants is limited by the supply of available donor organs.

### 2.2 Indications for Liver Transplantation

#### Major Indications

Indications for liver transplantation include a wide range of irreversible acute and chronic liver diseases with the most common indications for liver transplantation being listed below. In addition to these, over 50 other causes of liver failure have been successfully treated by transplantation across the world. These include a wide range of other metabolic and/or inherited disorders, large hepatic haemangiomas, abdominal situs inversus and liver trauma.<sup>3</sup>

#### **Indications for Liver Transplantation<sup>4</sup>**

Cholestatic liver diseases	- primary biliary cirrhosis - primary sclerosing cholangitis
Acute fulminant liver failure	
Alcoholic liver disease	
Autoimmune chronic hepatitis	
Biliary Atresia (paediatric)	
Chronic viral Hepatitis (Hep B/D, Hep C, Hep A)	
Cryptogenic cirrhosis	
Hepatic Malignancy	
Inherited and metabolic diseases of the liver	

For the majority of diseases listed above, transplantation has proven to be a well-established and effective procedure. For some diseases however, the decision to perform liver transplantation remains more controversial and primarily due to the uncertain long term survival often related to the risks of disease recurrence. This latter category includes alcoholic cirrhosis, chronic Hepatitis B and liver malignancies. These diseases make up a significant percentage of liver disease in Australia and are discussed further below.

### **Chronic Viral Hepatitis**

Transplantation for chronic viral Hepatitis, both B and C, is characterised by a high rate of recurrence of the virus in the transplanted liver. Recurrent Hepatitis B can be very severe in up to 50% of patients leading to graft failure and death. Overseas centres have shown that recurrent Hepatitis B can be reduced by extended doses of Hepatitis B immunoglobulin and antiviral therapy<sup>5</sup>. However this therapy can be very costly. Currently transplantation for Hepatitis B requires careful patient selection to assess the risk of disease recurrence and for this a range of biochemical and viral markers are used.

Recurrence of Hepatitis C following transplantation is virtually 100%. However this only occasionally causes significant short term graft problems with the majority of Hepatitis C transplant recipients having slowly progressive recurrent disease with five year survival rates equivalent to that of other transplant recipients. For this reason Hepatitis C is an accepted indication for liver transplantation.

### **Hepatic Malignancy**

Malignant disease was first thought to be an ideal indication for liver transplantation. Unfortunately, outcomes have been very poor because of the high rate of disease recurrence which has been demonstrated at approximately 40%, the majority of which occurs within the first two years<sup>2</sup>. Primary cholangiocarcinoma is a contraindication in most liver transplant units. Small hepatomas complicating cirrhosis are not necessarily a contraindication to transplantation, however patients with large or multi-focal hepatomas often do poorly.<sup>6,4</sup>

### **Alcoholic Liver Disease**

Liver Transplantation for alcoholic liver disease remains controversial due to the risk of recurrence and the perceived nature of the illness as being self-inflicted. However outcomes for patients who maintain genuine abstinence have been shown to be very good.<sup>7</sup> As such, transplantation for patients with alcoholic cirrhosis has become more common in overseas centres, particularly in the US.

Patient selection is based upon assessment of the risk of recidivism which includes abstinence from alcohol for at least six months, an adequate social support network with at least one close personal relationship, previous occupation, and genuine acceptance by the patient and their family of the diagnosis of alcoholism.<sup>2,7,5,15</sup>

## **Acute Fulminant Liver Failure**

Acute fulminant liver failure is a rapidly progressive, life threatening process of liver destruction in a previously healthy individual. Causes include Hepatitis B, autoimmune disease, acute toxic hepatitis secondary to a range of drugs or other substances and idiopathic cases. Though some of these patients survive with supportive medical therapy many do not and liver transplantation is the only effective treatment. A number of these patients die while waiting for an organ to become available.

To reduce mortality, techniques such as bioartificial liver support systems<sup>4,3</sup> have been developed as well as the use of living related donors,<sup>8</sup> most commonly in paediatric patients. Occasionally these patients may be suitable for an auxiliary transplant which can support them while their native liver recovers.

Because of the difficulties in treating these patients transplant units have developed a range of prognostic indicators, including biochemical and clinical markers, which are used to select patients appropriate to consider for transplantation.

## **Contraindications to Liver Transplantation**

The range of absolute and relative contraindications to liver transplantation varies widely from unit to unit. A list of absolute contraindications as reported by a number of North American Transplant Units is below:

### **Absolute Contraindications for Liver Transplantation<sup>2</sup>**

- HIV seropositivity
- Extrahepatic Malignancy
- Cholangiocarcinoma
- Hemangiosarcoma
- Active Sepsis
- Active alcoholism or substance abuse
- Fulminant hepatic failure with ICP > 50mmHg or CPP < 40mmHg
- Advanced cardiac or pulmonary disease
- Inability to comply with immunosuppression protocol
- Anatomical abnormalities precluding liver transplantation

Relative contraindications include diseases and conditions whereby careful patient selection is required to assess the benefits of transplantation before admission to the program. This includes chronic Hepatitis B; advanced age; significant extra-hepatic disease; renal failure; established previous extra-hepatic malignancies; and severe obesity.<sup>2</sup>

## **Timing of Liver Transplantation**

The decision to proceed with liver transplantation is influenced more by the timing and progress of liver failure rather than the disease itself. Studies have shown that patients with end-stage chronic liver disease who undergo earlier transplantation, particularly before the development of secondary complications, have better outcomes as well as incurring lower costs.<sup>2</sup> However, the needs of these patients must be balanced against the patients who are referred in fulminant liver failure and in need of urgent life saving transplantation.

For patients with chronic progressive liver disease a variety of clinical, biochemical and quality of life indicators are assessed. These are matched to knowledge of the patient's disease progression in order to determine the appropriateness and timing of transplantation for each patient.

### **2.3 Surgical Procedure**

#### **Donor Organs**

The standard criteria for donor organs are those taken from heart beating, brain dead donors who are less than 65 years old, HIV and Hepatitis B negative and with no underlying malignancy. Donor organs are matched for blood group compatibility but not usually for other immunological markers (HLA) or gender. The use of Hepatitis C positive donors have been reported though restricted to Hepatitis C positive recipients and those in need of urgent life saving transplantation.

Organs are transported in University of Wisconsin solution which allows preservation of the organ for up to 12 hours prior to transplantation. Studies have shown that worse graft function is associated with extended cold preservation time, steatosis (fatty liver) and livers from older donors.<sup>5</sup> However, due to the shortage of donor organs, many Transplant Units are now accepting older donors and achieving good outcomes.

#### **Orthotopic Liver Transplantation**

The recipient procedure is known as orthotopic liver transplantation, which involves removal of the recipient native liver and replacement with the transplanted donor liver. This is a technically difficult and demanding surgical procedure which can take from 8-12 hours.

In order to achieve good outcomes the transplant procedure requires a high degree of expertise and coordination between many hospital staff and departments. This includes the surgeons and anaesthetists, as well as the blood transfusion service, haematology, pathology and radiology services. In particular the blood transfusion service must be able to support the need for large quantities of blood and blood products at short notice during the operation. Fortunately, with advances in surgical techniques, the requirement for very large amounts of blood products has been reduced. The average blood transfusion is now approximately 10 units per operation.

Paediatric transplantation is more difficult because of the reduced size of recipients, which means that cut-down techniques must often be employed on the donor organ. The presence of scarring from previous surgery in paediatric patients often adds to the difficulty.

### **Heterotopic Liver Transplantation**

This procedure, often known as auxiliary liver transplantation, involves leaving the recipient organ in place while transplanting a donor liver in a different location. This procedure is most commonly used for reversible liver disease whereby the transplanted liver can be removed once the native liver recovers.

Where successful, this would remove the need for ongoing immunosuppression. However, in some centres, this technique has been associated with increased surgical complications and it is not suitable for liver diseases where there is a risk of further disease in the native liver. Overall, it is infrequently utilised compared with orthotopic transplantation.<sup>5,15</sup>

## **2.4 Outcomes of Liver Transplantation**

### **Overall Survival**

Improvements in patient management have increased survival rates and liver transplantation is now an accepted part of the management of end-stage liver disease. Most studies show that the most significant mortality occurs in the first year with most survival curves flattening out after twelve months. One and three year patient survival rates in the US for the period 1988 to 1995 were 77% and 68% respectively and for the same period in Europe, survival rates were 73% and 65%.<sup>5</sup> The trend for improved outcomes continues with a number of centres reporting one year survival rates of over 85%.<sup>2</sup>

Survival is influenced strongly by the primary disease of the liver, for example, diseases such as primary biliary cirrhosis and autoimmune hepatitis generally demonstrate better survival compared with malignancy and Hepatitis B. Patients whose procedure is urgent due to fulminant hepatic failure also have worse outcomes; though this is mostly in the first year with survival curves flattening out in subsequent years.

### **Complications**

The major complications of liver transplantation are listed in Table 1 below where they are divided into immediate, short term and long term. Direct surgical complications can occur in up to 50% of patients and they include bleeding, thrombosis and biliary tree complications. Bleeding is common and often made worse by the presence of coagulopathy related to the patient's liver failure. However, improvements in surgical and anaesthetic techniques in recent years have reduced the incidence of major bleeding.

TABLE 1: COMPLICATIONS OF LIVER TRANSPLANTATION<sup>4,9</sup>

<u>Immediate</u>	<u>Short Term</u>	<u>Long term</u>
Haemorrhage	Primary poor function	Allograft dysfunction
Primary graft non-function	Acute rejection	- biliary strictures
Acute renal failure	Chronic rejection	- disease recurrence
	Hepatic artery thrombosis	- viral hepatitis
	Portal vein thrombosis	- chronic rejection
	Cholangitis	Hypertension
	Bile leakage	Renal dysfunction
	Biliary obstruction	Osteoporosis
	Graft-verses-host disease	Hyperlipidaemia
	Bacterial infection	Skin malignancy
	Opportunistic infections	
	Neurological Complications	

Complications related to the graft include primary graft failure, acute or chronic rejection, and recurrent disease such as viral hepatitis. Primary graft failure can occur in 5-10% of transplants<sup>19</sup> and tends to be associated with prolonged preservation times and poor donor risk factors.

Rejection of liver transplants is less common than for other types of whole organ transplants due to the immunological characteristics of the liver. However, 50-70% of patients still experience some form of rejection. Most centres give prophylactic triple therapy immunosuppression and early rejection is treated with high dose steroid administration. If necessary, more advanced immunosuppressants are used such as OKT3 or tacrolimus. Long term or chronic rejection can lead to long term graft loss and this occurs in about 5% of cases.<sup>4,3</sup>

### Re-transplantation

Overall, the need for retransplantation varies from 10-20% of all transplants. Retransplantation can be an urgent procedure, as in the case of primary graft failure, or elective where there is a gradual reduction in function usually due to chronic rejection or recurrent viral hepatitis. Early retransplantation requires urgent identification of another donor organ. However, if one becomes available the operation is considered 'relatively' easy from a technical point of view. Late retransplantation is a more difficult procedure due to the formation of scars and adhesions following the primary procedure. The long term survival for retransplantation is inferior to that for primary transplantation.<sup>3,10</sup>

### Quality of Life

A number of studies have demonstrated improved quality of life in adults following liver transplantation. The evidence supports that the majority of patients overall attain a very good quality of life post transplantation despite the need for ongoing medical supervision or hospital admissions.<sup>11</sup> Much of the improvement is due to reduction in pre-transplant symptoms especially in patients with longstanding chronic liver disease.<sup>12</sup> The majority of patients return to the workforce, to school or to household duties.<sup>3,20</sup> The ability to return to employment has been associated with a single transplant, marital status, duration of liver disease and the presence of musculoskeletal symptoms.<sup>15</sup>

For children, some studies report a level of decreased intellectual and academic achievement following liver transplantation, however it is reported that this can be addressed with appropriate remedial therapy.<sup>11</sup>

## **2.5 Future Clinical and Technological Advances**

Greater experience and ongoing technological advances continue to reduce the complications and improve outcomes for many liver transplant recipients. Some of the most significant advances have included improvements in organ preservation, new immunosuppressive agents, antiviral therapies for Hepatitis B and C, and ongoing advances in surgical technique. Many of the advances currently under development are to address the shortage of donor organs. The details of some of these follow.

### **Donor Organs**

Split liver techniques and the use of living related donors have been used in various centres in order to address the shortfall in availability of donor organs. Split liver donation is where one donor organ is used for two recipients. The greater technical difficulty of this procedure can increase preservation time, surgical complications and graft failure. However surgical techniques are improving which now allow one liver to be shared effectively between one paediatric and one adult recipient.<sup>13</sup> It is likely that split liver techniques will increasingly be employed by Liver Transplant Units.

### **Living Related Donor**

The use of living relatives as donors is undertaken in some centres. Living Related Liver Transplantation (LRLT) involves a partial hepatectomy being performed on the donor and transplanted into the recipient. This is more commonly performed for paediatric recipients and in countries where there are cultural and religious factors preventing the use of brain dead donors such as Japan. There is not insignificant risk for the donor with mortality quoted at approximately 1% and the risk of a major perioperative complication for the donor approximately 5%.<sup>3</sup> The use of living donors also raises a number of legal and ethical issues apart from the surgical risk to the donor.<sup>14</sup>

Indications are that there have been less than ten LRLTs performed in Australia, the significant proportion on children. St George Hospital has expressed an interest in undertaking adult LRLT. These would be adult to adult transplants, resecting segments 2 and 3 of the left lobe of the liver, with segment 4 also resected if 2 and 3 are not of adequate volume for the recipient's metabolic needs. Progressing adult LRLT requires consideration in regard to a number of issues, including clinical and cost effectiveness, quality of care, and ethical issues. The Plunkett Centre for Ethics in Health Care undertook an ethics review of the proposal for the Department of Health in 2000. This review did not support the establishment of this type of transplant. In addition, in 2001 the Liver Transplant Standing Committee of the Transplant Society of Australia and New Zealand recommended that LRLT for elective cases awaiting cadaveric liver transplantation in Australia was not indicated at this stage.

### **Artificial Liver Support**

Even where organ donation rates are good patients with severe liver failure may still die before an organ becomes available. Therefore, efforts continue into the development of artificial liver support systems which are able to maintain patients in fulminant hepatic failure until a suitable organ becomes available. The systems being developed include bioartificial systems using hepatocytes or the use of temporary pig liver xenografts. The Australian National Liver Transplant Unit (ANLTU) in Sydney has had recent success with a bioartificial model which is currently under trial.<sup>4,3</sup> These systems can currently maintain patients for a number of days thus increasing their chances of receiving a donor organ.

### **Xenotransplantation**

The use of organs from animals for human transplantation has been a long-standing area of research. If successful, xenotransplants could theoretically provide an organ for every potential recipient. Researchers have made a number of advances in controlling rejection most recently using genetic engineering techniques. Despite this there are still a number of problems regarding the use of xenotransplants including those related to graft function, delayed rejection and concerns regarding infectious diseases. It appears likely that this technology will remain experimental for at least the short to medium term.

### 3.0 REVIEW OF CURRENT SERVICE PROFILE

#### 3.1 Delivery Sites

The modern age of liver transplantation in Australia started in Brisbane at the Princess Alexandra Hospital in 1985. The Royal Prince Alfred Hospital (RPAH) in Sydney followed soon after in 1986. In that same year RPAH was designated by the Federal Government as the ANLTU.

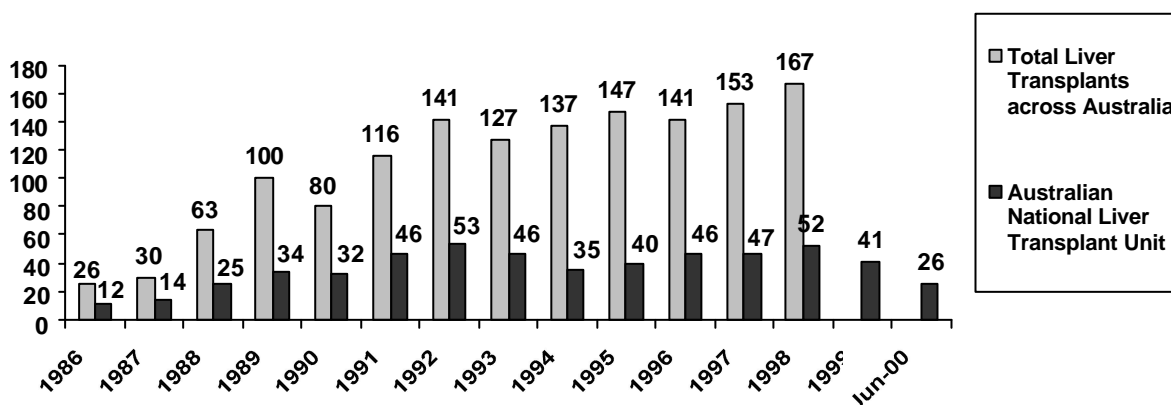
In addition to the Queensland and NSW units, adult liver transplantation units are located in Victoria, South Australia and Western Australia. Paediatric liver transplants are performed in NSW, Queensland and Victoria. New Zealand referred patients to Australian centres prior to the establishment of their own Liver Transplant Unit in 1998.

The ANLTU operates in two hospitals, RPAH and The Children’s Hospital at Westmead (TCHW). Prior to 1998 all liver transplant procedures for both adults and children in NSW were undertaken at RPAH. Paediatric patients would spend some time at TCHW but be transferred to RPAH for the procedure. In March 1998 TCHW began performing paediatric liver transplants on-site with assistance by surgeons from RPAH. This followed the move of TCHW from Camperdown to a new building at Westmead two years earlier.

#### 3.2 Activity

Figure 1 shows the number of liver transplants performed nationally to the end of 1998, with a breakdown of those performed at ANLTU to June 2000. The mean age of adult transplant recipients at the ANLTU is 44.6 years of age. However the unit has treated patients up the age of 67.

FIGURE 1 LIVER TRANSPLANT ACTIVITY ACROSS AUSTRALIA



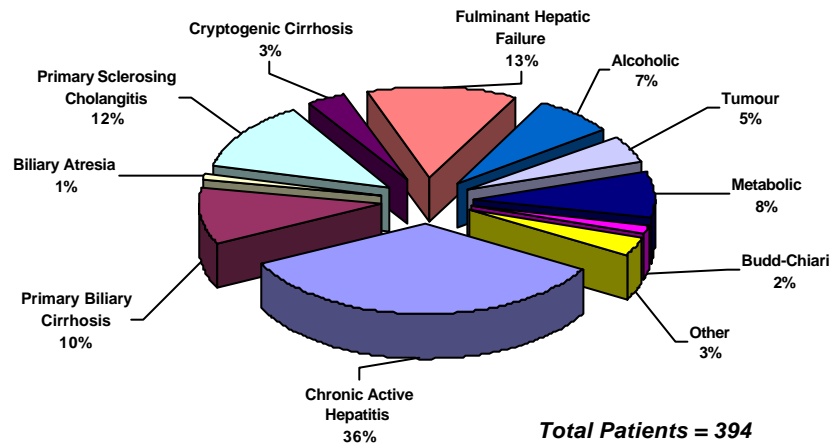
At the ANLTU, paediatric patients (up to approximately 14 years of age) account for approximately 18% of all liver transplants. Over the last few years the number of paediatric transplants in NSW has ranged from 7 to 5 per year.

A distinction is made for babies and very young children under three years of age. In these patients, small size and scarring from previous surgery renders liver transplantation technically more difficult. Overall, children under three years now make up at least half of all paediatric transplants (see Section 4.0 for more detail).

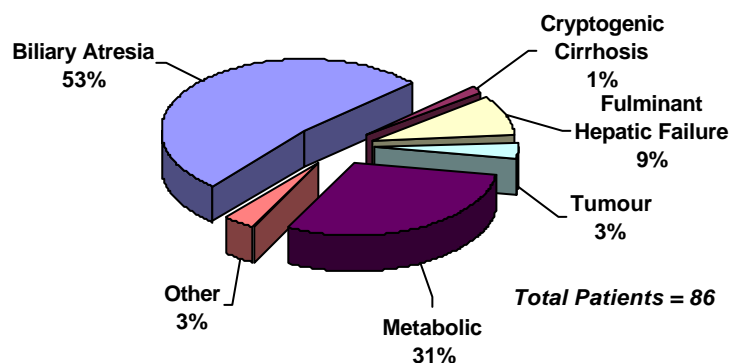
Figure 2 and Figure 3 show indications for transplantation for adults and paediatric patients at ANLTU between January 1986 and December 1999. The majority of adult transplantations are now for chronic active hepatitis. This includes Hepatitis C and Hepatitis B as well Autoimmune Hepatitis.

The number of patients being transplanted for Hepatitis C has been increasing over the last few years. The majority of paediatric transplants are for biliary atresia followed by in-born errors of metabolism and the incidence of these diseases is likely to remain stable in the future.

**FIGURE 2 AETIOLOGY OF PRIMARY LIVER DISEASE, ADULT TRANSPLANT RECIPIENTS JAN 1986 TO DECEMBER 1999**



**FIGURE 3: AETIOLOGY OF LIVER DISEASE, PAEDIATRIC TRANSPLANT RECIPIENTS, JANUARY 1986 TO DECEMBER 1999**



### **3.3 Patient Flow Analysis at the National Liver Transplantation Unit**

#### **Source of Patients**

The majority of transplants at the ANLTU (80%) have been performed on patients referred to the unit from within NSW and ACT. The number of interstate patients has fallen as other States have established their own units particularly since 1992. Currently most referrals are received from NSW and ACT residents as well as from South Australia for paediatric patients.

The ANLTU has occasionally performed transplants on overseas patients as has the Queensland and Victorian Transplant Units. The Queensland Unit has performed the majority of transplants for non-Australian residents, and predominantly on paediatric patients. It should be noted there is an undertaking by all Australian Transplant Units that no donor liver that could be used for an Australian citizen will be transplanted into a citizen from another country; this arrangement excludes New Zealand. With the increasing demand from local residents it is likely that liver transplants on overseas recipients will become less common.

#### **Patient Assessment and Selection Criteria at the ANLTU**

Referrals for liver transplantation are made directly to ANLTU Hepatologists or Surgeons. Current selection criteria includes most causes of end stage liver failure and acute fulminant liver failure. The only absolute contraindications to transplantation are HIV infection, continued alcohol or substance abuse, or significant disease outside of the liver which is not correctable by liver transplantation. For alcoholic liver disease at least six months of abstinence is required, along with a thorough psychological and social assessment, before these patients are admitted to the program.

The initial assessment involves admission to hospital for clinical work-up with a range of pathological and radiological investigations the most significant being angiography. Patients also undergo psychological and social assessment to determine their ability to cope with the pre and post-operative stresses of the procedure. The length of stay for the initial assessment has been progressively reduced and is now approximately two days.

After assessment, patients are either accepted onto the waiting list, rejected as not suitable for transplantation, or deferred for reassessment at a later date if their disease is considered at too early a stage for transplantation. The final decision regarding patient selection is very individually focussed and takes into account factors such as the underlying liver disease, the severity and progression of liver damage and the presence of other significant complications or illnesses. The overriding consideration is the likelihood of success of the operation and of long term benefit to the patient.

Between January 1986 and December 1999 the ANLTU was referred a total of 946 adult and 151 paediatric patients for assessment. Of these approximately 52% of adult patients and 73% of paediatric patients were accepted onto the program. Figure 4 shows the final proportion from both groups who were accepted, deferred or determined not suitable admission onto the program following assessment:

**FIGURE 4: OUTCOMES OF ASSESSMENT FOR ADULTS AND CHILDREN AT THE ANLTU JANUARY 1986 TO DECEMBER 1999**

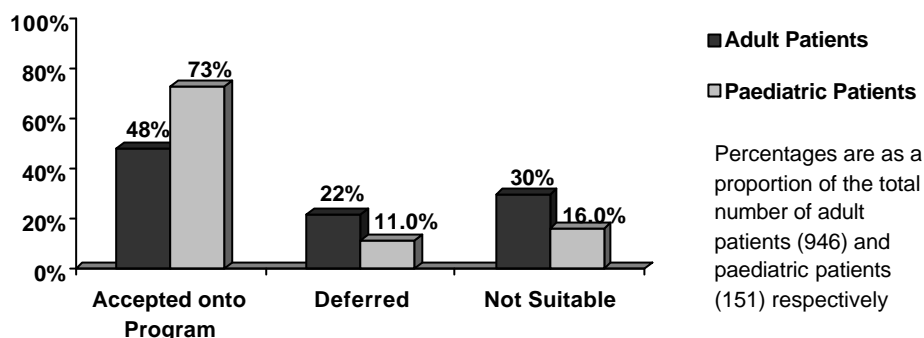


Table 2 summarises the main reasons patients were considered unsuitable and not admitted onto the transplant program:

**TABLE 2: REASONS PATIENTS CONSIDERED UNSUITABLE FOR TRANSPLANTATION January 1986 – December 1999**

<i>Reason Not Suitable</i>	<i>Number of Patients</i>	
Disease Too Advanced	109 (10%)	94 Adults 15 Paediatric
Tumour – Extra-hepatic Spread	45 (4%)	44 Adults 1 Paediatric
Psychological	47 (4%)	47 Adults
Good Prognosis	44 (4%)	39 Adults 5 Paediatric
Alcohol	38 (4%)	38 Adults
Patient's (Parents) Wish	17 (1%)	14 Adults 3 Paediatric
Age	3 (0.3%)	3 Adults
Alternative Therapy	3 (0.3%)	3 Adults
<b>Total</b>	<b>306</b>	<b>{Adult 282} {Paediatric 24}</b>

Patients who are accepted onto the waiting list are classified according to the severity and progression of their disease and this reflects the urgency of transplantation. Disease severity is classified according to the United Network for Organ Sharing (UNOS) codes.

- Status 1 patients (32% at ANLTU) are able to wait at home.
- Status 2 patients (39%) require repeated admissions to hospital to treat the complications of liver failure such as ascites or variceal haemorrhage.

- Status 3 patients (18%) are continuously in hospital.
- Status 4 patients (11%) are the most ill requiring admission directly to intensive care with fulminant hepatic failure.

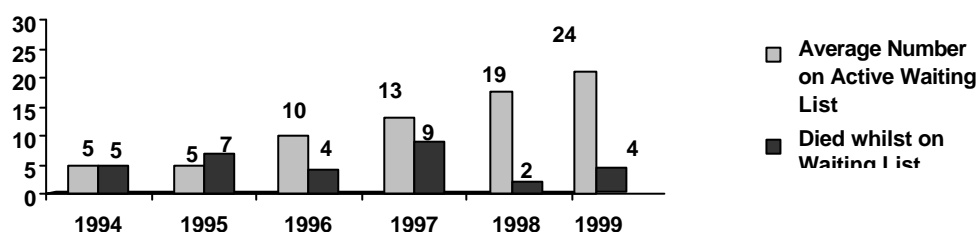
Approximately one-third of status 4 patients die in intensive care before receiving a transplant.<sup>16</sup>

### **Waiting List Status at the ANLTU**

Over the last 10 years over 84% of patients admitted to the waiting list have received transplants. Approximately 12% of patients die while waiting for a suitable donor.<sup>15,16</sup> The average waiting time for adult transplantation has been 52 days, but there has been a wide variation in waiting times from 0 to 567 days (up to 19 months).

For children, the average waiting time is 97 days with the range being 0 to 442 days (up to 15 months). Demand for admission to the program has been increasing steadily for a number of years and in the last 18 months there has been a dramatic increase in the number of people on the active waiting list. Figure 5 shows waiting list status at the ANLTU since 1994.

**FIGURE 5: WAITING STATUS AT ANLTU 1994 - 1999**



As previously stated, patients wait either in hospital or at home depending on their disease severity. Patients waiting at home attend regular pre-transplantation clinics in order to monitor their clinical status. Many require admission to hospital from time to time to manage complications of their liver disease. The clinical details of all patients on the waiting lists are kept up to date and reviewed at weekly Liver Transplant Grand Rounds.

### **Admission and Procedure**

When a donor organ becomes available it is matched to the most suitable recipient using blood group, patient size and considerations of clinical status. The potential recipient undergoes a number of investigations including a check for recent infections. The donor organ is retrieved by the surgical team which is then brought back to the Transplant Unit. The recipient procedure is complex and takes generally from eight to twelve hours. Post operatively patients spend three to five days in intensive care before being transferred to the transplant ward. Average length of stay for liver transplantation was 28 days for 1999 at RPAH.<sup>17</sup>

## Outpatient Care

After initial discharge, daily attendance is required at an outpatient clinic. This is reduced to two or three times a week as patients become more stable. Slow improvement occurs over several months and at twelve months most patients will have made a good functional recovery. In the long term, patients must be maintained on immunosuppressive therapy and have monthly full blood counts, liver function tests and immunosuppressive monitoring.

### **3.4 Outcomes at ANLTU**

Outcomes at ANLTU are equivalent to above average world results with one year patient and graft survival rates quoted at 82% and 78% respectively.<sup>18</sup> Longer term patient survival is shown in Figure 6.

Outcome varies depending upon the underlying patient disease as well as the patient's pre-transplant clinical status as demonstrated in Table 3 and Table 4. Causes of morbidity and mortality at the ANLTU are consistent with Liver Transplant Units in general. Table 5 shows the overall causes of mortality for the unit up until 31/12/99.

**TABLE 3 OUTCOME OF TRANSPLANTATION BY DISEASE AETIOLOGY<sup>16</sup>**

<b>Primary Liver Disease</b>	<b>Number of Patients</b>	<b>1 year survival</b>	<b>5 year survival</b>
Primary Biliary Cirrhosis	39	87%	79%
Chronic Active Hepatitis			
- Autoimmune	31	87%	79%
- Hepatitis B	49	74%	58%
- Hepatitis C	51	79%	70%
- Hepatitis B & C	4	100%	100%
- Hepatitis A	1	0%	0%
Inborn Errors of Metabolism	58	83%	70%
Primary Sclerosing Cholangitis	48	83%	65%
Alcoholic Cirrhosis	29	86%	86%
Cryptogenic Cirrhosis	14	57%	50%
Malignancy	23	82%	62%
Biliary Atresia	50	74%	71%
Fulminant Hepatic Failure	60	68%	66%
Other	24	71%	71%
<b>Total</b>	<b>480</b>	<b>78</b>	<b>70</b>

**TABLE 4: OUTCOME OF TRANSPLANTATION BY CLINICAL STATUS<sup>16</sup>**

<b>Clinical Status pre-Transplantation (UNOS coding)</b>	<b>Number of Patients</b>	<b>1 year survival</b>
Status 1 (outpatient)	154	87%
Status 2 (repeated admissions)	189	80%
Status 3 (hospitalised)	86	72%
Status 4 (intensive care)	51	59%

FIGURE 6: PATIENT SURVIVAL AT THE ANLTU

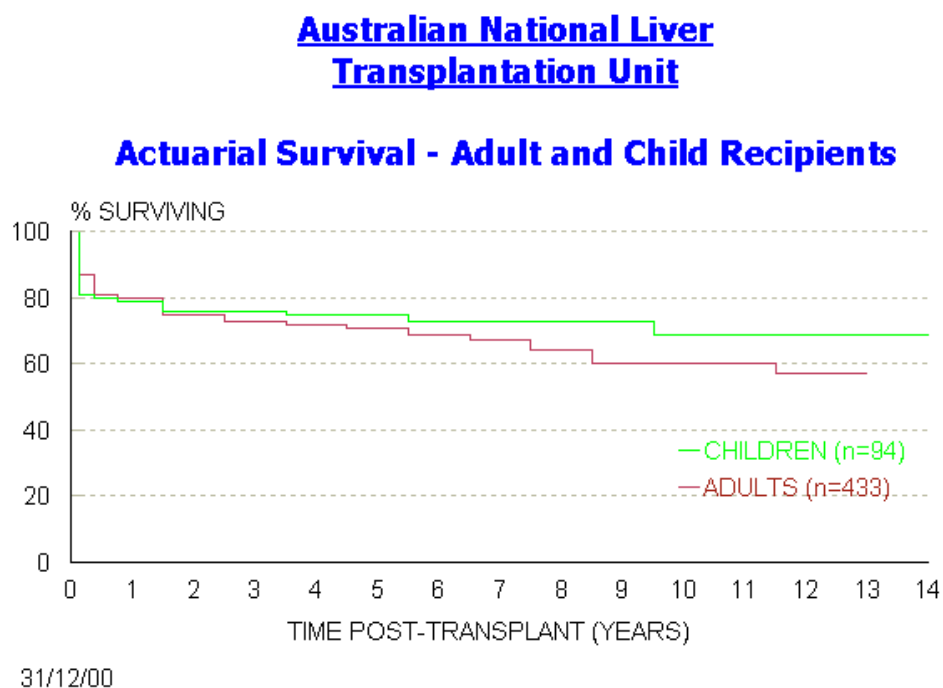


TABLE 5: CAUSES OF MORTALITY UP TO DECEMBER 1999

<b>Causes of Mortality ANLTU</b>	<b>Number (*)</b>
Sepsis	41 (27%)
Graft Failure	41 (27%)
- rejection	25
- recurrent Hep B	11
- recurrent Hep C	3
- PNF	2
Cerebral Catastrophe	20 (13%)
Malignancy	13 (9%)
- recurrent disease	8
- de novo	4
- transferred	1
Intra-operative death	8 (5%)
Vascular complications	6 (4%)
Respiratory failure	9 (6%)
Cardiovascular	5 (3%)
Renal failure	1 (1%)
Gastro-intestinal haemorrhage	1 (1%)
Other	6 (4%)
<b>Total</b>	<b>151 (31% of all patients)</b>

(\* percentage of total mortality)

It should be noted that the ANLTU has a very low rate of primary graft dysfunction (0.3%) compared with world figures (3%–10%).<sup>19,20</sup> This is most likely due to surgical technique and rapid organ retrieval, but in particular good organ preservation secondary to the high standard of intensive care management of donors.

### **3.5 Organ Donation**

The successful coordination of organ retrieval from cadaveric donors is a complex logistical exercise. The ANLTU employs a full time transplant coordinator who is central to the process. The most common causes of death for liver donors are cerebrovascular accidents (38%), road accidents (36%) and other trauma (16%). The average age of donors is approximately 34 years of age.<sup>21</sup>

The potential donor must be certified brain dead by two independent specialists. Following this consent is usually sought from the next of kin or person responsible. Most commonly consent is obtained by the intensive care clinician. The next most common method of consent is a voluntary offer by the family.<sup>22</sup>

Once consent is obtained the State Transplant Coordinator arranges appropriate blood tests including a viral screen and initial blood typing. The coordinator then notifies the appropriate organ Transplant Units. There are well established criteria which are followed to ensure equitable access by all units to available donors as they become available. Essentially this involves a rotation of donor offers from State to State until a suitable recipient is located for each organ.

The ANLTU Coordinator organises the Liver Retrieval Team which consists of a surgeon, assistant surgeon and perfusionist. They travel to the donor Hospital and undertake the retrieval procedure. Most commonly the ANLTU team remove the liver as well as both kidneys. It is common for more than one transplant team to be present at each retrieval for the removal of other organs including the heart and lungs and occasionally the pancreas. Improvements in surgical techniques have progressively reduced the time for the liver and kidney retrieval procedure which now takes about 1.5 hours.

The majority of transport is by road using various emergency or other hire vehicles. Long distance retrievals from country NSW or New Zealand have used a combination of fixed wing aircraft and road transport. Helicopter transport is used only occasionally. The liver is transported in University of Wisconsin solution which allows preservation for up to 12 hours.

With the establishment of Liver Transplant Units across Australia and in New Zealand, liver organs can now be retrieved by the nearest transplant team and then transported interstate to the suitable recipient thus greatly reducing the need for interstate travel by each Transplant Unit.

## 4.0 PAEDIATRIC LIVER TRANSPLANTATION

### 4.1 Activity

There are three centres which perform paediatric liver transplantation across Australia; the ANLTU in NSW, as well as units in both Queensland and Victoria. Since 1993 the ANLTU have performed paediatric liver transplants primarily on NSW and South Australian children. Prior to 1998 all transplant procedures in NSW were performed at RPAH. However, since March 1998 paediatric transplant procedures have been performed at the TCHW located at Westmead.

About half of all liver transplants in children are performed on under three year olds. In these patients, a much greater level of technical difficulty distinguishes the operation. The reasons for this include the smaller size of recipients; the need for reduced sized grafts and often, the presence of scarring from previous surgery.

Table 6 shows the number of paediatric liver transplants performed at the ANLTU and TCHW since 1985 for both over and under three year olds.<sup>23</sup>

**TABLE 6: ANLTU PAEDIATRIC LIVER TRANSPLANT ACTIVITY**

<i>Financial Year</i>	<i>Under 3 year olds</i>	<i>Over 3 year olds</i>	<i>Total Paediatric Transplants</i>
1985-1986	1	1	2
1986-1987	1	2	3
1987-1988	1	4	5
1988-1989	5	4	9
1989-1990	3	7	10
1990-1991	3	6	9
1991-1992	5	7	12
1992-1993	5	4	9
1993-1994	2	5	7
1994-1995	2	2	4
1995-1996	5	2	7
1996-1997	2	3	5
1997-1998	4	1	5
1998-1999	4	7	11
<b>Total</b>	<b>43</b>	<b>55</b>	<b>98</b>

The aetiology of liver disease in children leading to liver transplantation is shown in Figure 3. The majority of transplants are performed for congenital liver disorders including biliary atresia and in-born errors of metabolism. In these patients liver transplantation is currently the only effective long-term treatment.

It is not expected that there will be any significant changes to the indications or demand for paediatric liver transplantation in the near future. In the long term cell therapy or gene therapy techniques may provide an alternative treatment option for some of the enzyme deficiency diseases.

## 4.2 Outcomes of Paediatric Liver Transplantation

The first paediatric liver transplant performed at the ANLTU was on a two year old girl with a hereditary metabolic disorder in 1986. She is now a healthy 16 year old high school student. Survival rates for all paediatric patients are shown in Table 7. These are actual (not actuarial) rates at 1, 2, 5, and 10-year intervals.

TABLE 7: ACTUAL PAEDIATRIC SURVIVAL RATES<sup>24</sup>

	<i>Number of Patients</i>	<i>Number Surviving</i>	<i>% Survival</i>
1 year	70	53	78%
2 years	67	50	75%
5 years	49	36	73%
10 years and longer	9	5	70%

Most mortality occurs in the first three months after transplantation and is due to primary non-function of the graft, hepatic artery thrombosis, acute rejection, infection or cerebral complications. In general, survival rates tend to improve with the greater age of the recipient.

Chronic liver disorders cause delayed growth and development in most children. Liver transplantation has been shown to reverse this with most children exhibiting rapid catch up growth. Some Transplant Units use growth hormone to stimulate linear growth post-transplantation. However, long term paediatric survivors at the ANLTU have all shown normal growth without the need for growth hormone therapy.

Overall the unit reports that 92% of surviving paediatric transplant recipients are enjoying a normal quality of life.

## 4.3 Demand and Donor Organ Availability

As at July 2000, there were 14 children on the waiting list with 11 from NSW, one from Tasmania and two from ACT. Demand for paediatric transplantation is fairly steady however the availability of donor organs still limits the Unit's ability to treat all patients. Since 1986, 14 children have died while waiting a donor organ which represents 8% of the total placed on the waiting list.

Very early on in the program only whole liver transplants were performed which meant that donor organ supply was very limited. The program soon started using cut down techniques whereby an adult donor liver could be reduced in size and used for a paediatric recipient. This resulted in a dramatic improvement in available donor organs for children. More recently an increasing demand for adult liver transplantation has reduced the availability of donor organs for the paediatric recipients.

Surgical advances have led to the development of split liver techniques whereby the donor organ is dissected so that one part may be transplanted into a paediatric recipient and the other into an adult recipient. This technique cannot be used for all donor organs but the unit estimates that if only 20% of donors were suitable, the paediatric waiting time could be reduced from six months to one month.

Prior to March 1998, when all transplants were performed at RPAH, it was not possible to perform simultaneous transplants because only one operating theatre was available and this limited the ability to use split liver techniques. However, with paediatric transplants now being performed separately at TCHW split liver techniques are likely to become more common.

The use of living related donation has been used in a number of overseas centres for paediatric recipients. However, the technique involves not insignificant risks to the donors and has only been used once at the ANLTU. With the increasing use of split liver donations it appears unlikely that this technique will be used in the near future.

#### **4.4 Family Support and Follow-up**

The Liver Transplant Unit at TCHW provides extensive support and education for the families of transplant recipients. During the admission families are accommodated in the Hospital's hostel accommodation. Paediatric patients are followed up in the hospital's Liver Clinic. Spacing between appointments gradually increases to three months. In the long term all patients are reviewed in the TCHW Liver Clinic at three monthly intervals which continues indefinitely.

## 5.0 RESOURCE REQUIREMENTS OF LIVER TRANSPLANTATION

### 5.1 Specific Resource Requirements

#### Transplant Ward

A dedicated transplantation ward of 16 beds has been established at RPAH of which approximately 70% are occupied by liver transplant patients and 30% by renal transplant patients. As part of the 1998 RPAH redevelopment, the transplant ward will be increased to 24 beds.

#### Staffing

Effective running of the ANLTU requires the coordination of a large number of staff from many Hospital departments and across different disciplines. Medical staff include dedicated transplant surgeons, a vascular and an upper gastro-intestinal surgeon, anaesthetists, specialist physicians including a transplant hepatologist and psychiatrist as well as registrars and other supporting junior medical staff. The unit has a number of specialised nursing staff, scientific and technological support staff, allied health, research and administrative staff including a dedicated transplant coordinator.

Liver transplantation is a long and demanding surgical procedure and each operation requires the presence of the following staff:<sup>15</sup>

- Two transplant surgeons and one or two surgical assistants
- Two anaesthetists, one or two anaesthetic nurses or other assistants
- One perfusionist or technician
- Two or three operating room nurses
- One technician or orderly
- One haematology scientist in the laboratory

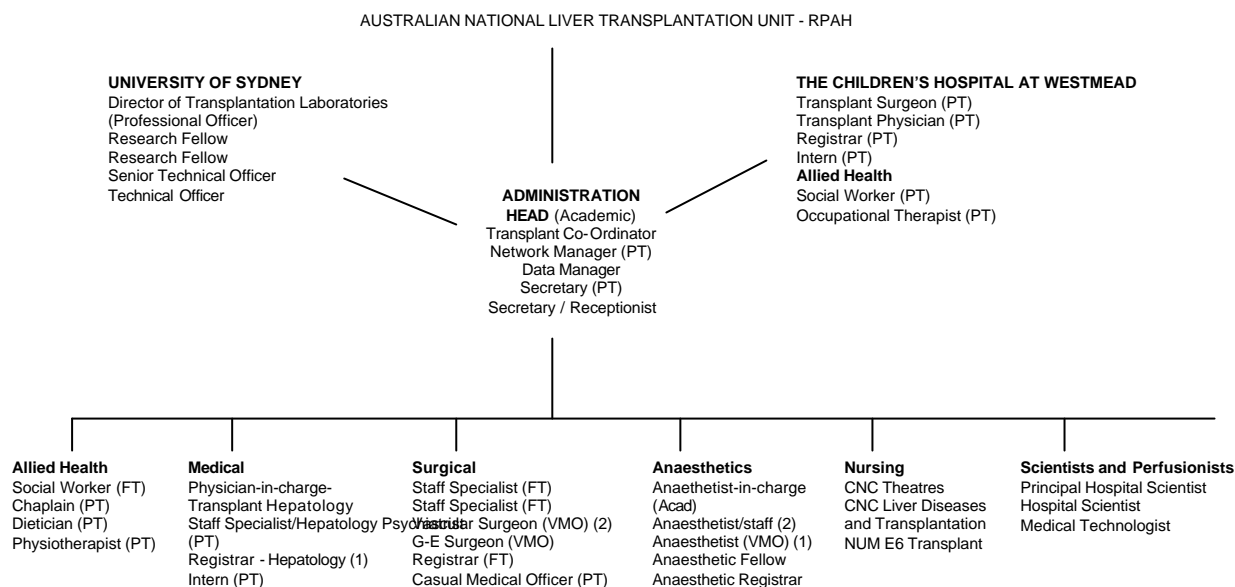
Because of the unpredictable nature of organ donation the Liver Transplant Team must provide a 24-hour service and the staff will often be called upon to work long shifts outside of normal working hours. In general, the Transplant Unit reports a low turnover rate for the majority of their staff.

The important exceptions to this are the transplant surgeons. The position of Liver Transplant Surgeon involves disruptive on-call and after hours commitments as well as stress from undertaking long, complex surgical procedures and the potential danger from exposure to blood borne viruses. These problems have contributed to a turnover of Transplant Surgeons at the ANLTU in previous years. The Unit is currently in the process of negotiating for additional surgical support to relieve some of the demands on existing surgeons.

The demands of liver transplantation on many medical staff have been recognised in the past through various salary supplementations for the Academic and Staff Specialist Surgeons, Anaesthetists and Intensivists. These include additional payments for on-call, call-back, outside-award, danger and in lieu of private practice.

For 1993/94 the ANLTU estimated the total cost for all staff dedicated to the Transplant Unit to be \$2.58 million per annum. The total staff profile of the ANLTU is as follows:

**FIGURE 7: STAFFING PROFILE AT THE ANLTU**



## **Hospital Support Services**

Many hospital departments provide specialised support to the ANLTU which often includes an after hours service; these are listed below:

- Haematology and Blood Bank - Cross Matching and blood products
- Radiology - Angiography; MRI; Cholangiogram
- Clinical Chemistry - Biochemical results including intra-operative and monitoring of the bioartificial liver support system
- Anatomical Pathology - Liver biopsy analysis; Histopathology on excised livers; Donor liver biopsy
- Microbiology - Microbiological monitoring especially on post-operative immunosuppressed patients

The presence of the Liver Transplant Unit has been reported as having a positive influence on many other Hospital departments in the development of clinical skills useful in the management of other patients.<sup>3,15</sup> The development of blood salvaging and rapid transfusion techniques used in liver transplantation can be applied to other major operative procedures and the management of trauma patients.

Advances in skills and knowledge are also likely to occur in intensive care, radiology, microbiology and infectious diseases, histopathology and immunology. In addition the Hospital also gains added expertise in the management of patients with severe liver failure including those who do not go on to liver transplantation.

## 5.2 Costs of Liver Transplantation

### Assessment of Cost

Liver transplantation and the operation of the ANLTU in NSW depend upon the use of a wide range of resources involving many departments across RPAH and TCHW. Because of this complexity it is difficult to determine the exact costs of liver transplantation. However, a number of estimates of the cost have been made using various methodologies. These include an internal estimate by the Transplant Unit in 1994<sup>16</sup>, the Australian Health Technology Advisory Committee (AHTAC) in 1995<sup>15</sup>, and costing studies by the NSW Health Department in 1997<sup>25</sup>. The results of these estimates are presented in Table 8. A study has also been undertaken by the Centre for Health Economics Research (CHERE) on the cost of organ retrieval.<sup>26</sup>

It is useful to consider the costs for transplant procedures as consisting of five components as follows:

1. *Patient assessment and waiting list maintenance*  
This includes the cost of assessment for patients who proceed as well as those who don't proceed to transplantation; and the cost of maintaining patients on the waiting list who often need repeated admissions and/or ongoing assessment.
2. *Patient transport*  
This is for the transport of patients from interstate or remote locations for assessment and admission. For the ANLTU the majority of patients are come from within NSW with a small number from the ACT.
3. *Organ Retrieval*  
The costs of transporting the surgical team and undertaking the retrieval procedure.
4. *Admission and Procedure Costs*
5. *Follow-up and long term care*  
This includes the cost of ongoing immunosuppression and review by the Transplant Unit

### Costs of Organ Retrieval

Studies have estimated the costs for organ retrieval to as high as \$8,000<sup>21</sup> per procedure. The most recent study undertaken by CHERE<sup>26</sup> estimated the total cost of liver retrieval at \$5,300 to \$5,800. This included the costs borne by the donor hospital of approximately \$1,800 which consisted of additional pharmacy and intensive care costs as well as theatre and anaesthetist time; and the costs borne by the retrieval team estimated at \$3,500 to \$4,000 for transportation and the provision of surgical and perfusion staff. It has been generally agreed that the donor hospital accepts the additional costs without reimbursement. For the recipient hospital these costs are absorbed into the total costs of transplantation.

## Comprehensive Costing Studies

The most comprehensive assessment of costs (see Table 8) is included in the AHTAC 1996 report which includes estimates for all components from patient assessment, organ retrieval, transplant procedure and follow-up care for five years<sup>15</sup>. These costs are based on the Commonwealth's 1994 National Costing Study. This report estimated the total cost at \$158,000 to \$177,000 per patient.

The ANLTUs cost estimate of \$125,000 per patient is based upon an averaging out of the unit's costs for 1993/94 over 40 transplants. This estimate does not include long term follow-up costs. The ANLTU believe their total costs are consistent with the AHTAC estimate.

The NSW costing study includes inpatient admission and procedure costs but excludes patient assessment, both for patients who do and do not proceed to transplantation, organ retrieval costs, and patient follow-up. As already noted the costs of organ retrieval to the Transplant Unit have been estimated at \$3,500 to \$4,000 per retrieval. According to the AHTAC report the total cost of assessment and retrieval is \$50,000 per patient. It should be noted that retrieval costs are significantly influenced by the use of air travel for distant retrievals. These are likely to have fallen as other States and New Zealand have established their own Transplant Units. The costs of follow-up care are \$6,500 per year and more for patients who have complicated courses. This includes the costs of ongoing immunosuppression which are not all borne by the Transplant Unit in the long term. Therefore the total costs to the Transplant Unit are probably best reflected at the lower end of AHTAC's 1995 estimates being approximately \$150,000 to \$160,000 per patient.

**TABLE 8: COST ESTIMATES FOR LIVER TRANSPLANTATION**

Source	Cost Estimates	Cost Assumptions
ANLTU 1994	\$125,000 per transplant	<ul style="list-style-type: none"> <li>▪ Averaged cost over 40 transplants (31 adults, 9 paediatric)</li> <li>▪ Does not include long term follow-up costs</li> </ul>
AHTAC* 1995	\$158,000 - \$177,000 per transplant	<ul style="list-style-type: none"> <li>• Comprehensive costing for five years follow-up including costs for assessment and organ retrieval (\$50,000), admission and procedure (\$75,000), drugs (\$6,100 per year), complications (\$2,300 per year) and follow-up care (\$380 per year)</li> </ul>
NSW Health 1996/97 costing study	\$95,485 per transplant	<ul style="list-style-type: none"> <li>• Clinical costing study based on detailed breakdown of costs for admission and procedure</li> <li>• No allowance for patient assessment, organ retrieval or follow-up care</li> </ul>

\* based of the Commonwealth's 1994 National Costing Study

Overseas reports support these cost estimates. In 1993, a comprehensive review of the costs of liver transplantation charges across the US showed the average charge was US\$145,795.<sup>27</sup> Similarly, 1994 UK cost estimates were UK£32,000 to UK£45,000 though it is not certain whether these included all components of care.<sup>11</sup>

### 5.3 Current Funding Arrangements

Prior to 1994, all liver transplants were funded through the Nationally Funded Centre (NFC) Program. As of July 1994, the majority of liver transplants were removed from the NFC program and became funded by NSW Health as a superspecialty service.

NFC funding was continued for liver transplants on patients under three years of age. It is important to note that up to the present time, all liver transplant patients have been classified as public patients regardless of their insurance status.

Funding for liver transplants on NSW residents is \$106,000 for each adult patient and each paediatric patient over three years of age. For interstate patients, the funding is \$76,255 per patient; the lower level of funding presumably reflects that part of the patient's care is expected to take place in the patient's home State. There are arrangements in place between the States for reimbursement of these interstate costs.

In 2000/01 liver transplants for patients under three years of age are funded at \$138,729 per patient. These funds come from the NFC funding pool to which NSW Health contributes. The higher rate for paediatric patients reflects the greater difficulty of the procedure and complexity in managing these patients.

The total funds for liver transplants are split between RPAH and TCHW depending upon relative activity. All funding for adult liver transplants is allocated to RPAH via Central Sydney Area Health Service (CSAHS) by NSW Health. From March 1998 all paediatric liver transplants (ie. patients up to 14 years of age) have been undertaken at TCHW.

The majority of funding for paediatric patients is allocated to TCHW; including NFC funding for infants under three years of age and funds from NSW Health for children over three years of age. RPAH receives an agreed portion of the paediatric funds in return for the support provided to TCHW which includes transplant coordination and surgical assistance.

Prior to March 1998 paediatric patients received their transplant at RPAH but were also admitted for some of their care to TCHW. This resulted in a complicated funding split between the two hospitals and, at times, this was the subject of some contention.

As of 1998/99 funding for liver transplants was allocated as a regular amount to CSAHS and TCHW and no longer subject to current year fluctuations. This means the budget is known in advance and the two health services are expected to manage expenditure within this budget on an annual basis. A more equitable method of charging for interstate patients has recently been negotiated in liaison with other ex-NFC funded transplant units across NSW. Charging is based on national AR-DRG cost weights. However, the *price* per cost weight differential between states means that variations exist.

## 5.4 Cost Effectiveness

Liver transplantation remains one of the most costly of all transplant procedures. As such it has been the subject of much debate as to its cost effectiveness as well as arguments regarding the appropriate use of resources.

The cost of the transplant procedure itself has been shown to vary depending upon factors such as the physiological state of the recipient, the number of post-operative complications, and whether the procedure is a primary transplant or retransplantation.<sup>11,28,29</sup> The economic benefits for transplant recipients depend primarily upon their quality of life post transplant and ability to make an economic contribution.

This is difficult to assess. However, some authors do suggest patients undergoing liver transplantation are, in general, younger than other patient groups to which they are compared in terms of economic analysis. Therefore, they are more likely to make an ongoing economic contribution if the procedure is successful.<sup>11</sup> Another important factor is the recognition of the costs of managing complications in patients with end-stage liver failure and who do not receive a transplant. For example, one study in the US estimated the costs of managing bleeding oesophageal varices, a common complication of end-stage liver failure patients, to range from US\$31,000 to US\$110,000 per admission.<sup>29</sup>

Overall, the economic analysis of liver transplantation is effected by a number of factors which vary widely from patient to patient. Consistent with this, some studies have shown that liver transplantation can be cost effective in comparison with other accepted health care services.<sup>27</sup> However, as with many medical procedures of this type where there is little alternative treatment available, a true assessment of cost benefit is very difficult.

## 6.0 PLANNING ISSUES

### 6.1 Projections of Need Statewide

#### Factors Influencing Demand

Demand for liver transplantation depends both on the incidence of end-stage liver disease and on the number of these patients who are considered suitable for transplantation. The latter factor depends very much on the effectiveness of liver transplantation in treating the various causes of liver disease. For adult patients there is strong evidence that both of these factors are contributing to an increase in demand for liver transplantation.

The incidence of end stage liver failure is increasing mostly due to epidemics of Hepatitis B and in particular Hepatitis C which is becoming one of the most common indications for liver transplantation both in Australia and overseas. It has also been postulated that many cases of transplantation for cryptogenic cirrhosis in the past may have in fact been due to Hepatitis C. Estimates of the incidence of Hepatitis C in Australia have been quoted as high as 0.4% or 150,000 to 200,000 persons<sup>20</sup> and it is estimated that up to 70% of this group will develop chronic hepatitis. Chronic Hepatitis C is a slowly progressive disease but it is expected that over 20 years or so 20 - 30% of patients may develop significant liver impairment.

It is also anticipated that there will be an increase in demand for retransplantation as the number of successful liver transplant recipients increases.

In addition to changes in the incidence of liver diseases, the effectiveness of liver transplantation to treat various causes of liver failure is also improving. Part of this is a general improvement in outcomes associated with development of the technology. This is reflected in widening of the acceptance criteria onto the program including the admission of older patients.

The other side is improvements in the management of specific diseases. Two significant areas of ongoing improvement are more effective antivirals to control Hepatitis B recurrence after liver transplantation; and advances in pharmacological control of malignant disease which may make liver transplantation more successful for primary liver tumours. The management of fulminant hepatic failure is also likely to improve as artificial liver support systems continue to develop.

#### Demand Estimates

Trends in activity at the ANLTU support the predictions of increasing demand. The current level of demand in NSW is approximately 8 million. The 1995 AHTAC Report<sup>15</sup> suggested various estimates of future demand ranging anywhere from 12-30 per million population by 2000. The ANLTU predictions are that NSW will reach a rate of approximately 15 per million population over the next few years, this is consistent with the rates in Europe and the US. .

To meet that level of demand by 2006 this would require that approximately 100 transplants were performed in NSW per year (at an estimated NSW population of 6.8 million<sup>30</sup>). This is nearly double the current number of transplantations. This demand cannot be met at the current rate of organ donation.

Paediatric patients account for about 18% of NSW liver transplants. For paediatric patients most transplants are for congenital liver disorders for which the incidence is not expected to change. Therefore the demand for paediatric transplantation is likely to remain stable.

## **6.2 Availability of Donor Organs**

### **Organ Donation Rate**

The supply of available donor organs is the most limiting factor on the ability of the liver transplant program to treat all suitable patients. Despite much publicity, organ donation rates in Australia have been low compared to other industrialised countries. The 1998 Organ Donation Registry showed Australia's overall organ donation rate to be 10.3 donors per million population.<sup>31</sup> This report also shows that organ donation rates have progressively decreased across Australia from a rate of 13 per million in 1993.

Figures for liver donation rates in Australia are slightly less than the overall organ donation rate. In 1996 the number of potential liver donors across Australia where consent was obtained was 170, of these 57 were from NSW. This equals a rate of liver donation of 9 per million population. Of the total consents obtained approximately 70% were suitable for retrieval and were subsequently transplanted. The two main reasons that consented organs were not retrieved was lack of suitable recipient or disease of the donor organ.<sup>22,32</sup>

In order to meet an estimated maximum demand of 15 transplants per million population by 2006, donation rates would need to increase to at least an equivalent level but more likely to a rate of 18 or 20 per million to allow for a percentage of organs which will be unsuitable for transplantation. An increase in the number of patients on the waiting list is likely to reduce the number of organs not transplanted because of a lack of a suitable recipient.

### **Overseas and Interstate Experience**

Australia's organ donation rate is one of the lowest in the western world. The highest rates of organ donation are found in Spain at 29 donors per million population followed by the US with 20.6 donors per million population. Donation rates across most European Countries varies from 14-15 donors per million population and in Canada the rate is 14.5 donors per million population.<sup>31</sup> These figures strongly suggest that an increase in the overall donation rate in Australia is possible.

Within Australia, the State with the highest rate of organ donation is South Australia at 17 donors per million population for 1997. The success of organ donation in South Australia follows the introduction of a system of organ donation based upon that used in Spain. The principle features of this model are a centralised organ donation coordination centre working in conjunction with a network of local organ donation teams within each Hospital.<sup>33</sup> Importantly, these teams include a medically qualified Transplant Coordinator based at each hospital.

The Medical Coordinator positions are funded on a part time basis and are usually filled by intensive care specialists working at the Hospital. Their role is to actively identify potential organ donors within the Hospital and assist in the appropriate management of these patients before death. The Coordinators are also responsible for communicating with the families of the potential organ donors and obtaining consent. The model includes extensive bereavement support for donor families as well as a system of auditing hospital deaths to identify missed donors. The success of this model in South Australia is demonstrated through an increase in donation rates from 14 donor per million population in 1994 to 17 per million in 1997. These rates are clearly well in excess of those in NSW and the Australian average.

### **Other Initiatives to Increase Organ Donation**

Some countries have introduced more radical changes in an attempt to improve organ donation rates. These include legislative changes based upon the principle of presumed consent whereby organ donation can be undertaken in any death unless the potential donor has registered their refusal during their lifetime. The success of these legislative changes is variable across different countries.<sup>34,35</sup> Other more controversial suggestions include forms of payment or compensation given to donor families<sup>14</sup> or the use of bonds whereby willingness to accept an organ if needed in the future legally binds people to be organ donors if the circumstances arrive.<sup>36</sup>

### **Increasing the Utilisation of Available Donor Organs**

Methods to take more advantage of the current pool of donors include split liver techniques as well as liberalisation of donor acceptance criteria. One example of the latter was reported in a US study which adopted what they called an "aggressive acceptance criteria". They reported an increase in transplants by 55% but this required transplantation of a number of "high-risk" donors. This was associated with an increase in ICU stay and other short term complications. However they reported no increase in primary graft failure or retransplantation and equivalent one year survival rates.<sup>37</sup> There is evidence locally that the criteria for donor selection is becoming broader in particular the acceptance of older donors.

### **Current Initiatives in Organ Donation Within NSW**

In NSW, coordination of organ donation and transplantation has traditionally been the responsibility of the NSW Red Cross Blood Transfusion Service. In July 1997, the NSW State Government allocated \$500,000 of recurrent funding to support strategies to increase the rate of organ donation in NSW.

This funding was used to establish the Coordination Centre for Organ and Tissue Donation as well as the setting up of an Area Health Service Network to support and promote organ donation activities in each major metropolitan region. It includes bereavement support services, review and audit processes as well as the development of additional strategies to increase awareness and support for organ donation in the community.<sup>38</sup>

These initiatives are based upon similar strategies to those adopted within South Australia. This system includes funding for local organ donation coordinators based within each Area Health Service. However, the organ donor coordinators are not necessarily medically qualified as in the South Australian model. This model is currently in the process of being implemented. It is likely that it will be a further one to two years before an assessment of the success of this new model can be undertaken.

In addition to the NSW strategies, there are initiatives being undertaken at a National level to improve organ donation within Australia. The Australian Coordinating Committee on Organ Registries and Donation (ACCORD) was replaced in 1996 by a new National network called 'Australian's Donate' which comprises representatives from organisations involved in organ and tissue donation across Australia. A National Director has been appointed and the organisation is working on projects to promote organ donation as well as the equitable distribution of organs across Australia and the use of uniform documentation.

### **Donation Retrieval Network**

Organ retrieval in NSW often involves the transport of more than one team to the donor hospital and the retrieval by each team of the appropriate organs. This recognises that specific expertise is required for the removal of each organ. However it has also been suggested that greater efficiency could be achieved through the use of single multi-organ retrieval teams.<sup>20</sup> Each team would need to comprise appropriate surgical expertise to enable procurement of all organs, this being key to the success of the system.

If this type of retrieval mechanism was considered appropriate it could have other benefits to Transplant Units. Teams could rotate on a regular roster. This would help to reduce some of the after-hours work burden (particularly for transplant surgeons) as separate retrieval teams would not be needed for each Transplant Unit. There is also potential to integrate this system with more central coordination of the organ donation pool which may help to improve donation rates as outlined above. Funding would most appropriately come from centrally pooled funds sourced from Area Health Services, all of whom would benefit from the service.

### **6.3 Caseload and Liver Transplant Unit Organisation**

An activity of 20 transplants per year is quoted by many studies to be the minimum required in order to maintain expertise and to encourage good outcomes.<sup>15</sup> In 2000 the ANLTU easily exceeded this level with 51 transplants (including paediatric patients) being performed. Both Queensland and Victorian Units exceed these minimum caseloads with 46 and 30 transplants respectively. The South Australian (8 transplants) and Western Australian (13 transplants) Centres fall below this level. The Western Australian unit has published survival results for their first 18 months. These results compare favourably with those from larger centres and provide some justification for the provision of a smaller service on the basis of geographical isolation.<sup>39</sup>

In terms of the caseload required for the establishment of a second Liver Transplant Unit in one city, the 1995 AHTAC report recommended this should only be considered if the first unit has a caseload of at least 60 per year and was not able to provide all transplantations for the particular State. It would also require an increase in the availability donor organs.

During the process of the review of liver transplantation services, other Centres expressed interest in establishing a second adult liver transplant unit in NSW if demand were sufficient. However, NSW will continue to provide liver transplantation at the ANLTU site only. The Selected Speciality and Statewide Service Plan will be reviewed in three to five years, when this service will again be assessed to determine the need for a second adult Liver Transplant Unit. Organ donation rates and technological change will be monitored to determine any need to reconsider the current recommendation.

The ongoing patient throughput at the ANLTU will lead to an increase in the number of patients being followed up by the unit. This is in addition to the increased demand for assessment of potential transplant patients. The ANLTU needs to develop strategies to cope with this increasing outpatient load. It may be appropriate to consider some sharing of expertise to allow other Area Health Services to assist in the routine assessment and longer term follow up of these patients where clinically appropriate. This would also be of benefit in providing clinicians at other hospitals some exposure to liver transplant recipients. In the longer term, this would assist in the development of interest in this technology by clinicians in training.

### **6.4 Funding**

Despite the high cost of liver transplantation services there has not been a comprehensive external costing study performed on this service. As already noted, the costing of liver transplant services is a complicated exercise. Liver transplantation is a high cost but relatively low volume service which requires a large amount of supporting infrastructure in the host institution. The procedure involves the use of many hospital services and the exact contribution of each is hard to quantify. In addition, many of the costing estimates performed so far have not necessarily included all components of cost and they have not appropriately differentiated between components of fixed and variable costs.

It would be appropriate for future costing estimates on liver transplantation to be based upon the following:

- Identification of the different components of cost using a system such as that outlined in Section 5 of this Plan. These components of cost should be designed so they can be consistently applied to the costing of other transplantation services.
- Appropriate estimation of the components of fixed and variable costs within activity parameters for the Transplant Unit.
- Estimation of the marginal cost of each transplant within the current infrastructure and activity parameters

In terms of the methodology of funding, the current central allocation of funds based upon cost estimates as outlined above, is an appropriate model for this type of superspecialty service. Cross area charging would not be appropriate due to the high cost and relatively low volume of the service. Appropriate interstate charging mechanisms need to be negotiated.

## **6.5 Staffing**

As already noted in Section 2 of this Plan, an effective liver transplantation service requires the coordination of a large number staff from various disciplines and, for many, the work can be demanding and stressful. Therefore, in order to maintain staff morale and enthusiasm for the program, leadership and commitment is required in at least one of the senior surgeons or physicians. On-call commitments can be high, particularly for the retrieval team and operating room staff. The overall staffing of the unit must be sufficient to account for these requirements and to allow for appropriate rotation of on-call commitments and relief of leave. In addition, there should be written protocols for on-call schedules and breaks.<sup>15</sup>

The difficulty in attracting surgical staff to a Transplant Unit is due to a number of factors. These positions require a large amount of on-call and subsequent after hours work. The surgical procedures themselves can be stressful and disruptive including both the retrieval, which often involves high speed travel by road and/or air, and the long and complex recipient procedures. There is also the risk to the surgical and assistant staff from potential exposure to Hepatitis C and other blood borne viruses. These stresses and risks also impact on the family members of transplant surgeons.

There must be an adequate number of surgeons with appropriate expertise so that the on-call and after hours commitments can be shared and regular leave granted. Remuneration arrangements should also take into account the added commitment and risks borne by staff in these positions.

## 7.0 RECOMMENDATIONS

### 7.1 *Technology Assessment*

- Liver transplantation has become a routine part of the management of end-stage liver failure for a large number of liver diseases in both adults and children

### 7.2 *Demand Estimates*

- Based upon the incidence of end-stage liver failure and the effectiveness of liver transplantation, there is likely to be a significant increase in demand over the next few years. Exact estimates are difficult to determine but a figure of 15 patients per million over the next three to five years is realistic. If donors could be found for all potential recipients, a total of 100 liver transplants per year within NSW would be required to meet this demand.
- Within these growth estimates paediatric demand is likely to remain stable.

### 7.3 *Organ Donation and Retrieval*

- The organ donation rate is currently the major factor inhibiting ability to meet demand for liver transplantation.
- The use of split liver donor techniques should improve the availability of donors for paediatric patients.
- International and interstate experience suggests that an increase in our organ donation rate is possible. Recent strategies within NSW to reorganise organ donation services in line with the South Australian model are likely to assist in improving organ donation rates. *These strategies should continue to be supported. As part of this reorganisation, it is important that the crucial role of Intensive Care Specialists in organ procurement is recognised and that their support and input into the process is obtained.*
- Greater efficiency could be achieved in organ retrieval through the use of a single, centrally coordinated, multi-organ retrieval team comprising of appropriate surgical expertise.

### 7.4 *Number and Organisation of Units*

- At current levels of activity a single Liver Transplant Unit within NSW is appropriate both in terms of efficiency and maintenance of expertise.
- No expansion in the number of units will be approved until a Review is undertaken in three to five years, and not unless there is a significant increase in organ donation rates.
- Strategies to encourage sharing of expertise in the pre-transplant assessment and the longer term management of liver transplant patients to clinicians outside the ANLTU should be explored.

### **7.5 Funding Recommendations**

- That funding for adult liver transplants will continue to be provided via a specific component of the Resource Distribution Formula (RDF) allocation to CSAHS. It is acknowledged that a review of funding for all selected specialty and statewide services is underway. The outcomes of this policy review may affect this position.

### **7.6 Review of the Plan**

- The Selected Specialty and Statewide Service Plans will be reviewed on a regular basis. It is expected that the Liver Transplantation Plan will be reviewed in three to five years time. However, changes in donor rates and technological change will be monitored in order to determine whether a shorter timeframe for review is required.

## **8.0 MEMBERSHIP: SELECTED SPECIALTY SERVICES STEERING COMMITTEE**

Dr Amanda Adrian	Director, Private Health Care Branch NSW Health Department
Ms Leonie Baden	Health Services, Technology and Capital Planning Unit, NSW Health Department
Professor James Bishop	Director, Sydney Cancer Centre Royal Prince Alfred Hospital
Mr Ken Brown	Chief Executive Officer South Western Sydney Area Health Service
Dr Vasco de Carvalho	Area Director Medical Services Central Coast Area Health Service
Dr Steevie Chan	Manager, Clinical Services Planning Unit NSW Health Department
Mr Richard Gilbert	Director, Health Services Development Central Sydney Area Health Service
Ms Deborah Green	Chief Executive Officer South Eastern Sydney Area Health Service
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Dr Nigel Lyons	Director, Health Services Development Hunter Area Health Service
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Ms Kathy Meleady	Director, Statewide Services Development Branch NSW Health Department
Ms Tineke Robinson	Director, Health Service Development Illawarra Area Health Service
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Dr Tim Smyth	Deputy Director General, Policy NSW Health Department
Mr Ric Sondalini	Structural and Funding Policy Branch NSW Health Department

## 9.0 MEMBERSHIP: GREATER METROPOLITAN SERVICES IMPLEMENTATION GROUP

### Membership

Professor Kerry Goulston	Co-Chair, Associate Dean, Northern Clinical School
Mr Jon Blackwell	Co-Chair, CEO, Central Coast AHS
A/Prof. Debora Picone	Deputy Director General, Policy
Dr Garth Alperstein	Community Paediatrician, Central Sydney AHS
Mr Peter Anderson	Member, Wentworth AHS Board
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Prof Peter Castaldi	Chairman, Western Sydney Area Health Service Board
Prof Michael Chapman	Professor, Obstetrics and Gynaecology, St George Hospital
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Dr Stephen Christley	CEO, Northern Sydney Area Health Service
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Prof John Dwyer	Chairman, Division of Medicine, Prince of Wales Hospital
Mr Peter Edwards	Consumer Representative
Ms Elizabeth Harris	Centre for Health Equity Training Research and Evaluation
Prof Michael Hensley	Division of Medicine, John Hunter Hospital
Dr Sue Hodgkinson	Director - Department of Neurology, Liverpool Hospital
Mr Michael Hollands	NSW State Comm, Royal Australasian College of Surgeons
Ms Lynne Johnstone	Lecturer, Health Service Management, Charles Sturt University
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Dr Meng Ngu	Director, Gastroenterology Unit, Concord Hospital
Dr Paul Nicolarakis	General Practitioner
Dr Stephen Nolan	Department of Critical Care, Manly District Hospital
Dr Tony O'Connell	Paediatric Intensivist, The Childrens Hospital at Westmead
Dr John O'Donnell	National Director, Clinical Services and Quality, Mayne Health
Prof Carol Pollock	Department of Medicine, Royal North Shore Hospital
Ms Tineke Robinson	Director, Health Services Development, Illawarra AHS
Dr Simon Roger	Medical Director, Division of Medicine, Central Coast AHS
Dr Stephen Ryan	Senior Associate, Hardses and Associates
Dr Tony Sherbon	Chief Executive Officer, Illawarra AHS
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Dr Warwick Stening	Director of Neurosurgery, Prince of Wales Private Hospital
Prof John Uther	Cardiologist, Westmead Hospital

### Department Coordination

Kathy Meleady	Secretariat / Director, Statewide Services Development
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**Selected Specialty and Statewide Service Plan  
NUMBER THREE - LIVER TRANSPLANTATION**