TSANZ

The Transplantation Society of Australia and New Zealand

Clinical Guidelines for Organ Transplantation from Deceased Donors

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Produced in partnership with

Australian Government

Organ and Tissue Authority

donatelife

Version 1.0 of the *Clinical Guidelines for Organ Transplantation from Deceased Donors* (the Clinical Guidelines) was released in April 2016. Updates are summarised in the version control table below.

Version control

Version #	Changes made	Approved by	Date
1.18	Updated Section 2.2.2 in alignment with OrganMatch Donor Chart launch Updated Section 3.2 to include responsibilities at time of organ offer Updated Appendix J	TSANZ Board, DSDC, OTA and OrganMatch	30 September 2026
1.17	Update to paediatric DCDD heart donation and allocation (Section 11.5)	Transplantation Society of Australia and New Zealand (TSANZ) Board, TSANZ Advisory Committees: Cardiac Transplant Advisory Committee (CTAC), and the Organ and Tissue Authority (OTA).	31 July 2026
1.16	Update to recommendations regarding suitability of paediatric donors with viral encephalitis (Section 2.3.5) Updated recommendations and references for donor-derived transmission of cutaneous melanoma (Section 2.4.4) Update to urgent liver listing process to include sub-category PELD 25 (Section 6.3.3) Update to liver transplant recipient exclusion criteria (Section 6.2.2) Update to Intestinal Transplant (Section 9) Update to histocompatibility assessment guidance aligning with most recent update to National Histocompatibility Assessment Guideline for solid organ transplantation (Sections 4.3.3, 5.2.6, 7.3.3 and 8.3.4)	Transplantation Society of Australia and New Zealand (TSANZ) Board, TSANZ Advisory Committees: Liver and Intestinal Transplant Advisory Committee (LITAC), Paediatric Transplant Advisory Committee (PTAC), Tissue Typing Advisory Committee (TTAC), Paediatric Donation Working Group (PDWG) and the Organ and Tissue Authority (OTA).	27 April 2026
1.15	Updated recommendations regarding risk of donor transmitted Malaria (Section 2.3.4.1 and Appendix I) Updated recommendations regarding risk of donor transmitted HHV-8 (Section 2.3.2.7 and Appendix I) Updated recommendations for donor-derived transmission of cutaneous melanoma (Section 2.4.4 and Table 2.7) Updated content to Chapter 6/Liver, including updates to acute and urgent patient (Section 6.3.3) and emerging issues (Section 6.7) Alignment with OrganMatch urgent patient listing process (Section 4.3.1, 6.3.3, 7.3.1 and Appendix F) Updated weight thresholds for paediatric kidney donation (Section 11.2) New Appendix B – Donor age/weight criteria per jurisdiction Updated Appendix H recognising the new North Queensland Kidney Transplant Unit New reference and links to the *TSANZ Clinical Guidelines Handbook* (replaces historical Appendix B/Process Report)	Transplantation Society of Australia and New Zealand (TSANZ) Board, TSANZ Infectious Diseases Special Interest Group (TIDSIG), and TSANZ Advisory Committees: Liver and Intestinal Transplant Advisory Committee (LITAC), Organ and Tissue Authority (OTA).	12 November 2025

Version #	Changes made	Approved by	Date
1.14	Updated recommendations regarding donor transmitted infectious diseases, risk of HBV and HIV, (Section 2.3.2.4, Section 2.3.2.8 and Appendix I) Updated advice related to renal cell carcinoma (Table 2.7 and Section 2.4.6.11) Updated kidney allocation algorithm (Chapter 5 and Appendix C) Updated references to NHMRC the *Ethical Guidelines for Cell, Tissue and Organ Donation and Transplantation in Australia, 2025*.	TSANZ Advisory Committees: Renal Transplant Advisory Committee (RTAC), TSANZ Infectious Diseases Special Interest Group (TIDSIG), Australasian Donation and Transplant Coordinators Association (ADTCA), Transplant Society of Australia and New Zealand (TSANZ) and the Organ and Tissue Authority (OTA).	30 June 2025
1.13	Updated recommendation for pre-donation imaging for liver donors (Section 2.4.2.3) Updated recommendations regarding risk of donor transmitted infectious diseases (Section 2.3.1, Section 2.3.2.5 and Appendix I) Updated advice related to testing in donors for COVID-19 (Section 2.2.2, 2.2.4, 2.3.2.1 and Appendix I) Inclusion of hyperlinks to National Histocompatibility Guidelines in relevant solid organ subsections Updated national organ allocation audit process (Section 3.2) Updated definition of a renal orphan recipient in alignment with ANZKX Guidelines (Section 5.2.5) Updated Heart matching algorithm in alignment with paediatric heart offering principles (Appendix G) Updated Kidney allocation algorithm (Appendix C)	TSANZ Advisory Committees: Liver Transplant Advisory Committee (LITAC), Renal Transplant Advisory Committee (RTAC), Cardiac Transplant Advisory Committee (CTAC), Lung Transplant Advisory Committee (LTAC), COVID-19 Australian Transplantation and Donation Rapid Response Taskforce, Australasian Donation and Transplant Coordinators Association (ADTCA), Transplant Society of Australia and New Zealand (TSANZ) and the Organ and Tissue Authority (OTA).	31 August 2024
1.12	Updated recommendation for the follow-up of recipients of organs from increased viral risk-donors (Section 2.3.1) New recommendation: Donors recently vaccinated with a live virus vaccine (Section 2.5.6) OrganMatch update – histocompatibility assessment must occur within 120 days of matching (Sections 4.3.3, 5.2.6, 7.3.3, 8.3.4) Broad revisions to Chapter 4 (Heart) and update to paediatric heart offering principles Update to paediatric heart donation and allocation (Section 11.5) and new Appendix O. Alignment with the ADTCA-TSANZ-OTA National Standard Operating Procedure (SOP): Organ Allocation, Organ Rotation, Urgent Listing, version 4.1	TSANZ Advisory Committees: Cardiac Transplant Advisory Committee (CTAC), Australasian Donation and Transplant Coordinators Association (ADTCA), Transplant Society of Australia and New Zealand (TSANZ) and the Organ and Tissue Authority (OTA).	13 Dec 2023

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1.11	Nomenclature changes throughout to DNDD & DCDD as per 'The ANZICS Statement on Death and Organ Donation, 2021' Alignment with the ADTCA-TSANZ-OTA National Standard Operating Procedure (SOP): Organ Allocation, Organ Rotation, Urgent Listing, version 4.0 Updated advice on International Eligibility (Section 1.2.2) Updated advice on Strongyloides (Section 2.3.4.2) Updated advice on consideration of lung donors and Covid-19 (Section 2.3.2.1) Revised content vigilance & surveillance (Section 2.8) Updated content to Chapter 4 (Heart) relating to urgent heart listing and OrganMatch heart algorithm Broad revisions to Chapter 5 (Renal) and update to kidney algorithm development New recommendations for small intrahepatic cholangiocarcinoma as an accepted primary indication for liver transplantation (Section 6.2.3.1 and 6.2.3.2) Broad revisions to Chapter 7 (Lung), revised Appendix E and F Review of Chapter 11 and alignment with National SOP Organ Allocation, Organ Rotation, Urgent Listing	TSANZ Advisory Committees: Cardiac Transplant Advisory Committee (CTAC), Lung Transplant Advisory Committee (LTAC), Renal Advisory Committee (RTAC), Liver & Intestinal Transplant Advisory Committee (LITAC), Australasian Donation and Transplant Coordinators Association (ADTCA), Transplant Society of Australia and New Zealand (TSANZ) and the Organ and Tissue Authority (OTA).	30 May 2023
1.10	Updated advice on exclusion criteria for hearts (Section 4.2.3) Updated advice to Chapter 6 – Liver inclusion, exclusion criteria, HCC and Alcoholic Hepatitis (Sections 6.2.1, 6.2.2, 6.2.3, 6.2.4) Updated advice to Chapter 8 (Pancreas) to include VXM, OrganMatch Kidney/Pancreas allocation algorithm (addition of Appendix N), and table of pancreas transplant units Updated map of recognised transplant units (Appendix H)	Cardiac Transplant Advisory Committee (CTAC), Liver & Intestinal Transplant Advisory Committee (LITAC), Pancreas & Islet Transplant Advisory Committee (PITAC), Australasian Donation and Transplant Coordinators Association (ADTCA), Transplant Society of Australia and New Zealand (TSANZ) and the Organ and Tissue Authority (OTA).	13 October 2022
1.9	Updated advice related to organ donation and transplantation from donors with a diagnosis of COVID-19 Updated in Section 2.2 and Section 2.3.2.1, including the addition of a flowchart for assessment of potential deceased donor	COVID-19 Australian Transplantation and Donation Rapid Response Taskforce, Australasian Donation and Transplant Coordinators Association (ADTCA), Transplant Society of Australia and New Zealand (TSANZ) and the Organ and Tissue Authority (OTA)	4 May 2022
1.8	Updated advice related to testing in donors for COVID-19 Addition of advice in Chapter 2 (Table 2.1 and Section 2.3.2.1)	COVID-19 Australian Transplantation and Donation Rapid Response Taskforce, Australasian Donation and Transplant Coordinators Association (ADTCA), Transplant Society of Australia and New Zealand (TSANZ) and the Organ and Tissue Authority (OTA)	14 December 2021

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1.7	Broad revisions to Donor derived malignancy (Section 2.4) Changes in relation to paediatric donors, with revisions to Section 6.5.3 paediatric donor liver allocation, Chapter 11 (Paediatric Donors): revision of the criteria for 11.4, paediatric lung donation and allocation,11.5 paediatric heart donation and allocation and the addition of 11.5.1 paediatric heart-lung blocs and allocation	Australasian Donation and Transplant Coordinators Association (ADTCA), Transplant Society of Australia and New Zealand (TSANZ) and Organ and Tissue Authority (OTA), Paediatric Transplant Advisory Committee (PTAC), Lung and Intestinal Advisory Committee (LITAC) and the Cardiac Transplant Advisory Committee (CTAC)	17 September 2021
1.6	The deceased donor kidney allocation algorithm underwent a review that has resulted in broad changes to Chapter 5 (Kidney) and Appendix C	Australasian Donation and Transplant Coordinators Association (ADTCA), Transplant Society of Australia and New Zealand (TSANZ), Organ and Tissue Authority (OTA) and the OrganMatch Strategic Governance Committee (OMSGC)	4 May 2021
1.5	Updated advice related COVID-19 (Section 2.3.2.1) Addition of advice in the event of reactive screening antibody results (Section 2.3.2.9) Addition of Section 2.5 on risks related to other donor conditions Updates relating to the Australian and New Zealand paired Kidney Exchange Program (ANZKX) (Sections 5.2.5 and 5.4.4)	Australasian Donation and Transplant Coordinators Association (ADTCA), Transplant Society of Australia and New Zealand (TSANZ) and Organ and Tissue Authority (OTA)	28 April 2021
1.4	Chapter 11 (Paediatric Donors) was added to the Guidelines, providing organ-specific advice on acceptability and allocation of organs from paediatric donors. Each of the organ-specific chapters in Part B were updated to reflect the new recommendations for paediatric donors Addition of advice on COVID-19 screening in deceased donors	Paediatric Donor Working Group. Australasian Donation and Transplant Coordinators Association (ADTCA) Transplant Society of Australia and New Zealand (TSANZ) and Organ and Tissue Authority (OTA)	24 July 2020
1.3	Broad revisions to donor assessment (Section 2.2) and donor transmitted infectious disease (Section 2.3) Addition of Appendix I: Summary of recommendations for infectious disease screening in deceased donors References to donor and transplant registry statistics have been updated throughout to reflect the most up-to-date data. Changes to Chapter 4 (Heart): removal of the criterion of at least 10 years expected post-transplant survival (section 4.2); clarification of acceptable duration of warm ischaemia time (section 4.4.1); clarification of policy regarding HCV NAT- positive donors (section 4.7) Changes to Chapter 6 (Liver): updates to Section 6.4.1 'Use of HCV infected livers into HCV negative recipients'	Australasian Donation and Transplant Coordinators Association (ADTCA), Transplant Society of Australia and New Zealand (TSANZ) and Organ and Tissue Authority (OTA)	31 May 2019

Version #	Changes made	Approved by	Date
1.2	Changes to Chapter 5 (Kidney): Rewording of the 80% five-year survival criterion for wait-listing eligibility. This now states that "significant benefit" is required from transplantation (Section 5.1) An adjustment to the rules surrounding return of deceased donor waiting time in the event of a failed live donor transplant within 12 months (Section 5.2) Removal of the 12-month waiting period for paediatric bonus score to be applied (Section 5.2.4)	Australasian Donation and Transplant Coordinators Association (ADTCA), Transplant Society of Australia and New Zealand (TSANZ) and Organ and Tissue Authority (OTA)	17 December 2018
1.1	Use of HCV infected donor livers into HCV negative recipients' has been added under section 6.4 on page 64. Minor consequential amendments to Recipient Eligibility in Section 1 and Organ Donor Eligibility in Section 2 have also been made	Australasian Donation and Transplant Coordinators Association (ADTCA), Transplant Society of Australia and New Zealand (TSANZ) and Organ and Tissue Authority (OTA)	17 May 2017

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It is not, nor is it intended to be a

a) complete or definitive statement on any area of medical practice or procedure

b) mandatory set of rules or guidelines.

Practitioners may determine their own approach to some guidance set out in this guideline document for their relevant or unique circumstances at their own risk.

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Rapid advances in medicine may cause information contained in this document to become out-dated or subject to debate.

Readers of this document who are not medical practitioners qualified in the field should seek further professional advice before any action is taken in relation to the matters described or referred to in the document.

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Introduction

Organ transplantation is a highly effective treatment for advanced organ failure that relies on the donation of organs from living or deceased persons. The focus of this document is on the transplantation of solid organs donated from deceased persons.

Currently, the number of patients who might potentially benefit from transplantation is far greater than the number of organs donated. For this reason, organ transplantation is offered primarily to patients who have end-stage organ disease and—with the exception of kidney transplantation—who have exhausted all alternative treatment options. Furthermore, transplantation is offered only to patients who have a reasonable prospect of achieving an acceptably good quality and duration of life after transplantation. Decision-making regarding the allocation and transplantation of donated organs seeks to balance the needs of individual patients against the need to maximise the overall benefit to the community from this scarce and valuable resource.

The Transplantation Society of Australia and New Zealand (TSANZ) is the body responsible for developing eligibility criteria for organ transplantation and protocols for the allocation of deceased donor organs to wait-listed patients. Specifically, TSANZ is funded by the Australian Government's Organ and Tissue Authority (OTA) to maintain:

1. Current, nationally uniform eligibility criteria to ensure that there are equitable and transparent criteria by which patients are listed for organ transplantation, and
2. Current, nationally uniform allocation protocols to ensure consistency in the criteria by which donated organs are allocated.

The TSANZ document Organ Transplantation from Deceased Donors: Consensus Statement on Eligibility Criteria and Allocation Protocols (version 1.1) was released in June 2011. The current document, Clinical Guidelines for Organ Transplantation from Deceased Donors, supersedes the previous Consensus Statement and was developed by the TSANZ Advisory Committees following a process of targeted written consultation. Version 1.0 of the Clinical Guidelines was released in April 2016, and in 2025 TSANZ developed the TSANZ Guidelines Handbook, which outlines the process by which TSANZ clinical guidelines are developed, reviewed, updated, and endorsed by TSANZ and OTA. The Handbook is intended to ensure that all TSANZ clinical guidance remains evidence-informed and is developed through comprehensive stakeholder consultation.

Central to the eligibility criteria and allocation protocols described in this document are the following ethical principles, which are embodied in the National Health and Medical Research Council (NHMRC) publication the *Ethical Guidelines for Cell, Tissue and Organ Donation and Transplantation in Australia*[1] which provide a framework to support ethical practice and inform decision-making by all those involved in Australia's donation and transplantation system:

1. Decision-making regarding allocation must involve explicit evaluation of the risk and benefits to the potential recipient as well as the need to ensure the appropriate use of scarce health resources.
2. There must be no unlawful or unreasonable discrimination against potential recipients on the basis of:
    - Race, religious belief, gender, marital status, sexual orientation, social or other status, disability or age
    - The need for a transplant arising from the medical consequences of past lifestyle
    - Capacity to pay for treatment
    - Location of residence (e.g. remote, rural, regional or metropolitan)
    - Previous refusal of an offer of an organ for transplantation
    - Refusal to participate in research.

3. Decisions regarding eligibility and allocation will take into account the following ethically relevant factors:
    - Relative urgency of need
    - Medical factors which affect likelihood of success (e.g. comorbidities, tissue matching)
    - Relative severity of illness and disability
    - Relative length of time on the waiting list
    - Likelihood that the recipient will be able to comply with the necessary ongoing treatment after transplantation.

To be eligible to be wait-listed for organ transplantation, patients must be referred for assessment and meet the relevant eligibility criteria as specified in this document. The transplant assessment process requires referred patients to be evaluated by a transplant unit; this evaluation process takes into consideration patients' medical history and other relevant factors. Once listed, patients are regularly reviewed to ensure that they remain eligible to receive a transplant.

Organ allocation processes vary according to the organ that is to be transplanted. Allocation of hearts, lungs, livers, and intestines involves transplant units making a clinical judgement when an organ becomes available as to which patient on the waiting list has the greatest need of that particular organ, at that particular time, based on a range of factors. Patients who require kidney or pancreas transplantation are generally stable over a prolonged period of time, and the allocation of these organs is currently based primarily on the closeness of tissue matching and the time spent on dialysis or on the transplant waiting list.

The criteria used to decide which patients are placed on a transplant waiting list and how deceased donor organs are allocated do not determine how many patients will be transplanted, but rather which patients are eligible to receive which donor organs. It is recognised that whatever process is used, there will still be many patients who might benefit from an organ transplant but will not be able to receive one because of the limited supply of organs.

The criteria and processes outlined in this document seek to achieve an appropriate balance between the needs of individuals with end-stage organ failure and the obligation of transplant teams to exercise responsible stewardship of the community's healthcare resources, including donated organs.

References

1 National Health and Medical Research Council (2025), Ethical guidelines for cell, tissue and organ donation and transplantation in Australia. Canberra: National Health and Medical Research Council.

Part A

General issues related to recipient eligibility and donor assessment

1 Recipient Eligibility

The relative scarcity of donor organs means that transparent eligibility criteria are required to ensure a just and equitable system for deciding which patients will have access to organ transplantation as a therapy. Determining eligibility in an environment where need exceeds availability involves balancing the potentially conflicting ethical principles of equity and utility. Equity, in its purest form, requires that every potential recipient who might benefit from an organ transplant has an equal opportunity to receive one. Utility, on the other hand, requires that the community should derive the maximum possible benefit from the limited number of organs available for transplantation. The eligibility criteria and allocation processes outlined in this document attempt to balance these ethical principles in a practical and transparent manner. It should be noted, however, that because the allocation of organs is a complex process with a range of factors informing the decision to offer a particular organ to a particular recipient, wait-listed patients will wait for variable periods of time regardless of their relative medical need.

1.1 Referral

Patients are referred to transplant units by their treating specialist physician for assessment of their eligibility to be entered onto a transplant waiting list. Eligibility is determined on the basis of organ-specific criteria that have been developed by the relevant Advisory Committee or Working Group of the Transplantation Society of Australia and New Zealand.

Comprehensive, multidisciplinary assessment of potential candidates for transplantation is a complex and time-consuming process. It is important that referral is timely to enable suitable patients to be listed as early as is medically appropriate. In some cases—particularly in the case of kidney transplantation where the patient is not at immediate risk of death—it would usually be appropriate to optimise the patient's medical, social and psychological situation prior to referral and evaluation for wait-listing.

1.2 Assessment for eligibility

1.2.1 General inclusion and exclusion criteria

The assessment process typically requires that patients undergo a standard set of consultations and investigations to evaluate their suitability for organ transplantation. Some patients will require further investigations depending on their specific circumstances. Clinical assessment should involve evaluation by a multidisciplinary transplant team that includes (as a minimum) both a suitably experienced transplant surgeon and a suitably experienced transplant physician (see Section 1.4).

The transplant team should regularly review wait-listed patients to ensure that they remain suitable for transplantation. Listed patients should be removed from the transplant waiting list if their condition changes (this could be either an improvement or a deterioration) to the point that they no longer meet the eligibility criteria outlined in this document.

While there are specific recipient inclusion and exclusion criteria for each organ, there are general conditions that apply across all organs. These are:

Age: with the increasing success of transplantation, the age range considered suitable for transplantation has steadily increased. Age is not by itself an exclusion criterion for most organs. However, the presence of multiple comorbidities in patients over 70 years of age is likely to exclude the majority of such patients from eligibility for transplantation.[1,2]

Comorbidities: exclusion criteria generally include conditions or combinations of conditions that would result in an unacceptably high risk of mortality or morbidity during or after transplantation (e.g. active malignancy, severe cardiac disease, or chronic infection).

Behavioural risk factors: the fact that an individual may require a transplant due to lifestyle choices they have made in the past is ethically irrelevant. However, ongoing substance abuse—including excessive alcohol consumption, cigarette smoking and illicit drug use—are generally considered contraindications to transplantation. These lifestyle factors increase the risk of poor transplant outcomes.[3-7]

Inability to adhere with complex medical therapy: for example chronic cognitive or neuropsychiatric deficits in the absence of a carer capable of facilitating adherence to therapy. [8-12]

All patients assessed for eligibility for transplantation have the right to know whether or not they have been placed on the transplant waiting list, and the reasons why they have not been listed if they are deemed ineligible.

Recognised transplant units in Australia and New Zealand are listed in Appendix H.

1.2.2 Eligibility for publicly funded access to deceased donor organs (or living non-directed donor organs) allocated by the national algorithms

TSANZ supports the Declaration of Istanbul on organ trafficking and transplant tourism.[13,14] and is committed to the principles of fairness and transparency in the processes of assessment and listing for organ transplantation.

TSANZ considers that all patients who reside* in Australia (AU) or New Zealand (NZ) *and* who are eligible for publicly funded treatment for end stage organ failure within AU/NZ are eligible for assessment, waitlisting and transplantation. Further organ specific information pertaining to transplant recipient inclusion and exclusion criteria can be found in chapters 4-10 of these Clinical Guidelines.

In view of the existing gap between the need for organs and their availability, TSANZ considers it inappropriate for patients who are not eligible for publicly funded healthcare to be assessed for transplantation except under exceptional circumstances. An exceptional circumstance may include a non-eligible patient who develops acute life threatening, non-reversible organ failure that would normally warrant consideration for transplantation and is too unwell to return to their home country to access care there. In this situation it needs to be established that the patient will return to a jurisdiction where there is access to safe and effective long-term care of the transplanted patient.

In addition to ensuring the relevant jurisdictional health oversight, we recommend that the appropriate TSANZ organ advisory committee be notified of such candidates. An annual audit of international patient waitlisting will be conducted by the TSANZ organ advisory committees.

*Further information on required residency status and eligibility for publicly funded healthcare can be found here: About Medicare | Australian Government Department of Health and Aged Care (AU) and Getting publicly funded health services | New Zealand Government (www.govt.nz) (NZ).

1.3 Consent

Consent is defined in the Ethical Guidelines as a person's or a group's agreement, based on adequate knowledge and understanding of relevant material.[15] As for all medical procedures, consent should be given before transplantation can proceed. If the individual does not have the capacity to give consent or is a minor, a representative should be involved in ongoing discussions and decision-making. Sufficient information about the procedure must be made available, including the risks, the benefits, and what will happen if the procedure does not go ahead.

The acceptability of donor organs that may pose an element of risk to the recipient should be discussed with both the potential recipient and their carer at the time of wait-listing (rather than at the time of the organ offer). With the introduction of new and safe antiviral therapy for Hepatitis C virus (HCV) infection this should include the possible use of an organ from a HCV infected donor into a recipient without HCV infection. The provision of adequate counselling and education is critical to the potential recipient's ability to consider their options and ultimately provide informed consent if they choose to proceed with transplantation in these circumstances.

It is imperative that the potential recipient receives comprehensive education regarding the transplant procedure and its potential short- and long-term outcomes. All patients are not equal in terms of their capacity to understand this information, and it is the clinician's role to ensure that information is provided at a level that is comprehensible to the patient. This should be done before surgery—ideally during the assessment phase—and over a series of meetings including consultations with clinicians and patient education sessions, with provision of supplementary reading material and/or electronic media.

Provision of written consent specific to the planned transplant must be sought. Provision of written consent should be preceded by discussion(s) of immunological and surgical risks, plus explicit discussion of any case-specific risks related to donor quality or risk of donor-derived disease (e.g. in the case of a tumorectomised kidney and cancer risk, or a hepatitis B core antibody positive donor or, more recently, the use of HCV positive organs in HCV negative transplant recipients – see Chapter 2) without compromising donor anonymity. In the case of children, both the patient and their carers should be educated and provide consent. For those deemed not legally competent, the appointed guardian should be educated and asked to provide consent.

1.4 Assessment and wait-listing

The referral of individuals with organ failure to a transplant unit for assessment of transplant eligibility should be initiated and completed in a timely manner to maximise the chances of successful transplantation. The transplant eligibility assessment should include:

> Patient education regarding treatment options: treatment options include transplantation versus no transplantation, or living donor versus deceased donor transplantation for those with kidney failure (and for some patients with liver failure). Patients should be educated regarding likely risks, estimated benefits, and expected outcomes of transplantation. Patients should also be educated about the range of donor characteristics and the potential risks and benefits of accepting a higher-risk organ.
>
> Medical assessment: both physical and psychological assessment is required to identify possible issues or contraindications to transplantation, and to enable an estimation of the risks and benefits of transplantation for each individual. This assessment should include clinical review by members of the transplanting team, including (at a minimum) a suitably experienced transplant surgeon and a suitably experienced transplant physician, plus any other clinicians deemed necessary. Assessment will include screening tests designed to ensure medical suitability for transplantation, as directed by the transplant team. The time required to complete medical assessment is variable, determined largely by case complexity.

Listing for deceased donor organ transplantation: this should be done by the transplant team following completion of the assessment to their satisfaction. Criteria for listing vary from organ to organ, and are detailed in each organ-specific chapter within this document. If the transplant team believe transplantation is either contraindicated or that the patient does not meet the criteria for listing—either due to the absence of an indication for transplantation or an unfavourable projected risk-benefit scenario if transplantation were to be attempted—then the patient and their referring clinician should be informed and advised as to the reasoning behind this decision. In some cases, where additional information is required, a listing decision may be deferred until such information becomes available. Every reasonable effort should be made to obtain the necessary information within a reasonable timeframe, and the referring clinician should be kept adequately informed regarding information requirements and timelines.

1.5 Appeals

Patients in Australia who are either (i) not referred for transplant assessment, or (ii) assessed by a transplant unit and deemed unsuitable for listing, have a right to appeal such decisions (see the NHMRC Ethical Guidelines[15]). The appropriate pathway for patients in scenario (i) who disagree with their assessment is to seek a second opinion from a specialist within the field. Potential outcomes of seeking a second opinion are: (a) the specialist from whom the second opinion is sought believes that referral for transplant is not indicated, in which case this should be explained to the patient, or (b) the second opinion is that referral is indicated, and that specialist refers the patient to a transplant service for assessment. In the case of scenario (ii), where the decision not to list a patient is appealed, the local unit will first review the clinical information to determine whether there are any factors that might lead to a change in the original decision. If the unit uphold their decision that the patient is not eligible for listing, however the patient, their family or other advocates still disagree with this assessment, then the appropriate pathway is to seek—via the patient's specialist, and with the impartial assistance of the local unit—referral to a second transplant unit within the patient's jurisdiction; an inter-state opinion may, if required, be sought by negotiation between the units and with the patient's consent. In the case of heart transplantation, given the logistical challenges and costs related to patient transport, the second unit should first conduct a data review, followed by a face-to-face review only if warranted. In all cases, the local unit should assist patients and families in pursuing a second opinion by providing clinical data to the second unit so that the patient does not have to undergo repeat investigations. Potential outcomes of referral to a second transplant unit are: (a) the second transplant unit agrees that the patient is not suitable for transplant listing, and this is explained to the patient; or (b) the second unit believes that the patient should be waitlisted, which should then be performed at either the primary or the secondary unit following discussion involving all parties.

In the case of intestinal transplantation and vascularised composite allotransplantation, for which only single transplant units currently exist, there is not the option of referral to a second unit within Australia or New Zealand if a patient appeals the decision of the transplant unit not to list. For intestinal transplantation, an understanding exists with the United Kingdom to refer cases for second opinion to the UK National Adult Intestinal Transplant forum, which convenes every two months.

New Zealand has a formalised process for appeals to the National Renal Transplant Leadership Team.

1.6 Ongoing review

Factors affecting patient suitability for transplantation may change over time. For this reason, patients wait-listed for organ transplantation should be monitored by their local physician. In addition, patients should be reviewed by the transplant unit (i) regularly, at an interval determined by the transplant unit based on patient comorbidity profile and stability (typically annually), AND (ii) ad-hoc, when the transplant unit is alerted to a potential change in suitability by the patient's usual treating physician or other medical staff. For example, unscheduled hospitalisations, intercurrent events such as myocardial infarction, or concerns with respect to non-adherence to therapy may warrant ad-hoc review by the transplant unit. If, upon review, the patient is determined to be no longer suitable for transplantation, they should be (i) delisted, if the change in status is deemed likely to be permanent, or (ii) temporarily moved to the inactive list, if the problem identified is felt to be remediable—in this case a plan for reassessment with a view to reinstatement to the active list should be made. The patient and their referring physician should be kept informed of any changes in listing status and, subsequently, of the steps involved in determining suitability for reinstatement to the active list.

1.7 Retransplantation

Organ transplant recipients who develop failure of the transplanted organ (e.g. a kidney transplant recipient who develops failure of the transplanted kidney) or another organ (e.g. a patient with a functioning liver transplant who develops kidney failure) are entitled to be assessed and listed for transplantation of a subsequent organ. The assessment should determine medical eligibility and the likelihood of successful transplantation in the same way as those seeking transplantation of a first organ. The presence or absence of a previous transplant should not affect access to transplantation, except where this impacts upon medical suitability.[15]

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2 Organ donor suitability

The majority of transplantation in Australia and New Zealand is possible because of deceased donation, including all heart, lung, pancreas, most liver, and approximately 70% of all kidney transplantation.[1] Deceased donation is based on altruistic decisions of individuals and/or their families to donate organs to benefit other people. In Australia and New Zealand, as in all countries, there are more people who might benefit from organ transplantation than there are donor organs available. This is largely due to the small proportion of people who die in the specific circumstances under which organ donation is currently medically feasible (approximately 2% of hospital deaths). The framework within which deceased organ donation occurs includes the laws and regulations that govern the determination of death and the use of human organs and tissues for transplantation, as well as the policies and guidelines that direct clinical practice.[2,3,4,5]

2.1 The organ donation process

2.1.1 Prerequisites for deceased organ donation

Before organ donation can take place:

- The donor must have been declared deceased by qualified physicians using accepted guidelines that are consistent with the laws and regulations of the jurisdiction in which the donor has died (see ANZICS statement[2]), and
- Consent to organ donation must have been given and documented according to the laws and regulations of that jurisdiction.

It is the formal responsibility of a designated officer appointed by the hospital authorities, reinforced by the Donation Specialist Coordinator and all surgeons in charge of donor surgical teams, to confirm that these laws and regulations have been fully complied with and documented appropriately before proceeding to the retrieval of organs.

2.1.2 Determination of death and pathways to organ donation

Criteria for declaring death in Australia and New Zealand are: [2,5]

- Irreversible cessation of all function of the brain of the person, or
- Irreversible cessation of the circulation of blood in the body of the person.

Death declared according to neurological criteria (brain death) is only possible when the person is maintained on a mechanical ventilator, usually whilst receiving treatment in an intensive care unit (ICU). Conditions causing sufficient brain injury to culminate in neurological death include haemorrhagic or occlusive stroke, trauma, hypoxic-ischaemic brain injury following a cardiac arrest, central nervous system infections and tumours. There are strict criteria and procedures for the determination of neurological death in Australia and New Zealand, which are outlined in the clinical guidelines of the Australian and New Zealand Intensive Care Society.[2] Donation after neurological determination of death (DNDD) results in better transplant outcomes for some organs, and is more predictable with only a small proportion of cases not proceeding to the surgical retrieval of transplantable organs. DNDD is limited by the low and decreasing incidence of stroke, brain trauma and other causes of neurological death observed in many developed countries including Australia and New Zealand. This means that DNDD is possible in fewer than 1% of the deaths that occur in hospital.

Death is more commonly determined using circulatory criteria and—in a limited number of such circumstances—organ donation may be possible. Donation after circulatory determination of death (DCDD) in Australia and New Zealand can occur after a decision has been made to withdraw treatment because it is considered no longer to be in the person's best interest.[4] This decision is usually reached by the healthcare staff and family, although in very rare and exceptional circumstances the decision may be made by the conscious, competent patient. The majority of patients suitable for DCDD are receiving mechanical ventilation and/or other cardio-respiratory supportive treatments in intensive care units. If loss of cardiac output with absence of circulation, and thus circulatory death, occurs within a short timeframe after withdrawal of cardio-respiratory supportive treatment (generally within 30 to 90 minutes), donated organs can be transplanted with successful outcomes.

Situations where DCDD is considered include severe brain injury that has not and is not likely to progress to neurological death, end-stage cardio-respiratory or other organ failure, high spinal cord injury, and progressive neuro-muscular conditions.

Donation after Circulatory Death gives individuals and their families the opportunity to donate organs when neurological death hasn't occurred, and provides additional organs for transplantation to the community. Currently, donors following a DCDD pathway comprise about 30% of organ donors in Australia and 16% of organ donors in New Zealand.[6] There are, on average, fewer organs transplanted per donor via a DCDD versus a DNDD pathway, given the narrower organ suitability criteria that are applied in the situation of DCDD.

Currently, approximately 30% of planned DCDD does not proceed to organ retrieval because death does not occur within the required time frames from withdrawal of cardio-respiratory support.[7] Clinical practice improvements to refer all patients at end of life in the intensive care and emergency department settings has enhanced access to patients for potential donation via the DCDD pathway. This has continued to demonstrate an increased donation rate via this pathway.[7]

2.1.3 Retrieval surgery

Each jurisdiction has processes in place to identify teams to undertake the surgical retrieval of abdominal or thoracic organs that have been assessed to be suitable for transplantation. Key team members from cardio-thoracic, liver or renal transplant units who will travel to the donor hospital may include surgeons, cardiac anaesthetists and perfusion technicians. Team members from the local hospital include theatre nursing staff, operating theatre technicians, anaesthetists and, sometimes, surgical assistants. The donation specialist coordinator also attends the retrieval surgery to coordinate the retrieval, assist with logistic arrangements, documentation of the process, support the theatre staff and care of the deceased post donation.

At surgical retrieval, organs are further assessed for suitability by retrieval surgeons in consultation with transplant surgeons and physicians. This may at times require adjunctive information such as the results of biopsies, which may not be available until after organ retrieval. Arrangements for the transportation of organs are made according to the organ type and whether organs are for local use or for transport interstate or between Australia and New Zealand.

There must be a reasonable prospect of at least one organ being transplantable before making the decision to proceed to retrieval surgery. The rate of non-utilisation of retrieved organs is expected to be small but greater than zero, since the final assessment of organ suitability can only be made at surgical retrieval. Information regarding organ quality and organ utilisation is collected and reviewed via the the 'Organ Retrieval Report Form' (ORRF).

2.2 Deceased donor and organ assessment

2.2.1 General evaluation of deceased organ donors

Organ suitability for transplantation is determined by the answers to two questions: (i) is the donor medically suitable to donate any organ, and (ii) is a particular organ suitable for transplantation.

Transplantation inevitably carries a small potential risk of transmission of infection or cancer from the donor to the recipient.[8] That risk may vary depending on the organ and is assessed by considering donor risk factors and by testing the donor. Donor-derived disease transmission complicates less than 1% of all transplantation procedures (excluding *Cytomegalovirus* [CMV] and Epstein-Barr virus [EBV]) but can result in significant morbidity and mortality.[9,10] While it is possible to quantify risks through screening and testing, the risks of transmission of infectious and other diseases cannot be completely eliminated.

The level of risk of disease transmission must be balanced against the risks to an individual patient of not proceeding with transplantation. The medical urgency of transplantation for some patients may mean that transplantation with an organ from a donor with increased risk of disease transmission is considered. Particularly where transplantation is life-saving, an increased risk of disease transmission may be regarded as acceptable to the recipient. Conversely, where transplantation is not immediately life-saving but instead aims to improve the quality of the recipient's life, a greater margin of safety is appropriate. Nonetheless, transmission of infectious or other disease to recipients always remains a possibility, as there are limitations on diagnostic capabilities and limited time frames for donor assessment. It is important that the recipient has an informed view of accepting or rejecting an organ of lower quality and/or increased risk of disease transmission, with an understanding of the likely benefits from transplantation with the organ on offer (in terms of survival and/or quality of life), the likelihood of subsequent organ offers, and the risk of deterioration of their health status whilst waiting for an alternative offer. The conversation with the patient regarding consent to receive organs of lower quality or increased risk of disease transmission should occur early, ideally at the time of consent to waitlisting, and should be revisited periodically to take into account changes in patient priorities and health status.

Suitability of a particular organ for transplantation is influenced by a range of factors including donor age, size, medical history (including co-morbidities), lifestyle choices and specific organ size and pathology. The donation pathway will also influence organ suitability; that is, suitability will be affected by whether the donation was via a DCDD or DNDD pathway, the cold ischaemic time, the warm ischaemic time in case of DCDD, the surgical retrieval process, organ perfusion, organ storage and logistics.

It is increasingly possible to grade the quality of donated organs in order to provide a more accurate prediction of the medium and long-term functional outcomes of the organ post-transplantation. It is also possible to grade the risk of transmissible disease associated with a given donor and organ. This grading of organ quality and risk of disease transmission allows acceptance decisions to be tailored to individual recipients' needs. That is, the potential benefit that is offered by a given organ may be insufficient for the needs of certain individuals (for example patients who are stable on medical therapy), however the same organ may increase the quality of life and survival prospects of other wait listed individuals (for example patients who are deteriorating on the waiting list or who are older).

2.2.2 Medical and social history

Obtaining a thorough medical, behavioural and travel history of the donor, performing a careful clinical examination and undertaking suitable investigations are critically important to the quality, safety and efficacy of organ donation. The accuracy of this information is critical to the assessment of the degree of risk to which the recipient of an organ from a given donor may be exposed. When interviewing next-of-kin and/or significant others regarding the history of a potential donor, it is important that this is done in a structured and standardised manner,

utilising best practice tools such as the Australian Donor Risk Assessment Interview (AUS DRAI), to balance the rigorous requirements of screening with compassion, patience and empathy. In Australia, the donor's medical history, examination and investigations are captured in the Electronic Donor Record (EDR) and then viewed across the OrganMatch Donor Chart data pages. Standard donor information includes the ABO report, Serology and NAT (when available) and the organ offer list. There may be supplementary donor organ relevant documents that are de-identified and uploaded to OrganMatch including, CXR, ECG, Echo, CT, angiography, ultrasound reports, GP summary and/or pathology reports. In New Zealand, the donor's medical history, examination and investigations are captured in a Confidential Donor Referral (CDR), which is completed for all donors, with the relevant information components provided to transplant units when organs are offered for transplantation.

There are specific requirements for determining the suitability of each individual organ being considered for transplantation and these are identified in each organ-specific chapter. The general evaluation of donor suitability includes obtaining detailed information about the donor's past medical and social history, paying particular attention to:

- History of diseases and surgery, especially those that may affect organ function
- History of diabetes, hypertension and other cardiovascular disease
- Smoking, alcohol intake and non-medical drug use
- History of tumours or cancer—including stage, pathology details, treatment and current status
- Recent symptoms that may be indicative of undiagnosed infection, neurological disease or malignancy
- Suggestion of underlying metabolic disorder
- Risk factors for the transmission of human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV), including non-medical injecting drug use, male to male sex, commercial sex work, time in prison, sex with a person at increased risk of these infections, or a young child of a mother at increased risk of these infections
- Risk factors for the transmission of Transmissible Spongiform Encephalopathies (TSE), including family history of early dementia, use of pituitary hormone extract, notification of treatment with pituitary hormone extract
- Place of birth and prior residence in countries outside of Australia and New Zealand
- Travel history, especially recent travel (past six months)
- History of animal contact

Information required regarding the donor's current medical status and recent medical history includes:

- Course of illness and cause of death
- Vital signs and cardio-respiratory status, including mechanical and pharmacological supports
- Function of potentially transplantable organs, including pathology, microbiological tests and imaging results
- Surgery or other procedures
- Medications
- Administration of intravenous fluids and blood products (noting especially that haemodilution from large volume intravenous fluid may result in false negative serological test results).

There are very few absolute exclusion criteria to organ donation, with the exception of disseminated metastatic cancer and donors with known specified factors for TSE (see Section 2.3.5.1). All other risk factors should be interpreted in the context of all other donor characteristics and recipient factors.

2.2.3 Physical examination

Physical examination provides information relevant to suitability, allocation, and possible disease transmission risks. This should include:

- Height and weight
- General assessment with respect to body habitus and state of health, major abnormalities related to past or present disease (e.g. obvious limb ischaemia, chest or spinal deformities, traumatic injuries)
- Inspection of skin, including the skin of the back and careful examination in skin folds and around the genital and anal areas, looking for surgical scars, skin lesions indicating possible cancers or infections, injection sites/needle track marks suggesting intravenous drug use (IVDU), or lumps, sores, tattoos, rashes or mole irregularity
- Look for obvious abnormalities, lumps or masses (e.g. neck, groin, axillae, breasts, abdomen).

An additional physical examination by an experienced surgeon(s) at the time of retrieval is also important, as this may reveal unexpected clinically occult lesions such as bowel cancers or renal or liver tumours.

2.2.4 Laboratory investigations

Blood group for ABO and Rhesus are mandatory investigations for all donors. For women of child-bearing potential dying from unexplained intracerebral haemorrhage, testing for beta human chronic gonadotrophin hormone is recommended to detect metastatic choriocarcinoma. Whilst routine post-mortem examination has become an uncommon procedure in clinical medicine, if an autopsy is performed then the results should be followed-up by the donation service and communicated back to the relevant transplanting units as the autopsy may detect potentially transmissible disease.

The list of possible pathogens for which potential donors might be screened is very long. Screening of these pathogens depends on whether:

- The pathogen is sufficiently prevalent in the population that screening would be useful
- There is evidence that the pathogen in question can be transmitted by organ transplantation
- Transmission of the pathogen could result in significant morbidity or mortality
- A sufficiently accurate, rapid and affordable screening test exists.

The rapid turn-around times necessary in the context of donor screening, the associated logistical and technical limitations, and the need to balance the risk of transmission of infection against the risks to the recipient of dying while awaiting transplantation, make the goals of screening potential organ donors different to screening blood or tissue donors. It is the goal of organ donation and transplantation programs to minimise unexpected infectious disease transmission events while simultaneously maximising opportunities for transplantation. All infectious disease screening recommendations, therefore, carefully consider turn-around times, test performance (i.e. the potential for false positive or false negative results), and other logistical issues that may pose a risk to the donation process and lead to the loss of transplantable organs. These considerations must be weighed against the benefits of screening to patient safety.

The following laboratory investigations to detect infections that may be transmitted by solid organ transplantation are recommended for all donors:

- HIV antigen/HIV-1/2 antibody combination assay (HIV Ag/Ab)
- Hepatitis B surface antibody (anti-HBs or HBsAb)
- Hepatitis B surface antigen (HBsAg)
- Hepatitis B core antibody (HBcAb)
- Hepatitis C antibody (anti-HCV or HCV Ab)
- Nucleic acid testing (NAT) for HBV, HCV and HIV, most commonly using polymerase chain reaction (PCR) assays
- *Cytomegalovirus* (CMV) immunoglobulin (IgG) antibody

- Epstein-Barr virus (EBV) capsid IgG antibody
- Syphilis serology (specific treponemal antibody test)
- Toxoplasmosis serology (IgG)
- Human T-cell-lymphotrophic virus (HTLV) 1/2 antibody
- Strongyloides stercoralis serology (IgG).

Urine microscopy and culture is recommended for all donors from whom a urine sample can be obtained, with the results of cultures and sensitivity testing to be followed up as soon as they become available (which may not be until after transplantation has occurred). Blood cultures are recommended only if there is clinical suspicion of bacteraemia. A respiratory tract sample (i.e; endotracheal aspirate, sputum or bronchoscopic sample), bacterial culture, fungal culture and SARS-CoV-2 PCR is recommended for all lung donors.

Diagnostic testing for tuberculosis is only recommended where there is suspicion of tuberculosis infection that is supported by epidemiological and clinical factors (see Section 2.3.3.5).

Table 2.1 provides details of which donors should receive the tests specified above and whether results are recommended prospectively. "Prospective results" in the context of organ donation refers to results that are made available prior to the transplantation of organs (as opposed to prior to organ retrieval). Test results that are not recommended to be made available prospectively should be obtained as early as possible, but transplantation may proceed prior to results being available.

Table 2.1: Recommended laboratory investigations for the detection of potentially transmissible infectious diseases in solid organ donors.

Test	Recommended for all donors	Recommended for specified donors	Comments
Serology and nucleic acid testing (NAT):			
HIV Ag/Ab (positive results confirmed with anti-HIV-1/2).	X		Results should be available prior to transplantation proceeding.
HBsAg, HBcAb and anti-HBs	X		Results should be available prior to transplantation proceeding.
anti-HCV	X		Results should be available prior to transplantation proceeding.
HIV/HBV/HCV NAT	X		Prospective NAT is required wherever this is logistically feasible, and is strongly advised for increased viral-risk donors (see Table 2.2 for definition of increased-risk donors). If results are not available in a timely manner transplantation may proceed at the discretion of the transplant team and with appropriate recipient consent.
anti-CMV (IgG)	X		Prospective results are preferable where possible.
anti-EBV (IgG)	X		Prospective results are preferable where possible.
anti-*T.pallidum* (IgG)	X		Prospective results are preferable where possible.
anti-*T.gondii* (IgG)	X		No urgency on test results.
Anti-HTLV-1/2	X[a]		Prospective results are preferable where possible.

Test	Recommended for all donors	Recommended for specified donors	Comments
Strongyloides (IgG)	X		No urgency on test results – retrospective results available within 7 days.
SARS-CoV-2 PCR from lower respiratory tract sample		X	For lung donors. Prospective results are preferable where possible.
Microbiological testing			
Urine microscopy and culture	X		Microbiological testing should be performed on all donors for whom a urine sample can be obtained, with results of urine culture and sensitivity testing to be followed up as they become available (post transplantation).
Blood culture		X	Recommended where there is clinical suspicion of bacteraemia.
Respiratory culture		X	Respiratory tract samples for all lung donors or if respiratory infection is suspected. Routine testing: Respiratory MCS and Fungal MCS.

[a] While HTLV-1/2 screening is recommended for all donors, donors at high risk of HTLV-1 include Aboriginal people from Central Australia and persons born in southwestern Japan, sub-Saharan Africa, the Middle East, the Caribbean, and parts of South America (French Guyana, Peru). Screening is recommended for all donors since information in the donor record might not identify all persons at high risk and outcomes in the rare event of transmission can be extremely severe or fatal. See Section 2.3.2.9.

2.2.5 Haemodilution assessment

Where the donor receives multiple blood transfusions or significant infusions of intravenous fluids prior to donation, haemodilution may occur such that circulating antigens, antibodies and targets for NAT are at a low concentration that is difficult to detect, introducing the potential for false negative results. False positive results may also occur due to interactions between serological tests and molecules present as a result of infused products. The degree to which a potential donor's plasma has been diluted is a product of blood loss as well as fluids infused.

Serological tests and NAT have not been validated for use on all haemodiluted samples, and therefore serological screening and NAT should ideally be performed on non-diluted blood samples. For all donors, blood products and colloids given in the 48 hours prior to the date and time the sample was drawn are entered into the EDR (Australia) or CDR (New Zealand). This information is used to autocalculate whether the sample is haemodiluted. If either plasma dilution or blood dilution exceed defined thresholds, a pre-transfusion/ infusion sample should be used for donor screening. If a suitable sample is not available, the risk of false negative results from testing a haemodiluted sample should be communicated to the transplanting teams.

2.2.6 Special donor groups

Donors under 18 months or breastfed children

Microbiological screening for neonatal and infant donors (of less than 18 months old, or up to 6 months beyond breast feeding) should be performed as for other donors, including HIV/HBV/HCV NAT, taking into account that positive antibody results may reflect passive transfer of antibodies from the mother. The potential for eclipse/ window period infections should also be considered, and prospective NAT is recommended in this context.

Given the limited volume of blood that can be taken from a neonate or infant for the purposes of screening and the likelihood of haemodilution, complementary testing of the mother is required in these cases. If the mother is not at increased-risk of infectious diseases (see Table 2.2) and is sero-negative for markers of infection, the successful screening of the neonate/infant is less critical. For mothers who are deemed an increased viral risk, discussion with an infectious diseases physician or microbiologist is strongly advised.

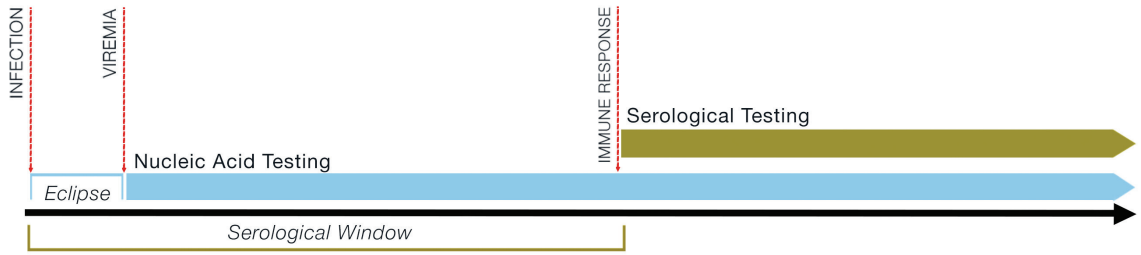
2.3 Risk of donor transmitted infectious disease

Acute or latent infections may be transmitted by the transplanted organ to the recipient. The intentional use of donors with certain infections may be considered where there is an acceptable risk of morbidity to the recipient, mitigated by serostatus matching, antimicrobial treatment or prophylaxis and/or monitoring. The unexpected transmission of an infectious disease from an organ donor to recipient(s) is a rare event; however, when it does occur, it is usually associated with significant morbidity and mortality.[9]

Donor history, examination and testing both reduce the risk of unexpected infection transmission and also inform risk-stratification where donors carry an increased risk of disease transmission. For instance, close attention must be paid to travel history: potential donors with recent travel to or previous residence in areas where they may have been exposed to endemic pathogens warrant additional screening.[10,11]

In addition, the concept of the "eclipse" or "window" period of infection is critical to understanding donor infectious disease risk mitigation. Following infection by a microbiological agent, there is a period of time during which no microbe can be readily detected in the host; this is called the "window period" for serological testing, or the "eclipse period" for NAT (see Figure 2.1). Unexpected transmissions are most likely to occur if the donor has recently acquired the infection and is still in the eclipse/window period before detection is possible. As such, test results must be interpreted in the context of the patient's full history, and the probability of false negative results needs to be considered against the donor's background of any reported risk factors such as IVDU or high-risk sexual contact.

Figure 2.1: Generalised diagram of eclipse and window periods.



2.3.1 Donors at increased risk of HIV, HBV and HCV

The unexpected transmission of HIV, HCV or HBV through transplantation is rare, particularly in the setting of thorough patient history, examination and laboratory testing (serology and NAT). While it is important to stratify donor risk of blood-borne virus acquisition, increasingly organs from otherwise suitable donors with increased risk for HIV, HCV or HBV infection are being used to expand the donor pool both in Australia and overseas. Recipients of increased risk donor organs have similar overall and graft survival compared to recipients from other donors.[12,13,14] Organ recipients in the United States who declined donors with increased risk had worse long-term survival than recipients who accepted increased risk donor, probably due to prolonged waiting times.[15,16,17]

Donors are classified as "increased risk" based on the presence of any of the risk factors listed in Table 2.2. In reality, the risk of unexpected donor-derived transmission of HIV, HBV and/or HCV exists on a spectrum, and varies by the type of risk behaviour, recency of behaviour and any risk-mitigation employed. It should be noted that information about behavioural risk factors obtained from the next of kin may be limited or inaccurate. The donor assessment interview must be supplemented with evidence from physical examination of the donor and/or their medical record. Donors whose social and medical history cannot be obtained should also be treated as increased risk.

The presence of HIV, HBV or HCV in the donor is not a contraindication to donation. Decisions about whether to proceed with donation and transplantation will depend on recipient informed consent, the nature of the infection, other recipient clinical factors and the availability of effective treatment. The presence of HIV usually rules out donation, with exceptions including for recipients living with HIV., similarly, recipients who are adequately immunised against or given prophylactic treatment for HBV may be transplanted with organs from donors with the potential to transmit HBV. The presence of HCV in a donor is no longer a barrier to transplantation given the availability of curative treatment. See Sections 2.3.2.4 and 2.3.2.5 for more detail.

Donor testing for HIV, HBV and HCV using serology and NAT should be undertaken using blood samples obtained from the donor prior to significant haemodilution. Such testing should be undertaken by laboratories with the appropriate accreditation (National Association of Testing Authorities [NATA] and Royal College of Pathologists of Australia [RCPA] or Therapeutic Goods Administration [TGA, licensed]). Serological testing for HIV, HBV and HCV is performed as part of the evaluation of all donors, with results obtained prior to proceeding with organ transplantation. NAT testing for HIV, HBV and HCV is also recommended for all donors, with results required prospectively wherever logistically feasible.

Table 2.2: Criteria for identifying organ donors at increased risk for HIV, HBV, and HCV infection (MSM= men who have sex with men; derived from Jones[18])

People who have injected drugs by intravenous, intramuscular, or subcutaneous route for non-medical reasons in the preceding 30 days*
MSM in the preceding 30 days
People who have been in lockup, jail, prison, or a juvenile correctional facility for more than 72 consecutive hours in the preceding 30 days
People who have had sex in exchange for money or drugs in the preceding 30 days
People who have had sex with a person in any of the above groups in the preceding 30 days
A child who is 18 months old or younger and born to a mother known to be infected with HIV, HBV or HCV infection
A child who has been breastfed within the preceding 6 months and the mother is known to be infected with HIV
When a deceased potential organ donor's medical/behavioural history cannot be obtained, or risk factors cannot be determined

* 30 days represents the maximum eclipse period for detection of HIV, HBV, and HCV via NAT.

If a donor has recently been infected with HIV, HBV or HCV, it is possible that the donor may still be in the eclipse or window period of infection (see Table 2.3) and transmission may still occur despite negative results on serology and NAT. The degree of residual infection risk associated with a specific donor is influenced by the nature of the donor's risk behaviour(s) and how recently the risk behaviour(s) occurred in relation to the time of donor testing.[19] Higher underlying incidence in an at-risk group or longer eclipse/window periods correspond with a higher residual risk of an undetected infection.

Table 2.3: Window and eclipse periods* for pathogen testing. Modified from Humar.[20]

Pathogen	Standard serology	Nucleic acid testing
HIV	17 – 22 days	5 – 6 days
HBV	35 – 44 days	20 – 22 days
HCV	~70 days	3 – 5 days

* Window period = the interval from infection to ability to detect that infection by serological testing; eclipse period = the interval after infection for which infection cannot be detected by either NAT or serological testing

Table 2.4 lists the estimated risks of undetected HIV, HBV or HCV infection in Australian donors by risk behaviour type, based on Australian epidemiological data.[21] These estimates of residual risk are based upon the best available local evidence, but are limited where the underlying data were sparse – notably in the case of commercial sex workers and high-risk partners. Data on the incidence of HBV in Australia is limited, therefore residual risk estimates were derived from estimates of the prevalence of hepatitis B core antibody (HBcAb) and hepatitis B surface antigen (HBsAg) in each risk group. It is also important to note that these residual risk estimates are based on historical data. Since 2019 when the residual risks in Table 2.4 were calculated, widespread uptake of HIV pre-exposure prophylaxis among MSM, and direct acting antiviral therapy for HCV, have led to reductions in the prevalence and incidence of these infections among their highest risk groups, and the stated estimates are likely to be over-estimates.[22,23,24,25]

As predicted by residual risk estimates, unexpected blood- borne virus (BBV) transmission is uncommon. The US CDC 2014-2017 investigated instances where recipient HBV or HCV NAT was positive within 18 months of transplantation, where donors were serology and NAT negative. There were 7 HBV NAT positive recipients, 5 were liver transplant recipients and 6 survived with functioning grafts. There were 20 HCV NAT positive recipients, 19 survived, 18 with functioning grafts. HBV was diagnosed 120-450 days and HCV at 20-190 days post-transplant. All donors were classified as increased risk, 70% had used intravenous drugs.[26] There are only a few occurrences of unintentional HIV donor derived infection in the literature since donors have been routinely tested with NAT and serology, mostly due to miscommunication of donor results.[27]

The risk of an undetected HIV infection is low. Donors with the highest residual risk, men who have recently had sex with men, have an estimated 1 in 1621 residual risk of undiagnosed HIV based on a negative enzyme immunoassay (EIA) result alone, and a 1 in 5092 residual risk based on a negative EIA + NAT. For recent intravenous drug users, prisoners, commercial sex workers and increased risk partners, the risk of undiagnosed HIV is less than 1 in 10,000.

It should be noted that the underlying risk behaviours within each risk factor category are not homogenous. The residual risks reported in Table 2.4 represent conservative estimates of the infectious risks associated with donors in each risk category; however, the actual risk of undetected infection in a given test-negative donor may be significantly lower depending on their history. For example, residual risks of HCV among IVDU may be lower for IVDU participating in needle exchange programs and receiving opioid substitution, compared to IVDU not participating in these programs.[28] For all donors, test results should be interpreted in the context of the donor's personal history and the residual risk estimates given in Table 2.4 should be used as a guide but not as definitive numbers.

Table 2.4: Residual risk[a] of undiagnosed HIV, HBV or HCV infection for Australian donors at increased risk, by risk factor and testing strategy. Adapted from Waller et al.[21]

		Residual infection risk			
		Enzyme immunoassay (EIA) serology[c]		EIA serology +nucleic acid testing (NAT)[d]	
Risk Factor	Incidence[b] (95% Confidence Interval) per 100 person-years	Risk estimate[e]	Upper risk	Risk estimate[e]	Upper risk
Human immunodeficiency virus					
Men who have sex with men	1.03 (0.72-1.33)	1 in 1621	1 in 1253	1 in 5092	1 in 3936
Intravenous drug use	0.16 (0.11-0.20)	1 in 10,619	1 in 8209	1 in 33,373	1 in 25,797
Prisoners	0.03 (0.02-0.04)	1 in 47,783	1 in 36,937	1 in 150,173	1 in 116,085
Commercial sex workers	0.05 (0.04-0.07)	1 in 31,856	1 in 24,625	1 in 100,116	1 in 77,390
Increased risk partners	0.03 (0.02-0.04)	1 in 47,783	1 in 36,937	1 in 150,173	1 in 116,085

Hepatitis C					
Men who have sex with men	1.3 (0.8-1.8)	1 in 409	1 in 292	1 in 5,719	1 in 4,076
Intravenous drug use	17.5 (10.4-24.5)	1 in 31	1 in 22	1 in 419	1 in 299
Prisoners	11.9 (2.6-21.3)	1 in 45	1 in 25	1 in 613	1 in 344
Commercial sex workers	4.5 (2.7-6.3)	1 in 116	1 in 83	1 in 1,616	1 in 1,152
Increased risk partners	5.6 (3.4-7.9)	1 in 94	1 in 67	1 in 1,301	1 in 927
Hepatitis B core antibody[f]					
Men who have sex with men	1.9 (0.7-3.7)	1 in 444	1 in 224	1 in 887	1 in 446
Intravenous drug use	8.1 (3.1-16.2)	1 in 103	1 in 52	1 in 205	1 in 104
Prisoners	3.5 (1.3-7.0)	1 in 237	1 in 120	1 in 473	1 in 239
Commercial sex workers	0.4 (0.2-0.9)	1 in 1,849	1 in 930	1 in 3,698	1 in 1,860
Increased risk partners	0.2 (0.1-0.3)	1 in 5,315	1 in 2,673	1 in 10,629	1 in 5,346
Hepatitis B surface antigen[f]					
Men who have sex with men	0.4 (0.2-0.9)	1 in 1,933	1 in 973	1 in 3,866	1 in 1,944
Intravenous drug use	0.7 (0.3-1.4)	1 in 1,216	1 in 612	1 in 2,430	1 in 1,223
Prisoners	0.6 (0.2-1.2)	1 in 1,418	1 in 714	1 in 2,835	1 in 1,426

[a] Residual infection risk is the predicted rate of undetected infection in donors who test negative for HIV, HCV or HBV, depending on risk factor and testing strategy, calculated as $RR = 1 - e^{(-incidence)*(eclipse\ period\ or\ serological\ window)}$

[b] Incidence estimates are based on a systematic review and meta-analysis of studies from 2000-2017 reporting original estimates of Australian HIV, HCV or HBV prevalence or incidence. Incidence rates and confidence intervals were estimated using random effects.

[c] Serological window period assumed in the calculation of residual risk estimates based on serological screening (EIA) alone: HIV=22 days, HCV=70 days, HBV=44 days[20]

[d] Eclipse period for NAT testing assumed in the calculation of residual risk estimates based on EIA + NAT: HIV=7 days, HCV=5 days, HBV=22 days.[20]

[e] Upper risk estimate is derived from the upper 95% confidence limit of the risk estimate.

[f] Data on the incidence of HBV in the Australian population are not available. It was therefore necessary to estimate the residual risk of undetected HBcAb and HBsAg separately. These estimates should be interpreted as the risk that, despite a negative test result, the donor is positive for either HBcAb (past, persistent or acute-phase infection) or HBsAg (active infection) respectively.

General considerations when transplanting organs from increased risk donors or donors with BBV

From an increased viral risk donor, the transmission risk is highest for HCV, which is now highly treatable after transplant, leading many units globally to routinely transplant organs from HCV NAT positive donor to HCV NAT negative recipients. The risk of HBV transmission is low, appears to occur predominately through liver transplantation, and is treatable. The risk of HIV transmission is very low. For these reasons **routine use of organs from increased viral risk donors can occur**, with informed consent and ensuring prospective donor NAT testing and routine testing of recipient post-transplant.

Follow-up of recipients of organs from increased viral risk donors

For all recipients of organs from donors identified by transplant clinicians as being at increased risk of infection with HIV, HBV or HCV, post-transplant surveillance for the appearance of infection should occur. NAT testing is required for HCV and preferred for HBV and HIV where possible; alternatives for the latter viruses are HBsAg and HIV antigen/antibody serological testing. Recommendations are for:

- one-time testing at 4-6 weeks post-transplantation
- HBV and HCV testing in the investigation of liver injury
- HBV testing at 1 year for liver recipients

Immediate verbal communication with the relevant donation agency needs to occur and subsequent documentation if testing indicates *de novo* infection with HIV, HBV or HCV in the follow-up period post transplantation.

2.3.2 Viral Infections

2.3.2.1 Coronavirus (SARS-CoV-2) causing COVID-19

Transmission of SARS-CoV-2 has not been documented via transplantation of organs from SARS-CoV-2 PCR positive donors, other than lung. Non-lung allograft outcomes appear equivalent for recipients of organs from SARS-CoV-2 PCR positive and negative donors alike.[29,30] Data on outcomes of recipients receiving lung transplantation from a donor testing positive by PCR for SARS-CoV-2 are limited to small cohort studies, with limited granular data regarding details of donor infection and/or recipient management.[31,32,33] SARS-CoV-2 PCR positive lung donation has occurred safely under specific circumstances and outcomes are expected to be better where there is no evidence of significant pneumonitis, where SARS-CoV-2 infection is in later stages (e.g. "weak" PCR results, higher CT value), where the recipient is immune from vaccination/prior infection and otherwise has a good, predicted outcome from lung transplantation.

Recommendations

Donation can proceed from non-lung donors with positive SARS-CoV-2 PCR provided the transplanting organ has not been damaged by the infection. Lung transplantation from SARS-CoV-2 PCR positive donor can be considered on a case-by-case basis.

2.3.2.2 Cytomegalovirus

Over 50% of the Australian adult population is latently infected with cytomegalovirus (CMV), based on rates of seropositivity in population studies.[34] No contraindications exist to organ donation in the case of latent CMV. However, organs from seropositive donors may transmit infection, potentially causing severe disease in the seronegative recipient.[35]

De novo CMV infection in the recipient can be largely managed by routine prophylaxis and post-transplant virological monitoring. Selecting CMV seronegative donors for CMV negative recipients avoids *de novo* CMV infection, however in practice there are often competing interests to seromatching.

Recommendation

Organs can be accepted irrespective of the CMV serostatus of the donor. If the donor or recipient is seropositive, suitable prophylaxis should be given and post-transplant virological monitoring is required.

2.3.2.3 Epstein-Barr virus

Over 90% of Australian adults are latently infected with Epstein-Barr virus (EBV).[36] Epstein Barr virus causes lifelong infection, and organs from seropositive donors may transmit infection to a seronegative recipient, increasing the risk of post-transplant lymphoproliferative disease (PTLD). The risk of PTLD is approximately six-times higher in cases of donor-derived primary EBV infection versus cases of EBV reactivation in seropositive recipients.[37]

Antiviral prophylaxis has not been shown to reduce the incidence of PTLD, therefore monitoring for the appearance of EBV deoxyribonucleic acid (DNA) and early treatment should be considered for all donor-positive/recipient-negative (D+/R-) transplants. In cases of suspected acute mononucleosis in the donor, diagnosis should be made on the basis of investigation of EBV-DNA in peripheral blood and EBV nuclear antigen.

Recommendation

Organs can be accepted irrespective of the EBV serostatus of the donor. If the donor is seropositive and the recipient seronegative, post-transplant virological monitoring is suggested.

2.3.2.4 Hepatitis B virus

Screening for hepatitis B virus (HBV) in potential organ donors uses hepatitis B surface antigen (HBsAg), hepatitis B core antibody (HBcAb) and hepatitis B surface antibody (HBsAb) to distinguish between current infection, prior cleared infection, vaccination, or no exposure.[38] HBV nucleic acid testing (NAT) is also recommended for all donors as occult HBV infection may occur. This is generally available prior to transplantation, but if NAT results are not yet available, the pathway for a NAT +ve donor should be followed (see Figure 2.2). Recipient immunity to HBV is usually defined by HBsAb titre >10IU/L, although weak evidence suggests possible additional benefits of titres >100IU/L where an increased risk of HBV transmission exists in the post-transplant setting.[39,40] Table 2.5 below summarises the interpretation of donor HBV screening and recommendations for utilisation. Figure 2.2 provides a further decision flow framework for the interpretation of HBV test results and utilisation of organs from HBV infected donors.

<u>HBsAg-positive and/or HBV NAT-positive donors</u>

HBsAg-positive and/or HBV NAT-positive donors are considered to have active HBV infection and pose a transmission risk.[41,42] Donors who are HBsAg-negative and HBV NAT-positive likely have occult HBV infection, typically with low HBV DNA viral load, but still pose a transmission risk. The risk of HBV transmission is lower where donor HBV DNA is undetectable, among non-liver organ recipients, recipients with a protective HBsAb titre, and with use of antiviral prophylaxis.[41,42,43]

HBsAg-positive and/or NAT-positive donors can be used for HBsAg-positive recipients (D+/R+), among whom lifelong antiviral therapy is routinely recommended regardless of donor HBV status.[44]

Additionally, the hepatitis D virus (HDV) status of the donor should be determined, including HDV ribonucleic acid (RNA) and HDV antibody assays. The results of these assays will often not be available until after transplantation. Where there is a suspected or known risk of HDV transmission, transplantation should be discussed with an infectious diseases physician or hepatologist prior to proceeding

Liver recipients

While HBsAg D+/R- liver transplants have been performed after exclusion of donor liver fibrosis[45,46] and can be considered in specific circumstances, there are increased risks in this setting, including the unproven but potential increased risk of hepatocellular carcinoma. Nonetheless, these transplants may be appropriate for some recipients. Lifelong antiviral therapy is recommended.

Non-liver recipients

Non-liver organs from HBsAg-positive and/or NAT-positive donors may also be used for HBsAg-negative recipients (D+/R-), with appropriate precautions and consent. Non-liver organs from donors who are HBsAg-positive/HBV NAT-positive have safely been used for HBsAg-negative recipients (D+/R-) in a number of cohorts,[47,48] including from deceased donors in non-endemic countries analogous to Australia.[46,49] Hepatitis B immunoglobulin can be used at the time of transplant for non-immune recipients. Entecavir or tenofovir are the optimal antiviral agents with antiviral strategies in existing studies ranging from short courses to indefinite duration. Monitoring for HBV reactivation after cessation of antivirals may mitigate adverse outcomes. Nonetheless, there are rare cases of significant recipient HBV reactivation and death in the setting of antiviral cessation or non-prescription.[50,51] As such, an optimal duration of treatment is difficult to recommend, and should be individualised based on donor and recipient factors, in conjunction with a hepatologist or infectious diseases physician experienced in HBV; however, treatment is often indefinite.

HBsAg-negative, HBV NAT-negative, HBcAb-positive donors

Interpretations include:

- Past infection
  - HBcAb of immunoglobulin M (IgM) class indicates a recent infection with HBV, while HBcAb of immunoglobulin G (IgG) class generally indicates a past infection
  - HBsAb will typically be positive but may be lost in the case of longstanding past infection, or may not have appeared after recent acute infection
- Persistent hepatocyte infection
  - The liver is a reservoir for HBV, and HBcAb-positive donor hepatocytes contain HBV cccDNA, with reactivation possible at any time in liver recipients[52,53]
- False-positive test result.

Liver recipients

For donors who are HBcAb-positive/HBsAg-negative, transmission rates are higher for liver transplantation than for the transplantation of other solid organs – 34% to 86% without prophylaxis in liver recipients[54,55] versus 0% to 5% for recipients of non-liver organs.[56] Prophylaxis for recipients of livers from HBcAb-positive donors has been shown to be effective, although transmission of HBV has been reported in rare instances despite this, mostly in the setting of lamivudine usage rather than antivirals with a high barrier to resistance (entecavir and tenofovir).[57,58,59]

While it is preferred that livers from HBcAb-positive donors be used for recipients with current or previous HBV infection, or recipients who have been successfully vaccinated, transplantation to naïve recipients can also be considered. Indefinite antiviral prophylaxis should be considered for all liver recipients given long-term risks of reactivation of infection within transplanted hepatocytes.

Non-liver recipients

For non-liver organs, the risk of transmission is negligible for recipients who are immune. Non-liver organs from donors who are HBcAb-positive and HBsAg-negative/NAT-negative may be used for HBV-naïve recipients after informed consent and with HBsAg and HBV DNA testing of the recipient. Short durations of antiviral prophylaxis (entecavir or tenofovir) for non-immune recipients may be considered.

Donors at increased risk of HBV

If the donor social or medical history is suggestive of increased risk of HBV infection (see Section 2.3.2), test results should be interpreted in the context of donor risk factors, particularly if NAT results are not available prior to transplantation. See Table 2.4 for the residual risks of an eclipse/window period HBV infection, by risk factor.

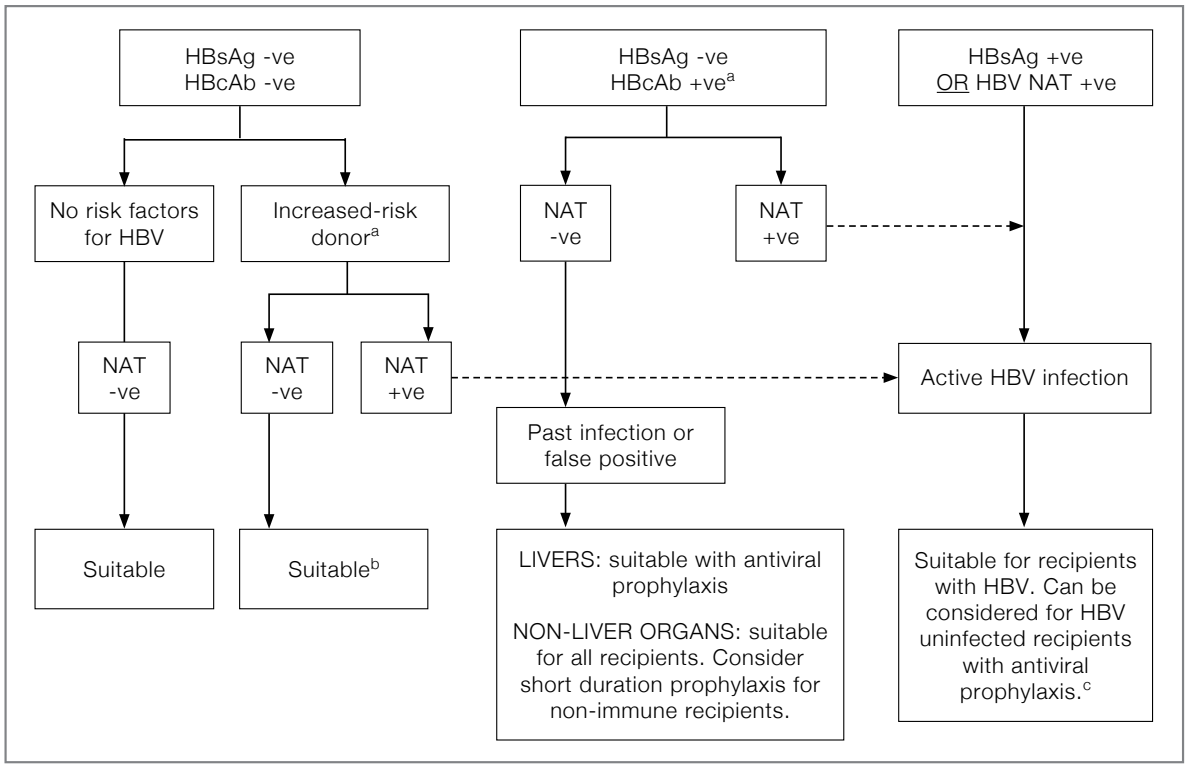
Table 2.5: Interpretation of results of HBV screening in organ donors and recommendations for utilisation

Test results	Interpretation	Implications for liver utilisation	Implication for utilisation of non-liver organs
HBV-NAT +ve HBsAg +ve	HBV infection	HBV transmission may occur. Organs may be transplanted to HBV infected recipients. Transplantation to non-infected recipients may be considered on a case-by-case basis, with antiviral prophylaxis. If proceeding with transplantation of HBsAg or HBV-NAT +ve organs, test for HDV and discuss results with a hepatologist or infectious diseases physician.	
HBsAg -ve HBV NAT -ve HBcAb +ve	Dormant hepatocyte infection	HBV transmission may occur in naïve recipients: ideally allocate livers to HBV-infected recipients or recipients with an immune response to vaccination and provide HBV prophylaxis.[a]	Transmission is unlikely: transplantation may proceed. Consider short durations of antiviral prophylaxis for non-immune recipients and monitor for HBV.[b]

[a] Recipient management would typically involve life-long entecavir or tenofovir with HBsAg and HBV DNA monitoring

[b] For the non-liver recipient with HBsAb >100 IU/L no prophylaxis is required. For the non-liver recipient with HBsAb < 100 IU/L, consider short durations of entecavir or tenofovir. Non-liver recipients should be tested by HBsAg and HBV DNA to 12 months post-transplant.

Figure 2.2: Decision flow-chart for HBV testing and utilisation of HBV-positive donors



[a] If NAT result is not available, follow the pathway for a NAT +ve donor, taking into account the nature of donor risk factors

[b] Consider the possibility of an eclipse period infection

[c] The use of donors with active HBV for non-infected recipients should have specialist hepatology or infectious diseases input, recipient consent, and antiviral prophylaxis.

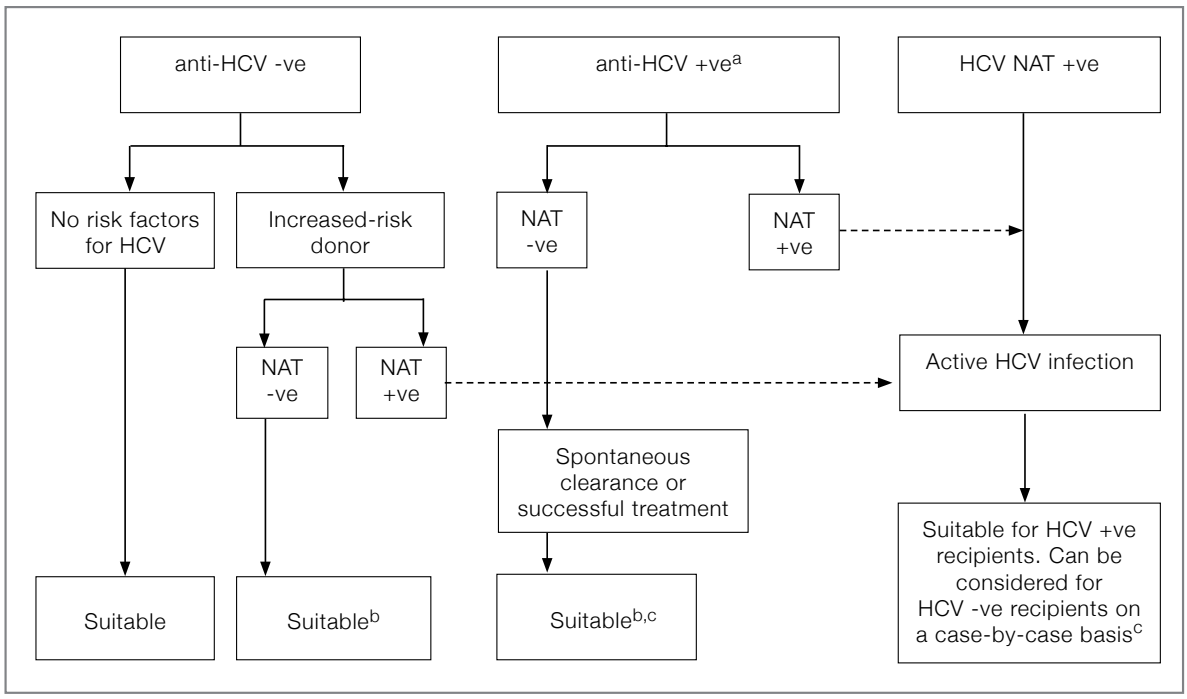
2.3.2.5 Hepatitis C virus

A positive HCV-NAT, with or without a positive anti-HCV, indicates active HCV infection. A positive anti-HCV with a negative HCV-NAT essentially excludes active HCV infection, given the low level of virus which can be detected with current RNA assays, excluding a short eclipse period risk of re-infection. Both anti-HCV and HCV-NAT are recommended for all donors. Figure 2.3 depicts the decision flow-chart for HCV testing, whilst Table 2.6 summarises the suggested organ utilisation and management implications.

Anti-HCV-positive, NAT negative donors

The risk of transmission from NAT-negative, anti-HCV-positive non-liver organs is very low.[60,61,62] Previous HCV infection is, however, a risk factor for reinfection, and classifies a donor as one of increased viral risk.[63] Should HCV transmission occur, HCV in the recipient is highly treatable. As such, routine use of anti-HCV positive, HCV NAT-negative non-liver donors can occur, with testing according to receipt of an increased viral risk organ.

Figure 2.3: Decision flow-chart for HCV testing and utilisation of HCV-positive donors



[a] If NAT result is not available, follow the pathway for a NAT +ve donor, taking into account the nature of donor risk factors

[b] Consider the possibility of an eclipse period infection

[c] Livers from donors who test HCV Ab pos NAT negative can transmit HCV, and from NAT positive donors would only be suitable in the absence of significant fibrosis/cirrhosis in the donor

Table 2.6: Interpretation of results of HCV screening in organ donors and recommendations for utilisation

Test results	Interpretation	Implications for organ utilisation
HCV-NAT +ve	Active infection	Transplantation should be considered for all recipients. HCV-negative recipients should provide informed consent and a plan for post-transplant antiviral treatment and monitoring should be followed.
Anti-HCV +ve HCV-NAT -ve	Active infection unlikely	Transplantation should be considered for all recipients. Represents spontaneous clearance of virus or successful treatment. HCV transmission is unlikely. Donor is classified as increased viral risk; recipient post-transplant monitoring is required.
Anti-HCV +ve HCV-NAT not available	Active infection cannot be ruled out	Transplantation should be considered for all recipients. All recipients should provide informed consent and a plan for post-transplant antiviral treatment and monitoring should be followed.

HCV-NAT-positive donors (active infection)

The reported cure rate of HCV after transplantation after first-line direct acting antiviral therapy is high (>90%),[64,65] including for liver transplantation, and receipt of HCV NAT positive organ does not appear to influence allograft outcomes.[66,67] Therefore, organs from HCV NAT positive donors can routinely be considered for transplantation into HCV-negative recipients.[65,67,68,69,70,71] Livers should only be transplanted in the absence of significant fibrosis, as per usual assessment. As transmission from HCV NAT positive donor organs is near universal, recipients are expected to require antiviral treatment, commenced early after transplantation (noting complications such as cholestatic hepatitis and glomerulonephritis occurred with delayed antiviral therapy). The potential risks, complications, and requirements for post- transplant antiviral therapy need to be discussed with potential recipients to ensure robust informed consent is obtained.

2.3.2.6 Herpes simplex virus

The overall seroprevalence of HSV-1 and HSV-2 in the Australian population is 76% and 12% respectively, although actual rates are highly variable by age group and according to risk factors for acquisition.[72] In the absence of appropriate prophylaxis, life-threatening de novo infections have occurred in naïve recipients of organs from latently-infected donors,[73,74] and due to reactivation in latently-infected recipients.[75] Given high rates of donor and recipient exposure, routine prophylaxis seems a more efficient approach than donor and recipient HSV-1 and HSV-2 IgG testing. Routine HSV prophylaxis is supported by a number of guidelines.[76] Where it is administered, CMV antiviral prophylaxis will also be effective against HSV. In the event that CMV prophylaxis is not given, acyclovir, famciclovir or valaciclovir would be the anti-HSV agents commonly utilised, usually recommended for at least one-month post-transplantation. Active infection in donors should also be considered where there are clinical features suggestive of HSV.

Recommendation

Organs can be accepted from donors with latent herpes family viral infections, and HSV screening is not required where antiviral prophylaxis is routinely administered. Organs from donors with acute herpes viraemia should only be considered with the administration of HSV-active antiviral treatment to the recipient.

2.3.2.7 Human herpesvirus-8 (Kaposi's sarcoma – associated herpesvirus)

Human herpesvirus-8 (HHV-8) is a rare but potentially fatal infection that can cause a spectrum of diseases in solid organ transplant recipients. Transmission occurs predominantly via saliva but also sexual, vertical and parenteral (including intravenous drug use). Following primary infection, HHV-8 may persist in a latent state with potential to reactivate and cause disease, particularly in immunosuppressed individuals. In solid organ transplant recipients, HHV-8 disease may result from donor-derived transmission, reactivation of latent infection in the recipient or de novo acquisition post-transplant.

Population level risk factors for HHV-8 infection

HHV-8 infection has significant geographic and social variation, although its epidemiology remains incompletely defined due to limited availability and reliability of serology testing. Globally, seroprevalence varies from <10% in North America and northern Europe to between 20-80% in the Mediterranean, parts of Africa and parts of China.[77]

Studies in Australia have reported HHV8 seroprevalence of 5.8% in blood donors,[78] compared with 18% in men who have sex with men (MSM).[79] Risk factors for HHV-8 infection in the Australian population hence include residence in an HHV-8 endemic region, and risk behaviors for other blood borne viruses (hepatitis B, hepatitis C and human immunodeficiency virus), such as MSM, commercial sex work, incarceration or a child with a mother with HHV-8 infection.[80,81]

Spectrum of HHV-8 diseases in solid organ transplant recipients

While most immunocompetent hosts are asymptomatic, the spectrum of disease manifestations associated with HHV-8 infection includes a range of malignant, lymphoproliferative and inflammatory conditions, which can co-exist. Diseases include:

- Visceral and cutaneous Kaposi sarcoma (KS)

  Malignancy of endothelial cells (blood vessels and lymphatics) with characteristics elongated 'spindle' cells. Visceral KS may occur without characteristic skin lesions post-transplant, affecting lymph nodes and/or organs, including the allograft.

- Multi-centric Castleman's disease (MCD)

  Lymphoproliferative disorder with multiple enlarged lymph nodes (and characteristic biopsy findings), associated with systemic symptoms.

- Primary effusion lymphoma (PEL) and other hematologic malignancies

  PEL is a rare diffuse large B cell lymphoma which accumulates in body cavities. Other HHV8 forms of PTLD have also been described.

- Kaposi Sarcoma Inflammatory Cytokine Syndrome (KICS)

  Non-malignant inflammatory condition associated with high level HHV-8 viraemia. Relatively recently described,82 occurring most commonly post-transplant among liver recipients, due to donor derived transmission (DDT).

- Hemophagocytic lymphohistiocytosis (HLH)[82,83,84,85,86]

  Inflammatory condition which can be triggered by HHV8 (often co-occurring with other HHV8 diseases).

The 90-day mortality for HHV-8 related diseases post-transplant (excluding cutaneous KS) is 29%,[86] with rates more than 50% reported in the setting of DDT.[87] The highest risk of DDT is from infected donors to uninfected recipients. Lymphoid rich organs such as liver and lungs appear to be associated with the greatest risk of HHV-8 DDT,88,89 although cases have been reported across the spectrum of transplanted organs.[86]

All solid organ transplant recipients, but especially those at increased risk due to donor or recipient risk factors, should be monitored closely for the development of disease manifestations consistent with a diagnosis of HHV-8 and investigated early, particularly during the first 12 months post-transplant when the risk of HHV-8-related disease is greatest.[80,81,86,88,89] Transplant clinicians should be aware of these rare diseases and seek expert advice on diagnosis and management, which is rapidly evolving. HHV-8 DNA monitoring should only be performed under guidance from a transplant infectious diseases specialist.

Mitigating strategies for donor-derived transmission

HHV-8 donor screening results to influence donor suitability

Currently there is insufficient evidence that donor HHV-8 results should influence donor suitability assessment. Internationally where donor HHV-8 screening is undertaken, results do not determine donor suitability.

HHV-8 donor screening to guide recipient monitoring and early intervention

Internationally, some centers (33% in one survey[90]), mostly in HHV-8 endemic regions, use donor screening to identify recipients at increased risk of donor-derived transmission of HHV-8 who may benefit from surveillance post-transplant. These screening programs have diverse methods and contrary results. In the United Kingdom (UK), a non-endemic region, nationwide donor screening was implemented in 2023, using HHV-8 serology followed by confirmation with HHV-8 DNA testing. Preliminary data from the UK found confirmed HHV-8 DDT events only occurred in the setting of donors with a positive DNAemia (10/3269 screening donors), with no instances of transmission from donors who were HHV-8 seropositive but DNA negative (unpublished data). In contrast, review of a universal serological screening program at an Italian center between 2011–2023 identified a seroprevalence of 3.3% among donors and 8.4% in recipients. In 49 instances of serological mismatch (D+/R-), 22 recipients (45%) experienced DDT and 13 recipients (26.5%) developed HHV-8 related disease complications.[88]

Protocols for management after identifying at-risk recipients are also limited and inconsistent. Antivirals have limited efficacy for HHV-8 and there is no role for primary prophylaxis. Pre-emptive monitoring of D+/R- using HHV-8 NAT has been described, with modulation of immunosuppression in response to detectable DNAemia as one possible strategy. However, not all patients with DDT will develop HHV-8 disease, and any benefits from pre-emptive immunosuppressive reduction may be offset by increased rejection rates. Close monitoring for disease and early initiation of B cell depletion with rituximab upon diagnosis of KICS has been described in an Italian cohort[88] associated with favorable outcomes. However, standardized screening tests, thresholds for intervention and treatment efficacy remain undefined.

Use of HHV-8 donor screening in Australia and New Zealand

Serological tests for HHV-8 are not currently available. HHV-8 NAT assays are available in some jurisdictions, however test performance for donor screening is uncertain and donor derived HHV-8 infection has occurred with negative donor NAT results.

Where a case of HHV-8 DDT has been confirmed, the recipients of other organs from the same donor should be notified with, at a minimum, clinical monitoring for HHV-8 disease, and optional HHV-8 PCR testing to assist risk stratification.

Recommendation

Routine donor screening for HHV-8 is not recommended.

Potential donors should not be excluded from donation based on perceived risk of HHV-8.

Solid organ transplant recipients should be tested for HHV-8 in the context of a compatible illness.

If a solid organ transplant recipient is found to have HHV-8 related disease, expert consultation should be sought for appropriate management. The possibility of donor-derived infection must be considered and reported through the appropriate channels, to facilitate monitoring of other recipients, as necessary, in accordance with expert guidance.

2.3.2.8 Human immunodeficiency virus

Screening for HIV should be performed using both NAT and a fourth-generation antigen/antibody combination immunoassay. These fourth-generation antigen/antibody combination immunoassays identify antibodies against both HIV-1 and HIV-2 as well as the presence of p24 antigen. If an initial test is positive, this result should be confirmed with subsequent testing according to jurisdictional policies, which may include separate antibody and p24 antigen assays, commercial western blotting assays, and/or nucleic acid tests.

The use of organs from donors with HIV for recipients with HIV (D+/R+) is supported by increasing evidence from both high and low HIV prevalence settings. Three studies of kidney HIV D+/R+ transplantation show favourable outcomes compared to HIV D-/R+ transplants, although one study demonstrated a trend towards increased rejection among HIV D+ kidney transplant recipients, which warrants additional investigation.[91,92,93] Notably, the risk of rejection was half as common in those receiving lymphocyte depleting induction, indicating that opportunities may exist to mitigate this risk. One cohort of D+/R+ liver transplants showed similar overall and graft survival, but increased opportunistic infections, mostly driven by CMV infection (among high risk CMV mismatch pairs, numerically higher in the HIV D+/R+ group) and HHV-8-related malignancies (not statistically significant).[94] Experience with other solid organs is more limited, but outcomes are not expected to be significantly different.[95] HIV superinfection with a drug-resistant strain is a theoretical concern, and while donor HIV is detectable in a proportion of recipients early after transplantation, the clinical relevance remains unclear.[94,96,97]

The number of transplant recipients with HIV internationally has been increasing, with good outcomes.[98,99,100,101] However, people with HIV face additional barriers to waitlisting and transplantation.[102,103,104] Data from the US indicate that a HIV D+/R+ strategy can provide a pathway to enhance access to transplantation for people with HIV and potentially higher quality organs, which may outweigh any potential additional risks.[105] Moreover, it

may enable utilisation of organs from donors with false-positive HIV screening tests, that would otherwise not be transplanted.[106] In Australia, the incidence of donor referrals with HIV is also small , but successful HIV D+/R+ kidney transplantation has been performed locally.[107] An infectious diseases specialist with expertise in HIV and transplant infectious diseases should be involved in these cases, and specific informed consent should be obtained from the recipient. Donors with HIV must have an HIV infection that can effectively be treated using antiretroviral therapy that accounts for both efficacy and potential drug interactions in a post-transplant setting.

Organ transplantation from donors with HIV into recipients without HIV is not routine practice, due to anticipated HIV transmission and limited evidence base. As such, there is insufficient published evidence to support the safety or clearly define the risks of this approach, even in exceptional cases. Should circumstances arise where a donor with HIV is appropriate to consider for a recipient without HIV (i.e. where the urgency and availability of transplantation is thought to outweigh the additional recipient risks of HIV transmission[108]), careful consideration would be required regarding consent processes, local approvals, and jurisdictional legal implications. Consultation of an infectious diseases specialist with expertise in HIV would be mandatory.

Recommendation

All donors should be screened for HIV using an HIV Ag/Ab combination assay and HIV-NAT. Use of organs from selected donors with an antibody and/or NAT-positive for HIV should be considered for waitlisted recipients with HIV, in consultation with a HIV specialist. Donation of organs from donors with HIV for recipients without HIV is not recommended; should exceptional circumstances arise, consultation with a HIV specialist, informed consent and careful consideration of risks would be required.

2.3.2.9 Human T-lymphotropic virus-1

Human T-lymphotropic virus-1 (HTLV-1) is an oncogenic retrovirus that is transmitted predominantly via breast-feeding, sexual intercourse or blood transfusion. While infection is usually asymptomatic, about 2-5% of infected individuals will subsequently develop acute T-cell leukemia/lymphoma (ATL), and a smaller proportion (0.25-4%) will develop HTLV-1 associated myelopathy (HAM).[109] Human T-lymphotropic virus-1 is not a ubiquitous virus; instead, it is understood to be distributed throughout the world in clusters of high endemicity. A high prevalence of HTLV-1 is found in sub-populations of southwestern Japan, sub-Saharan Africa, the Caribbean, parts of South America, parts of the Middle East, and among Aboriginal people of central Australia.[110] However, large global regions have not been investigated for the prevalence of HTLV-1, and its distribution remains unknown in much of the world. Similarly, outside of central Australia, little is known about the epidemiology of HTLV-1 in Australia and New Zealand. Studies conducted among mostly non-Aboriginal and Torres Strait Islander blood donors living in Australian cities have reported prevalence ranging from 0.001 to 0.032%.[110] It is important to note that HTLV screening assays do not distinguish between HTLV-1 and HTLV-2 infection, however HTLV-2 has not been convincingly associated with human disease.

To date, there have been 16 cases published worldwide of HTLV-associated disease following donor-derived transmission: 14 cases of HAM and 2 cases of cutaneous ATL, with onset of symptoms between 8 months and 4 years post-transplant.[111,112,113,114] A recent case series from Japan reported a rate of seroconversion of 87% for HTLV-1 negative recipients receiving a kidney transplant from an HTLV-1 positive donor, and a rate of HTLV-associated disease of 40% following donor-derived transmission (median incubation period 3.8 years).[114] Given the morbidity and mortality risk associated with HAM and ATL, utilisation of donors confirmed positive for HTLV1/2 is not recommended.

The HTLV-1/2 positivity rate among Australian organ donors is <0.1%, and to date there have been no reported cases of HTLV-1 transmission by organ donation in Australia or New Zealand. Nonetheless, universal screening of donors for HTLV-1/2 remains recommended at this time given the limitations of our understanding of HTLV-1 epidemiology, the practical challenges of targeted screening (i.e. accurately identifying individuals at high risk), the current lack of therapy for HTLV-1, and the severity of outcomes in the extremely rare event of donor-derived disease. In addition, HTLV-1/2 screening is currently an absolute requirement for eye and tissue donation (with the exception of cornea-only donation). The potential for false positive test results for HTLV-1/2 should be noted, based on international experience.[115]

Recommendation

HTLV-1/2 screening using serology is recommended for all organ donors, with prospective results preferable where possible. Where a serological screening test is reactive, confirmatory testing should be undertaken and donation should not proceed if HTLV-1/2 infection is confirmed. In the event of reactive screening antibody results which cannot be confirmed by subsequent testing in a timely manner, it is suggested to discuss with an infectious diseases physician or microbiologist the likelihood that results predict genuine HTLV infection, which is influenced by the strength of the test (e.g. signal to cut-off ratio) and the pre-test probability of infection. If a donor is retrospectively confirmed to be infected with HTLV-1 and organs are transplanted, monitoring of recipients for both infection and disease development is recommended.

2.3.2.10 Seasonal influenza

During each annual influenza season (June, July, August) approximately 5-10% of the population is affected.[116,117] During this period, a potential lung donor has about a 1-2% chance of transmitting influenza, based on 10% of the population being affected and given that influenza virus can be recovered from respiratory secretions of infected persons for approximately one week.[118]

In general, non-lung organs from donors with influenza infection can be safely used. As persons infected with influenza viruses generally do not have virus in non-lung tissues, the risk of transmitting infection to recipients of solid organs other than lungs is low.[119]

Evaluation of potential lung donors for influenza-like symptoms or respiratory tract infection is essential to avoid life-threatening infection in the recipient in the early post-transplant period.[120] In the event of donor-derived influenza transmission, however, successful antiviral treatment is possible.[118]

In the event of circulating influenza strains with antiviral resistance, influenza A subtyping may inform treatment options.

Recommendation

If influenza-like illness in the donor is suspected, influenza-specific NAT should be performed (although it is not essential to wait for the result before proceeding with transplantation). The presence of influenza is not a contraindication to the transplantation of non-lung organs. Utilisation of lungs should be considered on a case-by case basis. Post-transplant influenza treatment for 5–10 days is suggested for all recipients of organs from a donor infected with influenza.

2.3.2.11 West Nile virus

West Nile virus (WNV) is a mosquito borne virus commonly found in Africa, parts of Europe, the Middle East, North America and West Asia. West Nile virus infection is asymptomatic or associated with only mild-flu-like symptoms in the vast majority of cases (>99%). However, in some cases – and particularly among immunosuppressed persons – WNV may cause severe neuro-invasive disease, including meningitis, encephalitis and acute flaccid paralysis.[121] Multiple cases of WNV transmission from organ donors to recipients have been reported, with a high rate of adverse outcomes.[121,122] Compared to a mortality rate of 4% among symptomatic WNV cases in the general population, the mortality rate among transplant recipients with symptomatic WNV is approximately 25%.[123]

Suitable vectors for WNV have not been shown to exist in New Zealand, and to date there have been no notified cases of WNV, including cases acquired abroad. In Australia, the Kunjin lineage of WNV is endemic to tropical northern Australia, although notifications of WNV or Kunjin virus infection are rare – on average <2 per year – with some of these cases acquired in endemic countries.[124]

Given that locally acquired cases of WNV in Australia have not been recorded, targeted testing only is recommended for potential donors with compatible symptoms (similar to flu) and a history of recent travel to an endemic country or an area with an ongoing outbreak. The incubation period for WNV is approximately 3–15 days, and infected individuals are viraemic for up to a week, therefore history of travel up to 4 weeks prior is of interest. If WNV is suspected, advice should be sought from an infectious disease specialist regarding testing requirements and how to proceed in the event of a positive test. Testing should be performed using NAT, using PCR at the current time.

Recommendation

Screening of asymptomatic donors for WNV is not recommended. Targeted testing using serology and NAT (PCR) is recommended for potential donors with compatible symptoms and a recent history of travel (<4 weeks prior) to an endemic country or a region with an ongoing outbreak. If a donor is suspected or known to be infected with WNV, an infectious disease specialist should be consulted for advice on testing requirements and whether it is safe to proceed with donation.

2.3.2.12 Zika virus

Australia and New Zealand do not have local transmission of Zika virus, but suitable mosquito vectors exist in some parts of northern Australia and near neighbours. Of confirmed/probable cases of Zika virus infection diagnosed in Australia and New Zealand in 2017, the majority of these cases were acquired in Tonga, Fiji, Samoa, Mexico or Brazil.[125,126]

Zika virus should be considered in potential donors with compatible symptoms and a history of recent travel (<4 weeks) to Zika-affected areas (https://wwwnc.cdc.gov/travel/page/zika-information) The median incubation period of Zika virus associated disease is 5.9 days, with 99% of infected individuals clearing the virus within 23.4 days.[127] Although sexual contact with men who have been in an area of Zika virus transmission anytime in the prior 6 months is also theoretically a risk factor,[128] sexual transmission of Zika virus is extremely uncommon in Australia or New Zealand. Screening for Zika virus in asymptomatic donors is not recommended. For donors with a history of recent travel to Zika virus-affected areas who do not have any symptoms of viral infection, the risk of Zika virus infection is very low and the consequences of Zika virus infection in transplant recipients have not been shown to be severe.[129]

Recommendation

Screening of asymptomatic donors for Zika virus is not recommended. Zika serology should only be used as a diagnostic test in donors with compatible symptoms and epidemiological risk factors (i.e. travel to an endemic area within the previous 4 weeks). If the test is positive, seek advice from an infectious diseases specialist.

2.3.2.13 Other arboviruses

While the potential for donor-derived transmission exists, very little is known about the risks to organ transplant recipients of other arboviruses (dengue, chikungunya, Ross River virus, Murray Valley virus, Barmah forest virus, Japanese encephalitis). Importantly, arboviral infections are transient and there is no evidence for establishment of latency and latent disease. Donor testing is appropriate in the context of potential donors with compatible symptoms who have recently visited an endemic area. Targeted testing in this context would be warranted, typically with IgM, IgG and PCR, and the advice of an infectious disease specialist should be sought to guide appropriate testing and how to proceed in the event of a positive test. Decisions to proceed with transplantation should be made on a case by case basis, dependent on the organ(s) being considered for transplantation, availability of donor testing results prior to donation, and the nature of the infection.

Recommendation

If arboviral infection is suspected in a potential donor with compatible symptoms and a history of travel to an endemic area in the past 4 weeks, advice from an infectious disease specialist should be sought on appropriate testing procedures and what to do in the event of a positive test result.

2.3.3 Bacterial and fungal infections

2.3.3.1 Blood stream infections

Bacterial transmission through organ transplantation is probably common, as transient fever or infection with common organisms in recipients may not be recognised as donor-derived. An estimated 5% of organ donors have unrecognised bacteraemia at the time of donation, and abdominal contents are commonly contaminated during retrieval. Recipient outcomes are not adversely affected when the organisms are common, drug-sensitive pathogens and appropriate prophylactic antibiotics are administered.[130,131] When significant infection that is proven to be donor-derived does occur, it is more likely to be with resistant bacteria not covered by routine antibiotic prophylaxis or treatment in the donor and/or recipient (e.g. methicillin-resistant Staphylococcus aureus, vancomycin-resistant enterococci, and multidrug resistant gram negative bacilli).[9]

The routine culturing of preservation fluids in which organs are transported is of uncertain benefit and is currently not recommended. Contamination of preservation fluids is common, however contaminants are rarely of clinical significance.[132,133,134] In rare cases where contaminants are pathogenic, such organisms would typically be covered by routine prophylactic antibiotics.[132] The burden of clinically irrelevant positive test results that would be generated by routine culturing of bag fluids would outweigh the benefits to recipients.

The culturing of preservation fluids would, however be indicated in exceptional circumstances. Digestive tract breach at the time of multiorgan recovery has been linked to multiple cases of graft-transmitted candidiasis in kidney and liver recipients, resulting in fungal arteritis in several cases.[135] In the event of digestive tract rupture, appropriate specimens should be collected, including culture of organ preservation fluid, and surveillance cultures in the recipient where possible.

Donors with endocarditis should be treated on a case-by-case basis in a manner similar to bacteraemic donors, with consideration given to the potential for septic emboli in transplantable organs.

There is little data regarding donors with fungaemia. Given the difficulty treating fungi, guiding principles would suggest they will generally be unsuitable, however if donation is being considered the case should be discussed with an infectious diseases specialist. The assessment would consider such factors as whether the infection is controlled, whether there are signs of dissemination to the organ, the options for treatment including those relevant to the specific organ (e.g. some antifungals do not penetrate the urinary tract). A full course of antifungal treatment of a minimum duration of two weeks should be given to the organ recipients, with culture surveillance for the development of active infection.

For recommendations in the case of bacterial meningitis, see Section 2.3.5 (Central Nervous System Infection).

Recommendation

Bacteraemia is not a contraindication to donation, and organs may be used after the donor has been treated with antibiotics. Recipients of organs from donors with confirmed bacteraemia should receive a full course of antibiotic treatment, with monitoring for evidence of infection. Donors with ongoing sepsis and persistently positive blood cultures should not be utilised. Organs from donors with endocarditis may be transplanted after the donor has been treated with antibiotics and after consideration of the risk of emboli to organs for transplantation. Cases of fungaemia should be discussed with an infectious diseases specialist before proceeding to donation.

2.3.3.2 Pulmonary infections

Bacterial colonisation of donor lungs is common as (1) the lungs are in constant contact with the external environment and the airways are normally colonised with multiple organisms, (2) most donors require emergency intubation, which may result in aspiration and pneumonia, and (3) the rate of bronchopulmonary infections increases in proportion to the length of time spent in the ICU. Prior to donation, aspiration and consequent

pneumonia must therefore be ruled out or treated. In the case of pneumonia without bacteraemia, all other organs can be used safely. Following a period of antibiotic treatment and provided pulmonary function is not impaired, lungs may be considered for donation except where the pathogen is multi-drug resistant.

Invasive fungal infection of the lungs (including with endemic mycoses – e.g. histoplasmosis, coccidiodomycosis, blastomycosis) is very uncommon and the advice of an infectious diseases specialist should be sought in this situation if transplantation is being considered. Much more common is fungal colonisation of the donor airway, which is managed by routine antifungal prophylaxis and/or pre-emptive antifungal therapy according to unit policy.

Recommendation

In the case of pneumonia without bacteraemia, all other organs can be used safely for transplant. Lungs may be used after adequate and effective antibiotic therapy, with a full antibiotic course administered to the recipient. Fungal colonisation of the donor airway is not a contraindication to donation; however, in the case of invasive fungal infection the advice of an infectious diseases specialist should be sought.

2.3.3.3 Urinary tract infections

Urinary tract infection (UTI), with the risk of pyelonephritis, is common among potential donors due to bacteria or fungi ascending along the urethral catheter. Any suspected UTIs in potential donors should be confirmed by urine culture.

Prior to organ retrieval, the donor should be treated with antibiotics.[121] The final decision about organ utilisation should be made at the time of organ retrieval. Post-transplant treatment of the recipient is expected to reduce the risk of donor-derived infection. In general, however, there is no need to treat the recipient of a non-kidney organ from a deceased donor with nonbacteraemic, localised infection that does not involve the transplanted organ.

Candida infection early post kidney transplant has been associated with death and morbidity such as vascular and anastamotic complications.[136] *Candida* in the urinary tract of the donor is commonly thought to arrive there from contamination by faeces from intestinal perforation, directly infecting the kidneys from the external capsule then progressing inside the kidney. Culture of preservation fluids in cases where a breach of the digestive tract is identified during organ recovery is recommended for the early detection of *Candida sp.* Where donor or early recipient urinary tract cultures are positive for *Candida* sp. ongoing surveillance for complications should occur and antifungal therapy given to the recipient for a minimum 2 weeks.

Recommendation

In the case of UTI without bacteraemia, all non-kidney organs can be used safely for transplant. Uncomplicated UTI/bacteruria is in most cases not a contraindication to utilisation of kidneys if there has been adequate and effective antibiotic treatment (within time constraints of donation suitability assessment) and a full antibiotic treatment course is administered to the recipient. Where donor or early recipient urinary tract cultures are positive for *Candida*, ongoing surveillance for complications should occur and antifungal therapy be given to the recipient for a minimum of 2 weeks.

2.3.3.4 Multi-drug resistant bacteria

Donor exposure to multi-drug resistant (MDR) bacteria in the ICU is an increasing problem, in particular exposure to vancomycin-resistant enterococci, methicillin-resistant *Staphylococcus aureus*, extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae, carbapenem-resistant Enterobacteriaceae, multidrug-resistant *Pseudomonas aeruginosa*, and carbapenem-resistant *Acinetobacter baumanni*. Prolonged ICU stay, vasopressor use, need for cardiopulmonary resuscitation and injuries involving major blood loss increase the risk of infection or colonisation with MDR bacteria (although nosocomial infections may be acquired even with only a short hospital stay).[137,138] In addition, significant volume and blood product replacement in the donor with traumatic injury may result in a wash-out effect of prophylactic antibiotics and ineffective antibiotic coverage.[138] Donor country

of origin/prior residence is also a potential risk factor: donors from countries with high rates of gut colonisation with multi-drug-resistant bacteria pose a higher risk of transmission, as do donors who have previously been hospitalised overseas. Detection of MDR bacteria may be difficult due to antibiotic therapy, which may reduce the bacterial load to a level that is undetectable by standard culture protocols but is still able to transmit infection to an immunosuppressed individual.[139]

At this time there is no need for enhanced microbiological screening of potential donors for MDR bacteria over and above standard ICU practice. If MDR bacteria are identified prior to transplantation, the risks are highest for the bacteraemic donor or where the positive culture is taken from the organ that is to be transplanted: in these cases transplantation should be carefully considered and advice sought from an infectious diseases physician.[140] In all other circumstances, transplantation can be considered in consultation with an infectious diseases physician.[140] Colonisation by MDR bacteria is not a contraindication for donation provided the colonised tissue remains sealed from the rest of the body and any adjacent organs are not affected.

Recommendation

Organs from donors with positive cultures for MDR bacteria may be considered for transplantation with close recipient follow-up. Transplantation should be carefully considered in the event that the organ to be transplanted is itself colonised or the donor is bacteremic. A key consideration is whether safe antibiotic options are available to treat the bacterium. The case should be discussed with an infectious diseases physician and if donation proceeds, a full treatment course should be administered to the recipient.

2.3.3.5 Mycobacterium tuberculosis

The vast majority of tuberculosis cases in Australia and New Zealand occur in the overseas-born population, with other major risk factors including household or close contact with tuberculosis, employment in the health industry, incarceration, residence in an aged care facility, homelessness, and immunosuppression.[141] In the general Australian population, pulmonary tuberculosis accounts for approximately 60% of tuberculosis cases, with 40% being extrapulmonary.[141]

Reasonable efforts should be made to rule out active tuberculosis in donors with any epidemiological risk factors for tuberculosis or history of tuberculosis infection. However, there are no proven methods for screening deceased donors for tuberculosis. Chest X-ray and direct microscopy of bronchoalveolar lavage for acid-fast bacilli have a low sensitivity, and cultures may take up to eight weeks to turn positive.[142] Tuberculin skin testing and interferon gamma release assays are also impractical in the context of deceased donation given their slow turn-around times. NAT can identify *M. tuberculosis* in clinical specimens from donors with active infection only; a negative result does not definitively rule out infection with *M. tuberculosis*, as organisms can remain dormant in the host without causing disease for decades, without any detectable radiographic abnormality. Conversely, abnormal pulmonary findings from a range of causes are common in deceased donors and may confound donor evaluation.[142]

Given the limitations of tuberculosis screening tools in deceased donors, and given that it is unclear how to proceed on the basis of results from such screening, routine donor screening for tuberculosis is not recommended. Donor screening for tuberculosis can be triggered by the TB screening questions within the electronic donor record AUS-DRAI. Diagnostic testing for tuberculosis is recommended where there is clinical suspicion of tuberculosis infection that is supported by epidemiological factors.

Recommendation

Diagnostic testing for tuberculosis with microscopy (acid-fast bacillus staining) and PCR are recommended where infection is suspected based on epidemiological AND clinical factors that are suggestive of either active or latent tuberculosis. Donation of organs from donors currently being treated for tuberculosis or with positive results (e.g. AFB stain, NAT) is not recommended other than in exceptional circumstances after discussion with an infectious diseases physician. Donors with previous active or latent tuberculosis can be considered, taking into account tuberculosis antibiotic susceptibilities, completeness of donor treatment, and current evidence of infection in the organ. Discussion with an infectious diseases physician, close follow up of the recipient and consideration of tuberculosis prophylaxis for the recipient are recommended.

2.3.3.6 Treponema pallidum (syphilis)

The number of reported cases of syphilis has recently increased in both the Australian and New Zealand general population.[143,144,145] *Treponema pallidum* (syphilis) has been transmitted through organ transplantation.[146,147] All donors should be first screened for *T. pallidum* using a treponemal-specific enzyme immunoassay, with confirmation of positive results by a non-treponemal test such as the rapid plasma reagin (RPR) test. If the non- treponemal test is negative, then a second treponemal test based on different antigens to the original test should be performed. This approach differentiates potential donors who have been previously treated for syphilis from those with untreated or incompletely treated syphilis and those with an initial false positive result.[148] Treponemal test results should be interpreted in the context of what is known about the donor's history of treatment for syphilis and their sexual history, as there is always the possibility of previously treated persons having a recently reacquired syphilis infection.

The stage of syphilis needs to be considered in donors with positive syphilis serology and the case should be discussed with an infectious diseases physician. If secondary syphilis is likely, then the infection may be disseminated and donation should probably not proceed apart from exceptional circumstances. The possibility of tertiary syphilis of the aortic arch should be considered in the case of heart donation. For donors deemed to have primary, latent, or tertiary syphilis, donation may proceed with benzathine or intravenous penicillin prophylaxis given to the recipients with a regimen advised by an infectious diseases physician.

The presence of newly diagnosed syphilis in the donor indicates the donor is at increased risk of having also recently acquired HIV, HBV or HCV, and decisions regarding utilisation should be made accordingly.

Recommendation

If primary, latent or tertiary syphilis is detected in the donor, donation may proceed with appropriate prophylactic treatment of the recipient. A donor with secondary syphilis may be bacteraemic with the involvement of many organs, hence caution should be taken if clinical manifestations of secondary syphilis are present.

2.3.4 Parasitic infections

2.3.4.1 Malaria (*Plasmodium sp*)

Australia and New Zealand remain free of endemic malaria: all notifications are in travellers or those who have resided in endemic regions. Despite the absence of endemic malaria, suitable vector mosquitos for *Plasmodium sp* are present in northern Australia and the area is "malaria receptive". Limited transmission does also sometimes occur in the Torres Strait following importation.[149]

There are several Plasmodium spp. relevant to humans including *Plasmodium falciparum, Plasmodium ovale, Plasmodium vivax, Plasmodium malariae and Plasmodium knowlesi*.[150] Certain species of *Plasmodium* with partial immunity can allow development of asymptomatic parasitaemia. *P.ovale* and *P. vivax* have a hypnozoite phase in the liver that can reactivate into a blood stage years after initial infection. While *P.malariae* does not have a hypnozoite stage, it can cause illness years after leaving an endemic region.[151,152,153]

Although malaria is a rarely reported complication of organ transplantation outside of non-endemic countries, internationally and in Australia there have been a small number of documented cases of donor-derived malaria transmission involving all solid organ transplant recipients, frequently from donors with unrecognised asymptomatic parasitaemia involving *Plasmodium* spp. with a hypnozoite phase.[154,155,156,157,158,159,160,161,162,163,164] When donor-derived transmission does occur, if detected early it can be treated effectively.[165,166,167,168]

Thick and thin blood smears and rapid diagnostic antigen tests (RDTs) are insufficiently sensitive to exclude asymptomatic parasitaemia in donors. Nucleic acid tests (NATs) have high sensitivity for asymptomatic parasitaemia in most donors. Antibody testing is highly sensitive but does not differentiate prior from current infection. No diagnostic test is perfectly sensitive so in the event recipients develop a compatible clinical syndrome they should be investigated for malaria.[162,169,170]

Recommendation

All donors who have spent more than 3 months in a malaria endemic region, or who have visited (any duration) a malaria endemic region in the last 12 months (https://www.who.int/data/gho/data/themes/malaria), should be screened for *Plasmodium* infection using NAT or serology. Retrospective results are satisfactory. If NAT or serology is positive, transplantation may proceed, and recipients should be treated (and tested) for malaria. If donor testing is negative, recipients should be tested for malaria should compatible clinical syndrome develop.

2.3.4.2 Strongyloides stercoralis

Strongyloides is an intestinal nematode that is endemic to tropical or subtropical regions of the world. Once infection occurs, the *Strongyloides* parasite establishes an autoinoculation cycle that allow infection to persist in the host indefinitely. Infection is transmitted by skin contact with soil contaminated with human waste, and prevalence is therefore directly related to sanitation and hygiene conditions. Outside of the endemic regions of Southeast Asia, Central and South America, and Africa, *Strongyloides* infection is also found in poor communities, former war veterans, refugees, immigrants and travellers, and people occupationally exposed to soil (e.g. farmers and miners) in parts of the United States, Europe, United Kingdom, and Australia.[171,172] Groups with high rates of *Strongyloides* infection in Australia include war veterans, immigrants/refugees, and Aboriginal and Torres Strait Islander Australians (particularly children).[173,174,175,176,177] Infection with HTLV-1 is associated with increased prevalence of *S. stercoralis* infection.[178,179]

Donor screening with serology, using *Strongyloides* IgG EIA, is recommended for all donors due to the difficulty obtaining an accurate history for risk of exposure. Infection requires a period of residence in an endemic area (e.g. three months or more) and because of the longevity of the parasitic infection, screening is warranted even for very remote histories of travel to endemic regions.[180] *Strongyloides* testing may be retrospective, given that there is a window post-transplant in which infection can be treated effectively, although results should still be provided as soon as possible.

Recommendation

All potential donors should be tested for Strongyloides. Retrospective results are satisfactory and can guide recipient management post-operatively. If the donor tests positive, recipients should receive prophylactic treatment with ivermectin.[181]

2.3.4.3 Toxoplasma gondii

Exposure to *Toxoplasma gondii* is extremely common in all parts of the world, including Australia. A study of pregnant women in Australia found 35% had IgG antibodies to *T. gondii.*[182] Following infection, *T. gondii* spreads to organs and tissues and is able to multiply in almost any cell in the body.[183] Immunity does not eradicate the infection, as latent intracellular cysts can persist for years after acute infection mainly in muscle tissues and the brain (although visceral organs may also be infected).[183] Both acute and latent *T. gondii* infection in the donor pose a transmission risk, and *T. gondii* transmission by organ transplantation has been reported multiple times in the literature, most commonly by heart transplantation but also by kidney liver, bowel and pancreas transplantation.[184,185,186,187,188,189,190]

Numerous serological tests exist for the detection of *T. gondii* antibodies, including both IgM and IgG. IgM antibodies appear sooner after infection than IgG, and disappear following recovery (whereas IgG antibodies do not disappear). NAT can be used to diagnose active infection;[191,192] however, given that active infection is rare and the goal of donor screening is primarily to detect latent toxoplasma in the heart and other organs resulting from past infection, serological testing for toxoplasma IgG alone is recommended, with testing for acute toxoplasma (IgM, NAT) reserved for appropriate clinical scenarios.

While a positive serological test for *T. gondii* is not a contraindication to donation, it may inform the need for prophylaxis in the recipient. Trimethoprim-sulfamethoxazole prophylaxis for at least 3 months post-transplant is currently standard international practice for recipients at risk of *T. gondii* transmission.[193]

Recommendation

Toxoplasma gondii screening using serology is recommended for all potential donors, with results available either prospectively or retrospectively. For recipients at risk (donor and/or recipient seropositive), routine *Pneumocystis jiroveci* prophylaxis with cotrimoxazole is protective against toxoplasmosis. If cotrimoxazole is not tolerated, prophylaxis should be chosen which is active against *Pneumocystis* and *Toxoplasma gondii* (e.g. atovaquone, or dapsone plus pyrimethamine, not pentamidine).

2.3.4.4 Trypanosoma cruzi

Trypanosoma cruzi (Chagas disease) is a zoonotic protozoan endemic to Mexico, Central America and South America.[194] Following infection, trypomastigotes circulate in the blood stream, while intracellular amastigotes appear in muscle (including heart) and ganglion cells.[195] Acute infection is typically asymptomatic, with an initial period of high parasitaemia followed by chronic latent infection, which then progresses to cardiac, gastrointestinal and/or peripheral nervous system disease in approximately 30% of those infected.[195] In immunosuppressed persons, acute *T. cruzi* infection is associated with adverse outcomes, particularly where there is cardiac and/or central nervous system involvement.[195]

Routine travel to endemic regions carries a low risk of *T. cruzi* infection; at risk are those who have spent prolonged time in endemic areas (>3 months) and/or stayed in rural/disadvantaged areas. The risk of transmission from *T. cruzi* seropositive organ donors to seronegative recipients ranges from 10-20% for kidneys and livers, to >75% for hearts.[195] Evidence indicates kidneys and livers can be safely transplanted from *T. cruzi* positive donors if close post-transplant monitoring is in place for early diagnosis and treatment, should acute infection occur.[195] Recipients of *T. cruzi* positive organs should be monitored weekly for the first 2 months post transplant, every 2 weeks through months 3-6 and annually thereafter or after intensification of immunosuppression. Monitoring methods include blood microscopy for *T. cruzi*, blood nucleic acid tests, and serology. Given the high rate of transmission in the context of heart transplantation, hearts from donors infected with or screen-positive for *T.cruzi* should not be utilised.[194]

Chronic *T. cruzi* infection should be diagnosed on the basis of epidemiological factors and serological tests, using at least 2 serological methods (e.g. ELISA, indirect haemagglutination assay, indirect immunofluorescence assay) and with inconclusive results confirmed by PCR. Serological tests for *T.cruzi* have good sensitivity but poor specificity in chronically infected persons, whereas PCR has high specificity and low sensitivity.[195] Serological results are unlikely to be available within the donation timeframe but can inform post-transplant interventions.[11] Monitoring for evidence of transmission and prompt treatment of acute infection is preferred to the use of prophylaxis in D+/R- transplants.

Recommendation

Donors who have spent 3 months or more in Mexico, Central or South America at any time in their lives should be screened for *T.cruzi* using serology. Infection with *T. cruzi* is not a contraindication to the donation of non-cardiac organs, however recipients require close follow-up for 24 months post-transplant for the appearance of acute infection. Donors with known *T.cruzi* infection (acute or chronic infection) should be excluded from heart donation.

2.3.5 Central nervous system infection by various pathogens

Most central nervous system (CNS) infection is bacterial or viral meningitis and/or encephalitis. Individuals with meningitis and/or encephalitis sometimes deteriorate to the point of neurological death as a result of these infections, at which point they might be considered for organ donation.

Cases of donor-transmitted CNS infection reported in the international literature have also involved more unusual infectious agents, including *Mycobacterium tuberculosis*, lymphocytic choriomeningitis virus, rabies, *cryptococcus*, *coccidioides immitis*, *aspergillus*, and *balamuthia*, resulting in significant morbidity and mortality in recipients.[196] In some cases of donor-derived transmission, CNS infection was not suspected due other pathology such as trauma, stroke and hypoxic-ischaemic brain injury. Suspicion of any of the above agents as the cause of CNS infection in a potential donor should preclude donation.

By comparison, donors with microbiologically proven bacterial meningitis (e.g. *Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae, Escherichia coli*, or group B *streptococcus*) are acceptable if the donor has been receiving appropriate antibiotic therapy (ideally for 48 hours) and pathogen-directed prophylaxis is provided to the recipient. Donors infected with highly virulent organisms such as *Listeria* species should be excluded.[197]

Adult patients with viral encephalitis should generally be excluded as donors, given the potentially fatal risk of transmission of pathogens such as Murray Valley encephalitis, lymphocytic choriomeningitis virus, and bat-related lyssavirus.[195] In the case of encephalitis caused by HSV or Varicella-zoster virus (VZV), provided that the donor has received a period of antiviral treatment and is not viraemic, transplantation may proceed on a case-by-case basis. Recipients in this circumstance should receive a course of antivirals.

The aetiology and clinical presentation of encephalitis in children differs from that observed in adults, including variation in the spectrum of infectious agents. In selected cases, paediatric donors with encephalitis may still be considered suitable for utilisation (e.g. influenza-associated acute demyelinating encephalomyelitis), following consultation with senior medical staff and subject to the degree of diagnostic certainty. Viral encephalitis of unknown aetiology remains a contraindication.

Given that in some reports of donor-derived disease transmission CNS infection was not suspected, the following should raise the suspicion of possible CNS infection:[196]

- Stroke in a patient without risk factors (e.g. young or paediatric, without comorbidities such as diabetes, hypertension or prior cerebrovascular accident) or clear mechanism
- Fever early in presentation, or other features of CNS infection such as altered mental status or seizures (note that fever after hospitalisation in common in critically ill patients)
- Travel or contact history posing a risk of CNS infection (e.g. travel to endemic regions for WNV or recent bat contact)
- Donor is immunosuppressed either through medication or disease (e.g. autoimmune disease, cirrhosis or previous transplant)
- Cerebrospinal fluid pleocytosis with decreased glucose and increased protein.

If suspicious of the presence or uncertain of the cause of CNS infection, a lumbar puncture should be performed followed by polymerase chain reaction (PCR) and other rapid diagnostic techniques.

Recommendation

Donors should be carefully evaluated for the possibility of CNS infection, with the cause established wherever possible. Donors with microbiologically proven bacterial meningitis are generally suitable for transplantation, provided the donors has been treated with appropriately targeted antibiotic therapy and the recipients receive targeted prophylaxis. Potential donors with viral encephalitis should not be utilised, with the exception of proven and treated HSV/VZV encephalitis and paediatric cases as per the recommendation below. In the HSV/VZV encephalitis cases, transplantation may proceed on a case-by-case after a period of antiviral treatment in the donor and with recipients receiving a course of antivirals post-transplantation. Donors with CNS infection of unknown origin must not be utilised.

Paediatric Considerations: The potential aetiology and presentation of encephalitis in children differs to adults, including with regards to the spectrum of infectious agents observed. Some paediatric donors with encephalitis may be appropriate for utilisation (e.g. influenza associated acute demyelinating encephalomyelitis), following discussion with senior medical staff and dependent on the certainty of diagnosis. Viral encephalitis in children of unknown aetiology remains a contraindication.

2.3.5.1 Transmissible Spongiform Encephalopathies

Transmissible Spongiform Encephalopathies (TSEs) are a group of rare, transmissible, and lethal neurodegenerative disorders that can occur sporadically, due to genetic causes, or due to exposure to the transmissible agent (prion). Creutzfeld-Jakob disease (CJD) is the most common human TSE, and can occur in both sporadic (sCJD) and acquired (vCJD) forms. In the hospital setting, sCJD has been transmitted through medical or surgical procedures involving neurosurgical instruments, brain electrodes, tissue (human cornea and dura mater grafts) and tissue extracts (human pituitary hormones).[198] While there have been no known transmissions of vCJD via surgery or tissue or organ donation to date, there have been cases of vCJD transmission via transfusion of red blood cells and plasma.[199]

Prospective CJD surveillance in Australia has been performed since 1993. Persons with suspected CJD are notified to the Australian National Creutzfeldt-Jakob Disease Registry, typically as a result of referral for diagnostic cerebrospinal fluid 14-3-3 protein detection, or alternatively via personal communications from clinicians, hospitals, families or CJD-related groups, and through health record searches.[200] The CJD mortality rate in Australia is <2 per million population per year.[200] Acquired CJD has not been reported in Australia to date.

There is currently no minimally invasive test to detect TSE before the onset of symptoms, nor is the prevalence of asymptomatic TSE known. Definitive diagnosis can only be made, if at all, by neuropathological examination of brain tissue following biopsy or autopsy. In the context of deceased organ donation, minimising the risk of donor-derived TSE transmission relies on screening the patient's history for symptoms consistent with TSE, exposure to human blood, dura mater grafts, pituitary-derived hormones, contact with contaminated surgical instruments and/or prior notification from the department of health as being at increased-risk of TSE due to exposure to one or more risk factors.

The following people are at risk of TSE and should be excluded from the donation of organs and tissues (including blood and plasma):[201]

- People with a family history of CJD
- People who received human pituitary-derived hormones prior to 1986
- People who have received dura mater grafts, contact with contaminated surgical instruments, and/or prior notification from the department of health as being at increased risk of TSE due to exposure to one or more risk factors
- People who die with early onset dementia
- People who die with any obscure undiagnosed neurological disorder.

Residence in the in the United Kingdom for six months or more between 1980 to 1996 is NOT an exclusion for deceased organ donation in Australia or New Zealand.

Recommendation

Persons at risk of TSE (as defined above) should be excluded from organ donation.

2.4 Risk of donor transmitted malignancy

Active malignancy generally precludes organ donation, with some exceptions. Transmission of malignancy may nonetheless occur as a result of occult malignancy in the donor, or as a result of past or current malignancy that was judged to have a low chance of transmission at the time of donor evaluation. In these circumstances, transmission of cancer from donor to recipient is believed to occur in <0.1% of solid organ transplants.[202]

Some data on the occurrence of malignancy transmission through organ transplantation are available through tumour registries and other databases (see Appendix J). These data have significant limitations due to incomplete capture of adverse events and the inherent difficulties of attributing cancer in the recipient to donor origin. Registries such as the Israel Penn International Transplant Tumor Registry (IPITTR) rely on voluntary event-based reporting and lack routine follow-up data on all recipients therefore tend to over-estimate risk. Conversely, transplant recipient databases may incompletely track recipients over time and thus under-report the development of cancer, resulting in under-estimation of risk. There are currently no transplant registries with systems in place to capture all cancer diagnoses over the lifetime of the recipient. Nor is there a system to capture instances where donor cancer has not resulted in transmission to the recipient, further complicating the calculation of transmission risk.

When a recipient develops a cancer – even when the cancer is proven to be of donor origin (by HLA or other molecular typing technology) – it is not necessarily the case that the cancer was donor-transmitted, since the transplanted organ may have developed the cancer subsequent to transplantation. That is, cancer in the recipient may be donor-derived but not donor-transmitted. Known examples include late renal cell carcinoma many years post-transplant and cases of donor-origin lymphoma that are likely to have developed through EBV transformation of donor lymphocytes after transplantation, rather than having been transmitted at the time of transplantation.

Practices to avoid donor-transmitted cancer mean that there are relatively few published reports of transmission. These limited reports do not cover the range of cancers for which decisions may be necessary, nor are case reports a reliable indicator of risk for all cancers of a given type. The decision to proceed with a given donor will therefore need to be informed by a combination of:

i. Reported cases of donor-derived cancer
ii. Observed lack of transmissions in the case of certain cancers (e.g. low grade, low stage prostate cancer)
iii. Known biology of cancers in non-immunosuppressed individuals (especially known recurrence rate)
iv. Known biology of de novo cancers in immunosuppressed hosts.

While it is inevitable that there will always be occasional cases of inadvertent cancer transmission, every effort should be made to identify past or current malignancy and to obtain as much information as possible to assess the risk of cancer transmission. This will inform (i) the decision as to whether the donation of any organ is safe, (ii) the risk-benefit assessment for each potentially suitable organ against individual recipient circumstances, and (iii) necessary steps to mitigate risk if a decision is made to proceed. Investigations should include:

- Obtaining a full donor history, including details of any past cancer diagnosis and treatment and any other information relevant to assessing the risk of malignancy transmission based on current disease status
- Checking jurisdictional cancer registry (see Appendix L)
- Undertaking a careful physical examination at the time of donor workup and during the surgical retrieval procedure
- Reviewing test results including those available as part of patient care or routinely undertaken for donor assessment, and any additional tests indicated for further evaluation of cancer risk, including imaging and biopsy
- Seeking expert oncological and other advice, as required.

2.4.1 Summary recommendations for organ utilisation

Sections 2.4.3 to 2.4.7 of this document provide information on risks and recommendations for organ utilisation in the event of malignancy being detected in a potential donor. The estimated risks of donor-derived transmission associated with cancers of different sites are summarised in Table 2.7 below. Cancer types and stages associated with minimal-to-low risk of transmission and those associated with high-to-unacceptable risk are shown. For recommendations with respect to other cancer types and stages (including those associated with an intermediate risk of transmission), refer to the cancer site-specific section in this document. Recommendations for organ utilisation associated with each risk classification group are given in Table 2.8.

Table 2.7: Summary of risks associated with malignancies of different sites in the donor history or detected at retrieval.

Risk classification categories:
Minimal risk of transmission (<0.1%) – Likely to be acceptable for all organ types and recipients
Low risk of transmission (0.1% to <2%) – Likely to be acceptable for many organ types and recipients
High risk of transmission (≥10%) – May be acceptable in exceptional circumstances
Unacceptable risk – Use of organs is not recommended in any circumstance

Cancer site and type	Risk classification*			
Bladder (section 2.4.6.14)	Minimal	Low	High	Unacceptable
Single, Grade 1, Stage 0a papillary urothelial carcinoma	•			
Papillary urothelial neoplasm of low malignant potential (PUNLMP)	•			
Single, Grade 1, Stage I papillary urothelial carcinoma		•		
Treated Stage II-IV urothelial cancer >5 years cancer-free			•	
Low-grade urothelial carcinoma diagnosed at retrieval (ex PUNLMP)			•	
Recently diagnosed high-grade urothelial cancer				•
Multiple/recurrent urothelial cancer				•
Urothelial carcinoma *in situ* (CIS)				•
Breast (section 2.4.6.1)	Minimal	Low	High	Unacceptable
Ductal carcinoma *in situ*	•			
Stage Ia hormone negative breast cancer, >5 years cancer free		•		
Stage Ia hormone negative breast cancer, <5 years cancer free			•	
Stage Ib or higher hormone receptor positive breast cancer			•	
Breast cancer diagnosed at retrieval				•
Central nervous system (section 2.4.3)	Minimal	Low	High	Unacceptable
Primary brain tumours (see Table 2.10)	•	•		
Secondary brain tumours				•
Cerebral lymphoma				•
Colon and rectum (section 2.4.6.3)	Minimal	Low	High	Unacceptable
Carcinoma *in situ* of the colon or rectum	•			
Treated Stage I colorectal cancer (N0/M0), >5 years cancer free (excl familial adenomatous polyposis)		•		
Stage I colorectal cancer diagnosed during retrieval			•	
Stage IIa colorectal cancer, >10 years cancer free			•	
Stage II or higher colorectal cancer with ≤10 years cancer free				•
Gastrointestinal tract (section 2.4.6.4 & 2.4.6.7)	Minimal	Low	High	Unacceptable
Treated GIST ≤2cm (N0/M0) with mitotic count ≤5/50 HPFs and >3 years cancer free	•			
Branch duct intraductal papillary mucinous neoplasms (IPMNs) <3cm without a solid component or suspicious nodal disease		•		
Gastric GIST ≤2cm diagnosed during organ retrieval		•		

Gastric GIST ≤2cm, mitotic count >5/50 HPFs, treated and >3 years cancer free		•		
Gastric GIST >2-≤5cm, mitotic count ≤5/50 HPFs , treated and >3 years cancer free		•		
Branch duct IPMN >3cm without a solid component or suspicious nodal disease			•	
Gastric GIST >2cm diagnosed at retrieval			•	
Gastric GIST >10cm, mitotic count ≤5/50 HPFs, treated and >3 years cancer free			•	
Non-gastric GIST diagnosed during organ retrieval			•	
Non-gastric GIST >5cm, mitotic count ≤5/50 HPFs, treated and >3 years cancer free			•	
Non-gastric GIST ≤2cm, mitotic count >5/50 HPFs, treated and >3 years cancer free			•	
Any GIST >2cm with mitotic count >5/50 HPFs, treated and >3 years cancer free			•	
Main duct IPMN >10mm or any IPMN with a solid component or suspicious nodal disease				•
Any GIST diagnosed at retrieval or with distant metastases				•
GIST without complete prior surgical excision or GIST with <3 years cancer-free survival				•
Oesophageal, gastric, liver, pancreatic or biliary cancer				•
Gynaecological cancers (section 2.4.6.9 & 2.4.6.15)	Minimal	Low	High	Unacceptable
Adenocarcinoma *in situ* of the uterine cervix	•			
High grade squamous intraepithelial lesions	•			
Invasive cancer of the uterus or cervix in the donor history with a cancer-free interval >5 years			•	
Invasive cancer of the uterus of cervix diagnosed within the past 5 years				•
Ovarian cancer				•
Head and neck (section 2.4.6.8)	Minimal	Low	High	Unacceptable
Treated low stage oropharyngeal cancer and >5 cancer-free			•	
Oropharyngeal cancer diagnosed at retrieval				•
Kidney (section 2.4.6.11)	Minimal	Low	High	Unacceptable
Renal cell carcinoma <1cm, Nucleolar Grade I-II	•			
Renal cell carcinoma >1 and ≤4cm, Nucleolar Grade I-II		•		
Renal cell carcinoma >4-7cm, Nucleolar Grade I-II, diagnosed <5 years ago			•	
Renal cell carcinoma >7cm, Nucleolar Grade I-II, >5 years cancer free			•	
Renal cell carcinoma with extra-renal extension or >4cm tumours with Nucleolar Grade III-IV				•
Renal cell carcinoma >7cm diagnosed within the previous 5 years				•
Unconventional renal malignancy (e.g. collecting duct carcinoma, medullary, sarcoma, or any molecularly defined renal tumours such as fumarate hydratase-deficient RCC, or adverse features such as sarcomatoid or rhabdoid differentiation)				•
Lung (section 2.4.6.5)	Minimal	Low	High	Unacceptable
Any history of lung cancer				•

Prostate (section 2.4.6.10)	Minimal	Low	High	Unacceptable
Prostate cancer with Gleason score ≤6 (Grade 1, Stage I)	•			
Treated prostate cancer with Gleason score 7 (Grade 2/3, Stage II)	•			
Recently diagnosed prostate cancer with Gleason score 7 (Grade 2/3, Stage II)		•		
Prostate cancer with Gleason score >7 and extra-prostatic extension (Stage III)			•	
Neuroendocrine prostate cancer			•	
Prostate cancer with distant metastasis (Stage IV)				•
Skin (section 2.4.4 & 2.4.5)	Minimal	Low	High	Unacceptable
In situ cutaneous melanoma	•			
Basal cell carcinoma	•			
In situ squamous cell carcinoma	•			
Cutaneous squamous cell carcinoma T1, or T2 with >5 years cancer free		•		
Cutaneous squamous cell carcinoma T2 with <5 years cancer free		•		
Cutaneous melanoma <0.5mm without ulceration, located on an upper limb, completely resected		•		
Cutaneous melanoma 0.8–1mm with ulceration or 1–2mm without ulceration (T1b-T2a/N0/M0) with <10 years cancer free			•	
Cutaneous melanoma 1-2mm with ulceration (T2b/N0/M0) with >10 years cancer free			•	
Invasive cutaneous squamous cell carcinoma with nodal involvement or metastasis				•
Cutaneous melanoma T2b <10 years cancer free				•
Cutaneous melanoma stage T3 or T4				•
Cutaneous melanoma with nodal involvement or metastasis				•
Uveal or mucosal melanoma				•
Kaposi's sarcoma				•
Merkel cell carcinoma				•
Thyroid (section 2.4.6.13)	Minimal	Low	High	Unacceptable
Papillary thyroid microcarcinoma (micro PTC)	•			
Differentiated thyroid tumours ≤4cm limited to the thyroid (T1/T2)	•			
Newly diagnosed differentiated thyroid cancer >4cm (T3, M0)		•		
Differentiated thyroid cancer >4cm with extensive spread (T4), treated and ≥2 years cancer-free		•		
Differentiated thyroid cancer with aggressive histology or angio-invasion (T4b) with <2 years cancer-free survival			•	
Medullary thyroid cancer Stage III/IV, treated and >5 year cancer-free			•	
Newly diagnosed medullary thyroid cancers.				•
Any history of anaplastic thyroid cancer				•
Thyroid lymphomas, thyroid sarcomas and other rare tumours of the thyroid				•
Treated thyroid cancer with incomplete macroscopic tumour resection				•

Other/multiple sites	Minimal	Low	High	Unacceptable
Grade 1-2 neuroendocrine tumour (N0/M0), >5 years cancer free (section 2.4.6.6)		•		
Grade 3 neuroendocrine tumour (section 2.4.6.6)				•
Neuroendocrine tumour detected at retrieval (section 2.4.6.6)				•
Neuroendocrine carcinoma (section 2.4.6.6)				•
Sarcoma determined during retrieval (section 2.4.6.12)				•
Haematological cancers, <5 years recurrence-free survival (section 2.4.7)				•
Choriocarcinoma (section 2.4.6.2)				•

2.4.2 General recommendations for detecting malignancy in the donor and assessment of transmission risk

2.4.2.1 Donor history

At donor assessment, an interview is undertaken with the donor's family by the donation specialist coordinator or other health professional. This includes questions about past history of cancer and removal of any skin lesions, participation in regular cancer screening (e.g. prostate examinations in male donors and regular breast examinations and/or pap smears in female donors) and other factors that may indicate a risk of cancer, including smoking or recent weight loss. Donor assessment may also include a history of genetic testing identifying a cancer predisposition mutation in the donor or their first-degree blood relatives (see Appendix K).

If there is a reported history of cancer, details should be sought about the type, when and where it was diagnosed, treatments (e.g. surgery, radiotherapy, chemotherapy) and follow up. Pathology reports of removed skin lesions are often able to be obtained from the donor's general practitioner or pathology laboratories. Detailed information about a history of cancer should be obtained, including information from the patient's oncologist and treatment centre, stage of cancer, and histopathology reports. Reports related to disease surveillance, including imaging, should also be obtained if possible.

Details of all enquiries made in relation to donor history of cancer should be documented and communicated to the transplant centres. Where investigations were undertaken in response to a history of cancer reported by family, but no information was found, this should also be communicated to the transplant centres.

2.4.2.2 Donor physical examination

Physical examination occurs at two steps of the organ retrieval pathway: the first by the donation specialist coordinator or other health professional at the time potential donor is being considered, and the second at the time of organ retrieval by the surgical team. The physical examination undertaken by the donor coordinator ideally occurs as soon as possible after the family interview, so that information obtained from the family can be verified at the physical assessment and the coordinator can seek further clarification from the family about unexpected findings (e.g. scars from prior surgery). The physical examination includes a careful assessment to detect scars, skin lesions and obvious lumps or masses. Large scars that may indicate prior excision of a melanoma are of more concern than pigmented skin lesions, which are difficult to precisely identify and unlikely to represent an undiagnosed melanoma. The donor coordinator is not expected to make a precise diagnosis but rather to identify unusual or abnormal findings and seek further expertise from dermatology specialists, as well as documenting and conveying any abnormal findings to transplant units. The DonateLife physical assessment guideline provides further detail on donor physical examination.

The second physical examination undertaken by the surgeon(s) at the time of retrieval may reveal unexpected clinically occult lesions such as bowel cancers, renal or liver tumours. Abnormal lesions identified at this time may require biopsy to further evaluate the risk of malignancy. Perinephric fat should be excised sufficiently to ensure that the kidney is fully perfused. Careful dissection at the renal hilum is not routinely recommended at the donor hospital, but careful palpation of the kidney to exclude any renal mass is recommended.

2.4.2.3 Laboratory and imaging results

Pathology and imaging test results may be a) available as part of prior patient assessment, b) obtained as part of routine donation workup, and/or c) obtained through specific additional testing (e.g. imaging and biopsy).

Investigations that were undertaken as part of patient care and for the purpose of cancer treatment prior to the donation process beginning should be reviewed as part of the donor assessment process. These may include blood tests, imaging studies, biopsies or other information. Hospital medical record information, pathology results, and imaging study reports should be reviewed. Sometimes, an absence of any abnormalities is reassuring information that can be used to make a risk determination – e.g. computed tomography (CT) chest imaging revealing a lack of abnormalities in potential lung donors who are older and/or who have a heavy smoking history. If abnormalities are found, further evaluation and investigations may be warranted (see below).

Standard donor workup blood tests include a full blood examination and liver function tests. Occasionally, these can be abnormal as a result of an underlying malignancy. In female donors of child-bearing age, testing for beta human chronic gonadotrophin hormone is recommended to detect metastatic choriocarcinoma, especially if the cause of death is unexplained intracerebral haemorrhage. In all potential donors, a routine chest x-ray should also be carefully reviewed for any features that may suggest underlying primary or secondary pulmonary malignancy, or that might indicate bone metastatic disease in ribs or spine.

Abdominal CT imaging for potential liver donors may be requested, particularly if there are risk factors for malignancy or for anatomical evaluation (e.g. candidate for split &/or multivisceral donation). In general, such requests should be made with a provisional acceptance of the liver pending an acceptable CT scan result.

Additional tests, such as imaging, blood tests and/or biopsy, may be appropriate for further evaluation of cancer risk in certain, specific circumstances. Some centre-based or state-based protocols recommend CT chest studies to (i) exclude lung malignancy in potential lung donors aged over 70 years and/or those with a >20 pack year history of smoking, (ii) further evaluate concerning abnormalities identified on prior chest x-ray, or (iii) lung donors who test positive for SARS-CoV-2 on PCR from the upper respiratory tract to assess for any sequelae of COVID-19 (see Appendix E). A CT Chest that has already been undertaken as part of patient assessment ealier in the admission will usually suffice.

Routine screening for tumour markers is not recommended, since false-positive results may lead to unnecessary loss of donation and transplantation opportunities. If there is a confirmed malignancy in the donor history and previous tumour marker results are available, appropriate tumour markers may be tested as guided by oncological advice.

Careful consideration must be given to protocols or individual requests for additional tests, weighing their utility against the impact that undertaking such tests may have. Potential negative impacts include resource use (ICU and hospital), extending the donation workup timeframe and potential loss of family consent for donation as a result, and the potential for adverse impact on other organs. Additional investigations also introduce the risk of incidental findings (e.g. benign lesions identified on imaging, elevated prostatic specific antigen levels in catheterised male donors) that pose no risk to recipients and for which further evaluation is not possible in the donation timeframe, resulting in loss of transplantation opportunities. Hence, *ad hoc* requests for additional screening tests should only be carried out where there is a sound clinical or epidemiological basis for proceeding.

2.4.2.4 Biopsy and histopathology

Where a mass suspected of being malignant is known from the donor history or is found during donor workup and cannot clearly be determined as benign radiologically, a biopsy should be taken as part of the donor workup or planned ahead and performed during organ retrieval. For any mass or lymphadenopathy suspected of malignancy discovered during organ retrieval, an urgent histopathological examination must be performed by cytological smear and/or frozen section before any organ is transplanted. Where possible, discuss the appropriate sampling type with the on-call histopathologist. If possible, the mass should be completely resected and examined, without sacrificing a graft suitable for transplantation. The pathologist should be provided with as much clinical information as possible. If, however, after pathological examination the possibility that a suspicious mass is malignant cannot be ruled out, then the donor should be declined unless there is a suitable recipient facing an imminent risk to life (who has given informed consent).

When a donor malignancy (primary tumour or metastasis) is identified shortly after organ retrieval (e.g. during the implantation procedure), all recipient centres involved must be alerted immediately. In cases where organs have already been transplanted and histology reveals a malignancy (e.g. incidental cancer in a lung lobe discarded due to size reduction), a full donor autopsy should be requested whenever possible to obtain detailed information about tumour origin and dissemination. This is not necessary in cases of small primary renal cell carcinoma found in one kidney, which would not preclude the transplantation of other organs.

While routine post-mortem examination has become an uncommon procedure in clinical medicine, if an autopsy is performed then the results should be followed-up by the donation service up as the autopsy may detect potentially transmissible disease.

2.4.2.5 Assessment of transmission risk

For donors with a known history of cancer or where cancer is detected during donor work-up or organ retrieval, in deciding whether to proceed with donation it is important to not only consider to the natural history of the cancer in the donor, but also the potential impact of transplanting tumour cells of this type into an immunosuppressed recipient. Advice may be sought from the patient's treating oncologist or from oncologists and/or other specialists with particular expertise regarding the cancer under consideration (e.g. urologists who specialise in prostate cancer).

While the precise risk of transmission from donor to recipient of any given cancer is usually unknown, it is possible to broadly categorise the likely risk of transmission based on what is known about the cancer type and stage, its metastatic potential, and its patterns of recurrence in both the transplant and non-transplant setting (see Table 2.8). Newly diagnosed invasive cancer generally poses a higher risk of transmission than a history of treated invasive cancer followed by a significant disease-free interval. For potential donors with a confirmed history of cancer, the risk of transmission will be influenced by the treatment received, the length of the disease- free interval, and follow-up history.

Table 2.8: Risk categories for donor malignancy transmission (adapted from Nalesnik et al 2011). In all cases where the risk of donor malignancy transmission is non-standard, specific informed consent should be obtained from the recipient or their delegate prior to proceeding with transplantation.

	Definition		
Risk category	Description	Estimated risk of transmission	Recommendations for organ utilisation
Standard risk	No active malignant tumour or history of malignancy found during donor evaluation	Negligible	Acceptable for all organ types and recipients
Minimal risk	Existing evidence suggests minimal risk of transmission	<0.1%	Likely to be acceptable for all organ types and recipients
Low risk	Existing evidence suggests low risk of tumour transmission	≥0.1%-<2%	Likely to be acceptable for many organ types and recipients
Intermediate risk	Existing evidence suggests intermediate risk of tumour transmission	≥2%-<10%	May be acceptable for some organ types and recipients
High risk	Existing evidence suggests high risk of tumour transmission	≥10%	May be acceptable in exceptional circumstances e.g. where the recipient faces an imminent threat to life
Unacceptable risk	Existing evidence suggests very high risk of tumour transmission	NA	Use of organs is not recommended in any circumstance
Unknown risk	Evaluation for risk factors is incomplete or no literature exists on which to base risk assessment	NA	May be acceptable according to the circumstances and clinical judgement

Organs from deceased donors with cancers categorised as minimal risk may be safely used for transplantation without particular restrictions. Organs from donors with low- to intermediate-risk cancers may also be acceptable and provide benefit for many recipients, depending on organ type and recipient circumstances. Thorough donor assessment can help to inform decision-making, as can advice from oncologists and other specialists.

When donors are at high risk of transmitting cancer, early medical advice regarding suitability is recommended and transplant units should be contacted to determine whether there are suitable recipients in whom the risk may be deemed acceptable, before proceeding with detailed donor assessment. In particular, liver and thoracic transplant services should be consulted to determine if there are any urgently listed patients who might be considered suitable recipients and may be willing to accept the high risk of cancer transmission.

In all circumstances, it is necessary to weigh the potential risks and benefits of proceeding with transplantation given the characteristics of a donor organ and the circumstances of a particular recipient. This tailored risk assessment will differ according to the donor and cancer risk, the organ being transplanted, the transplant urgency for a given recipient and – if the organ were to be declined – the likelihood of a subsequent more suitable offer being received in an acceptable time period.

Patients who are waitlisted for organ transplantation should receive education about the risks of transplantation, including that of possible donor-derived malignancy. When there is a specific risk associated with the donor organ(s) at the time of organ offer, specific informed consent should be obtained from the recipient or their guardian/delegated decision-maker if the recipient lacks competence (for example, due to young age or illness) prior to proceeding with transplantation.

2.4.2.6 Role of cancer registries

Cancer at most sites is a notifiable disease in Australia and New Zealand. Operational and governance arrangements vary amongst Australian states and territories, however the Australian Association of Cancer Registries encourages a standard approach to cancer data collection and management across Australia.

New Zealand and the Australian states and territories operate cancer registries that assemble information about new cases of cancer and cancer deaths, though the breadth of data collected can vary between jurisdictions (Table 2.9). All registries record location, morphological type, topography, diagnosis date, and basis of diagnosis. The registries are “case-based” data collections: each piece of information provided to the registry is considered in the context of other information about the same person and used to progressively create a complete picture of tumours for that person. Cases are generally identified by name, sex and date of birth. An important exception to mandatory cancer reporting is keratinocyte cancers (particularly squamous cell carcinomas).

In Australia, arrangements exist in some jurisdictions (Table 2.9) for DonateLife staff to query the state-based registry (either directly or indirectly) to obtain the history of a potential donor once appropriate consent for donation is obtained from the next of kin. However, information from the registry is limited to those cancers diagnosed or treated within that state or territory and is identified primarily by name and date of birth. In order to obtain a complete history, it is important to ascertain if the donor previously resided in a different state or territory, and/or may have been diagnosed or treated under a different name. Where the potential donor previously resided in another jurisdiction, DonateLife staff in that jurisdiction would need to be contacted to proceed with further enquires.

The registries forward an agreed list of data elements to the Australian Institute of Health and Welfare (AIHW) annually to a national repository—the Australian Cancer Database—for national reporting and disease monitoring. This data collection is not available for interrogation to obtain the malignancy history of a potential donor.

More information about Australian cancer registries is provided in Appendix L, including an overview of cancer-specific information available through each of the state-based registries. It should be noted that the information in Table 2.9 and Appendix L may change over time through continual improvement in data reporting and capture.

Table 2.9: Historic cancer data availability to DonateLife and Organ Donation New Zealand

State	Cancer data availability	
New Zealand	Available to Organ Donation NZ	Yes
	Method of Access	Reports available on request
	Availability	–
	Restrictions on use	–
	Earliest year of data available	1948
	Contact details	data-enquiries@moh.govt.nz | https://www.health.govt.nz/nz-health-statistics/national-collections-and-surveys/collections/new-zealand-cancer-registry-nzcr
NSW	Available to DonateLife	Yes*
	Method of Access	Read-only access via web-based portal
	Availability	24/7
	Restrictions on use	–
	Earliest year of data available	1972
	Contact details	CINSW-DARenquiries@health.nsw.gov.au | P (02) 8374 3640
VIC	Available to DonateLife	Yes
	Method of Access	Reports accessible on request via secure portal
	Availability	9am-5pm; Monday-Friday
	Restrictions on use	–
	Earliest year of data available	1982
	Contact details	vcr@cancervic.org.au
QLD	Available to DonateLife	Yes
	Method of Access	Read-only real-time access
	Availability	24/7
	Restrictions on use	–
	Earliest year of data available	1982
	Contact details	https://CancerAllianceQld.health.qld.gov.au | P (07) 3176 4400
WA	Available to DonateLife	Yes
	Method of Access	Read-only real-time access
	Availability	24/7
	Restrictions on use	–
	Earliest year of data available	1982
	Contact details	wacanreg@health.wa.gov.au
SA	Available to DonateLife	Contact registry
	Method of Access	–
	Availability	–
	Restrictions on use	–
	Earliest year of data available	1977
	Contact details	WellbeingSACCSACancerRegistry@sa.gov.au

TAS	Available to DonateLife	Contact registry
	Method of Access	Read only access
	Availability	Mon – Fri business hours
	Restrictions on use	–
	Earliest year of data available	1982
	Contact details	https://menzies.utas.edu.au/research/research-centres/tasmanian-cancer-registry
NT	Available to DonateLife	Yes, once standing approval to receive data is requested from and given by Chief Health Officer under the NT *Cancer (Registration) Act*
	Method of Access	Email to NT Cancer Registry
	Availability	9am-5pm; Monday-Friday, unless otherwise negotiated
	Restrictions on use	Depends on CHO approval conditions
	Earliest year of data available	1991
	Contact details	NTCancerRegistry.DoH@nt.gov.au P 08 8985 8078 | F 08 8985 8075 W https://health.nt.gov.au/data-and-research/Innovation-and-research/northern-territory-cancer-registry/what-is-the-cancer-registry
ACT	Available to DonateLife	Yes – as per NSW Registry
	Method of Access	Read-only access via web-based portal
	Availability	24/7
	Restrictions on use	–
	Earliest year of data available	1972
	Contact details	CINSW-DARenquiries@health.nsw.gov.au | P (02) 8374 3640

* A lot of information is captured on the pathology report, the inpatient notification (surgical) or on the radiotherapy/chemotherapy treatment notification, which may not be explicitly listed in a data field.

2.4.3 Central nervous system tumours

Donor assessment and eligibility

Primary solid central nervous system (CNS) tumours may occasionally lead to death in circumstances where organ donation is possible. Extracranial spread of brain tumours is rare, though there are reports of malignancy transmission to the recipients of organs from such donors.[203,204,205,206,207,208,209,210,211,212]

Wherever possible, full histological characterisation of a CNS lesion should be accessed before any organ is retrieved. Where no histological diagnosis exists, organs from a donor with a CNS lesion should only be used in recipients whose probable waiting-list mortality justifies any extra risk, and only after fully informed consent has been given.

Assessment of transmission risk

Primary brain tumours

The World Health Organisation grades primary brain tumours from grade I to grade IV, based on biological behaviour and prognosis.[213] Grade IV tumours are cytologically malignant and generally fatal, and this has been interpreted as representing the highest risk of donor-to-recipient transmission. However, a number of transplants from donors with grade IV tumours have been reported that did not result in transmission of malignancy to the recipient. A UK review of 448 recipients of organs from 177 donors with primary CNS tumours, including 23 donors with grade IV gliomas and 9 with medulloblastoma, found no evidence of tumour transmission over a minimum follow-up period of 5 years.[214] A report of the Australian and New Zealand Organ Donor (ANZOD) registry found no transmission events from 46 donors, 9 with high-grade tumours, with organs transplanted into 153 recipients.[215] A UNOS database report that included 642 recipients of organs from donors with CNS tumours between 2000 and 2005, including 175 recipients of organs from donors with high-grade tumours, identified a single donor with glioblastoma multiforme who transmitted disease to three recipients.[216,217] A Czech report of 42 donors, 11 with high-grade tumours, found no transmission among 88 recipients followed for between 2 and 14 years.[218]

Overall, UK and European guidelines estimate the risk of tumour transmission from WHO grade I and II tumours to be minimal (<0.1%), and the risk of transmission from grade III tumours to be low (0.1 to <2%). WHO grade IV tumours are estimated to have a low-to-intermediate risk of transmission. SaBTO in the UK estimate the risk of transmission of WHO grade IV tumours as 2.2%, although combined data from the registries in the UK, United States and Australia and New Zealand would indicate the risk of transmission is lower than this (<1 in 200). A larger evidence base is needed to definitively quantify the transmission risks associated with grade IV CNS tumours.

Interventions such as brain irradiation, chemotherapy, previous craniotomy and ventriculo-peritoneal shunt may increase the risk of transmission of CNS malignancy from donors to recipients, possibly through breaching the blood brain barrier and so facilitating tumour spread.[219,220] There is considerable debate about the role and significance of such interventions, however, and it is difficult to differentiate between causality and coincidence—it may be that some interventions are more commonly employed in tumours that are more likely to spread.

There are case reports of tumour deposits identified around the peritoneal end of a ventriculoperitoneal shunt,[221] though the pattern of metastases is similar in those with and without shunts. The estimated increase in risk of extracranial metastasis attributable to the presence of a cerebrospinal fluid shunt is less than 1%.[222] The presence of a shunt should not contraindicate donation, provided that there is meticulous examination of the shunt tract at the time of retrieval surgery.[223] Similarly, prior craniotomy or biopsy should not contraindicate donation, however at the time of the retrieval procedure there should be a close examination of the craniotomy site and cervical nodes.[223] During the evaluation of a donor with a CNS tumour, a thorough thoracic and abdominal exploration with visualisation and palpation of organs should be performed.[223]

In summary, primary CNS tumours are not automatic contraindications to organ donation (with the exception of primary cerebral lymphoma – see below). In each case where a primary CNS tumour has been identified, the risk of not receiving a transplant should be weighed against the risk of transmission of donor malignancy. Based on reported data, the absolute risk of transmission of a primary CNS tumour is likely to be low, even with a high-grade malignancy. Craniotomy or other breach of the blood brain barrier does not contraindicate donation, though a ventriculo-systemic shunt may slightly increase the risk of transmission.[222] Informed consent of the recipient is required, with the (derived) risk estimates shown in Table 2.10 provided to inform the recipient's decision. More information on the possible transmission risks associated with specific CNS tumour types can be found in the European Guide to the Quality and Safety of Organs for Transplantation.[224]

Secondary brain tumours and cerebral lymphoma

Donors with cerebral lymphoma or secondary CNS tumours are considered an unacceptable risk for organ donation. Secondary malignancy in this context refers to metastatic cancer that has spread to the brain from a primary site elsewhere in the body. There is a risk that donors with brain metastases may be misdiagnosed as having a primary brain tumour or intracerebral haemorrhage. Metastases should therefore be considered for any patient with a history of cancer presenting with a non-traumatic cerebral haemorrhage and, if suspected, donation should not proceed.

Table 2.10: Recommendations on the use of organs from donors with primary CNS tumours, by tumour site. Derived from SaBTO[202] and the 2016 WHO classification of tumours of the central nervous system.[225] For a list ordered by risk category, see Appendix M.

	Risk classification*			
Diffuse astrocytic and oligodendroglial tumours	1	2	3	4
Diffuse astrocytoma, IDH-mutant	•			
Anaplastic astrocytoma, IDH-mutant		•		
Glioblastoma			•	
Diffuse midline glioma, H3K27 M-mutant			•	
Oligodendroglioma, IDH-mutant & 1p/19q-codeleted	•			
Anaplastic oligodendroglioma, IDH-mutant & 1p/19q-codeleted		•		
Other astrocytic tumours	1	2	3	4
Pilocytic/ Subependymal giant cell	•			
Pleomorphic xanthoastrocytoma	•			
Anaplastic pleomorphic xanthoastrocytoma		•		
Ependymal tumours	1	2	3	4
Subependymoma/ Myxopapillary ependymoma	•			
Ependymoma	•			
Ependymoma, *RELA* fusion-positive (II or III)		•		
Anaplastic ependymoma		•		
Other gliomas	1	2	3	4
Angiocentric glioma	•			
Chordoid glioma of the third ventricle	•			
Oligoastrocytoma	•			
Choroid plexus tumours	1	2	3	4
Choroid plexus/ Atypical choroid plexus papilloma	•			
Choroid plexus carcinoma		•		
Pineal tumours	1	2	3	4
Pineocytoma	•			
Pineal parenchymal tumour of intermediate differentiation (II or III)		•		
Pineoblastoma		•		
Papillary tumour of the pineal region (II or III)		•		
Meningiomas	1	2	3	4
Meningioma/ Atypical meningioma	•			
Anaplastic (malignant) meningioma		•		
Embryonal tumours	1	2	3	4
Medulloblastoma			•	
Embryonal tumour with multilayered rosettes, C19MC-altered			•	
Medulloepithelioma			•	
CNS embryonal tumour, NOS			•	
Atypical teratoid/rhabdoid tumour			•	

CNS embryonal tumour with rhabdoid features			•	
Ependymoblastoma			•	
Germinoma			•	
Immature teratoma			•	
Teratoma with malignant transformation			•	
Yolk sac tumour			•	
Embryonal carcinoma			•	
Non-gestational Choriocarcinoma			•	
Neuronal and mixed neoronal-glial tumours	1	2	3	4
Dysembryoplastic neuroepithelial tumour	•			
Gangliocytoma	•			
Ganglioglioma	•			
Anaplastic gangliomyoma		•		
Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos)	•			
Desmoplastic infantile astrocytoma and ganglioglioma	•			
Papillary glioneuronal tumour	•			
Rosette-forming glioneuronal tumour	•			
Central/ Extraventricular neurocytoma	•			
Cerebellar liponeurocytoma	•			
Tumours of the cranial and paraspinal nerves	1	2	3	4
Schwannoma	•			
Neurofibroma	•			
Perineurioma	•			
Malignant peripheral sheath tumour (II, III or IV)		•		
Mesenchymal, non-meningothelial tumours	1	2	3	4
Solitary fibrous tumour/ Haemangiopericytoma (I, II))	•			
Solitary fibrous tumour/Haemangiopericytoma (III)			•	
Haemangioblastoma	•			
Tumours of the sellar region	1	2	3	4
Craniopharyngioma	•			
Granular cell tumour	•			
Pituicytoma	•			
Spindle cell oncocytoma of the adenohypophysis	•			
Cerebral lymphoma	1	2	3	4
Primary cerebral lymphoma				•

Risk classification categories:

1 **Minimal risk of transmission (<0.1%)** – Likely to be acceptable for all organ types and recipients
2 **Low risk of transmission (0.1% to <2%)** – Likely to be acceptable for many organ types and recipients
3 **Low-to-intermediate risk of transmission**[a] – consider on a case-by-case basis
4 **Unacceptable risk**

[a] Best available evidence suggests that the risk of transmission from donor to recipient in the case of grade IV CNS tumours is ≤2%[146]

2.4.4 Melanoma

Melanoma is the third-most commonly diagnosed invasive cancer in Australia and New Zealand.[226,227] There are numerous reports of donor-derived transmission of cutaneous melanoma in the international literature, mostly where tumour diagnosis was missed in the donor.[216,228,229,230,231,232,233] Due to its high population prevalence, risk of non-detection, and tendency for early micrometastasis, invasive melanoma is the most commonly transmitted tumour type, accounting for approximately 30% of all reports of donor-transmitted cancers.[234,235] Transmission of melanoma from donor to recipient is also associated with a high recipient mortality rate – the IPITTR estimates this at 60%.[230]

The risk of donor-derived cutaneous melanoma transmission is closely associated with the tumour's thickness (also known as Breslow thickness) and stage at diagnosis and treatment.[236] It is important to note that Breslow thickness refers to the vertical depth of the tumour, rather than the extent of its superficial spread. In situ cutaneous melanoma is, by definition, non-invasive and poses minimal risk of donor-derived transmission, given that in situ melanoma is not associated with metastatic risk. In a series of 993 deceased organ donors (2010–2018), 9 had a history of melanoma, and 16 recipients received organs from donors with a history of in situ melanomas; no confirmed transmissions occurred.[237] This Australian cohort dataset highlights that overly cautious exclusion of donors with a history of low-risk melanoma may result in missed opportunities for transplantation. Further evidence from a systematic review and meta-analysis of patients with reported melanoma prior to solid organ transplantation, suggests that adverse post-transplant outcomes are primarily associated with prior invasive melanoma, while in situ melanoma appears to carry minimal risk.[238]

Invasive cutaneous melanoma, in contrast, may recur even after the donor has survived disease free after many years and is associated with a low to intermediate risk of transmission. True recurrence rates are difficult to estimate as people may die of a competing cause before recurrence is detected. Melanoma-specific survival rates in people with primary cutaneous melanoma may therefore be used as a guide to the potential risks of transmission. Using the latest staging (AJCC 8th edition)[239] individuals with melanomas < 0.8mm without ulceration are classified as T1a. In non-immunosuppressed individuals, the 10-year mortality risk associated with T1a melanoma is reported to be between 2–7%.[240,241] However, population-based studies have assessed 20-year melanoma-specific survival in patients with a melanoma less than 0.5mm and reported risks of melanoma death of less than 2%.[240,242] The most recent Australian population based study for transmission estimates recommend assigning 'low to intermediate' risk profiles to melanomas <0.8mm tumour thickness,[237] these risk profiles are also summarised in the table below.

For melanomas of thickness >0.8mm, risks of recurrence may be greater than 10%, depending on features and site.[241] In addition to tumour thickness, factors including ulceration, presence of mitoses, head and neck site,[243] nodular or acral subtype and male sex have an adverse impact on recurrence rates.[244] It is current practice to propose a sentinel lymph node biopsy to adequately stage melanomas thicker than 1mm with no detectable clinical evidence of metastases. Although a positive sentinel node should exclude such patients, negativity of the sentinel node is a reassuring feature and reduces dramatically the risk of recurrence.[242] Finally, studies reporting conditional survival in melanoma patients take into account the time elapsed since diagnosis and re-evaluate the risk of recurrence. Although this risk is dramatically reduced after 2 and 5 years for most invasive melanomas (except those with a positive sentinel node),[245] it does not exclude a late recurrence.[242] Melanoma Institute Australia (MIA) provides a risk calculator for estimating the recurrence risk associated with thin melanomas up to 1mm, as well as estimates of recurrence free survival for thicker (Stage II) melanomas, Risk Calculators | Melanoma Institute Australia.[239,240]

Melanoma cells may spread to distant sites in the early stages of cancer progression and can stay dormant and clinically undetectable for many years and even decades after resection of the primary tumour.[246] Transplantation of an organ with dormant melanoma micrometastases into an immunosuppressed host may lead to metastatic growth in the recipient,[247,248,249] with generally poor survival outcomes.[250,251] Use of life saving organs might still be considered in certain circumstances, however, after discussion with a melanoma specialist and with informed consent of the recipient.

Uveal and mucosal melanoma pose an unacceptable risk to donation, given their high risk of undetected micrometastases, regardless of the length of disease-free survival.[252,253,254] Cutaneous melanoma with a history of nodal metastasis or distant metastasis also poses an unacceptable risk.

Donors with a history of invasive melanoma should only be accepted in cases where sufficient information is available to make a determination of risk status. If sufficient information is not available to determine risk status (e.g. histology report unavailable or short duration of cancer follow-up time), donation should only be considered in exceptional circumstances.

Investigations	Risk calculation	Tumour details	Organs to consider
Obtain data about tumour stage (including thickness, ulceration and presence of mitoses), nodular or acral type, location of lesion, sentinel node status, previous therapy, type of follow-up or recurrence-free time and then evaluate risk of metastasis with a dermato-oncologist before considering for organ donation. *NB*: distant historical records of the removal of a melanoma may not be recorded in the donor's current home state cancer registry.	Minimal (<0.1%)	*In situ* cutaneous melanoma (T0)	All organs may be considered for transplantation
	Low (0.1% to <2.0%)	History of invasive cutaneous melanoma with tumour thickness <0.5mm, non-ulcerated, located on trunk, upper and/or lower limbs, completely resected. *NB*: history of invasive cutaneous melanoma of the head and/or neck sites carry a higher risk.[243]	Likely to be acceptable for many organ types and recipients
	Intermediate (2.0% to <10%)	Tumour thickness 0.5–0.8 mm (T1a), no ulceration, nodal status unknown, and completely resected **OR** Tumour thickness: — ≤1 mm with ulceration, or ≤2 mm without ulceration (T1b–T2a, N0, M0), **and** — Completely resected and cancer-free for >10 years, **or** — Sentinel node negative and cancer-free for >5 years *NB*: In this group, 10-year survival after 5 years cancer-free is ~92%.[255]	May be acceptable for some organ types and recipients. Consider on a case-by-case basis after consultation with a surgical oncologist or medical oncologist with expertise in melanoma management.
	High (>10%)	History of invasive cutaneous melanoma with: — Tumour thickness ≤1 mm with ulceration, or ≤2 mm without ulceration (T1b–T2a, N0, M0), **and** — completely resected and cancer-free for <10 years, or sentinel node negative for <5 years **OR** — Tumour thickness 1–2 mm with ulceration (T2b, N0, M0), **and** — completely resected and cancer-free for >10 years, or sentinel node negative for >5 years	Consider using organs where the recipient would be at imminent risk of death without the transplant. Consider on a case-by-case basis after discussion with a melanoma specialist and obtaining informed consent from the recipient
	Unacceptable risk	Any of the above melanoma categories **with a positive sentinel node**, or tumour thickness >2 mm (T3–T4) **OR** Tumour thickness 1–2 mm with ulceration (T2b) **and** cancer-free period <10 years **OR** Melanoma with: — Nodal involvement (N1 or higher), **or** — Distant metastasis (M1) **OR** Uveal melanoma **OR** Mucosal melanoma	None
	Unknown	Reasonable suspicion that the potential donor has had a cutaneous melanoma treated in the past and there is a surgical scar to confirm that a skin lesion has been widely excised, or a sentinel node biopsy has been performed but no further histological information or no cancer/ treatment follow-up details are available despite extensive enquiry	Consider only in exceptional circumstances where the recipient would be at imminent risk of death without the transplant

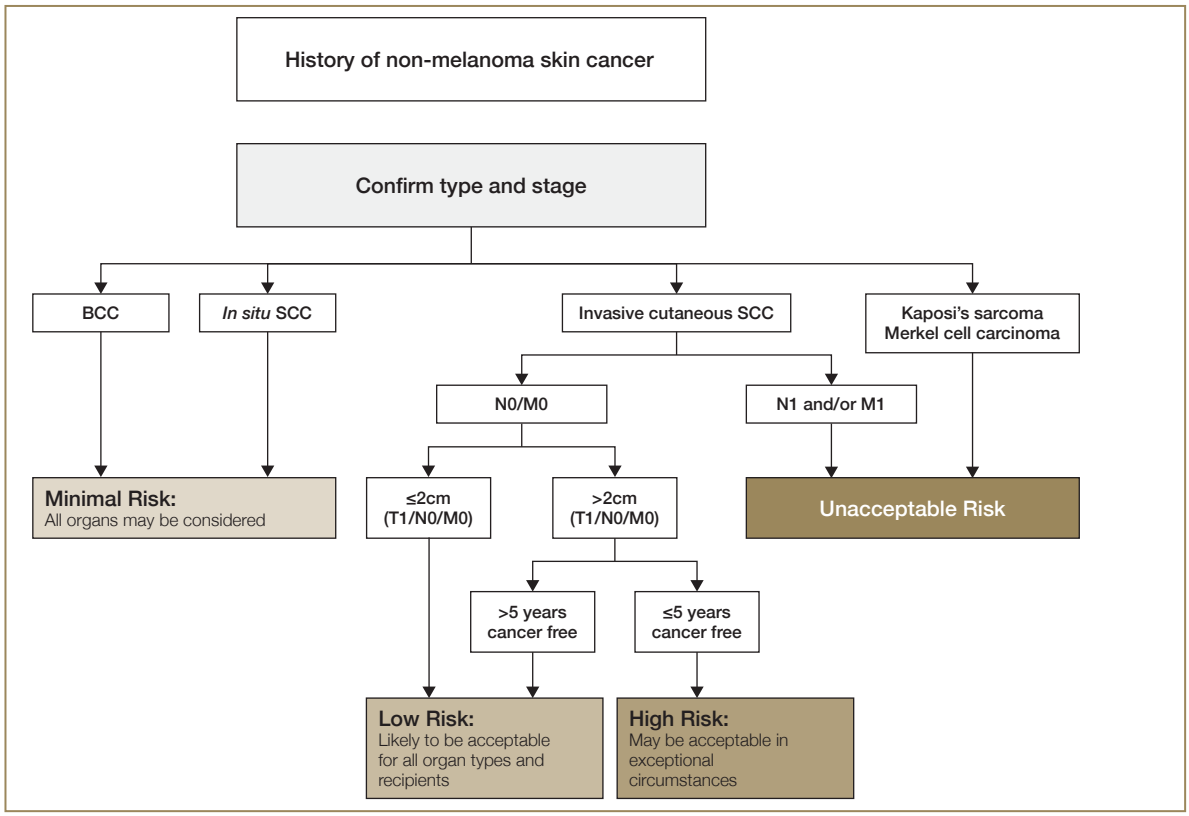
2.4.5 Non-melanoma skin cancers

Non-metastatic keratinocyte cancers (basal cell and squamous cell carcinoma of the skin) are the most common malignancy encountered in donors and are not considered a contraindication to donation. All basal cell carcinoma (BCC) and the majority of squamous cell carcinoma (SCC) are considered minimal-to-low risk of transmission: a UNOS database report including 776 recipients of organs from donors with BCC and SCC of the skin reported no incidence of disease transmission.[216]

Potential donors with a history of a large SCC (>2cm) and fewer than 5 years of recurrence free follow-up, however, pose a higher risk of transmission and should be considered on a case-by-case basis.[256] For donors with more than 5 years of recurrence-free follow-up, the risk of SCC transmission is low, regardless of tumour size.

Other types of cancers manifesting on the skin, such as Kaposi sarcoma (see Section 2.3.2.7), spindle cell carcinoma and Merkel cell carcinoma, pose an unacceptable risk to transplantation.

Figure 2.4: Decision flow chart for potential donors with a history non-melanoma skin cancer



Investigations	Risk	Tumour details	Organs to consider
Seek to obtain a pathology report for any skin lesion that has been widely excised (particularly on the head and neck) in the context of any reported history of skin cancer. Obtaining the pathology report will minimise the risk of missing a squamous cell carcinoma or melanoma misreported in the donor history as basal cell carcinoma. Consider tumour stage at diagnosis, previous therapy, type of follow-up or recurrence-free time and then evaluate metastatic risk before considering for organ donation.	Minimal (<0.1%)	Basal cell carcinoma *In situ* squamous cell carcinoma	All organs may be considered for transplantation.
	Low (0.1%-<2.0%)	History of invasive cutaneous squamous cell carcinoma, T1 (N0, M0) History of invasive cutaneous squamous cell carcinoma T2 and above (N0/M0) with curative surgery and cancer free period >5 years	Likely to be acceptable for all organ types and recipients.
	Intermediate (2.0%-<10%)	–	–
	High (≥10%)	History of invasive cutaneous squamous cell carcinoma T2 and above (N0, M0) with cancer free period <5 years	May be acceptable in exceptional circumstances e.g. where the recipient faces an imminent threat to life. Consider on a case-by-case basis with informed consent from the recipient.
	Unacceptable risk	Kaposi's sarcoma Merkel cell carcinoma History of SCC with nodal involvement and/or distant metastases	None.
	Unknown	Reasonable suspicion that the potential donor has had a non-melanoma skin cancer treated in the past and there is a surgical scar to confirm that a skin lesion has been widely excised but no further histological information is available despite extensive enquiry	May be acceptable according to the circumstances and clinical judgement.

2.4.6 Solid organ tumours

2.4.6.1 Breast cancer

Given the potential for late recurrence and metastasis, organs from donors with a history of invasive breast cancer should only be considered where specific criteria indicative a low risk of transmission are met.[257,258] Organs from donors with a history of Stage I (T1A, node-negative) hormone receptor-negative breast cancer may be considered where there has been full treatment and complete remission with follow-up for >5 years.[259] All other invasive breast cancer is considered high-risk of transmission, regardless of the duration of recurrence-free survival. For hormone positive breast cancer, the cumulative risk of recurrence at 20-25 years post-treatment is high, even for Stage 1 disease.[257,258] For Stage I oestrogen-receptor positive breast cancer without nodal involvement, there is a 13% risk of recurrence at 20 years.[257] Given the late recurrence associated with hormone-positive breast cancer, donors with a history of cancer of this type have a high risk of malignancy transmission.

While lobular breast cancer is usually of greater clinical concern, in terms of the risk of distant recurrence the risks are similar between lobular and ductal carcinoma of the breast.[260] Hence, in the context of assessing risk of transmission in the case of a Stage I breast cancer with >5 years recurrence free survival, it is reasonable to group lobular and ductal carcinoma together.

Where donors have a known history of invasive breast cancer but critical information on cancer pathology, treatment history, and/or receptor status are unavailable, donation should only be considered under exceptional circumstances for recipients facing an imminent threat to life. Invasive breast cancer diagnosed during retrieval poses an unacceptable risk to potential transplant recipients.

It is important to verify breast cancer history as reported by donor proxy/next of kin, to rule out the possibility of misreporting. Every effort should be made to establish that breast cancer was present as reported before excluding a potential donor from further investigation.

Ductal carcinoma *in situ* poses minimal risk of donor-derived transmission and does not preclude organ donation.

Investigations	Risk	Tumour details	Organs to consider
Investigations should include a thorough review of donor medical records and pathology reports to confirm existence of prior breast cancer and to determine stage, receptor status, treatment, and follow-up history	Minimal (<0.1%)	Ductal carcinoma *in situ*	All.
	Low (0.1%-<2.0%)	Stage Ia (T1/N0/M0) hormone negative breast cancer treated with curative surgery +/- chemotherapy and no recurrence for >5 years. Risk of transmission is estimated to be similar for lobular and ductal carcinoma with this staging.	All organs may be considered for donation with the informed consent of the recipient.
	Intermediate (2.0%-<10%)	–	–
	High (≥10%)	All other invasive breast cancer in the donor history (regardless of recurrence free period)	May be acceptable in exceptional circumstances e.g. where the recipient faces an imminent threat to life.
	Unacceptable risk	Breast cancer diagnosed during retrieval	None.
	Unknown	Where a donor has a confirmed history of invasive breast cancer, but critical information on cancer pathology, treatment history and/or receptor status is unavailable, donors should be considered high risk of cancer transmission	May be acceptable according to the circumstances and clinical judgement.

2.4.6.2 Choriocarcinoma

Choriocarcinoma of any stage is considered an unacceptable risk for organ transplantation. Choriocarcinoma is a highly aggressive, malignant trophoblastic cancer arising after hydatidiform mole, pregnancy, ectopic pregnancy, miscarriage or termination. Cases of undetected choriocarcinoma in donors resulting in multiple transmissions demonstrate the malignancy of choriocarcinoma in immunosuppressed recipients.[230,261] Female donors of child-bearing potential should have their blood levels of beta human chorionic gonadotrophin hormone tested to detect metastatic choriocarcinoma, especially if the cause of death is unexplained intracerebral haemorrhage.

2.4.6.3 Colorectal cancer

Based on an exceedingly low risk of nodal or metastatic disease associated with Stage I (T1, node-negative) colorectal cancers in the general population, a 2003 US consensus conference endorsed the use of such donors in certain circumstances.[262] In donors with Stage I familial adenomatous polyposis, however, the pancreas should be excluded from transplantation due to the increased risk of cancers in the duodenum, although some other organs may be acceptable according to the circumstances and clinical judgement. In donors with familial adenomatous polyposis where the colon remains *in situ*, given the immense number of polyps it would be impossible to rule out the presence of a malignant lesion. The risk of malignancy transmission in this circumstance would therefore most accurately be classified as unknown.

Stage II or higher colorectal cancer diagnosed at retrieval, or in the donor history with a cancer-free duration ≤10 years, poses an unacceptable risk of transmission to recipients. It is important that pathology reports are available to definitely establish cancer stage before proceeding with transplantation. Retrieval surgeons should carefully examine all intra-abdominal and intra-thoracic structures for suspicious lesions.

Investigations	Risk	Tumour details	Organs to consider
Investigations should include a thorough review of donor medical records, pathology reports and colonoscopy reports to confirm existence of prior colorectal cancer and to determine stage, treatment, and follow-up history. Absence of this information does not necessarily rule out donation, but it would be helpful as supporting evidence that the cancer history is low-risk. Donor surgeons should carefully examine all intra-abdominal and intra-thoracic structures for suspicious lesions at the time of organ retrieval.	Minimal (<0.1%)	Carcinoma *in situ*	All organs may be considered for transplantation.
	Low (0.1%-<2.0%)	Colorectal cancer Stage I (T1/N0/M0) with curative surgery and cancer free survival >5 years (excluding familial adenomatous polyposis)	Likely to be acceptable for many organ types and recipients.
	Intermediate (2.0%-<10%)	–	–
	High (≥10%)	Colorectal cancer Stage I (T1/N0/M0) diagnosed during organ retrieval History of Stage IIa (T3/N0/M0) colorectal cancer with curative surgery and cancer free survival >10 years	May be acceptable in exceptional circumstances e.g. where the recipient faces an imminent threat to life.
	Unacceptable risk	All other colorectal cancer	None.
	Unknown	Possible or confirmed history of colorectal cancer reported but pathology report not available Donor with familial adenomatous polyposis where the colon remains *in situ*	May be acceptable according to the circumstances and clinical judgement.

2.4.6.4 Gastrointestinal stromal tumour

Gastrointestinal stromal tumours (GIST) account for 4-5% of soft tissue sarcomas and 1-2% of all gastrointestinal malignancies.[263,264] Incidence of clinically diagnosed GIST is relatively low (an estimated 14 cases per million per year in Australia[265] and approximately 10-20 cases per million per year in Europe[266]); however, small, subclinical GISTs are common in adults.[267,268,269] The median age of people diagnosed with GIST is 60-65 years; paediatric GIST is a rare and clinically distinct subset of the disease.[270] GISTs can involve almost any segment of the gastrointestinal tract but most commonly occur in the stomach (60%), jejunum and ileum (30%), duodenum (4-5%), or rectum (4%).[266]

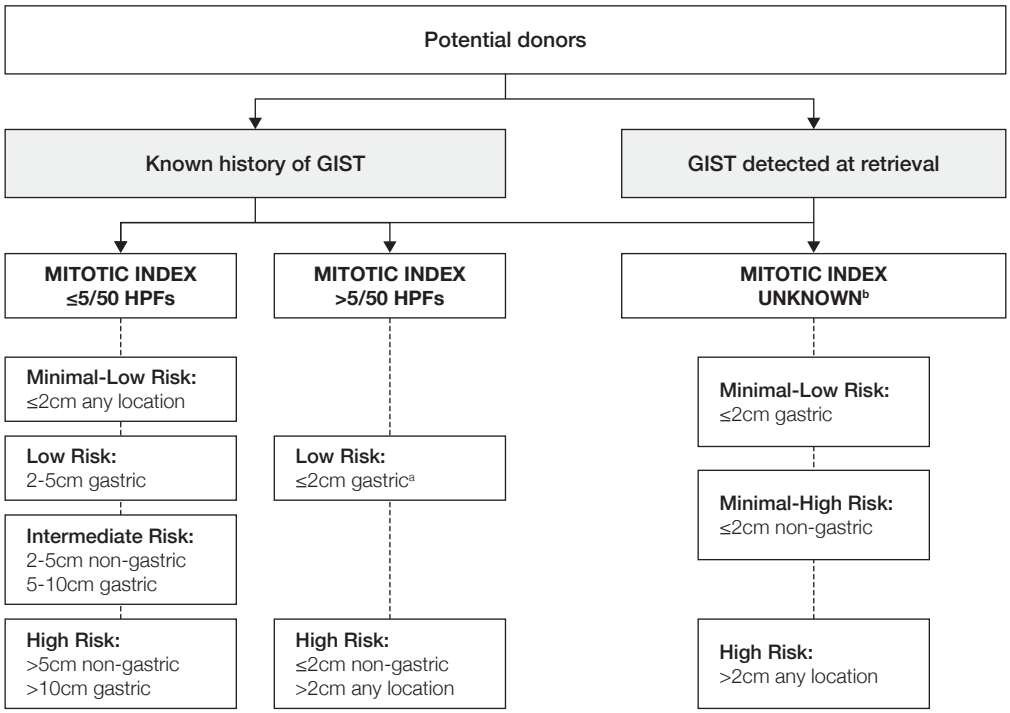
The median disease-free survival after GIST resection is approximately 3 years.[271] The main prognostic factors are: (i) tumour localisation (site and spread) (ii) mitotic index, (iii) tumour size, and (iv) tumour rupture before or during surgery.[271,272] Gastric GISTs have a more favourable prognosis and lower risk of metastases than GIST occurring at other primary sites, such as the small intestine.[266] The metastatic potential of GISTs exists on a spectrum from small, inactive tumours to larger, mitotically active tumours;[273] metastasis, where it occurs, is typically to the abdominal cavity or liver and may occur many years after treatment of the primary tumour.[266,269,274]

European guidelines state that donors with a history of gastric or duodenal GIST <2cm with mitotic index ≤5 per 50 high power fields (HPFs) have a low risk of metastases and may be acceptable for organ donation with low-to-intermediate risk of transmission.[224] A case series from Italy of five GISTs diagnosed during donor retrieval, all under 2cm and with mitotic index ≤5/50 HPFs, reported no evidence of transmission after a minimum of 18 months follow up from the three organs transplanted (two kidneys from a single donor and a liver from a second donor).[275] The Miettinen risk criteria define GISTs ≤2 cm as having zero risk of progressive disease over long term follow up, with gastric GISTS up to 5cm associated with a very low risk of progressive disease.[269]

GIST from primary sites other than the stomach that are >2cm and/or have a mitotic count >5/50 HPFs are likely to be associated with a higher risk of malignancy transmission, based on reported relapse rates on long-term follow-up of people with GIST.[269,271,274,276] The exact risk of transmission will also depend on the treatment received, follow-up time and duration of recurrence free survival. A disease-free period of more than 3 years is likely to indicate lower risk of transmission.[271]

In the context of GIST discovered during retrieval, the degree of risk is related to where the tumour is located, its size, and its mitotic count. As it is unlikely to be possible to obtain biopsy results and mitotic index in the timeframe required for organ transplantation, in this circumstance all known information about the tumour should be considered (i.e. size, location) and weighed against the risks to the recipient in the absence of transplantation. Gastric GISTS ≤2cm diagnosed at the time of retrieval are likely to be low risk, although minimal data are available on which to base recommendations.

Figure 2.5: Decision flow chart for potential donors with a history of gastrointestinal stromal tumour (GIST) or GIST detected at the time of organ retrieval



[a] Minimal data available on which to base risk assessment

[b] Where mitotic index is not available, all known information about the tumour should be considered and weighed against the risks to the recipient in the absence of transplantation

Investigations	Risk	Tumour details	Organs to consider
For donors with a history of GIST, information on mitotic index, tumour size prior to treatment, tumour site and the treatment delivered should be obtained. Where GIST is diagnosed during donor retrieval, excisional biopsy is recommended, noting however that it will be unlikely to be possible to obtain mitotic index prior to transplantation. Mitotic rate should still be requested, however, to support post-transplant management.	Minimal (<0.1%)	History of treated GIST ≤2cm (N0/M0) with mitotic count ≤5/50 HPFs and cancer free survival > 3 years	Likely to be acceptable for all organ types and recipients.
	Low (0.1%-<2.0%)	History of treated gastric GIST >2-≤5cm (N0/M0) with mitotic count ≤5/50 HPFs and cancer free survival > 3 years History of treated gastric GIST ≤2cm (N0/M0) with mitotic count ≥5/50 HPFs and cancer free survival > 3 years Gastric GIST ≤2cm diagnosed during organ retrieval	Likely to be acceptable for many organ types and recipients.
	Intermediate (2.0%-<10%)	History of treated gastric GIST 5-10cm (N0/M0) with mitotic count ≤5/50 HPFs and cancer free survival > 3 years History of treated non-gastric GIST >2-≤5cm (N0/M0) with mitotic count ≤5/50 HPFs and cancer free survival > 3 years	May be acceptable for some organ types and recipients.
	High (≥10%)	History of treated gastric GIST >10cm (N0/M0) with mitotic count ≤5/50 HPFs and cancer free survival > 3 years History of treated non-gastric GIST >5cm (N0/M0) with mitotic count ≤5/50 HPFs and cancer free survival > 3 years History of treated non-gastric GIST ≤2cm (N0/M0) with mitotic count >5/50 HPFs and cancer free survival > 3 years History of any treated GIST >2cm (N0/M0) with mitotic count >5/50 HPFs and cancer free survival > 3 years Any non-gastric GIST diagnosed during organ retrieval Any gastric GIST >2cm diagnosed at retrieval	May be acceptable in exceptional circumstances e.g. where the recipient faces an imminent threat to life. Risk of liver metastases may preclude use of the liver from a donor with history of high-risk GIST.
	Unacceptable risk	Any GIST diagnosed at retrieval or in the donor history with the presence of distant metastases. Any history of GIST without complete prior surgical excision or with <3 years cancer-free survival	None.
	Unknown	Reported history of GIST with unknown mitotic count	May be acceptable in exceptional circumstances according to the circumstances and clinical judgement.

2.4.6.5 Lung cancer

A history of lung cancer of any stage poses an unacceptable risk to organ transplantation. Registry and case reports of transmission of occult donor lung cancer by kidney transplantation, with generally fatal outcomes in recipients, are indicative of very aggressive behaviour of donor-transmitted lung cancers.[277,278,279]

Lung adenocarcinoma *in situ* (AIS) has a low risk of distant metastases and a low risk of recurrence, and therefore theoretically may be associated with a lower risk of transmission from organ donors to recipients. However, a definitive diagnosis of AIS is difficult to determine, as lesions may be multifocal and it is not possible to guarantee that there are no parts of the lesion with an invasive component. Theoretically – if a definitive diagnosis of AIS could be made – use of non-lung organs might be considered, recognising a small but real risk of disease transmission. In practice, donors with a diagnosis of AIS are unlikely to be suitable for donation of any organs.

Benign pulmonary nodules – such as hamartomas and papillomas – are relatively common especially after 45 years of age, hence it is important to distinguish between benign tumours in the lung and lung cancer in the donor. Donor assessment should include smoking history and appropriate imaging (CT) when indicated on the basis of an abnormality noted on chest x-ray or in the donor history, with review by a radiologist +/- respiratory physician. If available, any prior chest imaging should be reviewed for comparison. Lung bronchoscopy of potential lung donors is commonly deployed in all jurisdictions (where possible) and would permit visualisations of any endobronchial lesions.

Pulmonary hamartomas, which are common benign lesions, can be confidently diagnosed on CT. Other lesions may need to be assessed intraoperatively and a frozen section taken, especially in the context of significant smoking history or any suspicious signs on chest CT.

2.4.6.6 Neuroendocrine neoplasms

Neuroendocrine neoplasms mainly arise in gastrointestinal, lung or pancreatic tissue, but can be detected anywhere and may occur in multiple sites throughout the body. Although neuroendocrine neoplasms are rare, the rate of diagnosis of neuroendocrine neoplasms in Australia has doubled since the early 1980s and they are one of the most common incidental findings on organ retrieval.[280] Neuroendocrine neoplasms are divided based on histological differences into well-differentiated neuroendocrine tumours (NETs), poorly differentiated neuroendocrine carcinomas (NECs), and mixed neuroendocrine-non-neuroendocrine neoplasms (MiNENs).[281] Well-differentiated NETs are further divided into Grades 1 (low), 2 (intermediate), and 3 (high) based on mitotic rate and Ki-67 proliferation index; NECs are considered poorly differentiated and high-grade by definition and may be of small-cell or large-cell type.[282]

There have been multiple reports of donor-derived transmission of undetected high-grade NETs and small-cell NECs from liver and kidney donors, resulting in explant and/or death.[283,284,285] NETs and NECs detected during organ retrieval pose an unacceptable risk for organ transplantation, given the known metastatic potential of these cancers and the likelihood of undetected micrometastases[224] There may be certain circumstances of low-grade NETs found at the time of retrieval where the risk might be theoretically acceptable (e.g. small carcinoid tumours or multiple small NETs of the stomach), if supported by a good histological evaluation and if the recipient faces an imminent threat to life. In practical terms, however, it is unlikely that a full histological evaluation including Ki-67 and mitotic count could be performed within the donation window to permit accurate grading and prognostication. Without the additional reassurance of documented, long-term, recurrence free survival, any neuroendocrine neoplasm detected at retrieval poses an unacceptable risk to organ transplantation.

Donors with a history of Grade 1 or 2 NET, successfully treated with a recurrence-free survival of more than 5 years and without lymph node involvement or metastases, may be considered low risk for malignancy transmission, provided the history is well documented and the person had been closely followed up. Limited evidence exists, however, to guide practice with respect to well-differentiated, low-grade neuroendocrine tumours. Even low-grade NET can metastasise, depending on the location, with late metastases up to 20 years after initial resection possible.[286] Factors correlated with higher risk of NET spread include male gender, extra-adrenal location, greater tumour weight, confluent tumour necrosis, vascular invasion and extensive local invasion.[287] All information in the donor history should be taken into account and a careful risk-benefit assessment made when determining whether to proceed with donation.

A history of Grade 3 NET poses an unacceptable risk for organ donation regardless of the duration of recurrence-free follow-up, given the known risk of late metastases. Similarly, a history of MiNEN is an unacceptable risk for organ transplantation.

Table 2.11: Classification and grading criteria for neuroendocrine neoplasms of the gastrointestinal tract and hepatopancreatobiliary organs (source: The 2019 WHO classification of tumours of the digestive system, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7003895/)

Terminology	Differentiation	Grade	Mitotic rate[a] (mitoses/2mm^2)	Ki-67 index[b]
NET, Grade 1	Well-differentiated	Low	<2	<3%
NET, Grade 2		Intermediate	2-20	3-20%
NET, Grade 3		High	>20	>20%
NEC, small-cell type	Poorly differentiated	High[c]	>20	>20%
NEC, large-cell type			>20	>20%
MiNEN	Well or poorly differentiated[d]	Variable[d]	Variable[d]	Variable[d]

MiNEN, mixed neuroendocrine-non-neuroendocrine neoplasm; NET, neuroendocrine tumour; NEC, neuroendocrine carcinoma

[a] Mitotic rates are to be expressed as the number of mitoses/2mm^2 as determined by counting in 50 fields of 0.2 mm^2 (i.e. in a total area of 10 mm^2).

[b] The Ki-67 proliferation index value is determined by counting at least 500 cells in the regions of highest labelling (hot-spots), which are identified at scanning magnification; the final grade is based on whichever of the two proliferation indexes places the neoplasm in the higher-grade category.

[c] Poorly differentiated NECs are not formally graded, but are considered high grade by definition.

[d] In most MiNENs, both the neuroendocrine and non-neuroendocrine components are poorly differentiated, and the neuroendocrine component had proliferation indices in the same range as other NECs, but this conceptual category allows for the possibility that one or both components may be well-differentiated; when feasible, each component should therefore be graded separately.

Investigations	Risk	Tumour details	Organs to consider
For donors with a history of neuroendocrine neoplasm, information on differentiation, grade, mitotic index, Ki67 and nodal involvement, should be obtained. The type of treatment received (past or present), results from colonoscopies and any imaging for distant metastasis will also be relevant to donor risk assessment.	Minimal (<0.1%)	–	–
	Low (0.1%-<2.0%)	History of Grade 1 or 2 NET (N0/M0) with a well-documented history of cancer-free survival of >5 years	Likely to be acceptable for many organ types and recipients. Histological confirmation of tumour grade and prognostic classification*, details of tumour pathology, and documented follow-up are critical.
	Intermediate (2.0%-<10%)	–	–
	High (≥10%)	–	–
	Unacceptable risk	NET or NEC detected at retrieval History of Grade 3 NET Any history of NEC History of neuroendocrine neoplasm where pathology reports are unavailable or there is incomplete follow-up	None.

NET, neuroendocrine tumour; NEC, neuroendocrine carcinoma

* WHO 2019 Classification: Grade 1-3 well-differentiated NET defined by histological grade (low/intermediate/high), mitotic rate (<2/2-20/>20mitoses/2mm2) and ki67 index (<3%/3-20%/>20%).

2.4.6.7 Oesophageal, gastric, pancreatic, liver and biliary cancers

All oesophageal, gastric, pancreatic, liver or biliary cancers diagnosed during organ retrievalpose an unacceptable risk to organ transplantation. Given the number of fairly common benign liver tumours, however, it is important to confirm whether a tumour identified at retrieval is malignant before ruling out donation.

If identified in the donor history, treated tumours of these sites are also generally considered an unacceptable risk, given the aggressive nature of these cancers and a high risk of recurrence. Theoretically, risk may decrease following curative therapy and >5 years recurrence-free survival; however, given the high mortality rate for these cancers, this is not a common scenario and only a few isolated case reports of malignancy transmission exist involving donors with oesophageal,[288] gastric,[289] pancreatic,[290,291,292] liver[290] or biliary cancer.[293]

In the case of pancreatic cancer, an exception to the recommendations above are intraductal papillary mucinous neoplasms (IPMNs). Intraductal Papillary Mucinous Neoplasms (IPMNs) are considered potential precursors to the development of pancreatic cancer. They are a frequent finding on imaging in the ageing population and are for the most part benign. Persons with branch duct IPMN <3cm without any other "worrisome features"[294] of cancer are at low risk and may be considered for donation (excluding pancreas or islets). Branch duct IPMN ≥3cm is thought to carry greater risk of malignancy and whether to proceed will be at the discretion of the teams involved. Donation would usually not be appropriate in the context of features such as a solid component, suspicious nodal disease, or a main duct IPMN >10mm in diameter.

2.4.6.8 Oropharyngeal cancer

Oropharyngeal cancer diagnosed during orgretrievalposes an unacceptable risk to organ transplantation.

For donors with a history of treated oropharyngeal cancer and recurrence free survival >5 years, there may be certain acceptable risk scenarios, although minimal evidence exists on the outcomes of transplantation from donors with a history of oropharyngeal cancer.[295] In the context of early non-metastatic lesions that verge on being *in situ*-type lesions, donation may be acceptable in exceptional circumstances according to recipient need and clinical judgement. Oropharyngeal cancer associated with human papilloma virus (HPV) may also pose a lower risk of donor derived malignancy transmission, given that HPV-positive head and neck cancers have been demonstrated to respond better to treatment,[296] have better survival outcomes,[297,298] and lower rates of distant metastases than HPV-negative cancers.[299,300] Despite a more favourable prognosis, however, recurrence rates for HPV-positive cancers remain at 13-25% within 2 years, and up to 36% within 8 years of treatment.[297,301,302]

2.4.6.9 Ovarian cancer

Ovarian cancer is considered an unacceptable risk for organ donation.

Although risk may theoretically be diminished in the circumstance of curative surgery and lengthy recurrence-free survival (>10 years), this is an uncommon donation scenario and there are no data to support safe use of such donors.

In the event that an abnormal mass if found on the ovary during retrieval, a diagnosis on frozen section should be sought to inform if organs need to be respectfully disposed.

2.4.6.10 Prostate cancer

In Australia and New Zealand, there is a high prevalence of low-grade, non-aggressive prostate cancer among men over 50 years of age.[303] Prostate cancer confined to the prostate has a minimal-to-low risk of transmission and is likely to be present in many male donors without consequence for recipients. An autopsy series of "healthy" organ donors found that 23% of those aged 50-59 years, 35% of those aged 60-69 years, and 46% of those 70-81 years had undiagnosed prostate cancer.[304] There is no evidence, however, of increased rates of prostate cancer among transplant recipients relative to the general male population.[305,306] From 120 reports of organ transplants from donors with confirmed prostate cancer, there has been only one case of disease transmission.[307] In this case, prostate adenocarcinoma was transmitted by heart transplantation from a donor subsequently found to have metastatic disease involving the lymph nodes and adrenal gland.[308] A meta-analysis of the outcomes of kidney transplantation from donors with prostate cancer supports the conclusion that the risk of transmitting prostate cancer is lower than the risk of remaining on the waiting list.[309]

For donors with no history of prostate cancer, routine prostate specific antigen (PSA) screening is not recommended. PSA results in this group are likely to be unreliable due to elevation caused by catherization and routine PSA testing would likely result in unnecessary investigations. In addition, numerous benign prostate pathologies will cause an elevation in PSA.[310]

For donors with a known history of prostate cancer, PSA testing may be appropriate in situations where it is necessary to rule out prostate cancer recurrence or spread; in this circumstance, a PSA level that is undetectable or below 0.1 usually indicates minimal risk of transmission. If PSA is elevated (>6.5), organs may still be acceptable for many recipients. Isolated PSA results must, however, be interpreted with caution. In donors with a history of prostate cancer, results should ideally be interpreted in the context of past measures of PSA for that individual. Of greater importance to risk assessment is the prostate cancer grade, stage and disease-free interval.

For donors diagnosed with prostate cancer at the time of retrieval, or where there is a report of prostate cancer in the donor history, whether to proceed with donation will depend on the grade (Gleason score), stage and cancer-free survival for those who have previous surgical treatment. Grade group 1 (Gleason score 6) prostate cancer – which is the majority of prostate cancer diagnosed in Australia and New Zealand – is a largely indolent disease and is associated with minimal risk of transmission by organ donation.[300] There is an almost-zero risk of transmission of prostate cancer out of the prostate to a secondary site when Gleason score is 6.[311] Where Grade group 1 prostate cancer is detected at the time of retrieval or in the donor history, all organs may be safely transplanted. A donor history of treated Grade group 2/3 (Gleason score 7) prostate cancer may also be considered minimal risk, provided the tumour was organ-confined and the donor has been cancer-free for more than 3 years.

Where the donor history indicates the donor has previously received anti-androgen therapy (often delivered in conjunction with radiation therapy), consult with a urologist/oncologist before proceeding to donation. Anti-androgen therapy as a single agent therapy is suggestive of more aggressive disease prior to treatment, therefore risk of transmission is higher, even if PSA is low-to-undetectable at the time of donor evaluation.

Investigations	Risk	Tumour details	Organs to consider
Obtain all data about staging, past therapy, type of follow-up or recurrence-free time before considering for organ donation. PSA screening is not routinely recommended and should be used only for donors where there is clinical suspicion of potential for progressive/ metastatic cancer, depending on the circumstances and whether prior test results are available to compare against.	Minimal (<0.1%)	Prostate cancer with Gleason score ≤6 (Grade group 1, AJCC Stage I) diagnosed at the time of retrieval or in the donor history Past history of organ confined, margin negative, node negative prostate cancer with Gleason score 7 (Grade group 2/3, AJCC Stage II), with cancer-free survival >3 years	All organs may be considered for transplantation.
	Low (0.1%-<2.0%)	Organ confined, node negative tumours with Gleason score 7 (Grade group 2/3, AJCC Stage II), in the donor history or diagnosed at the time of retrieval	Likely to be acceptable for many organ types and recipients. Consider on a case-by-case basis taking into account treatment type (e.g. anti androgen therapy) and follow-up history. Minimal risk of transmission to female recipients.
	Intermediate (2.0%-<10%)	History of organ-confined prostate cancer with Gleason score >7 (Grade group 4, AJCC Stage IIC/IIIA), treated and with cancer free survival >3 years	May be acceptable for some organ types and recipients. Consider on a case-by-case basis after consultation with a urologist/ oncologist, taking into account cancer free duration, treatment and follow-up history. Minimal risk of transmission to female recipients.
	High (≥10%)	Extra-prostatic tumour extension, absent of nodal involvement or distant metastases (AJCC Stage III) in the donor history of diagnosed at the time of retrieval Neuroendocrine prostate cancer in the donor history or diagnosed at the time of retrieval	Consider on a case by case basis for transplantation into female recipients.
	Unacceptable risk	Prostate cancer with lymph nodal or distant metastases (AJCC Stage IV)	None.
	Unknown	Elevated PSA (>6.5) detected during donor work up and/or unconfirmed report of history of prostate cancer	Consider on a case by case basis.

2.4.6.11 Renal cell carcinoma

Suspicious lesions detected during retrieval

If a solid and/or suspicious lesion is found on the kidney at the time of organ retrieval or bench-top assessment, other organs should be assessed for possible involvement and other organ team members notified. Frozen section or urgent histopathology with limited immunostaining may be available to guide decisions. In a single-centre Italian study by Ambrosi et al, 51 incidental solid renal lesions (0.3-3.2cm) identified at the time of retrieval were assessed with frozen section.[312] Of these, 26 (51%) were found to be neoplastic and 25 (49%) were benign. Of all the renal tumours assessed with formal histopathology in this study, 69% were malignant and 31% benign (e.g. angiomyelolipoma, oncocytoma).

In certain situations, especially where cold ischemic time is prolonged, urgent frozen section/histopathological review may not be available or impractical. In these situations, non-renal organs and the contralateral kidney may be considered on a case-by-case basis after consulting with a subject expert and provided a recent imaging shows no evidence of involvement of these organs. Ideally, informed consent of the recipient should be sought prior to proceeding.

Renal cell carcinoma detected during retrieval

There are several case series documenting the safe transplantation of kidneys following renal cell carcinoma (RCC) resection for tumours up to 4cm in size detected at the time of organ retrieval. Pavlakis et al report no cases of malignancy transmission from 21 kidneys following excision of tumour (0.1–2.1cm), as well as no cases of transmission from the transplantation of 47 contralateral kidneys and 198 non-renal organs.[312] Yu et al report 97 cases of kidney transplantation after RCC resection of tumours up to 4cm without transmission. 22 cases of normal contralateral kidney transplants were reported, with one case of transmission (although the diagnosis of the original donor cancer has been questioned in this instance).[313] In the latest systematic review by Villani et al encompassing most available case reports and series, the risk of malignant recurrence after tumour resection prior to transplantation was 2.7%, where utilised kidneys included grade I-II (81.6%) and small tumours (1.26cm) with a mean follow up of 39.9 months.[314]

In the case of a solitary, well-differentiated RCC, the risk of malignancy transmission is minimal (<0.1%) where the tumour is ≤1.0 cm in size, or low (approximately 0.1 – 2.0%) for tumours >1.0 cm to ≤4 cm in size. All organs may be considered for transplantation in the context of an T1a RCC ≤4 cm with nucleolar grade I-II, including transplantation of the affected kidney following tumour resection, provided satisfactory margins are achieved and imaging of the urinary tract has excluded multifocal cancer deposits.[202,315,316] When imaging is not available, the risk assessment may include a discussion with a subject expert.

There are some caveats to utilising these kidneys. Sprott et al. reported a return-to-theatre risk at as high as 39% due to bleeding or urine leak after resection.[317] Although the risk is lower in other reports, this should be a part of the discussion with the potential recipient. Furthermore, careful and formal histopathological analysis with immunohistochemistry is required, as a small percentage of incidental tumours will have unacceptable features such as collecting duct, sarcoma, sarcomatoid or rhabdoid differentiation, or molecularly defined characteristics. Patients with adverse findings on the final histopathology may require early graft nephrectomy. Frozen section and formal histopathology results should be made available to other organ teams even though the risk of metastasis for a small renal cell carcinoma is very small.[318,319,320,321,322,323,324,325,326]

Ongoing surveillance by annual ultrasound is recommended for (i) recipients of kidneys with a resected tumour, given the small risk of recurrence and/or new primary cancer and (ii) recipients of contralateral kidneys, given the risk of developing a new primary.

Bosniak Cysts detected during retrieval

Bosniak cysts can only be defined by radiological imaging with contrast, most typically CT or MRI, which are performed prior to organ procurement.[327] The Bosniak classification of renal cysts describes radiological characteristics of a renal cyst, such as the presence of calcification or septum, septum with contrast enhancement or solid component (either enhancing or non-enhancing) of the lesion. In a systematic review by Sevcenco et al, the pooled risk of malignancy was 3.2% for Bosniak cyst I, 6 % for Bosniak cyst II, 6.7 % for Bosniak cyst IIF, 55.1% for Bosniak cyst III and 91 % for Bosniak cyst IV.[328] Lesions categorised as Bosniak I-II should not be manipulated prior to transplantation, whilst Bosniak cyst IIF could be considered for either monitoring or removal prior to transplantation. For lesions <4cm with Bosniak cyst III–IV, tumour resection prior to transplantation should be offered. The malignant potential of the Bosniak cysts is thought to be driven by the solid component within the lesion and therefore, in direct size comparison to solid lesions, Bosniak cysts may have lower risk of malignancy and transmission.

Renal cell carcinoma in the donor history

If the donor has been diagnosed with RCC <5 years prior to being considered for organ donation, the same risk thresholds defined above for RCC diagnosed at the time of organ retrieval apply. If the diagnosis in the donor was made >5 years ago and there has been recent follow up and/or CT scan showing nothing of concern, risk of transmission may be lower. Follow-up surveillance of recipients is recommended.

Donors with a history of treated RCC >4cm to 7cm in size with nucleolar grade I-II, with cancer-free survival for >5 years may be considered for transplantation of non-renal organs, provided that a recent CT scan shows nothing of concern. Donation of the contralateral kidney in the context of a history of RCC >4–7cm should be considered on a case-by-case basis, after reviewing donor history and follow-up.

A history of invasive RCC (Stage III or IV) or unconventional disease presents an unacceptable risk to organ transplantation.

Investigations	Risk	Tumour details	Organs to consider
If a suspicious renal lesion has been identified during donor work up, a renal US or CT abdo/pelvis (or MRI if indicated) could be performed to determine size, local invasion and position of tumour and presence of tumour in renal vein or IVC. Have a urological surgeon assess tumour in retrieval surgery if possible. Do frozen section or H&E stain histology.	Minimal (<0.1%)	RCC <1cm (diagnosed at retrieval or in the donor history)	All organs may be considered for transplantation, including affected kidney if tumour is close to the surface and resectable, and provided there are satisfactory surgical margins.
	Low (0.1%-<2.0%)	RCC >1 and ≤4 cm, Nucleolar grade I-II (diagnosed at retrieval or in the donor history)	All non-renal organs and the contralateral kidney may be considered for transplantation. The affected kidney may be considered for transplantation following resection, provided there are satisfactory surgical margins, with the informed consent of the recipient.
	Intermediate (2.0%-<10% risk of transmission)	Donor history of RCC >4-7cm with Nucleolar grade I-II, treated and with cancer-free survival for >5 years	Non-renal organs and the contralateral kidney may be considered on a case-by-case basis after consulting with a urologist/oncologist and provided a recent CT scan shows nothing of concern. Seek informed consent of the recipient.
	High (≥10%)	RCC >4-7cm and Nucleolar grade I-II diagnosed at retrieval or within the previous 5 years Donor history of RCC >7cm and Nucleolar grade I-II, treated and with cancer-free survival for >5 years	Non-renal organs and the contralateral kidney may be considered on a case-by-case basis after consulting with a urologist/oncologist and reviewing CT scan (CT needs to be a triple phase CT with 1mm cuts). Seek informed consent of the recipient.
	Unacceptable risk	RCC with extension beyond the kidney (Stages 3 or 4) or local invasion (T3-4), or >4cm tumours with Nucleolar grade III-IV Donor history of RCC >7cm diagnosed within the previous 5 years Unconventional renal malignancy e.g. collecting duct carcinoma, medullary, sarcoma, or any molecularly defined renal tumours such as fumarate hydratase-deficient RCC, or adverse features such as sarcomatoid or rhabdoid differentiation.	None.

2.4.6.12 Sarcoma

For recommendations regarding Kaposi's sarcoma (Human Herpes Virus 8) see Section 2.3.2.7.

Sarcoma detected during retrieval

Given the typically aggressive nature of these tumours, sarcoma diagnosed during retrieval poses an unacceptable risk to organ transplantation. While there are a number of low-grade sarcomas, obtaining a definitive diagnosis in the timeframe required for transplantation is unlikely to be feasible.

Sarcoma in the donor history

Isolated case reports from the literature demonstrate fatal outcomes of transplantation in the context of unrecognised donor sarcoma.[329,330] However, given the vast array of possible soft tissue and bone sarcomas and their heterogeneity with regards risk of recurrence and potential risk of transmission to recipients, potential donors with a history of treated sarcoma and a substantial recurrence-free period should be considered on a case by case basis.

Sarcoma type and associated long-term risk of recurrence, treatment type and era, and length of follow-up are key considerations in assessing transmission risk. As sarcomas are typically very aggressive, a person who is very late into follow-up (20-30 years) is unlikely to carry a high residual risk of cancer transmission.[331] Long term recurrence rates have reduced further in the current era due to improved treatment protocols. Organs from a donor with a distant history (30+ years) of Ewing sarcoma have previously been transplanted in Australia with good outcomes. The long-term data on recurrence of different sarcoma types should be taken into account when evaluating potential donors – particularly in the case of childhood cancers such as Ewing sarcoma.

2.4.6.13 Thyroid cancer

Over the past 30 years, the annual incidence of thyroid cancer diagnosed in Australia has steadily increased, from an age-standardised incidence rate of 3.3 per 100,000 in 1990, to an estimated rate of 14 cases per 100,000 in 2020.[275] Similar increases in the incidence of thyroid cancer have been reported globally, mostly driven by increases in lower stage papillary thyroid cancer and incidental findings of micro-papillary thyroid cancers during surgery for other conditions of the thyroid.[332] In Australia and globally, mortality from thyroid cancer has remained steady, suggesting a degree of overdiagnosis of thyroid cancer in the general population.[333]

The main types of thyroid cancer are:

- Differentiated (including papillary, follicular and Hürthle cell)
- Medullary
- Anaplastic.

Papillary thyroid cancer accounts for approximately 80% of thyroid cancers, and follicular thyroid cancer for another 10%.[334] These cancers generally grow very slowly and are typically low-stage at diagnosis, with only localised spread.[335] Overall, five year relative survival in people with thyroid cancer is 97% and the prognosis for differentiated thyroid cancer is very good until advanced stages of disease.[336,337] Distant metastases develop in 5-23% of people with differentiated thyroid cancer; when these do occur, it is mainly in the lungs and bones.[332] Current clinical practice guidelines recommend total thyroidectomy plus radioiodine for differentiated thyroid tumours greater than 4cm in diameter or tumours of any size associated with multifocal disease, bilateral disease, extra-thyroidal spread (pT3 and pT4a), familial disease or nodal involvement/distant metastases.[332] Post-operative risk of recurrence is low where there is complete resection and the tumour does not have aggressive histology.[338] Late recurrences can occur but can be successfully treated.[332]

The risk of transmission of differentiated thyroid cancer from a donor to a solid organ recipient relates to the size of the tumour and whether it has spread beyond the thyroid. Differentiated thyroid cancers of up to 4cm in size and confined to the thyroid pose minimal risk of donor-derived malignancy transmission, even if detected at the time of organ retrieval. It is important to note that thyroid cancers do not seem to be affected by immunosuppression: pre-existing thyroid cancers do not show increased rates of progression and incidence of thyroid cancer is not elevated in recipients of non-kidney organs – in kidney transplant recipients the incidence of thyroid cancer is not above that of dialysis patients.[339,340] In addition, even widely metastatic differentiated thyroid cancer is amenable to curative therapy, depending on its histology.[332] Hence, even in the event of donor-derived transmission, there could be a reasonable expectation of curative treatment.

Medullary thyroid cancer (MTC) accounts for <5% of thyroid cancer and may be sporadic (approximately 75% of MTC) or familial (approximately 25%).[332] Familial MTC has an earlier age of onset and is more aggressive, with a tendency to spread to the lungs, liver or bones. In confirmed cases of MTC, treatment is total thyroidectomy and central compartment node dissection. Lifelong follow-up is required and there is the potential for local recurrence or distant metastases.[332] For this reason, a history of MTC poses an intermediate-to-high risk to organ transplantation. A history of MTC with nodal involvement or distant metastasis is an unacceptable risk to organ transplantation.

Anaplastic thyroid cancer is a rare (approximately 2% of all thyroid cancers) and aggressive form of thyroid cancer that primarily occurs in people over 65 years of age.[332] All anaplastic thyroid cancers are Stage IV with a poor prognosis (5-year relative survival of 7%).[332] Any history of anaplastic thyroid cancer poses a unacceptable risk to organ transplantation.

Investigations	Risk	Tumour details	Organs to consider
For donors with a confirmed history of thyroid cancer, obtain all data about staging, histology, past therapy, type of follow-up or recurrence-free time before considering for organ donation.	Minimal (<0.1%)	Papillary thyroid microcarcinoma (micro PTC) Differentiated thyroid tumours ≤4cm in greatest dimension limited to the thyroid (T1-T2), with no spread to the lymph nodes (N0) and no metastasis (M0)	All organs can be considered for transplantation.
	Low (0.1%-<2.0%)	Newly diagnosed differentiated thyroid cancer >4cm (T3, M0) Donor history of differentiated thyroid cancer >4cm that has spread into the neck (T4), treated with total thyroidectomy and ≥2 years cancer-free survival	All organs may be considered for donation with the informed consent of the recipient.
	Intermediate (2.0%-<10%)	Differentiated thyroid cancer with extensive spread (T4a) with <2 years cancer-free survival Donor history of medullary thyroid cancer Stage I or II (N0, M0), treated with total thyroidectomy and >5 year cancer-free survival	May be acceptable for some organ types and recipients. Consider on a case-by-case basis, taking into account cancer free duration, treatment and follow-up history.
	High (≥10%)	Differentiated thyroid cancer with aggressive histology or angio-invasion (T4b) with <2 years cancer-free survival Donor history of medullary thyroid cancer Stage III or IV (N0/M0), treated with total thyroidectomy and >5 year cancer-free survival	May be acceptable in exceptional circumstances e.g. where the recipient faces an imminent threat to life. Consider on a case-by-case basis after discussion with an oncologist and obtaining informed consent from the recipient.
	Unacceptable risk	Newly diagnosed medullary thyroid cancers, or history of medullary thyroid cancer with nodal involvement or distant metastasis Any history of anaplastic thyroid cancer (diagnosed at retrieval or in the donor history) Other cancers of the thyroid, including thyroid lymphomas, thyroid sarcomas and other rare tumours History of treated thyroid cancer with incomplete macroscopic tumour resection.	None.

2.4.6.14 Urothelial carcinoma

Superficial, non-invasive papillary carcinoma of the bladder is not a contraindication to organ donation; however, it is important to establish that the cancer is low-grade before proceeding with donation. If urothelial cancer is diagnosed during retrieval, the advice of a urologist should be sought in assessing the tumour prognosis/behaviour in the donor.

If urothelial carcinoma is present in the donor history, donors should only be considered if there has been strict follow-up after primary diagnosis and complete histological information is available, given the high risk of recurrence of these tumours. Risk of recurrence increases (i) with increasing Stage and Grade, (ii) with greater tumour diameter, (ii) where multiple tumours are present, (iv) where there have been one or more prior recurrences, and/or (v) where there is concurrent carcinoma *in situ*.[341] A history of muscle-invasive bladder cancer (T2 and above) poses an unacceptable risk to organ transplantation, unless there is documented evidence of prolonged cancer-free survival. It is possible that the risk of transmission is lower from donors who have previously had a cystectomy and/or chemoradiation and have been cancer-free for >5 years, after which point the risk of recurrence is very low for patients with T1 or T2 disease.[342,343,344] For patients with T3 or T4 disease, the risk of recurrence at 5–10 years post-cystectomy is higher, at around 5%.[344] However, no data are available on the outcomes of transplantation in such circumstances.

Investigations	Risk	Tumour details	Organs to consider
For donors with a confirmed history of urothelial cancer, obtain all data about staging, histology, past therapy, type of follow-up or recurrence-free time before considering for organ donation.	Minimal (<0.1%)	Single low-grade (Grade 1), low stage (Stage 0 – Ta/N0/M0) papillary urothelial carcinoma OR papillary urothelial neoplasm of low malignant potential (PUNLMP)	All organs may be considered for transplantation. Surveillance of kidney recipients recommended due to risk of field changes.
	Low (0.1%-<2.0%)	History of single, low-grade (Grade 1), Stage I (N0/M0) carcinoma	–
	Intermediate (2.0%-<10%)	History of non-muscle invasive low stage (Stage 0-I) high grade (Grade 2-3) urothelial carcinoma, treated with surgery and chemotherapy and with cancer free survival >5 years	Consider on a case-by-case basis for selected recipients after discussion with a urologist. Risk will vary depending on the organ transplanted (e.g. higher risk for kidneys).
	High (≥10%)	Muscle invasive urothelial cancer (Stage II-IV) treated with surgery or radiation +/- chemotherapy and cancer-free survival >5 years Low-grade urothelial carcinoma diagnosed during donor retrieval (other than PUNLMP)	May be acceptable in exceptional circumstances e.g. where the recipient faces an imminent threat to life.
	Unacceptable risk	All other muscle invasive urothelial cancer, all recent high-grade urothelial cancer, donors with a history of recurrent urothelial carcinoma, and/or urothelial carcinoma *in situ* (CIS)	None.
	Unknown	Where a donor has a reported history of urothelial/bladder cancer, but critical information on cancer pathology is unavailable, donors should be considered unacceptable risk of cancer transmission.	None.

2.4.6.15 Uterus and uterine cervix cancer

Invasive uterus or uterine cervix cancer (Stage I or higher) diagnosed at the time of organ retrieval poses an unacceptable risk to organ transplantation. For donors with a history of invasive uterus or uterine cervix cancers, transmission risk may diminish after a disease-free interval of >5 years, however there are minimal data from the literature to support a recommendation, and donors should be assessed on a case-by-case basis.

Pre-cancerous cervical cell changes pose little to no risk to organ transplantation. Low grade squamous intraepithelial lesions (previously graded as CIN1) usually disappear without treatment. High grade squamous intraepithelial lesions (previously graded as CIN2 or 3) and adenocarcinoma *in situ* are pre-cancerous changes but pose minimal risk of donor-derived malignancy transmission.

Investigations	Risk	Tumour details	Organs to consider
For donors with a confirmed history of uterine/uterine cervix cancer, obtain all data about staging, histology, past therapy, type of follow-up or recurrence-free time before considering for organ donation.	Minimal (<0.1%)	Adenocarcinoma *in situ* of the uterine cervix High grade squamous intraepithelial lesions	All organs may be considered for transplantation.
	Low (0.1%-<2.0%)	–	–
	Intermediate (2.0%-<10%)	–	–
	High (≥10%)	Invasive cancer of the uterus or cervix in the donor history with a cancer-free interval >5 years	May be acceptable in exceptional circumstances e.g. where the recipient faces an imminent threat to life.
	Unacceptable risk	Invasive cancer of the uterus or cervix diagnosed at retrieval or in the donor history with a cancer-free interval <5 years	None.
	Unknown	Invasive cancer of the uterus or cervix reported in the donor history with incomplete or no follow-up documentation available	None.

2.4.7 Haematological cancers

Current haematological malignancy poses an unacceptable risk to organ transplantation.

A recent donor history of treated leukaemia, lymphoma or plasmacytoma and <5 years recurrence-free survival is also an unacceptable risk to donation.[345] In the context of donors with a history of treated acute leukaemia or lymphoma and 5 or more years of recurrence-free survival, including childhood leukaemia and Hodgkin's lymphoma survivors, seek expert advice from a haematologist on likely transmission risk.

Utilisation of donors with a history of low-grade haematological malignancies and other clonal haematological disorders has been proposed for certain recipients.[346] These include monoclonal gammopathy of uncertain significance (MGUS) and myeloproliferative neoplasms (MPN) – including polycythaemia vera, essential thrombocythaemia and monoclonal B cell lymphocytosis – all of which have a long natural median survival[347,348] and are becoming more common among donors as the donor population ages. MGUS are found in approximately 4% of the population older than 50 and are usually benign and asymptomatic,[349] hence are likely to be present in many organ donors without consequence for recipients. There have, however been reported instances of donor-derived lymphoproliferative disorders in recipients of solid organ transplants from donors

with MGUS,[350] hence the risk associated with such donors is not negligible. Donors with a known history of MGUS may be acceptable in certain circumstances, following advice from a haematologist. There are no data on transmission risk and the outcomes of transplantation from donors with MPN. Given that the goal of MPN treatment is usually symptom control rather than cure, even in treated patients there remains the potential for clonogenic stem cells to be transmitted with donor organs. It is not known how a transmitted MPN would behave in the immunosuppressed recipient, hence transplantation of organs from donors with a history of MPN is not recommended.

2.4.8 Suspicion of malignancy transmission in an organ recipient

2.4.8.1 Actions in the case of suspected or confirmed donor-transmitted malignancy

The potential for donor-derived malignancy may be identified at any one of three points on the donation pathway:

1. Before organ retrieval (during donor assessment and workup)
2. At organ retrieval (e.g. neoplasia discovered during retrieval surgery)
3. After the transplantation of at least one organ.

When malignancy is detected in the *donor* during workup, surgery, pretransplant organ preparation, or in the immediate post-transplant period, this is an urgent issue requiring immediate notification of all affected transplant units, DonateLife and eye and tissue banks.

In cases where organs have already been transplanted and histology reveals a malignancy (e.g. incidental cancer in a lung lobe discarded due to size reduction), a full donor autopsy should be requested whenever possible to obtain detailed information about tumour origin and dissemination. This will not be necessary in cases of small primary renal cell carcinoma found in one kidney, which would not preclude the transplantation of other organs.

Early diagnosis of donor-transmitted malignancy (within 6 weeks of transplantation) is associated with better survival outcomes. Analysis of the UK transplant registry found that 20% of recipients with a donor-derived cancer of the transplanted organ died as a direct result of cancer; however, where the donor transmitted cancer was detected early, there were no deaths related to the donor transmitted cancer.[202]

Where the possibility of a donor-derived cancer is identified in a recipient at some time after transplantation, DonateLife and Organ Donation New Zealand need to be informed as soon as possible and the origin of the cancer investigated.

Optimal recipient management in the event of a donor transmitted malignancy will depend on the type of tumour, the organ transplanted, the time from transplantation to diagnosis and the patient's immunosuppression regimen. How to proceed will be a joint decision of physician and recipient.

Table 2.11: Actions in the event of confirmed diagnosis of donor malignancy

Point in pathway	Diagnosed how	Actions
1 Before organ retrieval	Malignancy identified during donor assessment and workup	If donors are accepted despite malignant neoplasia: • Detailed histological reports, staging and imaging studies as well as all information and actual diagnostic findings are to be documented on the donor information form • Oncologist advice can be sought (may lead to recommendation for further tests, autopsy etc.) • Transplant centres may take decision to accept the organs • Obtain informed consent from the recipient/their family prior to transplantation • Carry out careful follow-up, bearing in mind the possibility of transmission • Report any possible transmission as per local and national reporting requirements.
2 At organ retrieval and before transplantation	Neoplasia incidentally found during organ retrieval surgery	• Immediately perform frozen section for preliminary diagnosis, subsequent work-up to be done for definite diagnosis: • Immediately alert all relevant transplant units • Transplant units may take decision to accept the organs • Oncologist advice can be sought (may lead to recommendation for further tests, autopsy, etc.) • Obtain informed consent from the recipient prior to transplantation • Carry out careful follow-up, bearing in mind the possibility of transmission • Report any possible transmission as per local and national reporting requirements.
3 After transplantation of at least one organ	a) Frozen section misinterpreted as benign, final diagnosis malignant, or b) neoplasia incidentally found during pre-transplant preparation of the organ in the recipient centre (other organs already transplanted), or c) donor autopsy results available after retrieval and transplantation of organs indicate neoplasia, or d) diagnosis in recipient at any time after transplantation.	• Immediately alert donation agency, relevant transplant units, eye and/or tissue banks • Report any possible transmission as per local and national reporting requirements • Oncologist advice can be sought; include consideration of donor autopsy to identify origin and extent of the primary tumour (not necessary in case of solitary, completely resected small renal cell carcinoma pT1a) • Joint decision of physician and recipient about further action (removal, therapy) on the basis of a risk–benefit analysis • Carry out strict follow-up.

2.5 Risks related to other donor conditions

In addition to the risks of donor-derived infection and malignancy, other pre-existing conditions in the donor may be transmitted via organ donation and transplantation, including some genetic diseases, allergies, and autoimmune diseases. It is critical that any such conditions are thoroughly characterised and conveyed to transplant units as they may influence general donor medical suitability, the suitability for transplantation of specific organs, or require transplant recipients to take particular preventatives measures or receive specific treatments.

2.5.1 Inherited or congenital disorders

There are inherited and genetic diseases which can be transmitted to recipients, depending on the organ transplanted.[351] Other genetic diseases may significantly compromise the function of the organ to be transplanted or cause connective tissue disorders, haematopoietic disorders, or predisposition for malignancy. The possibility of an underlying inherited or congenital disorder should be considered in donors with coagulation disturbance (see below), haemochromatosis, mitochondrial deficiency or mental disorder not related to infection, poisoning or malignancy. Presence of an inherited or congenital disorder in the donor must be defined as clearly as possible and communicated to the transplant programs. ALL known gene abnormalities should be communicated and considered in terms of risk of their transmission and degree of organ damage. If the transplant programs are uncertain about how to proceed, then specialist advice should be sought.

While it is beyond the scope of these guidelines to consider all potential inherited or congenital diseases that may affect the donation decision, some key examples are considered below.

<u>Ornithine transcarbamylase (OTC) deficiency</u>

OTC deficiency is an example of a latent genetic disorder which may cause cerebral oedema leading to neurological death. The onset of such an event can occur in childhood or later in life and may be precipitated by high protein consumption or unusual exercise. Hyperammonaemia is a key feature and should be measured in any patient with cerebral oedema without a clear cause. Transplantation of the liver from a donor with OTC deficiency carries a high risk of recipient fatality through cerebral oedema and is absolutely contraindicated, though other organs may be safely transplanted.[352,353,354]

<u>Alpha-1-antitrypsin deficiency</u>

Recipients of livers from donors with Alpha-1-antitrypsin deficiency are very likely to develop cirrhosis or fibrosis within months to years of transplantation, necessitating re-transplantation. Organ donation is possible, excluding liver and lung donation in the case of emphysematous patients.[355]

<u>Marfan syndrome and related conditions</u>

Due to the impact of Marfan syndrome on vessel walls and the potential for arterial anastomosis failure, organ donation is generally not recommended from donors with this syndrome.[356] Donation of the heart, heart valves, and tissues is absolutely contraindicated, while the utilisation of other organs would require careful consideration. A diagnosis of Marfan syndrome or any other known genetic collagen vascular disorders must be communicated to the transplant programs to allow for careful surgical decision making.

2.5.2 Coagulation disorders

Donation of non-liver organs may be considered from donors with inherited coagulation disorders. Liver transplantation is unlikely to be acceptable, although this depends on the nature of the gene defect and the individual risk-benefit assessment given the transplant urgency and likelihood other offers for a particular recipient. In the case of a donor with antithrombin III (ATIII), protein C, protein S or Factor V Leiden deficiency, the defect will be transmitted and the risk of serious thrombotic events in the recipient is increased.[357] If liver transplantation is to go ahead, recipients must be willing and able to receive anti-coagulation therapy after transplantation. Any severe form of inherited bleeding disorder such as haemophilia A, B or von Willebrand disease would generally contraindicate liver donation.

Autoimmune-related bleeding or pro-coagulant disorders may also influence suitability of organs for transplantation. Liver transplantation is absolutely contraindicated if high levels of factor VIII inhibitor are detected in the donor prior to organ retrieval.[358] A person dying as a result of catastrophic clot arising from anti-phospholipid syndrome would generally be unsuitable due to the risk of thrombosis in donor organs. However, a history of anti-phospholipid syndrome in itself would not contraindicate donation with decision making guided by the severity of the disease.

2.5.3 Allergy and anaphylaxis

Where a potential donor has died from anaphylactic allergy to a known allergen, or has a well-known history of serious allergic reactions, this information needs to be communicated to transplant programs and the recipient informed. Passive transfer of type 1 hypersensitivity reaction from donor to recipient has been reported following liver, lung, intestinal, kidney and heart transplantation.[359,360,361,362,363,364] Although the exact mechanism of this transfer is unknown, the risk of allergy transfer is higher the more lymphoid material that is transplanted, and is therefore greatest in the case of liver, lung, pancreas and intestinal transplantation.[365]

Recipients of organs from donors with a history of allergy and/or anaphylaxis may experience reactions to the same allergens for at least the first 3-6 months post-transplant and must be taught how to avoid such allergen exposure – especially food allergies such as peanut allergy – when the donor history includes anaphylactic reactions.[366]

2.5.4 Autoimmune disease

Donor history of autoimmune or chronic systemic diseases should be conveyed in detail to the transplant programs, as organ function can be affected and may influence suitability for transplantation. Organs from donors with autoimmune diseases can be used for transplantation after exclusion of significant organ damage and/or infections associated with immunosuppressive treatment of autoimmune disorders.

Certain autoimmune diseases may be transmitted by organ transplantation, such as immune haemolytic anaemia and autoimmune thrombocytopaenia, via the transfer of passenger lymphocytes from the donor to the recipient. This usually occurs in the context of liver or lung transplantation, given the greater number of lymphocytes transferred with these organs, but has also been observed in kidney transplantation.[367,368] In many cases this occurs without symptoms, since immunosuppression is also part of the treatment of autoimmune disease. In some cases, however, post-transplant immune-mediated haemolysis can occur, leading to anaemia in the recipient. The potential for immune-mediated haemolysis in the recipient does not preclude organ donation, although the presence of known erythrocyte antibodies in the donor (such as blood group O donor to blood group A or B recipients) indicates prospective monitoring of recipients would be reasonable.

2.5.5 Poisoning

Poisoning is generally not a contraindication to organ donation – people who have died with, or as a result of, drug toxicity or poisoning can become donors. Depending on the agent, organ function can be affected, which may limit the organs which are suitable for transplantation. The decision about whether to proceed depends on whether the organ being considered is functioning adequately, and assessment should be on an organ-by-organ basis. Most drugs and toxins will have been metabolised and excreted prior to organ donation and therefore residual toxicity to the recipient is not routinely a concern.

In the case of some poisoning agents – pesticides in particular – there may be a risk of delayed organ failure, primarily affecting the liver.[369] If the poisoning agent is unusual or if there is uncertainty regarding the impact on organ function, seek toxicology advice.

2.5.6 Donors who have had recent live vaccination

Live vaccines commonly used in Australia are the measles-mumps-rubella (MMR) vaccine, varicella vaccine, zostavax shingles vaccine, and the rotavirus vaccine. Less commonly used are the Bacillus Calmette-Gurin (BCG) tuberculosis vaccine, imojev Japanese encephalitis virus vaccine, yellow fever vaccine, and ACAM2000 mpox vaccine. Of these vaccines, donor transmission to recipients has only been reported for yellow fever vaccine through blood product transfusion, which led to seroconversion in the absence of clinical disease in 3 out of 4 tested recipients (who were all immunocompromised). One recipient died; it is unclear if this death was related to receipt of blood products.[370]

Viremia following vaccination is often studied by nucleic acid detection rather than viral culture.[371] Viremia has been found in a small percentage up to 4 weeks post varicella vaccination,[372] to 2 weeks post zostavax vaccination,[373] to 9 days post measles vaccination of macaque monkeys,[374] to 1-2 weeks post yellow fever vaccination,[375] and to 8 days after imojev vaccination.[376] Disseminated BCG after vaccination is very uncommon and has occurred predominantly in immunocompromised vaccinees.[377] Local injection site reactions are common and drainage which remains culture positive can occur up to 6 weeks after vaccination.[378] ACAM2000 is not commonly used for mpox vaccination in Australia. This vaccinia virus-based vaccine can be cultured from the inoculation site up to day 42 after vaccination, however, was not detected in blood in one study.[379] Rotavirus vaccine is given enterally to infants and remains in the gastrointestinal tract. The Australian Red Cross (Lifeblood) require waiting 4 weeks after live vaccines and 8 weeks after smallpox vaccine before donating blood or platelets.[380]

There is a high degree of uncertainty about the consequences of recent live vaccination of an organ donor for recipients of solid organs. Most live vaccines have not proven to be viscerotropic and viremia rates reduce over several weeks. Prophylactic measures to recipients may protect against clinical manifestations.

The consequences of live vaccine virus transmission may be ameliorated by antivirals or immunotherapies. Varicella zoster immunoglobulin (VZIG) and antivirals or recipient immunity could reduce the effects of varicella and zostavax vaccines. Normal human immunoglobulin (NHIG) or recipient immunity could reduce the effects of MMR vaccine. Mycobacterial agents (isoniazid, rifampicin, ethambutol, moxifloxacin, levofloxacin) are active against BCG vaccine.

Recommendation

Caution should be applied when considering solid organ transplantation from donors who have had live vaccination in the last 4 weeks. It is recommended to discuss risk and mitigation with an infectious diseases physician. Duration since donor vaccination (>2 weeks likely to have lower risk of transmission) and possible risk mitigation are factors to consider. Administration of VZIG and/or antivirals should be considered for organ recipients (particularly who are not immune to VZV) of a donor vaccinated recently with varicella vaccine or zostavax. NHIG should be considered for organ recipients (particularly who are not immune to measles, mumps or rubella) of a donor recently vaccinated with MMR. Anti–mycobacterial agents may be considered for organ recipients of a donor recently vaccinated with BCG.

2.6 Organ distribution and allocation

The allocation of organs is a complex process, influenced by a number of factors including medical need, medical urgency, recipient capacity to benefit, donor/recipient matching, and logistical factors.

The allocation process and specific allocation criteria vary depending on the type of organ to be transplanted, as outlined in Chapters 4 to 10 of this document. Clinical decisions about organ allocation can be very difficult due to the number and variability of factors that must be considered. The development of organ matching algorithms within OrganMatch has streamlined the offering and allocation of donor organs across Australia. Clinical input to assess the medical need and recipient capacity to benefit must be at the forefront of every decision, and it is for this reason that every attempt should be made to uphold the principles of allocation embodied in the Ethical Guidelines.[381]

Transplant units should use donated organs in a way that balances medical need with the likelihood of successful transplantation, taking into account the following general criteria when considering potential recipients for organs:

- Length of time waiting for a transplant, taken from the time that the illness progressed to a point that a transplant would be of immediate benefit
- Important medical factors, such as the closeness of tissue-matching and matching of organ quality to estimated recipient survival
- The urgency of the transplant given the likely deterioration of the patient's health without transplantation, especially if patient survival is immediately threatened by that deterioration
- Medical need, in terms of how sick the patient is without transplantation, and the prospects for transplantation to improve the patient's outcome (both in terms of survival and quality of life)
- Logistical considerations in making the transplant available to the recipient within an appropriate timeframe (see below)
- Anthropomorphic measurements for some organs, especially hearts and lungs.

The time between removal of the organ from the donor and its implantation into the recipient (the ischaemic time) is critical to post-transplantation outcomes. State based allocation (organs are allocated within their home state), assists in minimising this ischaemic time but is not always most appropriate. Further information on National Allocation of solid organs can be found in the TSANZ-OTA National Standard Operating Procedure, Organ Allocation, Organ Rotation, Urgent Listing.

Organs donated in New Zealand may be offered to Australian units, and vice versa where logistics and ischaemic times allow. If there is no suitable recipient in the donor country or as required by an urgent listing.

2.7 Vigilance and Surveillance

The Australian Vigilance and Surveillance System (AVSS) for Organ Donation for Transplantation is the central location and system for reporting SAERs (reported serious adverse events or reactions) relating to organs from deceased donors and is managed by the Organ and Tissue Authority (OTA).

The AVSS undertakes work in the following areas:

a. work in parallel with state and territory clinical incident management systems in deceased organ donation and transplantation
b. receive and coordinate responses to SAER notifications
c. monitor, record and retrospectively analyse SAER notifications
d. inform future processes in organ donation for transplantation, and
e. improve the safety and quality of organ donation and transplantation, thereby improving patient outcomes.

The National Vigilance and Surveillance system works in parallel with the existing jurisdictional clinical incident management systems. The clinical management and investigation of serious adverse events and reactions (SAERs) remains the responsibility of the hospital and jurisdictions in which the incident occurs. States and territories continue to be responsible for local reporting processes including communication with associated clinicians and patients, investigation of the incident; and the response to an incident including feedback, local policy and clinical practice review. While cases of donor derived disease transmission are rare, the immediate reporting and investigation of any post-transplant infection in the recipient and the notification of the donation agency and other recipients from the same donor is imperative to prevent/minimise harm to those exposed.

A key component of the Organ and Tissue Authority (OTA) National Vigilance and Surveillance System is the Vigilance and Surveillance Expert Advisory Committee (VSEAC). The purpose of VSEAC is to monitor the performance of the vigilance and surveillance system and advise OTA on emerging risks identified in the organ and tissue donation and transplantation sectors and provide recommendations for action where appropriate.

Further information can be obtained by emailing saen@donatelife.gov.au.

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3 Auditing and Monitoring

The distribution and allocation of organs for transplantation in Australia is supported by the national Standard Operating Procedure (SOP): *Organ Allocation, Organ Rotation, Urgent Listing*. The national SOP was first developed in 2016 by the Australasian Donation & Transplant Coordinators Association (ADTCA), the Transplantation Society of Australia and New Zealand (TSANZ) and the Organ and Tissue Authority (OTA).

3.1 TSANZ Advisory Committee Audits

TSANZ has a number of Advisory Committees that act as peak bodies for their organ-specific special interest groups, advising in the areas of recipient eligibility, donor organ retrieval, allocation and utilisation of organs for transplantation. TSANZ Advisory Committees undertake regular scheduled auditing of organ-specific allocation and transplantation activity at local, state and national levels. Activities and outcomes that are audited include organ utilisation, inter-jurisdictional organ sharing, and the reasons why potential donors do not proceed to transplantation. Audit outcomes are reviewed at Advisory Committee meetings twice yearly and discussed at meetings of the OTA's Transplant Liaison Reference Group, which are held three times per year.

3.2 TSANZ-OTA National Organ Allocation, Organ Rotation, Urgent Listing

Every DonateLife service within its jurisdiction conducts an audit of organ allocation to ensure compliance with the national SOP for organ allocation, rotation, inter-jurisdictional organ offers, and urgent listing. Data is collected on the number and characteristics of organs retrieved, utilisation outcomes, the number of offers made in each jurisdiction, and detailed reasons for declined offers. Deviations from the standard allocation rotation are documented and accompanied by a detailed explanation of clinical reasons supporting the decision. Urgent listings and their impact on the national rotation are also monitored and audited.

3.2.1 Standard Offering Practice

At time of organ offering, the following responsibilities apply.

The donation specialist is responsible for

i providing a donor verbal brief at the time of initial contact and

ii submitting the donor information as well as the available deidentified attachments to the OrganMatch Donor Chart.

The transplant unit/s are responsible for

i Confirming access to the Donor Chart in the OrganMatch Transplantation Portal

ii Review and assessment of the donor information provided electronically in OrganMatch.

The level of detail provided verbally should take into consideration:

- Repetition of data provided electronically
- Extended timeframe of organ offer process
- Transplant units responsibility to assess complete donor information provided electronically
- Risk of misinterpretation / translation of verbal information

3.3 Data collection

Data related to organ donation and transplantation activity are required for the purposes of monitoring, to demonstrate adherence to the national SOP, and to enable the identification of opportunities to improve the care of donors, the donation and transplantation process, and recipient outcomes. The Australia and New Zealand Organ Donation (ANZOD) Registry, together with the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA), the Australia and New Zealand Liver and Intestinal Transplant Registry (ANZLITR) and the Australian and New Zealand Islet and Pancreas Transplant Registry (ANZIPTR), record and report on organ donation and transplantation activities and outcomes within Australia and New Zealand.

Through these registries,[1,2] information is made publicly available on:

- The number of organs donated by deceased donors, including a comparison with international donation rates
- Organ donation pathways (e.g. whether donation occurred after neurological determination of death or donation after circulatory determination of death, whether donation proceeded and, if not, reasons why)
- The number of people awaiting transplantation for each organ type
- The number of organs transplanted, including reasons why donated organs were not transplanted
- Outcomes of organ transplantation.

The data collected on donation and transplantation are used by specialist advisory committees at the federal, state, and professional level to review, audit and monitor organ donation and transplantation practices. Registry reports do not include information that would allow identification of donors or recipients. However, in the event of a medical necessity the capacity exists to link donor data to the recipient(s) via transfer of medical (but not identifying) information about the donor to the transplant teams. An example of a reason for this to occur would be in the situation of an infection in a transplant recipient that might have been transmitted through the donated organ.

3.4 Governance

TSANZ is a company Limited by Guarantee and a registered health promotion charity that is governed by a constitution. TSANZ Advisory Committees operate under the governance of the TSANZ Board, elected from the broader TSANZ membership. The organ-specific Advisory Committees have individual terms of reference (see Appendix A), and Advisory Committee Chairs meet annually with the Chair of the TSANZ Advisory Committees and Working Groups who is a member of, and reports to, TSANZ Board.

The OTA is a statutory authority within the Australian Government Health portfolio and works with Australian states and territories, clinicians, and the community sector to implement the Australian Government's national reform programme to increase organ and tissue donation for transplantation.

The TSANZ Guidelines Handbook outlines the process by which clinical guidelines are developed, reviewed, updated, and endorsed under TSANZ/OTA governance. The handbook is intended to ensure that all TSANZ clinical guidance is evidence informed, transparent, and developed through broad stakeholder consultation. The process supports methodological rigour and responsiveness to emerging clinical needs or evidence, aligning with best practice in health policy development.The handbook serves as a reference for guideline authors,contributors, reviewers, and members of TSANZ advisory committees, working groups and special interest groups.It defines roles and responsibilities, outlines the stages of guideline development and consultation, and provides a framework for version control, endorsement, and publication. By following this process, TSANZ aims to uphold the integrity and clinical relevance of its guidelines across Australia and New Zealand. Access the TSANZ Guideline Handbook here.

References

1 http://www.anzdata.org.au

2 http://www.anzlitr.org

Part B

Organ-specific guidelines

4 Heart

4.1 Preamble

Heart transplantation is a highly effective, final therapeutic option for patients with end-stage heart disease of varying aetiologies. Over 6,000 heart transplants are performed annually worldwide[1] with over 120 heart transplants performed in Australia and New Zealand each year.[2]

Heart transplant recipients in Australia and New Zealand have a one-year post-transplant survival of 87.2%; 49.3% will survive for 15 years or longer and just over a third of all heart transplant recipients survive longer than 20 years.[2] This compares with an average survival of less than two years for eligible patients who do not receive a heart transplant.[3]

Current Australian estimates are that 30 000 patients are diagnosed with incident heart failure annually and that close to 500 000 people are living with long-standing chronic heart failure (CHF).[2] Between 2006 and 2011, deaths from CHF in Australia rose by 20%.[3] The prognosis for CHF remains poorer than for common forms of cancer.[4] Importantly, CHF is 1.7 times more common and occurs at a younger age among Aboriginal and Torres Strait Islander peoples than among other Australians. Death rates and hospitalisation for CHF are also significantly higher in these groups.[4]

4.2 Recipient eligibility criteria

4.2.1 Assessment and acceptance

Heart failure clinicians caring for potential transplant candidates should discuss referral with one of the heart transplant centres in Australia and New Zealand (see Appendix H) and, when appropriate, arrange for timely referral.[4] Paediatric patients will be referred to one of the three paediatric heart transplant centres, located within Victoria, New South Wales and Auckland. Early referral for heart transplant assessment is recommended to optimise time for thorough evaluation of the inclusion criteria outlined in Section 4.2.2. Early referral helps to facilitate transplant education for patients and their caregivers as well as allowing time to address barriers to transplant, which may include obesity, physical frailty, malnutrition, inadequate social supports, with pre-transplantation intervention.

On referral to heart transplant units, simultaneous referral to palliative care services is highly recommended to support the patient's journey through transplant assessment, potential waitlisting, heart transplantation surgery, and their post-transplant life. The decision to waitlist a patient for heart transplantation is at the discretion of the transplant centre and their multidisciplinary team who are involved with the transplant assessment 'work-up' process.

End-stage cardiac conditions suitable for referral for heart transplant assessment

The list below summarises the potential cardiac conditions that may be suitable for referral for heart transplant assessment. Upon referral for transplant assessment, patients need to have exhausted all alternative treatment options and have an expected survival benefit with a reasonable prospect of returning to an active lifestyle.

- End-stage heart disease, usually secondary to ischaemic heart disease or dilated cardiomyopathy with severe systolic dysfunction
- Severe systolic dysfunction secondary to valvular heart disease
- Diastolic dysfunction secondary to restrictive or hypertrophic cardiomyopathy
- Heart failure secondary to congenital heart disease
- Other conditions including specific heart muscle disease (other acquired, inherited) and those with intractable arrhythmias or intractable angina with no revascularisation option.

4.2.2 Inclusion criteria

Patients with one or more of the following criteria should be considered for heart transplant assessment:[5]

- Persistent New York Heart Association (NYHA) Class III/IV symptoms despite optimum medical therapy (including cardiac resynchronisation therapy, CRT, if indicated)
- Peak VO2 <14 ml/kg/min or <50% predicted in diagnostic cardiopulmonary exercise test (CPET)
- Unable to complete satisfactory CPET because of cardiac status
- B-Type Natriuretic Peptide (BNP) persistently >400 pg/ml or N-terminal proBNP (NT-proBNP) >1600 pg/mL, or increasing despite treatment
- Low cardiac index (<2 L/min/m^2)
- Two or more admissions with decompensated heart failure in last 12 months despite adequate medical therapy and adherence
- Heart Failure Survival Score of medium- to high-risk, or Seattle Heart Failure Model one-year estimated survival < 80%
- Deteriorating WHO Group II pulmonary hypertension
- Deteriorating renal function due to cardiorenal syndrome
- Persisting hyponatraemia (<130 mmol/L) despite optimum medical treatment
- Recurrent ventricular arrhythmia despite drug, ablation and device treatment
- Intractable angina despite optimum medical, interventional and surgical treatment
- Deteriorating liver function due to right heart failure despite optimum medical treatment
- Persistent/recurrent symptomatic pulmonary oedema or serious systemic congestion despite optimum medical treatment.

In addition to the above, patients with acute or acute-on-chronic heart failure requiring durable mechanical circulatory support (MCS) such as a left ventricular assist device (LVAD) should be considered for transplant candidacy. Detailed guidance on MCS, including candidacy, can be found within The International Society for Heart and Lung Transplantation (ISHLT) 2023 Guideline update.[6]

4.2.3 Recipient characteristics associated with post-transplant outcomes

Careful evaluation is recommended for potential heart transplant recipients who may display additional risk factors such as older age, and/or impaired renal function, as detailed below. The following list summaries one-year survival rates associated with each risk factor, as per the 2021 ISHLT Registry Report.[1]

- Age: one-year survival is lower in recipients aged >60 years compared to younger age groups in Europe, one-year survival for recipients aged >60 years is 75% compared to 86% for recipients aged 18-39; in North America, one-year survival for recipients >60 years is 88% compared to 90% for recipients aged 18-39, in other countries
- Kidney Function: one-year mortality exceeds 20% in patients with estimated glomerular filtration rate (eGFR) <30 ml/min/1.73m^2 at transplant, which lends evidence in support of simultaneous heart-kidney transplantation in these candidates. Patients on pre-transplant dialysis have high one-year mortality, which supports consideration of simultaneous or staged heart-kidney transplantation in these patients
- Mechanical support: one-year survival in LVAD recipients approximates that of non-LVAD recipients; but is lower in patients supported with biventricular assist device (BiVAD) and total artificial heart (TAH)
- Gender: lower recipient survival is observed where there is a donor-recipient gender mismatch (female donor to male recipient)
- Diabetes mellitus: five-year survival of recipients with diabetes has generally improved over time but remains inferior to that of patients without diabetes
- Body Mass Index (BMI): higher recipient BMI (>26 kg/m^2) at the time of transplant is significantly associated with increased risk for one-year mortality.

Sensitisation is not a factor in one-year survival. Sensitised patients, defined as Calculated Panel Reactive Antibody (cPRA)score > 80%, is similar to that of non-sensitised patients. Prior malignancy does not appear to influence short-term (one and five year) post-transplant survival.[1]

4.2.4 Exclusion criteria with considerations

Exclusion criteria include any condition or combination of conditions that would result in an unacceptably high mortality risk from heart transplant surgery, significantly and adversely affect post-transplant survival, or preclude active rehabilitation after transplantation.[7-9] If present, appropriate measures to reverse, treat and support should be undertaken in a multidisciplinary approach to enable potential candidacy.

Major exclusion criteria for heart transplantation are as follows:

Active malignancy:[7,10,11] an active malignancy, other than non-melanoma skin cancers, is usually a contraindication to heart transplantation; however, patients in permanent remission—as evidenced by prolonged disease-free survival—may be suitable for transplantation. With the availability of new cancer treatments this is an area undergoing rapid change. Best practice as to whether cancer treatment is required at all is also evolving; for example, low-risk, clinically localised prostate cancer may not need to be treated and 'cured' prior to the patient being considered eligible for heart transplantation. The decision as to whether or not to refer a patient with a history of malignancy for heart transplant assessment needs to be made on a case-by-case basis, and generally should only be made in consultation with the oncologist caring for the patient. In general, patients with a history of malignancy should only be considered for heart transplantation if their prior malignancy does not adversely impact their predicted post-transplant survival.

Complicated diabetes:[12] patients with diabetes mellitus and established significant microvascular complications, poor glycaemic control (HbA1c >59 mmol/mol or 7.5%), or diffuse peripheral vascular disease are generally considered unsuitable for heart transplantation.[7,12] On the other hand, patients with diabetes without secondary end-organ disease (proliferative retinopathy, nephropathy or neuropathy) have undergone heart transplantation with excellent long-term outcomes.[12] Therefore, in patients with diabetes, optimisation of glycaemic control to achieve HBA1c < 7.5% is recommended prior to listing.

Body Weight: several studies have identified obesity (body mass index ≥ 30 kg/m^2 or ≥140% of ideal body weight) as an independent risk factor for mortality in heart transplant recipients,[13-17] with one study reporting a doubling of mortality at five years post-transplant for patients with a BMI > 30 kg/m^2.[11] In light of these published findings, morbidly obese patients should be required to reduce their weight below a BMI of 35 kg/m^2 before being considered for heart transplantation.[18] While cachexia (BMI < 18.5 kg/m^2) is not an exclusion criterion, it is also an important risk factor for poor clinical outcomes after heart transplantation.[14] Emerging studies regarding prehabilitation, exercise, and nutrition interventions prior to cardiothoracic surgery have shown promising results with improved outcomes post-surgery.[19]

Infection: patients with HIV, hepatitis B and C may be suitable for heart transplantation with careful consideration and management by the transplantation unit.[20-24] This is described in more detail in Section 4.8 'Emerging Issues'.

Other infections—patients colonised with multi-resistant bacteria such as methicillin-resistant Staphylococcus aureus (MRSA) or vancomycin-resistant enterococcus (VRE) have undergone successful heart transplantation; however, active systemic infection with these organisms would still be regarded as an absolute contraindication to heart transplantation. The decision regarding whether to refer patients with a history of chronic infection for heart transplant assessment needs to be individualised and generally should only be made in consultation with an infectious disease specialist and any other specialists caring for the patient. The exception to this would be a patient with an infected VAD where removal of the device at the time of transplantation may be potentially curative.

Non-adherence or inability to comply with medical advice and complex medical therapy:[25-30] this includes chronic cognitive or neuropsychiatric deficits in the absence of a carer capable of taking on this role. Non-compliance with medical therapy after heart transplantation is a powerful predictor of increased morbidity and mortality.[27]

Non-compliance with recommended pre-transplantation vaccinations: the seroconversion rate after vaccinations is significantly higher in the non-immunosuppressed population compared to vaccination in immunosuppressed solid organ transplant recipients. It is therefore critical that potential transplant recipients are vaccinated before transplantation, to enable them to develop adequate immune responses to the pathogen.[31] Rates of COVID-19 infection, severity of illness and mortality rates have been reported to be lower in the fully vaccinated transplant recipients, compared to non or partially vaccinated recipients.[32-34] This highlights further the importance of adherence to transplant unit advice pertaining to recommended vaccination schedules.

Active substance abuse:[25,31] this includes smoking, excessive alcohol consumption, and illicit drug use. Recommencing smoking after heart transplantation has been identified as a risk factor for accelerated coronary artery disease (CAD), malignancy, kidney failure, and poor post-transplant survival.[35] For individuals with a history of substance abuse, a period of six months abstinence is strongly recommended (with confirmatory blood and/or urine testing if considered appropriate) before active listing is considered.[36] In the event of urgent clinical need, a shorter abstinence period may be considered if the patient shows motivation and compliance alongside a support network. Longer term support from the drug and alcohol services and/or support groups should also be implemented to ensure optimal post-transplant outcomes.

Irreversible degeneration/damage of other organ systems:[7,8] this refers to any degeneration or damage that precludes rehabilitation after heart transplantation (e.g., advanced neurodegenerative disease, advanced rheumatoid arthritis, or severe peripheral vascular disease not amenable to revascularisation). In cases where there is irreversible failure of multiple transplantable organs, combined organ transplantation may be considered (see Section 4.7).[37-39]

Acute medical conditions: a number of acute medical conditions may render a person temporarily unsuitable for heart transplantation. These include active peptic ulcer disease, acute pulmonary embolism, and active systemic bacterial or fungal infection. Patients can be reconsidered for transplantation once these diseases have been resolved with appropriate medical therapy.

Frailty:[40] frailty assessments should be performed in all patients with advanced heart failure who are being considered for heart transplant or LVAD. Whilst heart-transplant (and LVAD support) has been shown to reverse frailty post-transplant, prehabilitation is recommended to improve frailty status to enable candidacy.[41,42] Pre-transplant frailty is a key indicator of poor post-transplant outcomes across all solid-organ transplants. In an Australian study of 140 heart transplant patients, frailty assessed using six domains (fatigue, grip strength, gait speed, loss of appetite, physical activity and cognitive assessment) within the six months prior to transplant surgery predicted poorer outcomes post-transplant.[43] Frailty is also associated with increased mortality in patients undergoing BiVAD implantation, but not LVAD alone.[44] Frailty is reversible following LVAD implantation, thus providing an improved foundation for heart transplantation.

In summary, following assessment of physical frailty, cardiac rehabilitation is recommended in patients awaiting heart transplantation to decrease readmissions, waitlist mortality, and improve post-transplant outcomes.

Relative contraindications to heart transplantation include:

- uraemia with calculated (or measured) GFR <40 mL/min[1,10]
- hyperbilirubinaemia >50 mmol/L[1]
- intractable ascites with hypoalbuminaemia
- fixed pulmonary hypertension with transpulmonary gradient (TPG) >15 mmHg or pulmonary vascular resistance (PVR) >4 Woods Units after pulmonary vasodilator challenge.[7]

These clinical characteristics identify individuals with a marked increase in post-transplant mortality regardless of whether there is evidence of intrinsic kidney, liver, or lung disease.[1,10] Patients with evidence of renal and/or hepatic decompensation who otherwise meet eligibility criteria for heart transplantation, should be considered for MCS —so called 'bridge to decision'.[45,46] Similarly, patients with fixed pulmonary hypertension should be considered for combined heart-lung transplant (see below) or long-term MCS, which has been shown to reverse pulmonary hypertension over a three- to six-month period in a large proportion of patients.[46-48]

4.2.5 Special circumstances and considerations

Heterotopic (piggy-back) heart transplantation

Historically, the vast majority of heart transplants have been performed orthotopically (i.e., the donor heart is implanted in the normal anatomical site of the recipient heart following its removal). Heterotopic or 'piggy-back' heart transplantation refers to the circumstance where the recipient heart is not removed and the donor heart is implanted in the chest and connected 'in parallel' with the recipient's, so that the recipient now has two hearts pumping together. This may be considered in two clinical settings:

- Fixed pulmonary hypertension: patients who meet the above eligibility criteria for heart transplantation and who have fixed pulmonary hypertension as evidenced by a TPG >15mmHg after vasodilator challenge, who are otherwise not deemed suitable candidates for durable mechanical circulatory support such as LVAD.[47,48] Suitable agents for assessing acute pulmonary vascular reactivity include intravenous glyceryl trinitrate, intravenous prostacyclin and inhaled nitric oxide. Paediatric patients with a high pulmonary vascular resistance may be considered for orthotopic transplantation based on the presence of acute reactivity, expected regression post-transplantation, the magnitude of the perioperative risk, and the availability of other treatment options.
- Higher-risk donors: where donor heart function is judged to be suboptimal for orthotopic transplantation (but the heart is still potentially recoverable), donors may be considered for heterotopic heart transplantation subject to informed consent of the potential recipient.[49]

4.2.6 Retransplantation

Heart retransplantation is a rare occurrence in Australia and New Zealand, constituting only 1% of annual heart transplant procedures.[2] Globally, retransplantation makes up around 2-3% of all heart transplants performed.[50] The outcomes for heart retransplantation in cases of acute rejection and early graft failure are extremely poor.[50-51] Therefore, these patients are generally not recommended for retransplantation. Conversely, ISHLT registry data indicate that specific patients undergoing heart retransplantation due to late graft failure secondary to cardiac allograft vasculopathy can achieve excellent short and long-term survival.[50] In Australia and New Zealand, almost two-thirds of patients are alive at 15 years following retransplantation.[2] Patients may be considered for heart retransplantation provided they meet standard eligibility criteria.

4.3 Waiting list management

Heart transplant units will generally review patients listed for heart transplantation every 4-8 weeks in an outpatient clinic. This ongoing reassessment is critical to evaluate the patient's changing status against predicted peri-operative or post-transplant outcomes. Repetition of some assessments such a physical frailty, echocardiogram, right heart catheterisation and serum/urine nicotine and other drug levels may be required by transplant units to ensure waitlisted patients still meet eligibility criteria for transplantation or to re-evaluate candidacy for MCS. Occasionally it may also be appropriate to de-list patients to consider supportive/palliative care pathways after discussion with the multidisciplinary team, the patient, and their caregivers.

4.3.1 Urgent patients

Under some circumstances—for example, when transplant candidates are deemed unsuitable for MCS, develop life-threatening complications while on support, and if the patient's estimated survival is deemed to be within days to a few weeks without transplant—the patient may be placed on an urgent list.

Urgent listing for heart transplantation is at the discretion of the Transplant Unit Director. It is the responsibility of the Transplant Clinician to ensure the Cardiothoracic Transplant Units in Australia and New Zealand are notified of the urgent listing. The OrganMatch enrolment and urgent status is to be updated at this time to ensure the relevant donation and transplant clinicians are able to view this listing in OrganMatch. Donor hearts are offered to home state transplanting unit(s) first prior to offering to interstate urgent listing(s); it is at the discretion of each transplant unit to accept or decline a request for interstate urgent heart allocation. Urgently listed patients are to be considered *prior* to offering to paediatric transplant units as described in Section 4.6.2.

It is expected that the majority of individuals placed on the urgent waiting list will either die or be transplanted within two weeks of notification. In the event that a person remains urgently listed beyond two weeks, re-notification of all cardiothoracic transplant units is required at two-weekly intervals, as supported by the TSANZ-OTA National Standard Operating Procedure: Organ Allocation, Organ Rotation, Urgent Listing.

If there are simultaneously listed urgent patients, the following rule will apply:

- If a compatible donor becomes available outside the state of the urgently listed patients, the heart will be offered to the home state transplanting unit first and then to the patient who was *first* listed as urgent (subject to the home state transplant unit(s) wavering the offer to the urgent listing(s)).

The operation of the urgent waiting list will be subject to annual audit and review by the Cardiac Transplant Advisory Committee (CTAC) of TSANZ.

4.3.2 OrganMatch

Patients listed for heart transplant must be registered on OrganMatch under the heart transplant waiting list program. Initial collection of blood samples are required for Human Leukocyte Antigens (HLA) typing and identification of HLA antibodies using solid phase technique (Luminex). Samples are collected monthly and HLA antibody testing will be performed. Whilst it is optimal for all waitlisted patients to be screened every three months, screening must have occurred within 120 days to be included in matching. Any sensitising event (i.e., blood transfusion) will require repeat HLA antibody testing in addition to the routine monthly sample. Clinical parameters required for the OrganMatch Heart algorithm, must be entered in OrganMatch by the clinical team or transplant unit at the time of listing. Table 4.0 shows the relevant clinical parameters.

Table 4.0: Essential Clinical Parameters required for the OrganMatch heart transplant waitlisting and algorithm.

Height
Weight
ABO
Complete patient sensitisation history – i.e., blood transfusions, pregnancies, infection, VAD implantation, previous transplantation

In addition, the unacceptable antigen profile based on pre-defined criteria will be highlighted following consultation with the recipient transplant unit as described in Section 4.3.3 below.

4.3.3 Histocompatibility assessment

Each recipient must undergo a series of tests performed at the state Tissue Typing laboratories. This includes the following:

- HLA typing using molecular technique such as Next Generation Sequencing (NGS) at the following HLA loci – A , B, C, DRB1, DQB1, DQA1, DPB1, DPA1
- HLA antibody screening using Luminex single antigen beads. This screening must have occurred within 120 days to be included in matching.

These tests will be used in the histocompatibility assessment by the Tissue Typing labs and in consultation with the clinical unit to assign unacceptable antigens. These assigned unacceptable antigens can assist in excluding a waitlisted patient from incompatible donor offers. Additional comprehensive information is available within the National Histocompatibility Guidelines: https://tsanz.com.au/storage/Guidelines/TSANZ_NationalHistocompatibilityAssessmentGuidelineForSolidOrganTransplantation_Final.pdf

4.3.4 Management of sensitised waitlisted patients

There has been a substantial increase in the transplantation of sensitised patients, with the percentage of recipients with a pre-transplant calculated panel reactive antibody (cPRA) of >20% increasing from 5.2% to 17%.[1] This is reflective of the advances in antibody monitoring and management before and after heart transplants, especially with virtual crossmatching. There exists a fragile equilibrium in identifying unacceptable antigens in patients on the waiting list, potentially restricting access to organs for those with a designated 'high' cPRA. This cPRA serves as an estimate of the donor pool compatibility by assessing the frequency of antigens to be avoided due to the presence of corresponding cytotoxic antibodies. The most recent ISHLT Guidelines[31] provide updated recommendations which are summarised in Table 4.1 below:

Table 4.1: Management considerations of sensitised waitlisted patients[31]

Recipient histocompatibility assessment as per 4.3.3 above. When the cPRA is elevated (≥10%) further evaluation is recommended.
Each heart transplant centre should define the antibody threshold for unacceptable rejection risk. *(In Australia, a mean fluorescence intensity (MFI) less than 6,000 is the recommended acceptable threshold).*
Determine and report the cPRA based on recipient antibody specificity and population antigenemic prevalence
Each heart transplant centre to define a cPRA threshold for desensitisation (i.e., >50%). Therapies aimed at reducing allosensitisation may be considered in selected patients where the likelihood of a compatible donor match is low or to decrease the risk of donor heart rejection where unavoidable mismatches occur.
If known, presence of non-HLA antibodies, such as major histocompatibility complex (MHC) Class I polypeptide-related sequence A (MICA) or angiotensin II type 1 receptor-activating antibodies (AT1R), antibodies to self-antigens are reasonable to report and consider when assessing antibody mediated rejection (AMR) risk
A complete patient sensitisation history including previous cPRA determinations is required to assess the risk of AMR.
The presence of anti-HLA antibodies can be reassessed 1 to 2 weeks following a sensitising event (such as blood transfusion) to reduce the possibility of positive cross match, including those undergoing desensitisation therapies.

4.4 Donor assessment

The majority of hearts donated for transplantation in Australia and New Zealand are obtained following donation after neurological determination of death (DNDD). The quality of donor hearts varies enormously, and historically fewer than 30% of hearts in the setting of DNDD have been considered suitable for transplantation. In 2014/2015, a series of successful heart transplants were performed using hearts retrieved following donation after circulatory determination of death (DCDD).[52] Since 2014, the utilisation of donor hearts via the DCDD pathway has safely widened the donor pool, with excellent early,[53] and mid-range outcomes at one-, three- and five-year follow-up being reported and comparable to that of hearts transplanted via the DNDD pathway.[54,55] DCDD heart transplantation has become adopted as routine clinical practice for specialist transplanting centres, please see Section 4.5 for further information on DCDD.

Another rapidly advancing area shaping cardiac transplantation in Australia and New Zealand is hypothermic ex-vivo machine perfusion utilising the XVIVO heart preservation system. International and Australian trials using the XVIVO have demonstrated the safe extension of the donor heart ischemic time and a reduction in the risk of primary graft dysfunction. See Section 4.8 for more information regarding advances in machine perfusion.

Table 4.2 below summarises the broad suitability criteria for donor heart referral to heart transplanting units across Australia and New Zealand. Additional factors impacting donor heart quality are outlined in Section 4.4.1.

Table 4.2: Suitability criteria for heart donation.

Criteria	Comments
General organ donor criteria	See Chapter 2
≥3kg to ≤65 years (DNDD) ≥3kg to ≤55 years (DCDD)	Donors aged >45 years may require additional cardiac investigations such as coronary angiography detailed in section 4.4.3 to exclude CAD. Paediatric donors (*refer to section 4.6.2 and Chapter 11.5*).
No significant untreatable heart disease	Such as: hypertrophic cardiomyopathy, long-QT syndrome, Brugada syndrome, coronary anomalies including congenital heart disease.

4.4.1 Donor related risk factors

Several donor-related and procedural variables are known to affect the quality of the donor heart. These include donor age, the presence of cardiovascular risk factors (e.g., hypertension, smoking), known heart disease in the donor prior to death, or injury to the heart after death.

Age: the risk of death after heart transplantation increases progressively with donor age greater than 30 years.[56,57] A donor age of 50 years is associated with a 30% increase in the relative risk of death at one-year post-transplantation compared with a donor age of 30 years (an increase in the absolute risk of death at one-year post-transplant from 15% to 19%). The relative risk of death at one-year post-transplant rises to 50% for a donor age of 60 versus 30 years (absolute risk of 23% versus 15%).[50]

ISHLT Registry data continues to demonstrate older donor age, especially ≥50 years, is associated with reduced post-transplant survival as early as one month after transplantation.[57] Whilst globally the median age of donors is increasing, careful consideration is recommended in accepting hearts from donors older than 60 years due to the high risk of pre-existing CAD together with the heightened risk of cardiac allograft vasculopathy development.

DNDD vs DCDD: in DNDD, an intense sympathetic discharge that may occur during the development of brain death can result in severe (although usually reversible) myocardial dysfunction, as evidenced by a reduced left ventricular ejection fraction (LVEF) on echo, or a requirement for high doses of inotropic agents to maintain haemodynamic stability. In DCDD, warm ischaemic injury is an unavoidable consequence of withdrawal of life support. The duration of warm ischaemia is difficult to predict, however when this exceeds 30 minutes (from systolic blood pressure <90 mmHg to the administration of cardiac preservation solution) ischaemic damage to the heart is likely to be severe and not fully reversible.

Ischaemic time: the major procedural variable that affects donor heart quality is the ischaemic time—the interval between cross-clamp of the aorta in the donor (in the DNDD setting) and release of the aortic cross clamp in the recipient. The risk of death after heart transplantation increases progressively with ischaemic times exceeding 200 minutes. An ischaemic time of 360 minutes is associated with an 83% increase in the relative risk of death at one year post-transplantation (an increase in the absolute risk of death at one year post-transplant from 15% to 27%).[58] There is a strong interaction between donor age and ischaemia time in their effect on transplant outcomes, and both variables need to be considered when deciding whether to accept a donor heart—particularly from an interstate or remote donor hospital when a prolonged transport time is anticipated. With donors > 45 years of age, it is recommended to avoid long-distance transportation, or other factors such as redo sternotomy, and VAD explantation ¬- unless ex-vivo heart perfusion devices such as the XVIVO can be used to safely extend total donor heart ischaemic time.[59]

Infectious diseases: as with other solid organs transplanted from deceased donors, there is a risk of transmission of infectious diseases from donor to recipient (e.g. blood borne viruses such as HIV, hepatitis B or C). Donor screening for these and other transmissible diseases is discussed in Chapter 2. Screening may not detect all donor infections, including blood borne viruses recently acquired due increased risk behaviours.[60] The decision to transplant organs from such donors should only be undertaken after careful consideration of the risks and benefits to the recipient and with the informed consent of the recipient (or senior next of kin in the event the recipient is unable to provide consent). Information pertaining to safety of transplanting organs from deceased donors with a history of Covid-19 can be found in Section 2.3.2.1, and is also supported by ISHLT 2023 Guidelines: Donor heart selection: Evidence-based guidelines for providers (jhltonline.org)[59]

It is expected that all heart transplant units in Australia and New Zealand will make use of all viable donor hearts. The acceptability of various donor types to potential heart transplant recipients should be discussed with both the patient and the patient's carer at the time of waitlisting (rather than at the point of the heart offer). Informed consent should also be confirmed on the day of transplantation when there is a potential risk of transmission of donor infection (e.g. if the donor is positive for hepatitis B or C).

4.4.2 Donor information and testing

The assessment for heart donation suitability is outlined in Table 4.3.

Table 4.3: Donor information required for heart allocation.

1	Comprehensive medical history including donor age, gender, height and weight, coronary artery risk factors and history of any pre-existing cardiac disease
2	History of the presenting illness leading to death including any history of chest trauma (in the event of traumatic brain injury), cardiac arrest and duration of resuscitation prior to return of spontaneous circulation
3	Vital signs including central venous pressure (if available) and doses of vasopressor/inotropic agents
4	ABO Blood group
5	Laboratory tests General organ donor criteria for viral studies (see Chapter 2): HIV, HBsAG, HBsAb, HBcAb, HCVAb, CMV, EBV serology Donor HLA profile for virtual crossmatch (VXM) with potential recipients. N.B *A flow crossmatch (FXM) may be requested under defined circumstances to provide urgent additional immunological data that is not provided by the VXM*
6	Investigations Current chest x-ray Electrocardiogram (ECG) Echocardiogram Coronary angiography or computed tomography (CT) coronary angiography (CTCA) (selected cases)

4.4.3 Donor coronary angiography

Donor coronary angiography has been associated with significantly better heart transplant outcomes compared to no angiography in donors at high risk of CAD.[61] Moreover, the cost of donor coronary angiography is more than offset by the surgical retrieval costs avoided when a donor is found to have extensive coronary disease precluding heart transplantation.[61]

Coronary angiography should only be performed at the request of the heart transplant physician or surgeon and not solely upon the request of a transplant coordinator, as per the indications outlined in Table 4.4. This may necessitate direct communication between the heart transplant physician and the cardiologist/intensivist on duty at the donor hospital. Communication between the transplant physician and donor hospital will be facilitated by the transplant coordinator and the Donation Specialist Nurse Coordinator.

If a coronary angiogram is requested by the transplant physician/surgeon, this request should be made with a provisional acceptance of the heart pending an acceptable coronary angiogram result. If the heart is subsequently declined on the angiography result, national rotational offers should continue as per TSANZ-OTA National Standard Operating Procedure – Organ Allocation, Organ Rotation, Urgent Listing.

Right and left coronary artery angiogram is performed with minimal contrast. Investigations that should not be performed unless specifically requested are:

- Left ventricular angiogram
- Aortogram.

Coronary angiography should not be performed if:

- The donor is physiologically unstable
- There is a credible risk to the abdominal organs.

Table 4.4: Indications for coronary angiography[59]

Indications	Including but not limited to
History of suspected CAD	Myocardial infarct, angina
LV dysfunction on echo	Wall motion abnormalities, EF<45%
Risk factors	Age >45 years, BMI>30 kg/m^2, hypertension, hypercholesterolemia, diabetes, smoking, cocaine use and significant family history of CAD.

4.5 Heart donation after circulatory determination of death

The use of Donation after Circulatory Determination of Death (DCDD) hearts is reasonable at centres with: experience using marginal donor hearts, familiarity with the use of ex-vivo organ perfusion devices such as the Transmedics Organ Care System (OCS) for preservation and transportation, and experience instituting peri-operative mechanical support and its after-care for possible primary graft dysfunction.[63]

DCDD heart transplantation normally occurs where cardiac arrest is expected after cardio-respiratory support is withdrawn in a controlled setting such as an intensive care unit (ICU) or operating theatre (Maastricht Category III donors).

Illnesses that can lead to a person being a potential DCDD heart donor include but are not limited to; irreversible brain injury (traumatic, cerebrovascular or hypoxic-ischaemic) where there is little or no possibility of deterioration to neurological death; severe respiratory or liver failure; ventilator-dependent quadriplegia; and advanced neuromuscular disease with respiratory failure.[64]

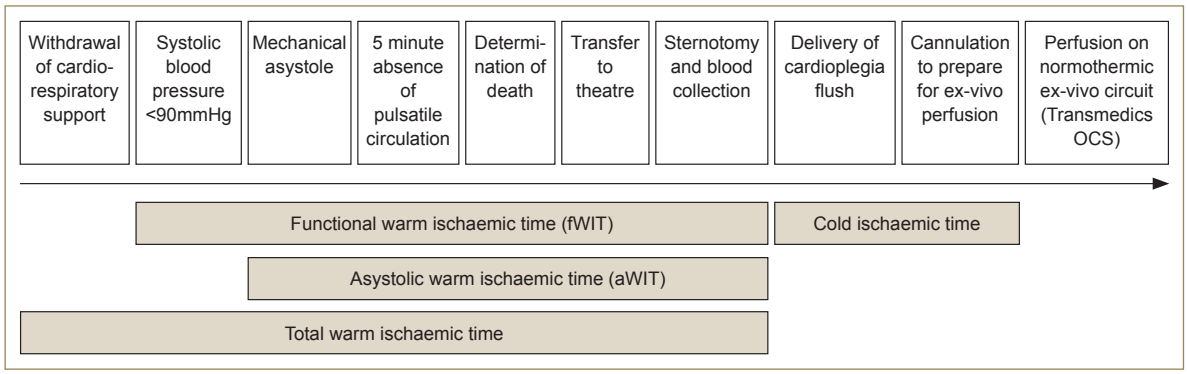
4.5.1 Withdrawal timing to candidacy

Patients who are consented and medically suitable to donate their heart for transplantation and in whom cessation of circulation is predicted to occur shortly after withdrawal of cardio-respiratory support (WCRS) will be considered for heart donation. WCRS in the setting of planned DCDD involves extubation with removal of mechanical ventilation and cessation of vasoactive agents (if present) provided for haemodynamic support, and/or removal of more advanced mechanical cardio-respiratory supports. This process should be performed in a controlled manner by the intensive care unit (ICU) staff either in the ICU or in the anaesthetic bay of the operating room in which the surgical retrieval procedure is to take place. If hospital infrastructure and established protocols allow a choice of location, each option should be explained to the family along with any impact on their experience and possible impact on donation and transplantation outcomes (e.g. affecting warm ischaemic times and organ utilisation). WCRS in the operating theatre complex will facilitate a shorter duration between death determination and organ retrieval, minimising organ warm ischaemic injury, and is the preferred site of WCRS when donation of the heart (or liver) is planned.[64] Following the onset of circulatory arrest, death is confirmed after five minutes of continuous absent pulsatility observed using intra-arterial blood pressure monitoring. The requirement is for mechanical asystole and not electrical asystole, noting that electrical activity may continue for many minutes after cessation of circulation. It is important to minimise warm ischaemic organ injury, so there should be prompt death confirmation after five minutes of absent circulation and followed by immediate movement of the patient to the operating theatre and table.[64]

The heart is very susceptible to warm ischaemic injury and, although exact safe timeframes are uncertain, current practice is to not proceed with heart retrieval for transplantation if the functional warm ischaemia time (fWIT) is likely to exceed 30 minutes. The fWIT for the heart is taken to be the time following WCRS from when there is a sustained fall in systolic blood pressure (SBP) below 90 mmHg to the administration of cardiac preservation solution/cardioplegia. After WCRS, the time for the SBP to fall to below 90 mmHg can vary. It is possible for death to occur well beyond 30 minutes following WCRS and for there still to be a satisfactory fWIT The DCDD process is usually stood down if death has not occurred within 90 minutes of WCRS. Prior to standing down the process there should be communication between the surgical retrieval team and staff attending the potential donor in case death is imminent with acceptable ischaemic times still possible.[64]

The asystolic warm ischaemic time (aWIT) is part of the fWIT and is the time from loss of circulation (mechanical asystole) to the administration of cardiac preservation solution/cardioplegia. The time taken from the delivery of cardioplegia until normothermic reperfusion of the heart on the Transmedics OCS is considered the cold ischemic time (CIT), or "back-table CIT", as it includes the time taken for back-table preparation of the heart before Transmedics OCS reperfusion. Figure 4.0 provides a schematic illustration of these timings.

Figure 4.0: DCDD timings for heart retrieval:[63]



4.5.2 Antemortem interventions

Ante-mortem interventions are procedures that are undertaken on the patient prior to death for the purpose of organ donation. Specific consent would usually be obtained for trans-oesophageal echocardiography, bronchoscopy, femoral cannulation, and blood product administration. Blood transfusion prior to donation may be requested by the accepting transplant unit if the donor's haemoglobin is < 100g/dL. A haemoglobin of > 100g/dL and a haematocrit of > 25% is desirable in order to facilitate delivery of warm oxygenated blood during normothermic machine perfusion (NMP) on the Transmedics OCS. The use of antemortem heparin is contingent on jurisdictional guidelines and hospital policy and is to be requested when permissible.[64]

4.5.3 Donor blood collection

Post cessation of circulation, approximately 1.2 – 1.5L of donor blood is to be collected in a heparin primed bag before the administration of cardioplegia, in the retrieval theatre. The addition of glycoprotein IIb/IIIa receptor antagonist such as tirofiban can be considered to prevent leucocyte filter clotting.[63]

The collected donor blood pH is usually <7.0 and partial correction to <7.2 (not to 7.4) with sodium bicarbonate should be performed. This is supported by pre-clinical studies demonstrating initial reperfusion of the ischaemic heart with an acidic perfusate reduced ischaemia-reperfusion injury.[65,66]

4.5.4 Donor heart viability assessment and lactate profiles

DCDD hearts are reperfused ex-situ using NMP systems such as the TransMedics OCS. Viability parameters include: (1) myocardial lactate extraction defined as a reduction in venous lactate levels compared to arterial lactate, (2) reduction in overall lactate, (3) visual inspection and, (4) haemodynamic parameters (mean aortic pressures between 65 and 90 mmHg; coronary flow between 650 and 950 mls/min on NMP).[67,68]

4.5.5 Controlled cooling

The heart on the Transmedics OCS is cooled at intervals of 2 °C (from 34 °C), by connection to a water heater cooler. Cold crystalloid cardioplegia (1 L) is administered once the heart has been cooled to 16 °C. The heart is then decannulated from the Transmedics OCS and placed in a bowl of ice and cold saline slurry for 15-20 minutes before implantation into recipient, This is to ensure adequate cold protection during the implantation process in the recipient. An additional dose of cold blood cardioplegia is administered immediately before the commencement of implantation, and further doses administered at 20- to 30-min intervals as needed during the implantation procedure.

4.6 Allocation

4.6.1 General allocation principles

The Donation Specialist Nurse Coordinator of the relevant jurisdictional DonateLife agency is responsible for referring potential cardiothoracic organ donors to the transplant coordinator for the corresponding heart transplant unit.

A donor heart is offered to the home state transplant unit first, except in donors who meet paediatric criteria (see Section 4.6.2 below). Each jurisdiction across Australia and New Zealand has an assigned home state heart transplant unit as listed below:

Jurisdiction of donor hospital	Heart transplant unit
NSW, ACT	NSW (adult and paediatric)
VIC, TAS	VIC (adult and paediatric)
QLD	QLD
WA	WA
SA, NT	No home state transplant unit – offer to unit first on rotation
NZ	NZ

If the home state heart transplant unit declines the offer, the donation offer is made on rotation to non-home state heart transplant units, with a 30-minute response time. For Victoria and New South Wales, both the adult and the paediatric heart transplant units must receive the offer before moving to the next state on the rotation.

Donor heart offers from South Australia and the Northern Territory are offered on rotation as for non-home state offers. Patients in South Australia or the Northern Territory who require heart transplantation are referred to interstate heart transplant units. New Zealand now receives donor heart offers from eastern states of Australia, and donor heart offers from New Zealand that are declined by the New Zealand heart transplant unit are offered to heart transplant units in the eastern states of Australia as per the TSANZ-OTA National Standard Operating Procedure: Organ Allocation, Organ Rotation, Urgent Listing.

4.6.2 Paediatric heart offering principles

All heart donors ≥17 years AND >50kg are to follow general allocation principles described above in Section 4.6.1. Donor hearts that are to follow the paediatric heart offering principles are defined as <17 years old AND/OR 3kg-≤50kg and are to be formally offered to paediatric recipients waitlisted at one of the three paediatric heart transplant units across Australia and New Zealand, please see Section 11.5. Urgently listed patients are to be considered prior to the paediatric heart offering principles. Please refer to Appendix O for Paediatric DNDD Heart Offering Principles, as well as the TSANZ-OTA National Standard Operating Procedure: Organ Allocation, Organ Rotation, Urgent Listing.

4.6.3 Allocation algorithm

Donor hearts are allocated according to the criteria shown in Table 4.5 below. Decisions about each individual offer and waiting list management are the responsibility of the local heart transplant unit.

Table 4.5: Matching criteria for heart donation

1. ABO compatibility*	Except paediatric patients aged <12 months[69]
2. Size and weight compatibility*	Recipient within +/- 30% of Predicted Heart Mass (PHM) Greater variability in the donor: recipient weight ratio may be acceptable depending on the ages of the donor and recipient, recipient transpulmonary gradient, especially in paediatric cases[70]
3. Histocompatibility Assessment*	VXM Refer to Section 4.3.3
4. Urgent status	See Section 4.3.1
5. Recipient waiting time	
6. Logistical considerations	Logistical considerations include coordination with other donor retrieval teams, transport of surgical teams and donor organs, type of heart transplant operation (orthotopic, heterotopic, or domino), number of transplants to be performed (usually heart and lung transplants are performed simultaneously in separate operating theatres), and the availability of intensive care unit beds.

Notes:

* Items 1–3 are absolute requirements for adult patients.

The OrganMatch Heart Transplant Waiting List (TWL) matching algorithm (See Appendix G) uses blood group compatibility, size matching (predicted heart mass) within a pre-specified perecentage range, and immunological compatibility to generate a list of potential recipients. The Tissue Typing Laboratory will perform Virtual Crossmatches (VXM) for the recipients on this potential recipient list. Patients with unacceptable antigens (above the pre-determined MFI threshold) to the donor HLA typing will be excluded from the match.

4.7 Multi-organ transplantation

Globally there has been an increase in the number of multiorgan transplants performed annually, although this still represents a small proportion of overall heart-alone transplants. According to ISHLT registry data, multiorgan (heart-kidney, heart-liver) transplants comprised just over 3% of adult heart transplants whilst heart-lung transplants comprised 1.6% of adult lung transplants.[71] Due to small numbers, outcomes data is limited to single centres and registries.

The following section will discuss the indications and risk factors associated with recipients receiving multiorgan transplants, the outcomes in recipients of multiorgan transplant, potential challenges regarding sensitisation and processes for listing for combined organ transplant. A recipient being considered for multiorgan transplantation needs to fulfil the eligibility criteria of both solid organs, with careful consideration of comorbidities and expected transplant survival.

4.7.1 Indications for multiorgan transplantation

Heart-lung transplant – Heart-Lung transplantation should be considered in patients with pulmonary arterial hypertension with severe cardiac dysfunction or those with Eisenmenger physiology/complex congenital heart disease and irreversible pulmonary hypertension.[72]

Heart-kidney transplant – Patients with end stage heart failure often have concomitant kidney disease. The challenge lies in differentiating those patients with a significant component of reversible kidney injury due to cardiorenal syndrome who may recover after restoration of cardiac performance versus those with intrinsic advanced kidney disease who may benefit from a simultaneous heart-kidney transplant. Potential heart transplant recipients with stage 4 chronic kidney disease should be referred to a nephrologist for evaluation and discussion of prognosis and treatment.[31] In a recent consensus conference on heart-kidney transplantation, it was felt that heart transplant candidates with an established GFR <30 ml/min/1.73m^2 may be considered for simultaneous heart-kidney transplantation.[73] An international heart/kidney workgroup also suggested that patients with established GFR of 30-44 ml/min/1.73m^2 with firm evidence of chronic kidney disease such as small kidney size or persistent proteinuria >0.5 g/day may also be considered for simultaneous heart-kidney transplant on an individual basis.[73] Recipients of multiorgan transplants had a higher prevalence of hypertension and diabetes, potentially reflecting the higher incidence of renal dysfunction in patients with these diagnoses.[71]

Heart-liver transplant – The common indications for heart-liver transplant are advanced heart failure with cardiac cirrhosis seen primarily in congenital heart disease, heart failure with concomitant noncardiac cirrhosis, or advanced heart failure with associated liver disease in which the liver is transplanted to avoid ongoing damage to the cardiac allograft such as in familial amyloid neuropathy.[73,74]

4.7.2 Processes for listing

Before patients are listed for combined organ transplantation, specific state transplant advisory committee (TAC) approval needs to be obtained. Patients being considered for heart-lung transplant will have their care primarily driven by the lung team with the thoracic organs implanted en-bloc. The decision for simultaneous versus sequential heart-kidney transplant is an individualised process with no current universally accepted criteria. Exploration and discussion for living kidney donation should occur contemporaneously with the evaluation process for heart-kidney transplant to maximise opportunities for evaluation and utilisation of such donors.[75]

4.7.3 Multiorgan transplant outcomes

Recommendations on the perioperative management of the multiorgan recipient and choice of induction and maintenance immunosuppression regimes have been previously outlined.[71,31] The early post-operative course for multiorgan transplants is more complex than that for isolated heart transplants. Approximately 30% of heart-kidney and heart-liver transplant recipients were hospitalised for at least 1-month post-transplant, compared with 17% for heart only transplants.[71] The incidence of severe renal dysfunction was similar in both the heart-kidney and the heart only transplant cohorts.[71]

As per the 2018 ISHLT registry report, the incidence of acute rejection and development of cardiac allograft vasculopathy (CAV) was lower after multiorgan transplantation compared with heart only transplantation (10% vs 24% for acute rejection, 24.3% vs 29.3% prevalence of CAV at 5 years).[71] Although not well understood, this is postulated to reflect immune modulation that results from introduction of higher volume of donor hematopoietic elements to the recipient receiving multiorgan transplants.[76,77] Overall survival was modestly improved in multiorgan transplant recipients, compared with heart only transplant recipients.[71] Deaths due to infectious causes predominated after multiorgan transplantation, whereas deaths due to graft failure and malignancy were more common after heart only transplantation.[71]

4.7.4 Retransplantation

Cardiac retransplantation accounts for a minority (2-3%) of heart transplants[78] and may be considered for a select group of patients with severe chronic allograft dysfunction.[31] In those patients with concomitant chronic renal dysfunction, combined heart-kidney transplantation should be considered. As per the 2018 ISHLT registry report, multiorgan transplants (mostly heart-kidney) comprised 12.8% of retransplants internationally, compared with 2.4% of heart only retransplantation.[71]

4.7.5 Sensitisation

In highly sensitised patients receiving multiorgan transplants, induction immunosuppression with anti-thymocyte globulin can be considered, with eventual maintenance immunosuppression comprising of tacrolimus, mycophenolate mofetil and prednisolone.[31,75]

4.8 Emerging Issues

Hepatitis B and C-positive recipients

Patients with chronic hepatitis B or hepatitis C infection may be suitable for heart transplantation depending on the presence and severity of chronic liver disease.[23,24,79,80] While hepatitis C antiviral treatment has improved dramatically over the last 10 years, immunosuppression post heart transplant may accelerate the course of the infection. Conversely, hepatitis C may accelerate coronary allograft vasculopathy, a leading cause of post-transplant mortality. Whether this is due to the virus itself or immunosuppression is unclear. Only few studies have assessed the outcome of heart transplantation in hepatitis C-positive recipients and—based on recent data—survival is reduced in this population.[79-81]

Human Immunodeficiency Virus (HIV) positive recipients

Improved survival of HIV-infected patients has shifted the profile of HIV infection from a rapidly fatal condition to that of a life-long chronic disease, with cardiovascular diseases now representing the leading cause of non–HIV-related death in this population.[20] Heart transplants have now been performed in patients with HIV infection internationally, and the small case series with limited follow-up data from international centres indicate that excellent survival can be achieved in carefully selected patients.[21,22] At this stage, the ideal HIV-positive heart transplant candidate remains speculative due to the limitations of the data published so far. Most of the

available data have been gained from liver and kidney transplantation in this group. Potentially, HIV patients with no detectable viral load, well maintained CD4+ T-cell counts, a stable anti-retroviral regimen, and no history of opportunistic or other concurrent infection may be considered for heart transplantation after careful discussion with an HIV specialist. Medical regimens, however, may be extremely complex due to multiple drug interactions. Rejection rates appear to be higher in liver and kidney transplant recipients with HIV.[22]

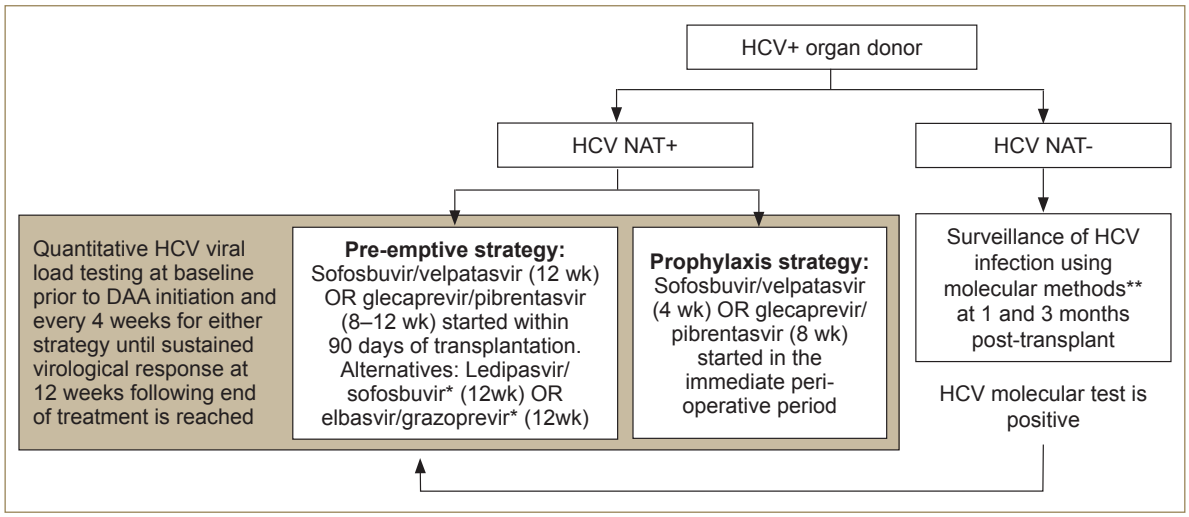
Utilisation of hepatitis C donors

The increasing availability of direct acting anti-viral (DAA) therapies for successful treatment of Hepatitis C Virus (HCV) has allowed the cardiothoracic transplant field to now safely consider the use of HCV-positive donors for heart transplantation.[80-83] The opportunity to safely expand the donor pool and potentially reduce the time on waitlist by accepting HCV-positive donors requires careful management pre and post transplantation. These management recommendations include but are not limited to:

- Patient education and associated informed consent specific to high viral risk donors prior to listing, and at time of transplantation
- Availability and assessment of waitlisted patient's recent serology i.e., pre-existing HBV infection.
- Careful pharmacological evaluation of drug interactions before initiation of DAAs to reduce decreased efficacy of HCV treatment
- Patient's ability to adhere with DAA medication protocol and prevent potential further HCV transmission
- Patient's ability to comply to surveillance monitoring of HCV RNA post transplantation as per transplant unit policy.

The ISHLT Consensus Statement on utilisation of hepatitis C virus-infected organ donors in cardiothoracic transplantation[80] provides further management considerations, guidance on recommended surveillance schedule and a potential DAA treatment strategy when utilising HCV-positive organs for cardiothoracic transplantation into HCV-negative recipients. See Figure 4.1 below.

Figure 4.1: ISHLT workflow recommendations when utilising HCV-positive organs for cardiothoracic transplantation into HCV-negative recipients.[80]



*Based on appropriate genotype as per manufacturer recommendations.

**Molecular methods include NAT and quantitative RNA PCR and/or viral load.

+, positive; -, negative; DAA, direct-acting antiviral; HCV, hepatitis C virus; NAT, nucleic acid test; PCR, polymerase chain reaction; wk, week.

Advances in machine perfusion and the anticipated impact on the donor pool

The traditional approach to donor heart preservation involves flushing the donor heart with a cold preservation solution and subsequent transport with the donor organ packed in ice (cold static storage preservation). Several groups have now established alternative methods of donor heart preservation, including hypothermic (XVIVO) and normothermic ex vivo perfusion (Transmedics OCS) described in Section 4.5.[52-54] The latest advancement in technology, the XVIVO Heart Preservation System, safeguards donor hearts using non-ischaemic heart preservation (NIHP). In 2021, the initial trial showcased the device's safe application in cardiac transplantation. Recently, a multicentre trial in Australia and New Zealand focused on extended NIHP (6–8 hours) for donor heart preservation using the XVIVO system.[84] This trial demonstrates the safe prolonged preservation periods, crucial to the often-challenging logistics of remote and regional donor hospitals across Australia and New Zealand. Further research in this area of machine perfusion is vital for optimising organ utilisation and widening the donor pool.

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5 Kidney

Most patients with kidney failure would live longer, feel healthier, and have a better quality of life with a kidney transplant compared to staying on dialysis.[1–4] The quality-of-life benefits from transplantation mean that some patients may still wish to receive a kidney transplant even if it might not increase their life expectancy.

For approximately 30 years, the Renal Transplant Advisory Committee (RTAC) and state Transplant Advisory Committees have continually developed, reviewed, and updated kidney transplantation and allocation protocols. This process takes account of changes in donor numbers and characteristics, transplant outcomes, tissue typing technology, and improved allocation practices.

In New Zealand, the National Kidney Allocation Scheme (NKAS) is managed by the National Renal Transplant Leadership Team (NRTLT). NKAS allocates deceased donor kidneys nationally, based predominantly on waiting time on dialysis and Human Leukocyte Antigen (HLA) matching. For details, visit: NZ Kidney Allocation Scheme December 2022 (health.govt.nz)

At the forefront of Australia's kidney allocation protocols is the Kidney National Allocation Algorithm, (see Section 5.4.2 and Appendix C). This includes a National Allocation Algorithm and a State Allocation Algorithm. The National Allocation Algorithm is designed to facilitate the allocation of kidneys to recipients who are (i) highly sensitised (those with many HLA-antibodies) and may otherwise wait a very long time to find an immunologically compatible donor, (ii) medically urgent, or (iii) a good immunological match with the donor, especially if also young. If the donor kidneys are not both allocated via the National Algorithm the available kidney(s) will be allocated within the state in which they were donated, according to the State Allocation Algorithm.

5.1 Recipient eligibility criteria

The number of deceased donor kidneys available for transplantation is far lower than the number of patients who might benefit from a kidney transplant.[5,6] In Australia, only patients who have commenced dialysis are eligible to be listed to receive a deceased donor kidney transplant (with very rare exceptions). In New Zealand, patients with progressive chronic kidney disease and an estimated GFR of less than 15 ml/min/1.73m^2 who are within 6 months of requiring dialysis are eligible for inclusion on the kidney transplant waiting list (regardless of whether they have commenced dialysis). The Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) report on the incidence, prevalence and outcomes of dialysis and transplant treatment for patients with kidney failure across Australia and New Zealand.[7,8,9,10] In Australia and New Zealand, unadjusted one-year patient and graft survival rates for primary deceased donor grafts have been stable at around 98% and 96% respectively for the past ten years.

Receiving a transplant has inherent risks associated with surgery and immunosuppression that need to be weighed up against the possible benefits. Patients need to be well informed by their clinical teams and accept their own individual transplant-related risks prior to listing.

Prior to 2018, it was an Australian requirement that patients have an 80% likelihood of survival at five years post-transplant to be eligible for deceased donor kidney wait-listing. This is no longer an absolute requirement. Eligibility for deceased donor kidney transplant wait-listing in Australia now requires that potential kidney transplant candidates have a high likelihood of significant benefit from kidney transplantation. Any significant risk of death post-transplant from complications (e.g. heart disease, vascular disease, cancer, infection) or general frailty would be a contraindication to kidney transplantation. This risk-benefit assessment is a clinical decision best made by the local multidisciplinary transplant team comprising of transplant physicians, surgeons, coordinators, psychiatrists, psychologists and social workers who are experienced in managing both dialysis and transplant patients.

In New Zealand, an estimated 80% likelihood of survival at five years post-transplantation remains an eligibility requirement for deceased donor kidney transplantation. While this may be difficult to determine, New Zealand units use an algorithm to estimate survival probability.[11] These calculation tools are also used by other centres around the world to estimate an individual's post-transplant survival based on various factors.[12]

5.1.1 Inclusion criteria

Inclusion criteria for being listed for deceased donor kidney transplantation are:

- Kidney failure requiring dialysis (Australia) or progressive chronic kidney disease in patients who are within 6 months of requiring dialysis and a GFR <15 ml/min/1.73m^2 (New Zealand);
- Low anticipated likelihood of perioperative mortality and a reasonable estimated post-transplant patient and allograft survival. Factors that may influence graft survival include primary causes of kidney failure that are likely to recur after transplantation (therefore resulting in premature graft failure), infection risk and concerns regarding non-adherence with immunosuppression.
- Age: advanced age in the absence of significant medical comorbidity and cognitive or neuropsychiatric deficits is not a contraindication to kidney transplantation; however only 2% of the dialysis patients in Australia aged over 65 were on the waiting list for kidney transplantation at 31 December 2023 due to the high rates of comorbidities in this population.[7,9] A number of patients over the age of 70 with limited comorbidities have been transplanted successfully.

5.1.2 Exclusion criteria

Criteria that are considered relative or absolute contraindications for deceased donor kidney transplantation wait-listing include:

- Australia: if the perioperative and post-transplant risks outweigh the likelihood of deriving significant benefit from transplantation; New Zealand: if there is a lower than 80% likelihood of surviving at least five years following transplantation.
- Comorbidities that might have a significant impact on the life expectancy of a kidney transplant recipient include cardiac disease, vascular disease, infection risk and malignancies.[13–18]
- Cardiovascular disease: severe, non-correctable cardiovascular disease is an absolute exclusion criteria. Lesser degrees of disease would also potentially contribute to a lower anticipated post-transplant survival, and hence would be considered a relative contraindication.[19,20]
- Diabetes mellitus: uncomplicated diabetes mellitus is not a contraindication to transplantation. Patients with diabetes should undergo a detailed assessment for any vascular complications that may affect their anticipated post-transplant survival; such vascular complications would be a relative consideration.[21,22]
- Infection: uncontrolled infection is a contraindication to transplantation. Patients may be listed and transplanted once the infection has been adequately treated.

- Malignancy: active malignancy is generally considered a contraindication to kidney transplantation (see Table 2.7). However, patients with a history of malignancy deemed to be cured may be suitable for transplantation. The decision whether to refer a patient with a history of malignancy for kidney transplant assessment needs to be made on a case-by-case basis, and generally should only be made in consultation with an oncologist or other appropriate specialist.
- Non-adherence to complex medical management: the ability to correctly follow a treatment plan—particularly with respect to anti-rejection medications—is an important factor in successful outcomes following kidney transplantation and, as such, is a requirement for listing. Likelihood of adherence is assessed by the transplanting units social and psychiatry team; every effort should be made to assist patients and their carers to optimise adherence to therapy.
- Other medical conditions: patients with kidney failure can have any number of comorbid medical conditions that may affect the risk of complications and survival after transplantation. These include but are not limited to, cardiac disease, chronic lung disease, cirrhosis of the liver, peripheral vascular disease, and cerebrovascular disease. Whether the existence of any such conditions is an absolute or relative contraindication to kidney transplantation needs to be considered on a case-by-case basis.
- Surgical exclusions including complex vascular anatomy and heightened risks associated with significant obesity.

5.1.3 Assessment and acceptance

Patients referred for kidney transplantation (from kidney/dialysis units) should be initially assessed by the transplanting hospital team, with regular review of patients after listing to ensure ongoing medical, psychological and surgical suitability. Initial and subsequent patient assessments and decisions regarding acceptance onto the waiting list in OrganMatch and continued eligibility for listing should involve a transplant nurse, physician and surgeon. The Director of a transplant unit (or their delegate which may include transplant clinicians and transplant coordinators) has the authority to add or remove patients from the kidney transplant waiting list.

5.1.4 Retransplantation

Patients who are being considered for a second or subsequent kidney transplant should be assessed according to the same criteria as candidates who are being assessed for their first kidney transplant. The vast majority of kidney transplant procedures are performed in first-time recipients. In Australia and New Zealand over the past decade, approximately 10% of recipients have received two or more kidney transplants. Only 1–2% of recipients receive a third or subsequent kidney transplant.

5.2 Waiting list management

The waiting list is comprised of patients who have been assessed by a transplant physician and surgeon and determined to be suitable to undergo kidney transplantation. Where possible, this assessment process should commence *prior* to initiation of dialysis. The total time from referral for transplant assessment to activation on the TWL can vary considerably depending on each individual's underlying medical and surgical concerns, the investigations required, the need for opinions from other specialists and many other factors. For referred patients who are relatively healthy with few comorbidities, activation on the TWL should ideally occur within the first 6 months of commencing dialysis.

Patients must be enrolled in the Kidney TWL program in OrganMatch in order to be matched with deceased organ donors. It is not a chronological list: organs are offered to waitlisted candidates according to the national and state allocation protocols (see Sections 5.4 and 5.5) which take into account recipient sensitisation, donor-recipient HLA-match and waiting time. There are certain circumstances in which a patient may be given priority (e.g., patients under 18 years of age; see Section 5.2.4). Once a patient is accepted onto the TWL and enrolled in OrganMatch, blood samples should then be sent to the state tissue-typing laboratory. The status of TWL

candidates is made "ready" when tissue- typing and HLA antibody (luminex) screening (Section 5.2.6) is complete. Once a patient's status is "ready" in OrganMatch the patient can be matched with deceased organ donors.

To maintain an accurate HLA profile for each waitlisted patient, monthly tissue typing bloods are required and sensitisation events such as blood transfusions, vaccinations, infections, should be monitored closely and reported back to state tissue-typing laboratories. Further details on sensitisation history can be found in section 5.2.6.1

When patients develop a lot of antibodies against other peoples' tissue type (HLA-antibodies) – sensitisation—it can be very difficult to find a suitable kidney for them (i.e., one that they do not have antibodies against). These patients require preferential access to a well-immunologically matched kidney if one becomes available. The ability to measure a patient's level of sensitisation has improved, along with an enhanced allocation algorithm that can provide priority matching to best meet the needs of these sensitised patients.

5.2.1 Calculation of waiting time

In Australia, waiting time is calculated from the date that long-term dialysis was commenced (not from the date of acceptance onto the waiting list). This is because delays in active listing may arise due to medical issues or delays in completing the necessary investigations that are outside the control of the patient. It is critical that all patients are adequately tested and prepared for transplantation, and therefore it is important for work-up investigations to be completed thoroughly. When calculating waiting time, periods of acute or temporary dialysis prior to the date that long-term dialysis was commenced do not contribute to waiting time.

In New Zealand, waiting time is calculated as the number of months from the date of chronic dialysis initiation for treatment of end stage renal failure (or recommencement after a failed kidney transplant) to the date of offer of a kidney. Where patients recover independent renal function unexpectedly after chronic dialysis initiation for the treatment of end stage renal failure, waiting time shall be calculated from the date of subsequent initiation of chronic dialysis for treatment of end stage renal failure.

For a second or subsequent transplant, waiting time is calculated from the date that dialysis was recommenced (Australia and New Zealand), following failure of the previous transplant. Sometimes, a kidney transplant will fail very early or never function at all. When a deceased donor kidney transplant fails very early, as a result of technical issues or the poor quality of the donor kidney, it may be possible for the patient to retain their original waiting time credit (This would not apply in the case of graft loss due to non-adherence to treatment).

In Australia, if a kidney transplant fails within the first 12 months, the recipient is able to retain their original accrued waiting time credit when/if they are re-listed for a subsequent transplant. This makes allowance for kidney transplants that are performed but never functioned very well or had technical issues. Approval for reinstatement of waiting time in these circumstances needs to be obtained from the relevant state-based renal transplant advisory committee.

Live donor kidney recipients in whom the graft fails within the first 12 months post-transplant may be able to retain their previously accrued waiting time, if approved by the relevant state or national transplant advisory committees. This removes the risk of the possible loss of accrued waiting time as a disincentive to proceed with a live donor. The number of live donor kidney transplants that are lost in the first year are very low.

In New Zealand, if a patient meets renal failure criteria for listing within one year after kidney transplantation, the recipient will be reinstated on the waiting list with the same waiting start date they had prior to the most recent transplant if they otherwise are or subsequently become eligible for deceased donor listing.

5.2.2 Ongoing review

To remain active on the TWL, patients must continue to be medically, psychologically and surgically suitable to receive a kidney transplant, and should undergo regular reassessment by the transplant unit. Reassessment of patients on the TWL should occur at least annually; usually this would be a face-to-face assessment. It is expected that to remain on the TWL a patient should continue to fulfil the same inclusion criteria as at their initial listing. Transplant units should have a process to formally ensure that ongoing patient reassessment occurs and that actively listed patients are suitable to receive a kidney transplant.

Sometimes an event occurs requiring a patient's enrolment status to be changed to "on hold". On hold status is temporary. If a patient is no longer suitable for transplant, the enrolment must be ended in OrganMatch. For example, the development of un-correctable substantial cardiac disease would mean that a waitlisted person is no longer suitable and so their enrolment in OrganMatch would be ended. If, however, a patient had a treatable infection, such as peritonitis, their status would simply change to "on hold" until the infection resolved, provided no other changes occur that affect eligibility. Patients should be kept informed of their status on the TWL.

5.2.3 Urgent patients

In rare circumstances (applicable in Australia but not in New Zealand) a patient who is active on the transplant waiting list may be deemed 'urgent'; for example, if they have very limited or failing dialysis access without which their survival is threatened. The decision to give a patient urgent status is state-based and is reviewed by each state's transplant advisory committee. It is expected that—unless there is a compelling reason—the first suitable kidney offer should be accepted for patients deemed as urgent. In OrganMatch a patient needs to be flagged with a state urgency index.

5.2.4 Paediatric priority

Paediatric kidney failure patients are few in number (approximately <2% of the prevalent kidney failure population in Australian and New Zealand), and have special needs with respect to physical and psychological development that are best met by transplantation.[23,24] In Australia, patients who are under the age of 18 years and have commenced dialysis are eligible for paediatric prioritisation under the National and State-based allocation algorithms. Bonus points are awarded for paediatric priority taper to zero by age 25 years.

Given this extra priority, paediatric recipients can expect to receive offers of kidneys that vary with respect to kidney quality and the degree of HLA matching. Transplant units need to weigh up the implications of these offers with respect to immunological considerations and projected graft longevity. In some paediatric units, both immunological exclusions (eplet based) and quality-based exclusions (e.g. setting an upper limit for donor age or donor co-morbidity) are being set for individual patients, and this approach is strongly advised. This will tend to increase the waiting time in favour of a kidney with a better immunological match and prognosis match.

In New Zealand, patients under the age of 15 at the time of allocation receive paediatric prioritisation.

5.2.5 Australian and New Zealand Paired Kidney Exchange (ANZKX) Priority

If the intended recipient of a kidney from a living donor matched through the Australian and New Zealand Paired Kidney Exchange (ANZKX)[25] is unable to receive that kidney but their co-registered living donor has already donated, the "orphan recipient" will be eligible for priority listing from the national deceased donor organ pool in their country of residence.

If the orphaned recipient is in Australia and pre-emptive (i.e. has not yet started dialysis) then an exception will be made so that these patients can be prioritised to receive a kidney from the deceased donor pool once approved by RTAC.[25] In OrganMatch, these patients are listed with National Urgency status.

If an ANZKX kidney is transplanted and kidney reperfusion has been established, the recipient will not be considered an orphan recipient, even if the kidney never functioned. However, if the transplant surgeon finds that the kidney is visibly damaged prior to surgery and proceeds but early graft loss occurs, the recipient would still be eligible to be prioritised according to the Orphaned Recipient protocol if approved by RTAC. In this situation the transplant surgeon needs to have informed the ANZKX Coordination Centre prior to proceeding with surgery.

If the orphaned recipient is in New Zealand, prioritisation for a deceased donor kidney will be discussed and approved by the New Zealand NRLT.

This ability to prioritise ANZKX recipients in case of unforeseen circumstances safeguards the live donors and recipients participating in the ANZKX program. Since 2021, ANZKX has moved to continuous matching and no longer performs match runs. By performing continuous matching, the program aims to reduce the waiting time from match offer to transplant to approximately 60 days or less. Historically, with match runs the average waiting time was around 100 days.

5.2.6 Histocompatibility Assessment

Prior to waitlisting, each transplant candidate must undergo a series of tests performed at the state Tissue Typing laboratories. These include:

- HLA typing using the molecular technique Next Generation Sequencing (NGS) at the following HLA loci: A, B, C, DRB1, DQB1, DQA1, DPB1, DPA1. If present, DRB3, DRB4, DRB5 should also be included.
- HLA antibody screening using Luminex single antigen technology to detect the antibodies to HLA-A, -B, -C, -DRB1, -DRB3, -DRB4, -DRB5, -DQA1, -DQB1, -DPA1, and -DPB1. This screening must have occurred within 120 days to be included in matching. It is optimal for all waitlisted patients to be screened every 3 months.

5.2.6.1 Defining Unacceptable Antigens

On completion of patients' HLA typing and HLA antibody screening results, the histocompatibility laboratory provides an evaluation of histocompatibility data and recipient immunologic risk that will allow the clinical unit to decide on appropriate induction and immunosuppression approaches to transplantation. The assessment should provide an individualised list of HLA antigens that would be unacceptable in a donor and should consider:

1. The recipient's sensitisation history
   a. Previous transfusion of blood products
   b. Numbers of pregnancies and age of youngest child
   c. Repeat mismatches from previous transplants
2. Detection and characterisation of HLA-specific antibodies
   a. The strength of the various HLA-specific antibodies
   b. Stability of antibody strength over time - decreasing or increasing
3. Likelihood of repeat transplant in the future
   a. Consider avoidance of potential donor HLA mismatches with high eplet loads.

All HLA antigens to be avoided in potential donors will be defined unacceptable antigens and listed in the following categories:

- Antibody sourced (antigens to which there is evidence of historical or current HLA antibodies)
- Previous donor mismatches
- Other antigens for exclusion (e.g., potential high eplet load mismatches)

Once defined, the unacceptable antigens are used in the TWL matching algorithms to exclude potential recipients from incompatible organ offers. Waitlisted patient's HLA antibodies must be performed every 120 days – if this is not done the patient will not be matched with deceased organ donors. The waitlisted patients' assigned unacceptable antigens are also assessed and reviewed after every antibody screen. Additional comprehensive information is available within the National Histocompatibility Guidelines: https://tsanz.com.au/storage/Guidelines/TSANZ_NationalHistocompatibilityAssessmentGuidelineForSolidOrganTransplantation_Final.pdf

5.3 Donor assessment

Various medical factors have been found to influence long term kidney graft function, in particular donor age and history of diabetes, hypertension or vascular disease.[26,27] Internationally, transplant centres are increasingly using donor characteristics in allocation decisions in an effort to optimise the transplant outcomes from each donated kidney.[28,29] In 2021, implementation of a revised kidney matching algorithm included, in part, KDPI-EPTS matching (prognosis matching) to improve organ utilisation. This is described in more detail in Section 5.4

5.3.1 Donor information and testing

As described in Chapter 2, all deceased donors undergo a detailed general assessment of medical suitability, which includes kidney function assessment through the patient's past and current medical history and medical investigations. In some cases, a kidney biopsy of the donor kidney is performed, which can be useful particularly in the case of donors with significant cormorbidities.[30]

Given an increasing number of older donors, often with significant cardiovascular disease, some donated kidneys are thought to not be able to provide adequate function after transplantation. In a proportion of these cases, both of the kidneys from the one adult donor are offered to a single recipient (dual). This is to ensure that at least one patient can be transplanted with a successful outcome.[30]

For information on kidney donation from paediatric donors, see Chapter 11.

5.3.2 Donor-related risk

The quality of kidneys retrieved from deceased donors can vary significantly. Donor age may be anywhere from 3 months to 75 years or above. In 2023, the mean age of deceased donors was 47 years in Australia and 43 years in New Zealand.[31] Donors aged over 65 years accounted for 15% and 11% of all deceased donors in Australia and New Zealand respectively.[31] Kidney function can also vary depending on the existence of any underlying disease processes in the donor (e.g., hypertension, diabetes, or vascular disease). Studies support the utility of transplanting kidneys from donors who are older or have diabetes, hypertension, or vascular disease, as this increases the total number of kidneys available and gives more people the opportunity to be transplanted. Whilst recipients benefit from transplantation over remaining on dialysis, long-term recipient outcomes with these kidneys are poorer.[26,27]

The concept of a "Kidney Donor Risk Index" (or KDRI) has been developed in order to rank the quality of each donor kidney.[32] The KDRI is converted to a Kidney Donor Profile Index (KDPI) by remapping onto a percentage scale. Kidneys with a low KDPI are expected to have longer post-transplant survival than those at the other end of the spectrum. Factors included in the calculation of this index are donor age, donor kidney function, presence of diabetes or hypertension, cause of death, and donation pathway (neurological death or circulatory determination of death).

Within OrganMatch it is now possible for a patient with their nephrologist to indicate a specific maximum level of KDPI (KDPI max) that they are willing to accept.

It is important to note that, in estimating kidney quality, it is not possible to account for all potential donor-related risk factors and there is always the possibility that some unknown factor may affect the transplant outcome. All transplantation procedures carry some risk and recipients should be made aware of these general risks before being listed for transplantation. Units are expected to have a thorough patient education process that discusses these issues in detail prior to patients being listed and then transplanted. Some states use a consent form that is discussed with the patient and signed prior to listing, in order to communicate the various risks and expectations of the transplant process.

In some cases, there may be important additional factors that need to be discussed with the recipient before they consent to proceed with a specific transplant. This is important if there appears to be some additional risk related to the donor, or if other factors have been identified that may influence the transplant outcome. Examples include:

- The likelihood the kidney will have delayed function requiring dialysis for a period of time after the transplant surgery—approximately one-third of kidneys transplanted do not function immediately
- The possibility that the kidney will have poor function
- The risk of infection or cancer transmission if there are factors in the donor history that increase their risk, even though screening tests may be negative
- Anatomical problems that may have been identified in the donor kidney
- Greater than usual immunological barriers between the donor and recipient, such as the identification of donor-specific HLA-antibodies in the recipient—these may lead to an increased risk of rejection and/or the need for additional treatment such as plasma exchange.

5.4 Allocation: Australia

Kidney allocation processes are based on certain principles (see Section 5.4.1), which have been refined over time and are under frequent review to ensure that allocation outcomes remain consistent with these stated principles. Allocation algorithms (see Sections 5.4.2 and 5.4.3) refer to the practical application of these principles and are dynamic because they need to respond to changes in medical knowledge and to shifts in donor and recipient characteristics over the longer term. To ensure that kidneys are not wasted, allocation algorithms also need to be sufficiently flexible to accommodate changes in the medical status of recipients and/or donors that necessitate deviation from the usual allocation pathway.

Similar to many practices in medicine, there may be instances where the allocation process cannot always be rigidly applied, and clinical discretion may sometimes be necessary to overcome unexpected impediments to normal allocation (see Section 5.4.5). In these rare circumstances, all cases that deviate from normal allocation practice are audited by experienced transplant clinicians through RTAC and the respective state transplant advisory committees to ensure that the deviation was acceptable and justified. Where deviations occur, the over-riding principle remains to ensure that all kidneys that can be used are effectively and fairly allocated to a wait-listed patient. In addition to unplanned allocation deviations, certain authorised deviations from usual allocation rules are also recognised. These may occur in the case of urgent listings, the Australian and New Zealand Paired Kidney Exchange Program or donors with a rare blood type (see Section 5.4.4).

To ensure the best use of kidneys from deceased donors, it is important to try to maximise the benefit to the whole community from this scarce and valuable resource.[11,12] In several international programs, donor kidneys with greater estimated survival are preferentially allocated to recipients predicted to have a longer life-expectancy after transplantation; donor kidneys with shorter estimated survival are preferentially allocated to recipients predicted to have a shorter life expectancy. Acceptance of a kidney with shorter estimated survival is often with the expectation of a shorter waiting time.

Matching the quality of the donor kidney to the likely longer-term survival of the recipient is now seen as an important principle in allocation policy (as described in Section 5.3.2).[11,33,34] In basic terms, kidneys with a longer predicted life span are best allocated to recipients with a longer predicted life expectancy and vice versa. This is referred to as prognosis matching. Prognosis matching aims to optimise graft survival outcomes from the available donor pool, while giving a wide range of people on dialysis the opportunity to benefit from transplantation. As of May 2021, the principle of prognosis matching was introduced into kidney matching algorithms in Australia. The Kidney Allocation Algorithm continues to be enhanced and further work is underway to improve outcomes for patients and the community.

The ongoing development of the Australian Kidney Allocation Algorithm has also enabled greater HLA matching for younger, healthier patients who are likely to require re-transplantation in their lifetime. Kidney transplantation is one way that patients become sensitised against future transplants and this can limit the patient's ability to find a suitable second (or subsequent) kidney if they require retransplantation in the future. Younger, healthier patients are most likely to need a second or subsequent transplant because in many cases they outlive their original graft.

Better immunological matching may improve their chances of successful retransplant in the future. Changes to the Kidney Allocation Algorithm in 2021 made a first step in this direction, by initially preferentially allocating well-matched donor kidneys to waitlisted candidates with longer estimated post-transplant survival.

5.4.1 Principles

The principle intention of the Australian Kidney Allocation Algorithm is to ensure all deceased donor kidneys are allocated to a recipient by a process that is transparent, equitable and standardised. Currently this is done according to the following criteria:

- Blood group compatible (e.g., A to A) and blood group acceptable (e.g., O to B) See Appendix C for ABO selection rules
- Waiting time (see Section 5.2.1)
- HLA matching (tissue typing to determine the level of immunological compatibility between a donor and recipient)
- HLA-antibody detection (which can identify unacceptable HLA antigens, and be used to preclude certain donors)
- Certain priority allocations (e.g., paediatric recipients defined as age <18 years, combined organ recipients such as kidney-pancreas, highly sensitised recipients)
- The requirement to maintain an equitable flow of kidneys between states and territories
- Usually, the higher ranked recipient will be offered the left kidney, unless it is significantly smaller, poorly perfused, damaged or has challenging complex vascular anatomy, in which case it will be allocated to the lower ranked recipient.

5.4.2 Australian Allocation Algorithms

An overview of the Australian allocation process is shown in Figure 5.1 below. The specific algorithms for national and state-based allocation are transparent and available to all potential recipients (see Appendix C).

The first step of the allocation process is HLA typing of the donor to establish whether there is a recipient in any Australian state or territory who would receive a particular advantage or benefit from a specific kidney, based on a combination of their HLA-matching and unacceptable antigens. For these reasons, a proportion of kidneys are allocated based on immunological match according to the national allocation algorithm. In these situations, the kidney(s) may therefore be transported interstate. If not matched at the national level, the kidney(s) will be allocated according to the state algorithm.

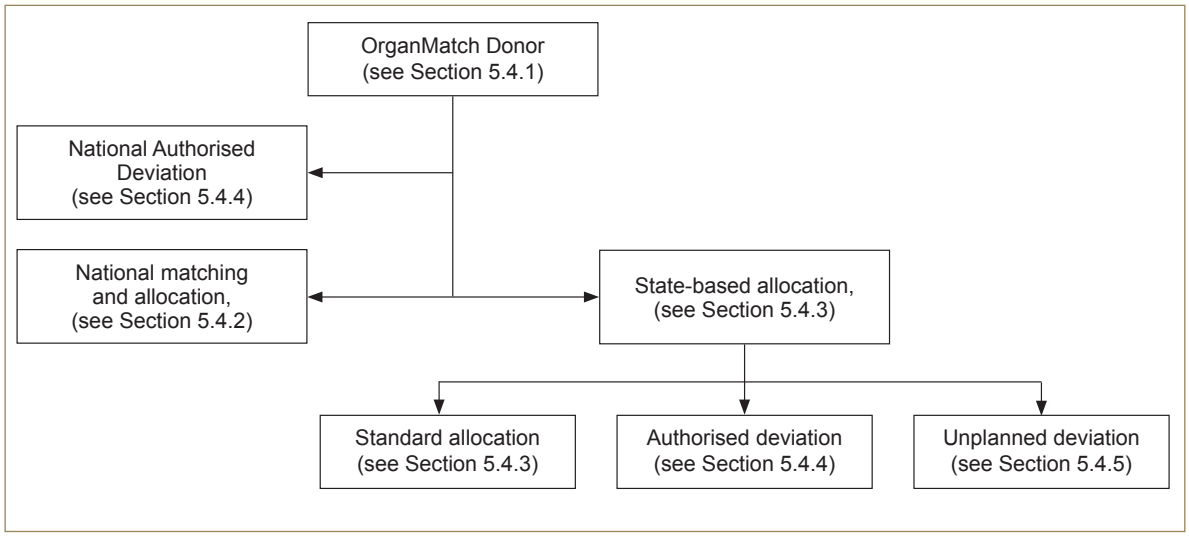
The national and state kidney allocation algorithms are complex and are continuously monitored and reviewed. Previously, on average, about 20% of deceased donor kidneys are transported interstate through national allocation. The remaining 80% of kidneys remain in their donor state and are allocated according to state algorithms. However, since the updated algorithm was implemented in May 2021, giving increased priority to the very highly sensitised waitlisted candidates, there has been an increase in the proportion of kidneys being allocated via the national algorithm.

For younger recipients who have longer life expectancies and thus may need more than one transplant in their lifetime, a good immunological match) is considered more important than it is in older recipients, as a better match may minimise the formation of HLA antibodies that may lead to difficulties in finding a compatible donor in the future. For older patients and those with multiple co-morbidities, the longer-term benefit of good immunological matching is less crucial as there is a lower likelihood of requiring a subsequent transplant.

5.4.3 State-based allocation using the state allocation algorithms

The state algorithms are primarily based on waiting time and immunological matching, although to lesser degree than the national algorithm (Appendix C). It is important to note that the majority of recipients overall do not receive highly immunologically matched kidney as this is usually not possible. However, excellent graft and patient outcomes are still achieved.

Figure 5.1: Flow diagram representing an overview of the pathway by which kidney allocation proceeds after initial matching within OrganMatch.



From a practical viewpoint, state-based allocation helps to minimise cold ischaemic time and allows for a more efficient use of local donation, laboratory, and retrieval team resources. There is good evidence that shorter ischaemic times improve transplant outcomes, especially for kidneys of lower quality. An additional advantage of state-based allocation is that it allows for state-based transplant advisory committees to continually review and improve the local allocation algorithm in order to reduce inequities and imbalances within their state. It also allows states to streamline their processes for allocating kidneys that are of lower quality or pose certain additional risks (e.g., possible infection or malignancy or anatomical difficulties). These kidneys are often very difficult to successfully allocate, and efficient local systems help to achieve the best use of these organs. The state transplant advisory committees review, audit and guide the principles applied in achieving successful allocation in these less typical cases that assist in maximising organ utilisation rates.[14,35] Some of these state-based scenarios are described below in Section 5.4.4 (dual organ allocation) and Section 5.4.5 (unplanned deviation).

5.4.4 Authorised deviations in allocation

Kidney allocation algorithms allow for certain exceptions or authorised allocation deviations using the rules defined below.

> Simultaneous pancreas and kidney (SPK) transplantation: SPK offers the best clinical outcomes for certain patients with type 1 diabetes mellitus and kidney failure.[36] When a suitable pancreas is donated for SPK transplant, one of the donor kidneys is also allocated to the same recipient. The second kidney is then available to be allocated to a kidney-alone recipient. If, however, there are two highly-sensitised (and hence more difficult to match) kidney-alone recipients who have a very good immunological match (Level 1 or 2 National Matching Score—see Appendix C) the allocation to the SPK patient will not occur (i.e., it will be vetoed) and the kidneys will be allocated to the two kidney-alone patients.

Children (paediatric recipients <18 years): because of the special needs of children with kidney failure, mechanisms for priority allocation exist for paediatric recipients in each jurisdiction to promote timely transplantation. Details of state-specific policies are provided in Appendix C.

Increased Viral Risk Donor (IVRD): donors with recent increased infectious risk behaviours (defined in Section 2.3.1) proceeding to donation within the eclipse periods for detection of HIV, HBV and HCV by nucleic acid testing (NAT) (see Table 2.3) may be allocated to well informed and consenting recipients. Recipients that consent to transplantation from an increased viral risk donor accept the small but increased risk, compared to standard-risk donors, that HIV, HBV and HCV transmission may occur, due to undetectable levels of virus at the time of testing and/or false-negative results.

Dual organ allocation (two kidneys to one recipient): occasionally, a deceased donor may have kidneys that are considered unsuitable to be used individually but still thought to provide benefit to a single individual recipient when transplanted together. In adult donors, 'dual' allocation may occur when the donor is elderly and has significant comorbidities which impact kidney function for example. This may also occur with the use of very small paediatric donors who are <20kg (1 to 5 year-old), or on rare instances there may be an allocation of a donor <10kg (3 to 12 month-old) to dedicated specialist centers, with relevant expertise to accept and implant infant en bloc kidneys into an adult recipient (for details see Chapter 11). The decision to offer both kidneys to one individual is made by the retrieving surgical and medical team after consultation and review of the donor and potential recipient's characteristics. The recipient is fully informed of the risks and benefits of dual allocation.

Multiple organ transplantation (other than SPK transplantation): In some carefully selected patients, a combination of a kidney and another solid organ (usually a heart or liver) is requested in order to achieve a satisfactory patient outcome. Requests for multiple organ retrieval are made via each state's transplant advisory committee. The organs in these cases are usually allocated within the donor state (see also Section 5.6).

Exceptional circumstances arising in the Australian and New Zealand Paired Kidney Exchange (ANZKX) Program:

There are two potential situations in which authorised allocation deviations may occur in relation to donors and recipients participating in the ANZKX:

- Orphaned kidney—this is a situation where a kidney removed from a living donor participating in a kidney exchange cannot be transplanted into the matched recipient because of a problem such as the recipient has an acute deterioration at the time of anaesthetic. Under these circumstances, the "orphaned kidney" may be reallocated to a patient on the deceased donor list in the country that the kidney is located in at the point it is orphaned. Kidneys in transit between countries will be allocated in the country of arrival. Under some circumstances, input from RTAC/ANZKX Clinical Oversight Subcommittee (RACOS) might be sought if required. In Australia, the allocation of the kidney will take into account the current location of the kidney, whether there are any potential recipients at Level 1-3 on the National Allocation formula and the logistics of transporting the kidney, as described in the ANZKX National Protocol. In New Zealand, the kidney will be allocated according to New Zealand's NKAS.[37]
- Orphaned recipient—this is a situation where a living donor kidney allocated to a recipient in the ANZKX program is surgically removed but is unusable, damaged, lost, or unable to be implanted into the intended paired recipient, even though the co-registered living donor for that recipient has already successfully donated to the other recipient in the paired exchange. This also includes the situation in which a kidney is damaged, the damage is identified by the recipient transplant surgeon prior to implantation and the kidney fails early after transplant. New Zealand and Australia will be responsible for the subsequent allocation of a kidney to an orphaned recipient enrolled in their country. In Australia, the 'orphaned recipient' will receive priority listing on the transplant waiting list (Level 3 interstate exchange) for a suitable kidney from the national deceased donor organ pool. In the case of a very highly sensitised recipient (very high calculated panel reactive antibody level) who is likely to be difficult to match, the degree of prioritisation can be altered following discussion with RTAC. Given that pre-emptive recipients are not on the deceased donor wait list in OrganMatch, approval will be sought from RTAC to allow orphaned pre-emptive recipients to be made active on the transplant waiting list and receive priority allocation. In New Zealand, prioritisation for orphaned recipients is defined in the NKAS algorithm.[37]

These agreements have been made with the approval of the Organ and Tissue Authority, New Zealand's NRLT Team, and RTAC endorsement. (For more information on the ANZKX, see the following link: https://donatelife.gov.au/ANZKX)

5.4.5 Unplanned (exceptional) deviations in allocation

In clinical medicine, circumstances often arise that require immediate decision-making, and it is not possible to predict all potential deviations from the usual allocation process. In every case, the overriding principle is to ensure every donated kidney is allocated to a suitable recipient and not wasted. These exceptional cases are audited and reviewed by RTAC and state-based transplant advisory committees, to ensure the principles of allocation are followed as far as possible and, if not, that the reasons for deviations are acceptable. Exceptions to usual allocation procedures often occur for the sake of patient safety, or to minimise the risk of discard of an organ. Examples of such circumstances are listed below.

Prolonged ischaemic time: if there is a prolonged cold ischaemic time, it may be particularly important to transplant the kidney as quickly as possible and therefore it may not be possible to transport the kidney interstate, as it would be deemed unusable on arrival. In these cases, the kidney needs to be allocated in the state in which it was donated, using the state-based allocation algorithm.

Technical issues: where there are technical issues that make it safer for the local surgical team who removed the deceased kidney to be involved in transplanting the organ. Examples include:

- Kidneys removed from living patients as a treatment for renal cancer. A small cancer is removed, the kidney repaired, and the kidney transplanted into a recipient who often has borderline eligibility for listing, who understands the additional risks of possible cancer transmission and surgical complications.[38]
- Kidneys that have significant anatomical abnormalities of the blood vessels (e.g. an aneurysm), ureter or parenchyma (e.g. large cysts, possible tumours that require biopsy). These kidneys may also pose an increased risk to the recipient and will generally be acceptable only to some patients on the TWL.

Intended interstate recipient is medically unfit: where the intended recipient is found to be medically unfit to undergo transplantation after the organ is shipped. For example, a kidney from Sydney may be on its way to Perth, however the intended recipient in Perth is found to be medically unsuitable due to a previously unrecognised problem. In order to prevent discard of this kidney, it may be necessary to reallocate the kidney to another patient located in Perth, rather than attempting to ship the kidney interstate a second time. In this example, the "urgency" of need for the next patient on the allocation list as well as the feasibility of getting the kidney to that patient should be considered.

No blood group/ immunological compatible recipient: for example where the donor is blood group AB and there is no one on the TWL of that blood group who is also HLA-compatible. In order to promote organ utilisation, transplanting units and/or donor coordinators may explore the following possible recipients: (i) an AB patient on dialysis that is not yet active in OrganMatch TWL but is deemed suitable to receive the organ (this is usually someone about to be made active within OrganMatch who has met all the requirements for listing including tissue typing); or (ii) someone who is close to needing dialysis but has not yet commenced and is deemed suitable to receive the organ, or (iii) someone with an incompatible blood group who may be able to receive the organ with additional treatment (such as plasma exchange).

5.4.6 Allocation of living donor kidneys to patients waitlisted for a deceased donor kidney

In very rare cases, when a kidney is required to be removed from an otherwise healthy individual with a kidney-specific disorder (e.g., a small tumour), the patient may indicate a wish to donate that kidney to someone awaiting kidney transplantation. Such kidneys can be repaired and offered to patients on the deceased donor waiting list according to the state-based allocation algorithm. Patients who are offered this type of kidney should be informed, counselled, and consent to the risks and benefits of receiving this organ before transplantation proceeds.

Non-directed altruistic donors (NDAD) are living donors who come forward wishing to donate a kidney but without an identified recipient. NDAD are fully assessed medically, surgically and psychologically as per standard protocols.

In Australia, if they are deemed suitable their donated kidney will be allocated according to the policy of the relevant state transplant advisory committee. This is usually done through the ANZKX program, and a chain of transplants will be performed with a donor kidney remaining at the end of the chain. This kidney is then allocated by OrganMatch to an Australian recipient on the deceased donor TWL as per ANZKX guidelines. This recipient on the TWL should be within the state of the NDAD if possible.

In New Zealand, the NRLT Team encourages units to consider entering suitable NDAD into the ANZKX. If NDAD donate directly, they are allocated according to the NKAS. If NDAD donate into the kidney exchange, the kidney at the end of the chain is allocated as a NDAD within the NKAS.[37]

5.5 Allocation: New Zealand

All deceased donor kidneys are allocated on a New Zealand-wide basis.

Kidneys must be offered to recipients according to the rules specified under the New Zealand Kidney Allocation Scheme[37]. For details, visit:

https://www.health.govt.nz/about-ministry/leadership-ministry/expert-groups/national-renal-transplant-service/nrts-papers-and-reports

5.6 Multi-organ transplantation

Uncommonly, a patient may require a multi-organ transplant, for example a liver and a kidney or a heart and a kidney at the same time. If, after detailed assessment by the treating specialists, a patient is deemed suitable, a request for consideration of a multi-organ transplant is jointly submitted to the local/state advisory committees. Each request is considered on a case-by-case basis.

Some patients may be considered for multi-organ transplantation prior to reaching kidney failure but will have significantly reduced kidney function to warrant a combined transplant.

The allocation of kidneys in the context of multi-organ transplantation follows different rules to standard allocation. For example, in the case of a patient deemed suitable for combined liver-kidney transplantation, when a liver is allocated to this patient the kidney from the same donor will be simultaneously offered. Whilst there is no confirmed process for multi-organ listing, it is currently under review by TSANZ.

In New Zealand, if the non-kidney transplant team consider that their patient also needs a kidney transplant, then a request is made and assessed by a kidney transplant physician at Auckland Transplant Centre. If the Auckland transplant group agrees to the multi-organ transplant, then the patient will be listed for multi-organ transplantation including a kidney.

5.7 Emerging Issues

The next review of the Australian Kidney Allocation protocol has now commenced and will build on further developing a more graded allocation algorithm, to ensure ongoing improvements in balancing utility and equity of organ allocation and kidney transplant outcomes.

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6 Liver

6.1 Preamble

Liver transplantation is a highly successful treatment for advanced liver disease, both in terms of extending and improving quality of life. The demand for liver transplantation and the shortfall in the number of donor organs available means that it is not currently possible to transplant every patient who might individually derive benefit from the procedure. This imbalance means that if every patient who stood to benefit from liver transplantation—even if only marginally—was placed on the waiting list then the list, and therefore waiting times, would become so long that most patients would die before ever being offered a transplant. In this scenario, many patients receiving a liver transplant would have their lives extended only marginally, while others—for whom liver transplantation might extend their lives by decades—would die on the waiting list. Therefore, liver transplantation is offered only to patients whose liver disease is of such a severity that their risk of dying within two years without a transplant exceeds 50%.

At the same time, it is necessary to strike a balance between maximising access to liver transplantation for those who would die without it and achieving the best possible outcome from each transplant. This balance is the single most difficult issue in liver transplantation because there is no "maintenance" treatment equivalent to renal dialysis, and thus there is only a finite time that patients can wait for a liver transplant. For the past 20 years, it has been agreed by the liver transplant units in Australia and New Zealand that eligibility for entry to the liver transplant waiting list should be set at an expectation that a patient has a greater than 50% likelihood of surviving at least five years after liver transplantation; this aligns with international benchmarks. In 2021, five-year patient survival among liver transplant recipients in Australia and New Zealand was 84%, while waiting list mortality (died on waiting list or within one year of delisting) was approximately 5%.[1]

There are arguments for and against setting such minimal listing criteria or "survivorship thresholds"; this difficult area—of balancing utility versus individual equity—is informed by the Ethical Guidelines.[2] It should also be appreciated that there are some patients with liver disease who would not benefit from liver transplantation. Liver transplantation is a massive surgical procedure, and the associated risks can outweigh the risks associated with the natural history of the underlying liver disease. Minimal listing criteria are therefore needed in order to prevent patients with less severe liver disease from being offered a liver transplant that would be riskier than continuing to live with their liver disease.

Additional complexity arises because the manifestations of liver disease are varied. There is no single indicator of liver dysfunction (unlike, by comparison, serum creatinine level in chronic kidney disease) that allows transplant units to track the decline of patients with liver disease, or to compare the severity of liver disease between patients (although the MELD score comes closer than many other systems; see below). Furthermore, not all patients in need of a liver transplant will die from liver failure without one. A common example is patients with Hepatocellular Carcinoma (HCC)—these patients have underlying chronic liver disease, but their survival is usually determined by the progression of the cancer rather than the failure of liver function. The particular relationship between HCC and eligibility for liver transplantation is covered in Section 6.2.3. Thus, it is difficult to "rank" the urgency of the need for liver transplant for patients on the waiting list. This is discussed in more detail in Section 6.3.

In the case of liver allocation, unlike other forms of solid organ transplantation, tissue matching beyond simple ABO blood group compatibility has little impact on transplant outcomes. However, there are other factors that are very important considerations in liver allocation, from technical factors such as size (a liver retrieved from a very large donor may not fit in a small transplant recipient and conversely a small liver may not provide adequate function in a large recipient), to how well the graft is likely to work initially (very sick recipients do not tolerate donor livers that have impaired function immediately after transplant), to complex logistical issues related to organ transportation (long preservation times resulting from transporting a donor liver over a great distance can have serious negative effects on the transplant outcome). The general principle is that a donor liver is allocated to the sickest patient for whom the liver is suitable; if the liver is of an incompatible blood type or there is a size mismatch then it would not

be helpful to transplant it into the sickest patient on the waiting list—in this case it would be offered to the next sickest patient for whom there would be an acceptable chance of successful transplantation with that organ. In this way, allocation decisions are made to enable the best outcome from every transplant.

Most deceased donor livers are allocated to patients with chronic liver disease on a state-based allocation system. However, there are situations where the liver can suddenly fail without warning, such as in acute Hepatitis B infection or paracetamol poisoning – in these situations patients can present to hospital and die within days. Additionally, children with a rare form of liver cancer called hepatoblastoma need access to liver transplantation in a time-sensitive manner (liver transplantation needs to occur rapidly after chemotherapy treatment is completed to secure the best chance of cure). The circumstances of urgent liver transplantation are very different from the circumstances under which patients with chronic liver disease are transplanted, and therefore waiting list management for acute and urgent patients is discussed separately in Section 6.3.3.

Organisation of liver transplantation in Australia and New Zealand

Each state in Australia has a single liver transplant unit. There is a single unit in Auckland that serves New Zealand. The New Zealand unit is broadly aligned with the units in Australia and participates in the sharing of donor livers between the jurisdictions as described in Section 6.5. The liver transplant units and their corresponding donor jurisdictions are as follows:

Jurisdiction of donor hospital	Location of liver transplant unit
WA, SA, NT	WA, SA
QLD	QLD
NSW, ACT	NSW
VIC, TAS	VIC
NZ	NZ

Each of the liver transplant units also undertakes multi-organ donor retrieval procedures as a service for the organ donation agencies that exist in each jurisdiction. Although the population of Australia and New Zealand is small compared to many European countries, the geography is very different – each liver transplant unit in Australia covers an area bigger than Western Europe and this is one of the reasons why organ allocation is organised on a jurisdictional, rather than national, basis.

6.2 Recipient eligibility criteria

6.2.1 Inclusion criteria

As a general principle, eligibility is restricted to patients for whom quality and quantity of life is expected to be enhanced by liver transplantation. Given the limited availability of donor organs and the risks to the patient of liver transplant surgery, patients will only be listed for liver transplantation once their liver disease poses an imminent threat to their survival or their quality of life has become intolerably poor.

Liver disease has many different manifestations and, in contrast to renal disease, it is difficult to describe the severity of an individual's liver disease with a single metric. In the United States in the late 1990s it was recognised that access to and timing of liver transplantation varied greatly around the country—some patients whose health was barely impacted by their liver disease were receiving transplants whilst many others died before receiving a lifesaving transplant. This stimulated the development of a scoring system, the Model for End-Stage Liver Disease (MELD) score, which correlates with how long a patient is likely to survive without a liver transplant (Table 6.1: Calculation of MELD, PELD and HCC MELD scores).

MELD score is a measure of the severity of an individual's liver failure, calculated using a mathematical formula based on blood tests: the higher the score, the greater the severity of liver failure. The Paediatric End-Stage Liver Disease (PELD) score is an equivalent system adjusted for children. The score has a reasonable, but not perfect,

ability to predict the risk of dying from liver failure in the near future (3 months). It has allowed jurisdictions in the United States to allocate livers based on need alone. This is particularly important where many centres 'compete' for donor livers, and the MELD score-based allocation system has been implemented to reduce 'gaming' of the system by individual centres for their own, and their patient's benefit. It must be recognised, however, that it is quite common to have severe liver disease, posing an imminent threat to life, where the MELD score is still relatively low. In Australia and New Zealand, where all livers go to a single centre (i.e. there is no competition) the liver can be allocated to the individual with the truly greatest need even if they do not have the highest MELD score. In Australia and New Zealand, the patients are ranked within each transplant centre according to clinical need, which takes into account their MELD scores but also other less easily measured factors.

There are some patients who, although their survival is not immediately threatened, have an intolerably poor quality of life as a result of their liver disease. The best example would be patients with polycystic liver and kidney disease, for whom liver function may not be impaired but the liver can reach such a size that it completely fills their abdominal cavity and results in starvation because the patient becomes physically unable to eat.

Typical indications for liver transplantation in patients with chronic liver disease are:

- MELD score of >15 in an adult or a PELD score of >17 in a child (see Table 6.1: Calculation of MELD, PELD and HCC MELD scores)[3]
- HCC that fulfils accepted transplant eligibility criteria (see 6.2.3) criteria[4]
- Liver disease that would result in a two-year mortality risk of >50% without liver transplantation
- Diuretic-resistant ascites
- Recurrent hepatic encephalopathy
- Recurrent spontaneous bacterial peritonitis
- Recurrent or persistent gastrointestinal haemorrhage
- Intractable cholangitis (in primary or secondary sclerosing cholangitis patients)
- Hepatopulmonary syndrome[5]
- Portopulmonary hypertension[5]
- Metabolic syndromes (with severe or life-threatening symptoms) that are curable with liver transplantation (e.g. familial amyloidosis, urea cycle disorders, oxalosis etc.)
- Polycystic liver disease with severe or life-threatening symptoms
- Intractable itch secondary to cholestatic liver disease
- Hepatoblastoma in children
- Severe alcoholic hepatitis not responding to medical therapy in appropriately selected patients (see Section 6.2.4).

Table 6.1: Calculation of MELD, PELD and HCC MELD scores[a]

MELD score	=0.957 x Log_e(creatinine mg/dL) + 0.378 x Log_e(bilirubin mg/dL) + 1.120 xLog_e(INR) + 0.643 Multiply the score by 10 and round to the nearest whole number Notes: Laboratory values of <1.0 are set to 1.0 for the purposes of the MELD calculation The maximum serum creatinine is 4.0 mg/dL. This includes those patients on dialysis.
PELD score	= 0.480 x Log_e(bilirubin mg/dL) + 1.857 x Log_e(INR) – 0.687 x Log_e(albumin g/dL) + 0.436 if patient is <1 year old + 0.667 if the patient has growth failure (<2 standard deviations below the mean) Multiply the score by 10 and round to the nearest whole number Notes Laboratory values of <1.0 are set to 1.0 for the purposes of the PELD calculation
HCC MELD	If the maximum tumour diameter is >2cm but total tumour burden is within UCSF criteria (i.e. tumour not >6.5 cm in diameter and total diameter of all tumours not more than 8cm), and without evidence of vascular invasion, then a score of 22 will be allocated to the patient. An additional 2 points will be allocated for every 3 months on the waiting list. If the maximum tumour diameter is ≤2cm there will be no HCC MELD points allocated to the patient. This patient's score will be the standard MELD score only.

[a] http://www.unos.org/resources/meldpeldcalculator.asp

6.2.2 Exclusion criteria

Patients who are estimated to have less than a 50% likelihood of surviving at least five years after liver transplantation, and patients who are predicted to have an unacceptably poor quality of life post-transplant, are considered ineligible for wait-listing. Exclusion criteria therefore include those conditions or circumstances (medical or psychosocial) that would make the risk of mortality at five years post-transplant exceed 50%. The assessment of risk associated with coexisting conditions is complex and many patients require detailed appraisal by specialists across multiple fields before determining whether a patient should be excluded from entry to the waiting list. The NHMRC Ethical Guidelines underpin the specified exclusion criteria.[2] Past behaviours such as intravenous drug use or alcohol dependence are not acceptable as reasons for exclusion from the liver transplant waiting list, but if these behaviours are ongoing then they would be considered exclusionary as they threaten the outcome of the transplant. The following list of contraindications to liver transplantation is indicative but not exhaustive:

- Malignancy: prior or current, except for HCC within criteria outlined in 6.2.3.1 and small intrahepatic cholangiocarcinoma 6.2.3.2).[6] These cases often require detailed discussion between transplant units and oncologists prior to the patient being assessed for transplantation because the prognosis of different cancers varies widely
- Active infection (other than hepatitis B, hepatitis C, or HIV)—tuberculosis would be an example
- Coronary artery disease that is irremediable or associated with a poor prognosis
- Cerebrovascular disease that is irremediable or associated with a poor prognosis
- Severe metabolic syndrome (hypertension, morbid obesity, hyperlipidaemia, and type II diabetes, with or without obstructive sleep apnoea)[7]
- Extreme inanition or frailty not thought to be reversible by liver transplantation
- Patients at significant risk of a return to hazardous alcohol intake: for those patients where alcohol was a contributing factor in their liver disease, careful assessment by a multidisciplinary team of the risk to post-transplant outcomes posed by recidivism is required. As a general rule, a period of abstinence of not less than six months will need to be observed before acceptance onto the waiting list to exclude patients with alcohol related liver disease whose liver function will improve with abstinence to the point where liver transplantation is no longer needed.[8] Patients with decompensated alcohol related cirrhosis, who are unlikely to survive until observing 6 months of abstinence, should be evaluated and assessed by a multidisciplinary team* prior to acceptance on the transplant waiting list. Access to the multidisciplinary team* and adherence to long-term relapse prevention should be available for patients who are on the waiting list and following transplantation. Ultimately, the decision to assess and list a patient is determined by the individual transplant centre's team, focusing on the likelihood of survival in the absence of transplantation, and the long-term benefit and ability to manage the risk of return to harmful drinking after the transplant. If assessment of a return to hazardous drinking risk is unfavourable then this is a contra-indication to proceeding with transplantation because of the risk of compromised outcomes. Patients considered for transplantation for severe acute alcoholic hepatitis (AH) do not require a specified period abstinence but must fulfil additional inclusion and exclusion criteria (6.2.4).
- Ongoing misuse of any substance that might compromise survival of the graft
- A likelihood that the recipient will be unable to adhere to the necessary ongoing treatment regimen and health advice after transplantation
- Tobacco use is a relative contraindication to liver transplantation (because of an increased risk of malignancy and cardiovascular disease)[9,10]
- Inadequate or absent social support is a relative contraindication to liver transplantation (because of an increased risk of non-adherence)[11,12]
- Hepatopulmonary Syndrome: current evidence shows that patients with this condition who have a partial pressure of oxygen on room air of <40 mmHg have an unacceptably high perioperative mortality rate (30 to 40%)[5]

* A multidisciplinary team assessing an individuals suitability for transplantation should include a transplant hepatologist, transplant surgeon, counsellor, psychiatrist and addiction specialist who should be involved in all stages of the transplant journey. This includes the assessment period, ongoing evaluation whilst waitlisted, and in long-term follow-up.

- Portopulmonary hypertension: current evidence shows that patients with this condition who have, despite treatment, a mean pulmonary artery pressure of >35 mmHg and a pulmonary vascular resistance of >250 dynes.sec.cm^{-5} (3.1 Woods units)[7] have an unacceptably high perioperative mortality rate (30 to 40%, with patients often succumbing during the transplant surgery)[5]
- Neurocognitive impairment is not an absolute exclusion criterion, but all units are aware that such patients and their carers may find that the outcome of transplantation is not as good as they hoped, with little improvement in quality of life. Patients with severe neurocognitive impairment require an exceptionally careful evaluation.

6.2.3 Malignancy assessment

6.2.3.1 Hepatocellular carcinoma (HCC)

In Australia and New Zealand, hepatocellular carcinoma (HCC) accounts for 25% of liver transplants either as a primary or a secondary indication and currently carries a 5-year post-transplant survival of approximately 84%[13]. HCC typically arises in a setting of chronic liver disease and is an unusual malignancy in an otherwise normal liver. Any patient with cirrhosis has an increased risk of HCC, but that risk is greater in liver disease arising from certain causes such as hepatitis B and hepatitis C. While patients with a single small HCC can sometimes be treated with liver resection or ablation, others can only be cured by liver transplantation. Establishing which HCC patients are eligible for transplantation is complex. There is substantial heterogeneity in the way that tumours behave, and predicting the natural history of disease progression in the HCC patient is not straight forward. Furthermore, the "severity" or stage of a HCC is variable, and it has been established for more than two decades that there is a high risk of recurrence and death if liver transplantation is performed in the context of advanced HCC.

Several transplant eligibility criteria have been developed for HCC by correlating pre transplant HCC characteristics with survival outcomes. The Milan criteria established that limiting tumour burden to a solitary lesion less than 5cm or up to 3 lesions each no more than 3cm in diameter and in the absence of vascular invasion or extrahepatic disease, improved post-transplant recurrence-free survival.[14] Expansion of the original Milan criteria, as proposed by the University of California San Francisco (UCSF) group,[15] or the extended Milan "up-to-7 rule"[16] amongst others, has demonstrated that less restrictive criteria can be used without impacting survival.

UCSF eligibility criteria

In Australia and New Zealand, the UCSF criteria of up to 3 lesions measuring no larger than 4.5cm in diameter and adding to a total tumour diameter of 8cm or less, or a single tumour up to 6.5cm, have been adopted for liver transplant waitlisting. The prognostic value of alpha fetoprotein (AFP) as a surrogate of microvascular invasion and as a predictor of poor post-transplant outcomes in HCC has also been established.[17-19] An AFP cut-off of >1000 ng/mL has been recommended in Australia and New Zealand as an exclusion for liver transplantation in line with current US guidelines,[20] however more restrictive cut-offs have been used in other countries.[21] By adding AFP cut-offs to waitlisting and/or downstaging models, improvements in predicting post-transplant outcomes have been demonstrated.[18, 22-24]

Metroticket 2.0 eligibility criteria

The Metroticket 2.0 model uses pre-transplant imaging and AFP to predict post-transplant HCC-recurrence free and overall survival[24]. This model has several potential advantages over existing criteria based on tumour size alone. Firstly, the model was derived and validated using pre-transplant radiology tumour characteristics rather than explant histology, pragmatically representing the point of decision making in clinical practice. Secondly, a competing risks analysis was performed, which identified non-HCC related death as a competing risk with HCC-related death and provided more accurate survival estimates. Thirdly, the Metroticket 2.0 model can be used as an individual risk calculator for five-year HCC-specific and overall survival or as a dichotomous (in/out) criteria. Validation of the Metroticket 2.0 model using data from all the Australian and New Zealand liver transplant units found that patients fulfilling the Metroticket 2.0 criteria on explant have a survival comparable to those using UCSF criteria, which was similar to single-centre Australian data using pre-transplant imaging. Thus, expansion of criteria to MT2 is justifiable.[25]

There are several important caveats to using the Metroticket 2.0 model. The vast majority of patients in the derivation cohort of the Metrocket 2.0 model received TACE or other neoadjuvant treatments. The measurements that were used to derive the model were based on the most recent imaging and AFP prior to transplant, not the measurements at listing. Nodules were only counted if they remained arterialized after neoadjuvant treatment and nodule size was taken to include the largest diameter of both viable and non-viable portions. It follows that in applying the prognostic model, tumour number and size need to be defined and measured in the same way.

Downstaging

Factors such as lack of tumour response to transarterial chemoembolization (TACE) or atypically aggressive tumour biology have been correlated with poor post-transplant outcomes[26]. A period of close observation may be required to confirm that tumour burden remains firmly within transplant eligibility criteria. In the setting where potential transplant candidates have tumour burden in excess of UCSF or Metroticket 2.0, loco-regional therapy such as TACE may be offered to reduce the tumour burden to downstage to within transplant criteria. If downstaging is offered, then potential transplant recipients must demonstrate that they remain within transplant eligibility criteria for a minimum observation period of 3 months before being considered for waitlisting[27]. As aforementioned, the Metroticket 2.0 prognostic model was derived using measurements that include the influence of downstaging, although the model has not been specifically validated in this setting. Patients may be downstaged to within Metroticket 2.0, UCSF or Milan criteria, depending on individual transplant unit preference, however such patients should be reassessed after a minimum 3-month observation period before being activated on the waiting list.

Allocation priority

Another complex issue is determining the priority of HCC patients on the liver transplant waiting list. The is no confirmed optimal method of prioritising HCC patients to ensure they are transplanted before they are ineligible due to tumour progression, while also ensuring non-HCC patients are not disadvantaged. Assigning additional MELD points to HCC patients on the waiting list and other systems have been suggested, but with varying degrees of success[28]. In Australia and New Zealand, waiting list prioritisation remains the responsibility of the individual transplant unit. The burden of HCC continues to rise and ensuring equitable organ allocation remains a pertinent issue for the future.

Recommendation

UCSF criteria or Metroticket 2.0 are the eligibility criteria for liver transplant waitlisting in Australia and New Zealand.

AFP >1000 ng/mL should be considered as an exclusion for liver transplant waitlisting.

The Metroticket 2.0 model is acceptable for liver transplant waitlisting. The listing threshold may be set by individual units but must be predictive of at least 70% HCC-specific 5-year survival.

Metroticket 2.0, UCSF or Milan may be used as downstaging criteria. Any patient who is offered downstaging must remain within the respective criteria for a minimum 3-month observation period prior to activation on the waiting list.

6.2.3.2 Intrahepatic Cholangiocarcinoma

Small intrahepatic cholangiocarcinoma is now accepted as a primary indication for liver transplantation.

Although actual or suspected cholangiocarcinoma has historically been a major contraindication to liver transplantation, recent international publications have demonstrated good outcomes for a subset of patients with the following strict criteria:

- solitary (although there could be co-existing HCC within HCC criteria (6.2.3.1))
- small ≤ 20mm
- intra-hepatic
- unresectable, and in the presence of cirrhosis of the liver
- have no evidence of metastasis (including local lymph nodes).

The lesion can be the primary indication for transplantation if the diagnosis is relatively certain or there is another co-existing indication such as chronic liver disease. Biopsy of suspicious lesions is discouraged due to the small risk of tumour seeding. PET scanning is not required prior to transplantation.

Reasonable efforts to rule out other diagnoses such as metastasis from the GI tract should be undertaken (such as CT imaging, tumour markers, and appropriate endoscopic examinations). There is no requirement for neo-adjuvant therapy prior to transplantation.

Screening for new or metastatic lesions and lesion growth beyond 20mm while awaiting transplant should occur at least every 3 months by CT or MRI imaging. Delisting will occur if the tumour breaches the criteria above.

The role of post-transplant adjuvant chemotherapy or immunosuppressive modulation will be based on the post-transplant histology and be at the discretion of the local transplant team and oncology recommendations.

6.2.4 Early transplantation for severe acute alcoholic hepatitis

Alcoholic hepatitis (AH) is a clinical entity that is usually, but not always, diagnosed by biopsy. Severe AH that fails to respond to medical therapy has a mortality of 70% at two months.[29] Liver transplantation is the only lifesaving treatment for these patients. International data suggests that the three-year survival of carefully selected patients transplanted for a first episode of alcoholic hepatitis is equivalent to that of patients transplanted for other indications.[30-32] The survival and comparatively low alcohol relapse rates suggest the feasibility of performing liver transplantation in this group of patients in Australia in those units that have the necessary resources for patient assessment and post-transplant alcohol related follow up. In those units that have an active AH policy the following are required.

Inclusion criteria:

1. Patients must meet the specific definition of severe AH:[33]
   a. Onset of jaundice within prior 8 weeks
   b. Ongoing consumption of at least >40g for women and >60g for men of alcohol/day for six months or more, with less than 60 days of abstinence before onset of jaundice
   c. AST and ALT > 50 IU/L but <400 IU/L
   d. Bilirubin > 50mmol/L
   e. Liver biopsy confirmation (strongly recommended)
   f. Maddrey Score of >32 AND MELD score >20
2. Patient must be a non-responder to appropriate medical therapy—for most patients this will be corticosteroids managed as per Lille criteria, though some patients will have a contraindication to steroids
3. Presentation of severe AH must be the first liver decompensating event
4. Favorable psychosocial profile as determined by multidisciplinary team
5. Consensus agreement by the unit's transplant committee.

Exclusion criteria (in addition to those listed in Section 6.2.2)

1. Prior documented diagnosis of advanced alcohol related liver disease such as cirrhosis or previous decompensating liver event (e.g. jaundice, ascites, variceal bleed)
2. Presence of severe alcohol use disorder as classified by DSM V (previously termed alcohol dependence)
3. Absence of insight into alcohol as cause of liver disease / current presentation
4. Absence of agreement by patient to adhere to lifelong total alcohol abstinence and participate in long term post-transplant relapse and monitoring.

At the outset, patients should be diagnosed with dual pathology of both alcohol use disorder and liver disease. For optimal outcomes, both conditions should be managed in the long term with equal attention. Alcohol relapse prevention should be integrated into post transplant management in a structured way, preferably with regular alcohol biomarker monitoring. Relapse prevention should be multidisciplinary and evidence based, performed by an experienced practitioner skilled in a variety of psychotherapeutic techniques. Consideration should be given to pharmacotherapy for patients with ongoing cravings. There should be rapid identification and simple pathways to escalate support for those patients identified as having "slipped" to prevent the return to the pattern of sustained drinking.

6.2.5 Retransplantation

Patients are eligible for re-transplantation if they fulfil the same criteria for either acute or chronic liver disease as stated above, with an estimated likelihood of surviving at least five years post-retransplantation exceeding 50%.

6.3 Waiting list management

6.3.1 Principles of prioritisation for liver transplantation

For patients with chronic liver disease who are waitlisted for liver transplantation, care is provided at one of the Australian or New Zealand liver transplant units, which co-align with organ donation services. It is logistically complex to transport donor livers around Australia and New Zealand; furthermore, organ donation rates are such that it is most efficient to organise liver transplant services at the state level. Therefore livers donated in a given jurisdiction are allocated to patients on the waiting lists of the transplant units that correspond to that donor jurisdiction (unless there is a patient on the urgent waiting list—see Section). It is therefore necessary for each liver transplant unit to be very familiar with the patients on their waiting list and to prioritise them according to clinical urgency in order to minimise waiting list mortality.

Patients on the liver transplant waiting list are grouped according to the blood group of the donor liver that the patient on the waiting list would ideally receive, and then prioritised according to clinical urgency within each blood group. The waiting list is organised in this way to promote equitable outcomes across recipient blood groups. Usually this will mean that recipients will receive only a liver with the identical blood group to their own. However, in some circumstances where a patient is extremely unwell, they might receive a liver that would otherwise have been allocated to other blood group lists. For example, a blood group O liver can be transplanted into a patient of any blood group, and this may occasionally be necessary to save the life of a very sick patient of another blood group. Conversely, subtype 2 of blood group A is compatible with blood group O, and hence A2 livers can be transplanted into O recipients. Blood group incompatible transplants can also be performed, but these are rare and only performed when patient risk assessment suggests that it is justified and certain technical manipulations are undertaken.

Prioritisation is NOT based on the length of time that patients have been on the liver transplant waiting list: the principle guiding liver allocation is always "sickest first". Prioritisation is based largely on MELD score, but other features of liver disease (such as encephalopathy) may justify prioritisation above patients with higher MELD scores. In the United States, such patients are termed "MELD exceptions" in recognition that their MELD scores don't serve them equitably, and there is a complex protocol in place to enhance their priority. An example would be patients with primary sclerosing cholangitis, who are prone to serious recurrent bacterial cholangitis with blood poisoning yet who frequently have low MELD scores. There are also a number of rare diseases where the liver doesn't fail but has a metabolic defect—in the manufacture of an important protein for example—which leads to life threatening disease in another organ system (amyloidosis is an example). The liver transplant units in Australia and New Zealand work out how to prioritise such patients on their own individual waiting lists.

Each unit reviews their waiting list at least weekly and discusses the priority of listed patients. In this way, patients who deteriorate—especially if this isn't reflected in their MELD score—can be re-prioritised. In Australia and New Zealand, prioritisation occurs by clinical consensus among all members of the transplant unit. At the time of a liver donor offer the selection of a recipient is then relatively straightforward and can be made by one or two individuals rather than the entire clinical group, as patients have been ranked by need ahead of time.

6.3.2 Ongoing review

In the same way that a patient listed for urgent liver transplantation can deteriorate to a point where transplantation becomes futile, so might non-urgent patients need to be delisted because their situation has changed in such a way that they are no longer likely to benefit a from liver transplant. The commonest reason for this is cancer progression in patients with HCC, where the tumour(s) has grown to the point where the risk of recurrence after transplant is unacceptably high.

Clinical circumstances can arise that mean that a patient needs to be temporarily removed from the 'active' waiting list. An example would be a significant infection, causing an acute illness such that liver transplantation at that time would be hazardous. These patients are placed on a 'hold' list that allows them to still be reviewed at the transplant unit clinical meetings and, when appropriate (e.g. after the infection is successfully treated), they can be returned to the active list or permanently delisted if necessary. Patients are informed of such changes in listing status whenever they occur. The reasons for the status change should be made clear to the patient or, if appropriate, to their next of kin.

6.3.3 Acute and urgent patients

There are situations in which the need for liver transplantation occurs suddenly and without a history of pre-existing liver disease. This can happen in patients newly infected with hepatitis B where the liver is rapidly overwhelmed by the virus. Paracetamol poisoning is another example. However, in some patients no cause of acute liver failure can be established. There is also a small risk in patients who have recently undergone liver transplantation that the donor liver may not work, due either to primary non-function or hepatic arterial thrombosis. Many patients with acute liver dysfunction will recover spontaneously as the liver cells overcome the causative insult—only a few patients will actually require urgent liver transplantation.

In Australia and New Zealand, the King's College criteria, first devised in 1989, are used to guide whether a patient might need urgent liver transplantation. It is recognised that there are limitations to the use of the King's College Criteria in the era of early renal replacement therapy for neuroprotection, and markedly improved transplant-free outcomes than were originally reported related to critical-care improvements. It is recognised that the urgency of the situation is not always the same from one patient to another—in the most extreme cases, where the patient is in a coma and on a ventilator (life support), the patient may have less than 24 hours to live and is placed in Category 1. Less serious cases, where the data indicate severely impaired liver function, but the patient is not yet ventilated, are placed in Category 2a. See Table 6.2 for all urgent liver listing categories.

King's College Hospital criteria for liver transplantation in acute liver failure

Paracetamol (acetaminophen)-induced liver failure:

pH of arterial blood (after rehydration) of <7.3, OR all three of the following criteria on the same day:

- International normalised ratio (INR) >6.5
- Serum creatinine >300 micromol/L
- Grade III or IV encephalopathy.

Non-paracetamol-induced acute liver failure:

INR >6.5, OR three of the following five criteria:

- Age <11 or >40
- Serum bilirubin >300 micromol/L
- jaundice-to-encephalopathy time of >7 days
- INR >3.5
- Drug-induced liver injury or viral hepatitis as aetiology.

For urgent liver transplantation, recipient prioritisation and allocation of donor livers is conducted on an Australia and New Zealand-wide basis (i.e. binational listing). This is because the populations served by the individual jurisdictions (Australian States and New Zealand) are too small to realistically offer a good chance of a donor liver becoming available for urgent patients in the necessary timeframe. It has been agreed that patients fitting the criteria for urgent listing should have access to donor livers across all of Australia and New Zealand. Since less than 10% of liver transplants are performed in urgent patients, this does not seriously impact upon waitlisted patients with chronic liver disease. However, to reduce the possibility that patients with chronic liver disease might be adversely affected by urgent listings, two categories of urgency exist.

Extremely sick patients are placed in Category 1: any donor liver that becomes available anywhere in Australia or New Zealand is automatically offered to a patient in Category 1. It is possible, however, that there might be patients with chronic liver disease who are on the waiting list and, although not listed as urgent, may be at greater risk of dying than an urgent patient in Category 2a. Thus, when a donor liver becomes available in a given jurisdiction and there is a Category 2a patient listed elsewhere in Australia or New Zealand, a discussion needs to occur between the transplant unit in the jurisdiction listing the Category 2a patient, and the transplant team in the donor home state to ensure that the liver is in fact directed to the sickest patient. In practice, this is usually to the Category 2a patient.

There are two further types of Category 2 patients. Category 2b, which refers to children with hepatoblastoma in whom liver transplantation needs to occur quickly at the conclusion of chemotherapy treatment so that cure can confidently be achieved; and Category 2c, which refers to patients who need combined liver and intestinal (small bowel) transplantation.

It is exceptionally difficult to find suitable grafts for Category 2c patients, who also present a formidable surgical challenge as well as having a high risk of dying whilst they await transplantation. It has been agreed across all liver transplant units that Category 2c patients will be assigned national prioritisation, however, it has also been agreed that donor livers will not be sent to the National Intestinal Transplant Unit (part of the Liver Transplant Unit Victoria) if the jurisdiction in which the liver was donated has a patient on their waiting list with a MELD score of 25 or greater (such patients have a 50% chance of death within a month).

In the case of both Category 2b and Category 2c patients, discussion regarding liver allocation needs to take place between the urgent listing unit and donor home state transplant unit before allocation takes place.

Patients with high MELD (or PELD) scores in Australia and New Zealand historically had limited access to deceased donor livers. To address this, binational sharing of donor livers for patients with a MELD score ≥35 was introduced in February 2016, now known as Share 35. The Share 35 process is a liver transplant allocation policy aimed at reducing waiting list mortality and maximising the utility of donated livers. It prioritises patients with a MELD score of 35 or higher, offering waitlisted patients with MELD ≥35 an opportunity to be considered for a transplant, beyond that of home state offers. Since the implementation of the Share 35 policy, there has been a 78% reduction in waiting list mortality, with post-transplant survival remaining equivalent and overall intention-to-treat survival improving.[34] A discussion regarding liver allocation between the Share 35 listing unit and the donor home state transplant unit is encouraged, though not compulsory, prior to allocation.

The PELD score (see Table 6.1) is an evidence-based tool used to quantify disease severity and prioritise liver transplantation in children under 12 years of age. A score of ≥=25 has been identified as a threshold representing a high risk of waitlist mortality and significant risk of clinical deterioration.

The PELD 25 category ensures that these paediatric patients are recognised as a priority group within the national allocation framework. This approach reflects both the prognostic value of the PELD score and the ethical imperative to provide equitable access for highly vulnerable paediatric recipients.

Table 6.2: Categories of patients eligible for urgent liver transplantation

Category 1	
Patients suitable for transplantation with acute liver failure who are ventilated and in an ICU at risk of imminent death. When such patients are listed, allocation to them is mandatory.	
Category 2	
When a donor liver becomes available, discussion occurs between the urgent listing unit and the donor home state transplanting unit to determine optimal allocation	
Category 2a	Patients suitable for transplantation with acute liver failure from whatever cause who are not yet ventilated but who meet the King's College criteria. This includes patients who have acute liver failure because of vascular thrombosis in a liver allograft. In addition, this category includes paediatric candidates with severe acute or chronic liver disease who have deteriorated and are in a paediatric intensive care unit. When such patients are listed, allocation to them is usual but not mandatory. It is subject to discussion between the directors (or delegates) of donor and recipient state liver transplant centres across Australia and New Zealand.
Category 2b	Paediatric patients suitable for transplantation who suffer from severe metabolic disorders or hepatoblastoma (after initial treatment) for whom a limited time period exists during which liver transplant is possible.
Category 2c	Patients awaiting combined liver-intestinal transplantation by the National Intestinal Transplantation programme in Victoria. If a potentially suitable donor is identified, the donor home state transplant unit must discuss allocation of donor organs with the Victoria unit unless the donor home state transplant unit has a suitable liver recipient with a MELD score of 25 or greater.

Share 35

Patients with chronic liver disease awaiting liver transplant who have, or progress to, a MELD score of 35 or higher can be listed under the Share 35 programme. Share 35 patients are listed across all liver transplant units in Australia and New Zealand; however, they are categorised separately from urgent listings.

It is not compulsory to offer to Share 35 patients, a decision is made by the donor home state transplant unit whether to offer on or not. A discussion between units is encouraged but not compulsory.

PELD 25

Paediatric patients on the liver transplant waitlist who have, or reach, a PELD score of 25 or above may be listed under the PELD 25 programme. These patients are included across all liver transplant units in Australia and New Zealand, but are categorised separately from urgent paediatric listings (Categories 2a and 2b).

Listing and delisting of acute and urgent patients

Patients meeting criteria for Urgent or Share 35 PELD 25 listing are registered on OrganMatch by the home-unit. The assessment of patients needing urgent liver transplantation is complex, and the situation is never static. Some acute patients improve while they are waiting for a donor organ, and therefore can be removed from the waiting list (delisted) because they no longer need a transplant to survive. Other patients unfortunately deteriorate while waiting for an urgent liver transplant and may reach a point where transplantation is futile, in which case they must be delisted. An example of this would be the onset of brain swelling when, even if a transplant is undertaken, the ensuing brain damage cannot be reversed and would prove fatal.

Patients listed for urgent liver transplantation must be frequently re-assessed. The listing automatically expires after 72 hours for Category 1 and Category 2a patients, and after 7 days for category 2b, Share 35, and PELD 25 patients. Patients must be formally relisted in OrganMatch at these time points if liver transplantation is still required. Category 2c are exempted from the relisting requirements because they are not in a situation where their condition is expected to improve (however, they may require delisting if there is a change in circumstances such that transplantation is no longer appropriate). Please also refer to the OTA/TSANZ National Standard Operating Procedure: Organ Allocation, Organ Rotation, Urgent Listing for urgent listing procedures.

6.4 Donor assessment

All donor organs are precious, and the altruistic act by donor families of consenting to deceased donation in the most difficult and tragic of circumstances is gratefully and respectfully acknowledged. The goal of organ transplantation is to save and improve lives; in some circumstances, however, a potential donor liver may carry some risk of not achieving this goal. The worst case scenario is that the liver does not function after transplantation, in which case the recipient of that liver will die (unless a second donor liver quickly becomes available). There is also the potential transmission of infection or cancer from the organ donor to the recipient via the donor liver (see Chapter 2).

The assessment of donor eligibility and the suitability of organs for transplantation is one of the most difficult and complex areas of liver transplantation. Decision-making is frequently not straightforward: patients on the waiting list are at risk of dying without a transplant so it may be preferable to accept a higher-risk donor liver when offered rather than wait for a lower-risk one, not knowing how long that wait might be. Of course, the risk-benefit calculation is not the same for all patients. The HCC patient with a tumour that is approaching the size threshold for delisting will present a different risk-benefit scenario with regards to utilisation of a higher-risk donor liver as compared to stable a patient with cirrhosis from hepatitis C. Balancing the risks associated with a given donor organ against recipient urgency is one of the most difficult tasks faced by liver transplant units.

During the assessment and workup of potential liver transplant recipients, donor-related risk as it relates to the individual patient needs to be thoroughly explained as part of the consent process. Thus, a patient who is very unwell and at high risk of imminent death may be advised to accept a higher-risk liver—for example, a liver retrieved from a donor carrying the hepatitis B virus. The recipient of this graft may then require lifelong anti-viral treatment, but this may be acceptable if such a donor liver represents the only opportunity for this very sick patient to receive a transplant. On the other hand, a liver from a hepatitis B-positive donor or other higher-risk donor might not be suitable for a young child.

As well as the general donor eligibility criteria described in Chapter 2, there are some specific donor considerations relevant to liver transplantation. In contrast to the considerations related to higher-risk donor organs, it is also possible to identify donor livers that carry very low risk of either immediate or long-term dysfunction. In the case of low-risk livers, there is a commitment in Australia and New Zealand that these will be “split” wherever possible—typically generating a small left-sided graft and a larger right-sided one. Thus the single donor liver can be transplanted into two people. This is especially relevant to the transplantation of children, who usually only require a small graft—the left side being ideal. Such donors are young (less than 50 years of age), have been diagnosed with neurological death, have no risks factors for infection or malignancy, and their management in ICU has been straightforward, without any cardiovascular instability and little requirement for blood pressure support with drugs.

6.4.1 Donor-related risk

Risks to liver function

Certain donor-related factors are likely to influence the post-transplantation outcomes of their liver, including:

- Age
- Length of hospital stay
- Length of ICU stay
- Cold ischaemia time
- Fatty liver
- Cause of death
- Donation after circulatory determination of death (DCDD).

Risk assessment of liver donors is recognised to require considerable experience in the field of liver transplantation. The Donor Risk Index (DRI), developed in Michigan, is an "integrated" measure of liver donor risk widely used in the United States.[35] However, the United States DRI has been found to have poor discriminatory power when applied to European donor cohorts, and would be expected to perform similarly poorly if applied in Australia and New Zealand. Efforts are therefore underway to develop an Australian and New Zealand DRI and it is likely that this tool will be available in the next 5 years. Extra investigations may also sometimes be helpful in determining suitability for liver donation, such as CT scanning or a biopsy of a donor liver to examine the extent of steatosis (fat) in the liver (severe steatosis can pose a severe threat of a liver transplant failing to function).

Use of HCV infected donor livers into HCV negative recipients

The use of HCV-positive liver donors for HCV-positive recipients is accepted practice.[36] With the recent introduction of direct-acting anti-viral (DAA) therapies for HCV, yielding cure rates of greater than 95%,[37,38] transplantation with a liver from an HCV-NAT positive donor might now also be considered for HCV-negative recipients who are at high risk of dying on the waiting list or delisting due to progression of liver failure or tumour.[i]

However, an HCV-NAT positive donor will transmit HCV infection to the recipient, who should be treated with DAAs in the early post-transplant period.[39]

Issues that need to be considered when using HCV-NAT positive livers in HCV-negative recipients are listed below.

1. Possible chronic damage in HCV positive livers

   Chronic HCV infection in many patients is a mild illness and HCV-positive livers are currently used in HCV-NAT positive recipients. The possibility of an HCV-positive donor liver having chronic damage from the infection requires evaluation by an experienced donor surgeon and will require frozen section biopsies.

2. Donor hepatitis C genotype

   Pan genomic direct acting anti-viral drugs are so effective that HCV genotype has become less important in the allocation and possible use of an HCV-NAT positive donor liver.

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i The types of recipients that might be considered for transplantation with a liver from an HCV-NAT positive donor include:

1 Patients with Fulminant Hepatic Failure

2 Patients with severe end-stage liver disease largely based on MELD score although other features of liver disease (such as encephalopathy, Hepatorenal syndrome) may justify use in patients who have been on the waiting list for a period of time without receiving donor organ.

3 Patients with low MELD scores and hepatocellular cancer where there is progression of the hepatocellular cancer (but still within transplant criteria). The use of such hepatitis C positive donors may minimise progression of HCC in this situation and withdrawal of patients from the waiting list.

4 Possible expansion to all recipients would be considered following a review of Australia and New Zealand and or international data as it becomes available (certainly within the first 12 months following introduction). ANZ data on all cases would be reported to the ANZ Liver Transplant Registry).

3. Increased donor HIV risk

   The circumstances of death in a donor actively infected with HCV may carry a small risk of transmitting HIV infection. However, this risk is mitigated by NAT testing and a good donor social history.

4. Monitoring of HCV dynamics post-transplant

   Transplantation of an untreated HCV-NAT positive recipient will result in re-infection of an HCV-negative allograft within the first 24 hours post-transplant,[40] and maximum replication of virus occurs somewhere between one and three months post-transplant. Recurrence of HCV is universal. The infection is more aggressive and can result in liver failure within 6-12 months.

   Viral replication is accelerated by immunosuppression, and therefore monitoring of HCV loads in the weeks after transplantation is routine.

   The genotype of a previously infected HCV-positive recipient should be checked following transplantation with an HCV-NAT positive donor liver.

5. Commencing Directly Acting Antivirals (DAA) post-transplant

   The Gastroenterological Society of Australia has recently published a consensus statement on the management of HCV after liver transplantation, recommending that, when possible, treatment should be initiated early after transplantation to prevent fibrosis progression. The decision to treat actively infected patients on the waiting list should be made on a case by case basis and can be commenced pre- or post-transplantation. The treatment regimen and the duration of treatment should be based on current recommendations for the treatment of compensated and decompensated cirrhotic patients.[39]

6. Legal issues

   The risks and complications of an HCV positive organ and post-transplant anti-viral therapy need to be discussed with potential recipients to ensure informed consent is obtained. Clinicians should refer to their own jurisdictional governance and legal authorities for advice where there is a lack of clarity or policy direction in relation to informed consent.

Summary

Transplanting HCV-NAT positive livers into HCV-negative recipients has risks that need to be explicitly discussed during the consent process with potential recipients, in particular:

- underestimation of liver fibrosis in the donor liver, and
- the very small possibility of transmitting other infections such as HIV if the donor death occurs during the window period for this infection e.g. recent intravenous drug use.

Given the above, a HCV-NAT positive donor liver with minimal fibrosis could be transplanted safely into a consenting HCV-negative recipient with the plan to treat with DAAs as soon as practical post-transplant. The predicted cure rate of HCV infection with DAAs is currently greater than 95%; however, the risk of transplanting HCV-NAT positive donor livers into HCV-negative recipients is low but not zero. Therefore, at the present time, such donor livers can be considered for transplantation into recipients where the risk of not receiving that transplant is greater than the risk of waiting longer for another donor liver offer.

Technical considerations

There is emerging use of very small liver donors, including neonatal donors. For advice on paediatric liver donation and allocation, see Chapter 11.

With the increasing number of referrals of older potential donors, the possibility of severe vascular disease in organs from older donors is noted. On occasion, this can be so severe that the donor liver cannot be safely transplanted.

6.5 Allocation

6.5.1 General allocation principles

Given the adverse impact of longer ischaemia times on transplant outcomes, the transportation of donor livers over long distances is considered to be undesirable. Therefore, for efficiency and optimal transplant outcomes, the allocation of donor livers is organised at the level of the states and New Zealand (as opposed to binational allocation for urgently listed patients). The principle of allocation is to provide the best possible outcome for the highest priority patient on the waiting list for whom that liver would be a suitable match. Organ quality is not uniform, and therefore liver allocation must strike a balance between the expected outcomes of transplantation with a particular donor liver (i.e. benefit/utility) versus the risk of remaining on the waiting list for an unknown length of time (i.e. urgency/justice).

There are fewer problems of tissue compatibility in liver transplantation than there are for other forms of solid organ transplantation. Mismatches of HLA tissue types are of lessor relevance in liver transplantation and hence tissue crossmatching is not routinely taken into consideration. In contrast however, while liver transplantation between incompatible ABO blood groups is possible, it is a complex and higher risk undertaking (with the exception of very young children). Therefore, the first principle of liver allocation is to match donors with recipients of the same, or at least compatible, blood group. It is appreciated that there is the potential for blood group O livers, because they are universally compatible, to be allocated to recipients of other blood groups to the detriment of blood group O patients on the waiting list. All units make every effort to avoid this situation. Additionally, there is an argument in favour of transplanting blood group A subtype 2 (A2) livers into blood group O recipients (blood types A2 and O are compatible) to redress some of the inequity in allocation faced by the blood group O waitlisted population.

Other factors to be considered in liver allocation include organ size, risks of poor or delayed graft function, and hepatitis C status of the donor. Gross size discrepancy between the organ donor and the recipient may lead to situations where the donor liver is too big to be physically transplanted into the recipient or, conversely, where it is too small to support life. More difficult, however, are allocation decisions in a situation where the donor liver carries several risk factors that indicate it may not function well post-transplant. On the one hand, such a liver may prove disastrous if transplanted into a very sick recipient who would tolerate graft dysfunction poorly. On the other hand, that patient might die if they were to wait for another, hopefully better, organ. Allocation decisions are often very difficult to make but are guided by the principle of trying to provide the best possible outcome for the highest priority patient on the waiting list for whom that liver would be a suitable match.

Allocation decisions occasionally deviate from the predetermined order of waiting list priority. For example, if a unit were undertaking two liver transplants in one day, resources may be stretched and therefore the second liver may be allocated to a lower-priority patients who is anticipated to be more straight-forward surgically. Itis therefore important that allocation activity and decision-making is recorded, audited, and reviewed at the binational level. For some years, the Liver and Intestinal Transplantation Advisory Committee (LITAC) have annually reviewed allocation decisions made by all transplant jurisdictions in Australia and New Zealand. Recently, LITAC has determined that the results of this annual audit will in future be made available to the public.

6.5.2 Allocation pathway

Any liver becoming available from a deceased donor within Australia or New Zealand is first to be offered to patients listed as urgent. If there are no suitable urgent (including paediatric) candidates on the waiting list, the liver will go to the ABO blood group identical recipient with the highest clinical priority.

Often, but not always, clinical priority will align with MELD/PELD score ranking. However, there are other considerations that influence how a donor liver is allocated. The following factors may be relevant (and the reasons for the variance in allocation must be prospectively recorded):

- The presence of a patient on the list with HCC
- The quality of the donor liver—higher-risk donor livers may be utilised but can be problematic in patients with very high MELD scores (although it is recognised that such patients also have a higher risk of dying whilst waiting for a better liver to be offered)[1–3]
- The presence of a paediatric patient on the waiting list in need of a split or reduced-size liver, provided the donor liver is of suitable quality[ii]
- Donor size—overly large size discrepancies result in poor outcomes, therefore size matching may mean that the patient with the highest MELD/PELD score is not allocated a particular liver
- Logistical considerations—transport, cold storage preservation time, surgeon and operating room staffs kill mix and availability, and anticipated hepatectomy time may impact on allocation decisions and result in the patients with the highest MELD/PELD score not being allocated a particular liver.

6.5.3 Paediatric donor liver allocation

Paediatric organ donors comprise only approximately 5% of all organ donors in Australia and New Zealand, however there is a consensus amongst the liver transplant units in Australia and New Zealand that the allocation of these grafts involves considerations that are separate from the rest of the organ donor pool. It has been agreed that livers retrieved from donors less than 18 years old will be used for paediatric recipients. The reason for this is partly that the grieving parents of a paediatric organ donor may be comforted by knowing their child's liver has gone to another sick child. However, this is also a situation where to do otherwise would potentially deny the possibility of finding an ideal donor for an older child (for whom it can sometimes be very difficult to find a suitably sized liver), and secondly would permit a marked donor-recipient age mismatch. In some cases, the paediatric donor liver is big enough to split into 2 grafts. In this circumstance the home state may allocate both left and right grafts to paediatric recipients on their waiting list. In the event the home state does not have a second suitable paediatric recipient, the remaining graft (either left or right) will be offered on the Paediatric Liver Allocation Rotation. In the event the split liver segment cannot be allocated to a paediatric recipient within Australia and New Zealand, the home state may allocate to an adult recipient. For detailed recommendations on paediatric liver donation and allocation, see Chapter 11.

Since the number of children awaiting liver transplant in Australia and New Zealand is low (typically less than 10 at any given point in time), it is often necessary to consider the whole list of children waiting for liver transplantation in Australia and New Zealand to achieve the goal of allocating paediatric donor livers to paediatric recipients.

6.5.4 Organ sharing and rotation

It is important that all donor livers suitable for transplantation are used. After determining that there are no urgent patients to whom a donor liver must be allocated automatically, the organ is available for allocation to the local waiting list in the jurisdiction of retrieval according to the allocation principles already described. On occasion, when no suitable local recipient can be identified, the liver will be offered on to other units around Australia and New Zealand for allocation under an agreed rotation.

6.6 Multi organ transplantation

There are patients who have multi-system diseases for whom to transplant only one organ would not improve their survival. Cystic Fibrosis (CF), for example, not only affects the lungs but also may affect the liver (as well as other body systems). Uncommonly, both the lungs and the liver may need to be transplanted for an improvement in survival to be gained.

ii In the event that a donor liver is suitable for splitting between a child and an adult, it may be necessary to allocate the left-sided graft to a paediatric recipient and the right-sided graft to an adult smaller than one who would have been chosen had the liver been used whole. If there is a waiting adult patient in extremis for whom it would only be suitable to use the liver whole (rather than the small right hemigraft), then splitting may be deferred.

The ethical tension that exists in multi-organ transplantation arises because one patient receives organs that could otherwise have been transplanted into two or more patients. However, to give a patient one organ when they need two (or more) is also inefficient because it may not lead to the desired improvement in survival.

Combined liver and kidney transplantation

Transplanting a kidney in conjunction with another organ is the commonest form of multi-organ transplantation. Australian eligibility criteria for combined liver-kidney transplantation are as follows:

- Known end-stage kidney disease requiring dialysis
- Chronic kidney disease not requiring dialysis but with an estimated GFR of <30 mL/min and proteinuria of >3 g/day, or with a GFR of <20 mL/min for >3 months
- Acute kidney injury (including hepatorenal syndrome) not requiring dialysis but with an estimated GFR of<25 mL/min for >6 weeks, and
- Known metabolic disease including hyperoxaluria, atypical haemolytic uraemic syndrome with H factor deficiency, or familial amyloidosis affecting primarily the kidney.

Patients who meet these criteria can be considered for combined liver-kidney transplantation. These criteria are concordant with those currently defined by the United States United Network for Organ Sharing.[41] The decision to list a patient for a combined liver/kidney transplant should be taken after workup and assessment by, and discussion between, both the liver and renal transplant teams.

6.7 Emerging issues

The landscape of liver transplantation is evolving rapidly in response to significant shifts in epidemiology, technology, and clinical practice. Several key developments are shaping current and future challenges in liver transplantation in Australia and New Zealand:

Changing Recipient Demographics and Disease Burden

There is a notable increase in the age and complexity of liver transplant candidates and recipients. This is largely due to a shift in the predominant indications for liver transplantation, with Metabolic Dysfunction-Associated Steatotic Liver disease (MASLD) and Alcohol-related Liver Disease (ARLD) being the leading causes of end-stage liver disease. These patient populations often present with multiple comorbidities, necessitating more nuanced assessment, perioperative management, and long-term follow-up strategies.

Advances in Organ Preservation Technologies

The progressive implementation of machine perfusion technologies, including Hypothermic Oxygenated Machine Perfusion (HOPE) and Normothermic Machine Perfusion (NMP), is transforming donor liver assessment and preservation. These technologies offer potential benefits such as extended preservation times, viability assessment, and improved utilisation of marginal or extended criteria donors. Transplant units across Australia and New Zealand are at varying stages of adopting these technologies, and national data collection and collaborative evaluation efforts are critical to guiding best practice and policy development.

Internationally, the use of Normothermic Regional Perfusion (NRP) is having dramatic impacts by safely expanding the donor pool by permitting utilisation of organs that would previously not have been able to be used. Such an advance is yet to be introduced in Australia and New Zealand.

The Rise of Transplant Oncology

Liver transplantation for selected malignancies is becoming increasingly accepted, representing a paradigm shift in transplant candidacy. Conditions that were historically considered absolute contraindications—such as colorectal liver metastases and unresectable cholangiocarcinoma—are now being reconsidered under strict selection criteria and within clinical trials or protocolised programs. This emerging field of transplant oncology necessitates careful ethical and clinical scrutiny, equitable access considerations, and close monitoring of outcomes to ensure appropriate patient selection and optimal graft use.

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7 Lung

7.1 Preamble

Lung transplantation is a highly effective treatment for advanced lung disease. Generally, a 60% five-year and 40% ten-year survival rate is expected following lung transplantation as per the International Society for Heart and Lung Transplantation (ISHLT) registry report.[1] However, only approximately one in twenty of those individuals with severe lung disease who might benefit from a lung transplant will actually receive one.[1,2]

Due to the scarcity of donor lungs, lung transplantation should be considered for patients with chronic end-stage lung disease who have a two-year likelihood of survival predicted at less than 50% without transplantation[3] and who have no alternative treatment options. Infant lung transplants (currently not available in Australia and New Zealand) and living-related lung transplants have their own specific issues and are not discussed in this document. Information pertaining to peadiatric lung donation can be found in Section 11.4.

Lung transplantation is a complex therapy with significant risks, and therefore the careful evaluation of all organ systems (with appropriate specialist advice as needed) is a mandatory part of the assessment to evaluate a potential patient's risk of short and long-term morbidity and mortality post-transplantation. As significant contraindications may exist, it follows that not all potential recipients will prove suitable for lung transplantation.[2]

It is also possible that, even after active listing for lung transplantation, an individual may subsequently develop a new complication or become too frail to successfully undergo transplantation. In this circumstance, an individual may then be delisted temporarily (if the situation can be resolved) or permanently (if the condition is unresolvable). Intensive interventions such as mechanical ventilation or extracorporeal membrane oxygenation (ECMO) may be used to provide a short-term 'bridge' to lung transplantation, but these are complex therapies that can themselves be associated with patient deterioration to the extent that ultimately transplantation may not be feasible.

The ISHLT guidelines on patient eligibility and selection for lung transplantation were revised in 2021 with input from Australia and New Zealand clinicians. Australian and New Zealand lung transplant units follow the recommendations contained within these guidelines.[2,3]

7.1.1 Ethical Principles for the Allocation of Donor Lungs

- **Utility:** To maximise net benefit (e.g., using years of survival gained to prioritise allocation)
- **Justice:** To distribute the benefits and burdens of organ allocation system in a fair way (e.g., using medical urgency to prioritise allocation, allowing special consideration for candidates for whom it is difficult to find a suitable organ)
- **Respect for persons:** To treat persons as autonomous with the right for self-determination (e.g., the right to give or withhold informed consent for lung transplantation).

7.2 Recipient eligibility criteria

Early referral for lung transplant assessment is recommended to optimise time for thorough evaluation of the inclusion criteria outlined below in 7.2.1, especially for interstitial lung disease patients whose referral for transplant assessment should occur at the time of diagnosis. Early referral helps to facilitate transplant education for patients and their caregivers as well as allowing time to address barriers to transplant, which may include obesity, physical frailty, malnutrition, or inadequate social supports, with pre-transplantation therapy. On referral to lung transplant units, simultaneous referral to palliative care services is highly recommended to support the patient's journey through transplant assessment, potential waitlisting, lung transplantation surgery, and their post-transplant life.

7.2.1 Inclusion criteria

Indications for lung transplantation are:

- Progressive respiratory failure despite optimal medical, interventional and surgical treatment, and/or
- Poor quality of life, potentially with intractable symptoms and repeated hospital admissions (e.g. New York Heart Association [NYHA] Class III-IV).

Additional disease-specific candidate selection criteria at time of listing

Chronic obstructive pulmonary disease:

- Forced expiratory volume in one second (FEV_1) <25 % predicted
- Body-mass, airflow obstruction, dyspnea and exercise (BODE) index ≥7
- Clinical deterioration: severe exacerbation with hypercapnoic respiratory failure or recurrent exacerbations despite maximal treatment, pulmonary rehabilitation, and oxygen therapy
- Moderate to severe pulmonary hypertension
- Chronic hypercapnia.

Cystic Fibrosis:

- FEV_1 <30% predicted especially if a rapid downward trajectory is observed (<40% predicted in children)
- Frequent hospitalisation, (>28 days/year) despite optimal medical therapy i.e., trial of elexacaftor/tezacaftor/ivacaftor
- Massive haemoptysis (>240ml) despite bronchial artery embolization
- Pneumothorax
- Exacerbations requiring non-invasive ventilation and/or intravenous antibiotics
- 6-minute walk test <400m
- Worsening nutritional status despite nutritional interventions (BMI <18kg/m^2)
- Development of pulmonary hypertension (PASP >50mmHg or RV dysfunction)
- PCO_2 >50 mmHg and/or PO_2 <60 mmHg.

Interstitial Lung Disease (ILD):

- Any form of pulmonary fibrosis with forced vital capacity (FVC) of <80% predicted or diffusing capacity of the lungs for carbon monoxide (DLCO) <40% predicted
- Decline in FVC of >10% or decline in DLCO > 10% within the prior 6 months
- Supplementary oxygen requirement at rest and/or exertion
- Development of pulmonary hypertension demonstrated by echo or right-heart catheter
- Hospitalisation because of respiratory decline, acute exacerbation, or pneumothorax
- Desaturation to < 88% on 6 minute walk test or >50 m decline in 6 minute walk test distance in the past 6 months
- Inflammatory ILD – progressive decline of pulmonary function with radiographic progression despite treatment

  For patients with connective tissue disease or familial pulmonary fibrosis, early referral is recommended as extrapulmonary manifestations may require special consideration.

Pulmonary vascular diseases:

- NYHA Functional class III or IV/REVEAL risk score >10 despite escalation of pulmonary vasodilator therapy
- Progressive hypoxemia
- Significant right ventricle dysfunction despite pulmonary hypertension (PAH) therapy

- Secondary organ decline due to PAH i.e., kidney, liver.
- Known or suspected high-risk variants such as Pulmonary veno-occlusive disease/Pulmonary capilliary hemangiomatosis (PVOD/PCH), scleroderma or large pulmonary artery aneurysms
- Life-threatening complications such as: hemoptysis.

Lymphangioleiomyomatosis (LAM)

- FEV1 <30% predicted + diseases progression despite mTOR inhibitor therapy
- NYHA Class III or IV
- Hypoxemia at rest
- Pulmonary Hypertension
- Refractory Pneumothorax.

7.2.2 Exclusion criteria

Absolute contraindications to lung transplantation include any condition or combination of conditions that result in an unacceptably high risk of mortality or morbidity, limiting the likely survival benefit from transplantation or the predicted gain in quality of life. Absolute contraindications include (but are not limited to):[2–8]

Lack of patient willingness or acceptance of transplant
Malignancy with high risk of recurrence or death related to cancer
Glomerular filtration rate < 40 mL/min/1.73m^2 unless being considered for multi-organ transplant
Acute coronary syndrome or myocardial infarction within 30 days (excluding demand ischemia)
Stroke within 30 days
Liver cirrhosis with portal hypertension or synthetic dysfunction unless being considered for multi-organ transplant
Acute liver failure
Acute renal failure with rising creatinine or on dialysis and low likelihood of recovery
Septic shock
Active extrapulmonary or disseminated infection
Active tuberculosis infection
HIV infection with detectable viral load
Limited functional status (e.g., non-ambulatory) with poor potential for post-transplant rehabilitation
Progressive cognitive impairment
Repeated episodes of non-adherence without evidence of improvement *(Note: For pediatric patients this is not an absolute contraindication and ongoing assessment of non-adherence should occur)*
Active substance use or dependence including current tobacco use, vaping, marijuana smoking, or illicit drug use
Other severe uncontrolled medical condition expected to limit survival after transplant
Non-compliance with pre-transplantation vaccinations as recommended by the local transplant unit - the seroconversion rate after vaccinations is significantly higher in the non-immunosuppressed population compared to vaccination in immunosuppressed solid organ transplant recipients[9,10]

Risk factors with high or substantially increased risk of adverse patient outcome post lung transplantation.

Candidates with these risk factors may be considered in some transplant units with specific expertise[3], it is likely that the presence of multiple comorbidities alongside low physiologic reserve in patients over 70 years of age will exclude many of such patients from consideration for lung transplantation.

Age > 70 years
Severe coronary artery disease that requires coronary artery bypass grafting at time of transplant
Reduced left ventricular ejection fraction < 40%
Significant cerebrovascular disease
Severe esophageal dysmotility
Untreatable hematologic disorders including bleeding diathesis, thrombophilia or severe bone marrow dysfunction
BMI > 35 kg/m^2
BMI < 16 kg/m^2
Limited functional status with potential for post-transplant rehabilitation
Psychiatric, psychological or cognitive conditions with potential to interfere with medical adherence without sufficient support systems
Unreliable support system or caregiving plan
Lack of understanding of disease and / or transplant despite teaching
Mycobacterium abscessus infection
Lomentospora prolificans infection
Burkholderia cenocepacia or gladioli infection
Hepatitis B or C infection with detectable viral load and liver fibrosis
Chest wall or spinal deformity expected to cause restriction after transplant
Extracorporeal life support
Retransplant <1 year following initial lung transplant
Retransplant for restrictive chronic lung allograft dysfunction (CLAD)
Retransplant for AMR as etiology for CLAD

7.2.3 Retransplantation

Retransplantation may be an appropriate consideration in select candidates should an individual deteriorate after receiving a lung transplant and re-qualifies for waitlisting according to the inclusion and exclusion criteria stated above. Evaluation of retransplantation should explore possible reasons for graft failure, rate of deterioration, donor lung availability and the management of patient's sensitisation/potential high panel-reactive antibody.

7.3 Waiting list management

Lung transplant units will generally review patients listed for lung transplantation every 4-8 weeks in an outpatient clinic. This ongoing reassessment is critical to evaluate the patient's changing status against predicted peri-operative or post-transplant outcomes. Repetition of some assessments such a physical frailty, CT Chest imaging and serum nicotine/cotinine levels may be required by transplant units to ensure waitlisted patients still meet eligibility criteria for transplantation.

Patients eligible for the transplant waiting list (TWL) must be registered in OrganMatch, in the Lung- TWL program. Initial collection of samples is required for Human Leukocyte Antigen (HLA) typing and identification of HLA antibodies using solid phase technique (Luminex). Samples are collected monthly, and HLA antibody testing will be performed every three months. Clinical parameters required for the Organmatch Lung algorithm, must be entered in OrganMatch by the clinical or transplant unit at the time of listing. Table 7.0 shows the relevant clinical parameters.

Table 7.0: Clinical Parameters required for OrganMatch Lung Transplant waitlisting and algorithm

Essential OrganMatch Clinical Parameters:
Height
Weight
ABO
Sensitising events – i.e., blood transfusion, previous pregnancies, infection

7.3.1 Urgent patients

Although there is no defined national priority/urgent lung listing category, under some circumstances a lung transplant waitlisted patient from one state may be notified to other state Lung Transplant Programmes in an attempt to increase their opportunities for lung allocation and transplantation. This process is termed National Notification. Urgent patients are incorporated into the lung matching algorithm described in Section 7.5.2 and are offered deceased donor lungs as per the TSANZ-OTA National Standard Operating Procedure: Organ Allocation, Organ Rotation, Urgent Listing, also described in Appendix F. National notification for lung transplantation is at the discretion of the Lung Transplant Unit Director. It is the responsibility of the Lung Transplant Director (or their delegate) to notify all other Lung Transplant Units. Updating the recipients OrganMatch enrolment must occur to ensure appropriate identification and matching. The listing can be viewed within OrganMatch by the donation and transplant clinicians as required.

7.3.2 Paediatric patients

The paediatric lung transplantation centre resides at the Alfred Bayside Health in Melbourne, Victoria, with a recommended age range for referral from four to sixteen years.

7.3.3 Histocompatibility Assessment

Each recipient must undergo a series of tests performed at the state Tissue Typing laboratories. These include:

1. HLA typing using molecular technique such as Next Generation Sequencing (NGS) at the following HLA loci: A, B, C, DRB1, DQB1, DQA1, DPB1, DPA1,
2. HLA antibody screening using Luminex single antigen beads. This screening must have occurred within 120 days to be included in matching. It is optimal that all waitlisted patients are screened every 3 months.

These tests will be used in the histocompatibility assessment by the Tissue Typing labs and in consultation with the clinical unit to assign unacceptable antigens. These assigned unacceptable antigens can assist in excluding a waitlisted patient from incompatible donor offers. Additional comprehensive information is available within the National Histocompatibility Guidelines: https://tsanz.com.au/storage/Guidelines/TSANZ_NationalHistocompatibilityAssessmentGuidelineForSolidOrganTransplantation_Final.pdf

7.4 Donor assessment

7.4.1 Donor-related risk

Table 7.1 outlines standard criteria for lung donation. Historically, approximately 35-40% of deceased donor lungs offered for donation in Australia and New Zealand have been considered acceptable for clinical transplantation.[11] This compares with international retrieval rates of only 15-20%.[12,13,14] Specific management protocols have evolved for the potential lung donor that address common scenarios such as retained secretions, aspiration, ventilator-associated pneumonia, barotrauma prevention, atelectasis and neurogenic pulmonary oedema. A higher-risk lung donor is one who has characteristics that may adversely influence the early and/or long-term transplant outcomes of the chosen recipient. Traditionally, a higher-risk donor has been defined as possessing one of the following characteristics: age >60 years, smoking history >20 pack years, PaO2 <300 mmHg, chest x-ray positive for infiltrates or trauma, persistent purulent secretions at bronchoscopy or prolonged ischaemic time. Nonetheless, many potential donors with these characteristics will prove suitable for lung donation following careful organ assessment and retrieval.[15–23] The evolution of ex-vivo lung perfusion (EVLP) will further enhance acceptance rates for lung donation especially those donors considered very high risk or with multiple risk factors. The EVLP system consists of a perfusion circuit with tubing and a reservoir, enabling lungs to be sustained ex-vivo at normal temperature with an extracellular perfusate rich in human albumin to maintain high colloid pressure. The principles of EVLP are to reduce interstitial oedema within the donated lung and to perform maneuvers to facilitate alveolar recruitment, whilst monitoring the trajectory of key physiological measures including PO2, pulmonary vascular resistance and lung compliance.

Table 7.1: Suitability criteria for lung donation[23,24]

Criteria	Comments
General organ donor criteria	See Chapter 2
≥8kg to ≤75 years	Paediatric donors as small as 8kg may be suitable lung donors (see Chapter 11)
No significant untreatable lung disease	Also no known significant pleural disease in the case of DCDD lung donation
Arterial blood gases on 100% fractional inspired oxygen (FiO_2) and 5 cm positive end-expiratory pressure (PEEP) >250 mmHg	Or equivalent partial pressure of oxygen in the blood (PaO_2)/FiO_2 – ratio

7.4.2 Donor information and testing

Table 7.2: Donor information required for lung allocation

1	Lung disease and treatment history	Especially smoking (cigarettes and cannabis), asthma, and aspiration may determine single versus bilateral lung transplant considerations. Any history of TB or contact with TB
2	Accurate height, gender and ethnicity	Used to estimate total lung capacity
3	Weight	Only used in consideration of combined heart/lung transplant and for small paediatric lung donors
4	Investigations	ABO blood group Arterial blood gases on 100% FiO_2 and 5 cm PEEP Chest x-ray and lung field measurements within 24 hours Fibreoptic bronchoscopy* (if possible) CT Chest (selected patients)* Donor/recipient virtual crossmatch (VXM). N.B *A flow crossmatch (FXM) may be requested under defined circumstances to provide urgent additional immunological data that is not provided by the VXM.* Donor microbiology, serology & NAT testing, see Table 2.1 Coronavirus (SARS-CoV-2) PCR lower respiratory tract sample – for further donor suitability information please refer to Section 2.3.2.1

* See Appendix E. Ante mortem interventions such as lung bronchoscopy and CT Chest are commonly deployed in all jurisdictions with minor variations between states and, in some jurisdictions, between hospitals.

7.5 Allocation

7.5.1 General allocation principles

The lung transplant unit in the home state receives the donor offer as detailed below and given 30 minutes to respond to the offer. If the home state lung transplant unit declines the offer, the donation offer is made on rotation to non-home state lung transplant units – with a 30-minute response time, as per the TSANZ-OTA National Standard Operating Procedure – Organ Allocation, Organ Rotation, Urgent Listing.

State of donor hospital	Lung Transplant Unit
NSW, ACT	NSW
VIC, TAS	VIC
QLD	QLD
WA	WA
SA, NT	No home state transplant unit – offer to unit first on rotation
NZ	NZ

The acceptance of lungs by a transplant unit depends on a large variety of technical and logistic factors, including the existence of a suitable recipient (see Table 7.3). Although it is known that a variety of factors may manifest as apparent donor lung 'quality' (and be measured as oxygenation, chest X-ray abnormalities and bronchoscopy findings), no specific higher-risk donor category is used when allocating lungs or making acceptance decisions.

7.5.2 Lung Matching Algorithm

Considerable logistical issues and the various combinations of potential lung and/or heart transplantation that heart and lung transplant units must consider when donor organs are offered add complexity to the development of a lung matching algorithm.[25–27]

The OrganMatch Lung TWL matching algorithm uses blood group compatibility, size matching and immunological compatibility to generate a list of potential recipients. The tissue typing laboratory will perform virtual crossmatches (VXM) on the recipients on the waitlist. Patients with unacceptable antigens to the donor HLA typing will be excluded from the match. Whilst OrganMatch enhances the process of recipient matching, the final allocation decision is always at the discretion of the accepting lung transplant unit. Further information on OrganMatch and the lung matching algorithm can be found here: https://www.donatelife.gov.au/for-healthcare-workers/organmatch/training-hub#Transplantation_Portal

For allocation of lungs from paediatric donors, please refer to Section 11.4.

Table 7.3: Individual patient allocation criteria for donor lungs

1	ABO compatibility
2	Size compatibility based on chest x-ray measurements and total lung capacity values
3	Histocompatibility assessment (see section 7.3.3)
Where more than one potential recipient meets the above criteria, the first choice will be determined by the following process	
4	Clinical urgency* Logistics** Long-term outcome benefit*** CMV status of donor and recipient
5	Recipient waiting time, all other factors being equal

Notes:

* *Clinical urgency:* Graded by level of support required and evidence of rapidity of deterioration of underlying indication for transplant. Level of support includes, but not limited to the following:

- Extracorporeal membrane oxygenator (ECMO)
- Invasive mechanical ventilation
- Non-invasive ventilation
- High-flow O_2 requirement
- Low-flow O_2 requirement
- Prolonged or recurrent hospitalisation
- Other support devices such as continuous intravenous therapies.

Rapidity of deterioration includes, but not limited to

- Change in NYHA functional Class or Medical Research Council(MRC) grade
- Significant fall in lung function parameters
- Significant fall in PaO2
- Significant rise in partial pressure of carbon dioxide in the blood (PaCO2)
- Significant fall in 6-minute walk test distance
- Need for escalation in level of support as above
- Time course of progression of radiological changes
- Development of symptomatic pulmonary hypertension
- Development of refractory right heart failure.

** Logistical considerations include: operation type (lobar, single, bilateral, heart/lung); availability of required team members for the retrieval, lung transplant(s) and related cardiac transplants (paired donor heart or domino heart transplant); timely availability of all recipients; coordination between all involved transplant units arranging and performing the transplant procedures.

***Consideration of long-term outcome benefit includes: Comorbidities such as osteoporosis, gastroesophageal reflux, known coronary or peripheral vascular disease, carriage of pan-resistant organisms, poor rehabilitation potential, history of malignancy, advanced age, lack of compliance, morbid obesity or malnutrition and other relative contraindications for lung transplantation which have been shown to be associated with an inferior outcome benefit.

7.6 Multi-organ transplantation

Patients with respiratory failure and concurrent disease of another solid organ—typically heart, kidney, or liver—may be considered for combined organ transplantation. The general eligibility criteria for multi-organ transplantation follow the individual eligibility criteria for each organ to be transplanted. Multi-organ transplant is a more complicated surgical procedure with associated unique medical and other post-operative complications. As such, it is recommended for younger patients with functional reserve and with an ability to withstand the heightened surgical risks and prolonged rehabilitation associated with this complicated procedure. Referral for consideration of multi-organ transplantation should occur earlier in the disease course in alignment with expected longer waitlisted time.[3]

7.7 Emerging Issues

Utilisation of Hepatitis C donors[28-31]

The increasing availability of direct acting anti-viral (DAA) therapies for successful treatment of Hepatitis C Virus (HCV) has allowed the cardiothoracic transplant community to now consider the use of HCV-positive donors for lung transplantation.[28–31] The opportunity to safely expand the donor pool and potentially reduce the time on waitlist by accepting HCV-positive donors requires careful management pre and post transplantation. These management recommendations include but are not limited to:

- Patient education and associated informed consent specific to high viral risk donors prior to listing, and at time of transplantation
- Availability and assessment of waitlisted patient's recent serology i.e., pre-existing HBV infection
- Careful pharmacological evaluation of drug interactions before initiation of DAAs to reduce decreased efficacy of HCV treatment
- Patient's ability to adhere with DAA medication protocol and prevent potential further HCV transmission
- Patient's ability to comply to surveillance monitoring of HCV RNA post transplantation as per transplant unit policy.

The ISHLT Consensus Statement on utilisation of hepatitis C virus-infected organ donors in cardiothoracic transplantation[28] provides; further management considerations, guidance on recommended surveillance schedule, and a potential DAA treatment strategy when utilising HCV-positive organs for cardiothoracic transplantation into HCV-negative recipients.

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8 Pancreas and Islet

8.1 Preamble

Pancreas transplantation is undertaken as a treatment for type 1 or insulin-deficient diabetes in two ways:[1]

- Either the whole pancreas organ is transplanted,[2] or
- The insulin producing pancreatic islet cells are separated from the organ and transplanted.[3]

There are four units in Australia and one in New Zealand that perform solid organ pancreas transplantation (see Appendix H). The vast majority of solid organ pancreas transplants are undertaken as simultaneous pancreas and kidney (SPK) transplants in recipients with both type 1 diabetes and kidney failure.[4] A small minority of transplants are undertaken as solid organ pancreas transplants alone, either after kidney transplantation or in patients with good kidney function who do not require a kidney transplant. There are only a very small number of patients with exceptional circumstances for whom pancreas-alone transplantation is deemed appropriate.[2] There are also some patients that require a pancreas transplant along with other organs (for example, combined liver/pancreas, liver/pancreas/kidney, or lung/pancreas transplantation in patients with conditions such as cystic fibrosis). These are uncommon transplant procedures and often referred to as multi-organ transplants.

There are two pancreatic islet isolation laboratories in Australia and New Zealand: Westmead Hospital in Sydney and St Vincent's Institute of Medical Research in Melbourne. Pancreatic islet cell transplantation is currently undertaken at the following infusion centres: Westmead Hospital, St Vincent's Hospital and Royal Adelaide Hospital.

Simultaneous pancreas (solid organ) and kidney transplantation

As the solid organ pancreas transplant units are national centres with referrals often coming from interstate, patients must first meet broad minimum eligibility criteria to be referred to and undergo subsequent assessment at one of the three units. Further criteria must then be met in order for patients to be entered onto the solid organ pancreas transplant waiting list.

This two-step waitlisting process allows potential recipients to be seen and preliminarily assessed at a transplant unit before their disease progresses to the point that they meet the final criteria for waitlisting for SPK transplantation. This process also minimises the referral of patients who would ultimately be deemed unsuitable for SPK transplantation. The minimum eligibility criteria for referral are based on data demonstrating poor outcomes in subgroups of patients with, for example, significant cardiac disease,[5-7] increasing age,[8] or obesity.[9] Eligibility criteria are also based on feasibility; for example significant bilateral disease of the iliac vessels or marked obesity in the recipient make transplant surgery technically difficult or impossible.[9-11]

Multiorgan transplantation including a solid organ pancreas

These are infrequently performed and will require a collaborative approach involving several transplant centres, each specialising in the specific organs required. As an example, if both a liver and pancreas transplant are required, then the liver transplant centre will be the primary team. They will co-ordinate plans with the centre that performs pancreas transplantation.

8.2 Recipient eligibility criteria

8.2.1 Criteria for referral for solid pancreas transplantation

Patients must be referred to a pancreas transplant unit by their treating nephrologist and/or endocrinologist. Patients will be reviewed by the pancreas transplant unit if they meet the following criteria:

- Type I diabetes with insulin dependence
- eGFR <30 mL/min
- Absence of significant cardiac disease, or adequately treated cardiac disease
- Patent iliac vessels bilaterally
- Age ideally <50 years (unless medically fit, see below).

In the case of age, individual subjects older than 50 years may still be deemed eligible for solid organ pancreas transplantation if they are otherwise very medically fit.[6,8] It must be taken into account, however, that patients generally face a waiting time of approximately two to three years from listing to the time of transplantation. As older age affects the likelihood of a successful outcome from SPK,[6,8] alternative transplant options (e.g. kidney alone transplantation, living donor kidney transplantation) also need to be very strongly considered.[12]

In the case of cardiovascular and/or iliac vessel disease, referral may still be considered if the referring team have a strong expectation that these problems can be significantly resolved. Individual cases may need to be discussed directly with one of the national transplant units before the transplant unit can decide to formally assess the patient's overall suitability.

8.2.2 Inclusion criteria: solid organ pancreas transplant waiting list

Patients may be referred and assessed if they meet the above criteria for solid pancreas transplantation, however they will not be actively listed for transplantation until they also meet all of the following criteria:

- Insulin dependence deemed by the national pancreas transplant unit to be reversible by pancreas transplantation
- eGFR <15 mL/min and dialysis impending
- Absence of significant cardiac disease, or adequately treated cardiac disease
- Patent iliac vessels bilaterally
- BMI <35 kg/m^2 (is a relative contraindication)
- Non-smoker or permanent cessation of smoking for more than 3 months (see below).

The expectation that a solid organ pancreas transplant can fully reverse the need for insulin is based on a pattern of insulin deficiency rather than one of insulin resistance (signifying type 1 rather than type 2 diabetes). This is not always straightforward to determine but relies partly on the demonstration of absent or low C-peptide levels (a marker of native insulin production).[13,14]

Smoking has been found to adversely affect transplant outcomes.[6,15] For this reason, patients are expected to demonstrate commitment to permanent smoking cessation before they can be transplanted.

While outcomes are significantly improved if patients can be transplanted early in the course of their kidney disease progression,[16-18] the limited supply of organs and the needs of the kidney-only waiting list restrict the ability to transplant patients before the point of kidney failure. The majority of patients are transplanted after they commence dialysis (typical eGFR <10 mL/min), however some may receive a transplant just prior to dialysis (10–15%). The ability to transplant patients prior to dialysis is important, as the window of opportunity for transplantation is small for some patients due to the presence of multiple comorbidities. The current mortality rate on the SPK waiting list is approximately 10% per year—significantly higher than age matched patients on the kidney-only waiting list.[4,19-21]

8.2.3 Exclusion criteria: solid organ pancreas transplant waiting list

Exclusion criteria for pancreas transplantation are:

- Exclusion criteria as per kidney-only transplantation (see Section 5.1.2)
- Significant cardiac disease, or inadequately treated cardiac disease
- Significant vascular disease

- Continuous dual antiplatelet therapy that cannot be safely ceased (in the short term) to allow surgery to proceed (e.g. recent coronary artery stenting at risk of thrombosis); single agent antiplatelet therapy is not an exclusion
- Significant psychiatric disease (affecting ability to cope and comply with surgery and treatment)
- Ongoing cigarette smoking
- Inability to comply with complex medical therapy (e.g. chronic cognitive or neuropsychiatric deficits in the absence of a carer capable of taking on this role)
- Addiction to non-prescription illicit drugs (e.g. narcotic or cannabis abuse).

8.2.4 Inclusion criteria: pancreatic islet transplant waiting list

Patients are entered onto the national islet transplant waiting list by recognised Clinical Islet Transplant Programmes. Patients on the national Islet transplant waiting list will be assigned to a recognised Clinical Islet Separation Laboratory by the Clinical Islet Transplant Programme.

Inclusion criteria for pancreatic islet transplantation are:

- Type 1 diabetes for five years or more
- Severe hypoglycaemic unawareness (documented blood sugar level <3 mmol/l without awareness) that has not responded to optimal conventional insulin therapy, as assessed by an endocrinologist
- Age >18
- Creatinine clearance >75 mL/min/1.73m^2
- Serum creatinine <130 umol/L
- 24 hour urine protein estimation <300 mg/day
- Weight ideally <80 kg
- The patient has read and signed the islet-specific informed consent form
- Absence of donor reactive antibodies by Luminex and virtual crossmatch
- Willingness to use effective contraception measures
- Ability to understand the protocol and provide informed consent.

8.2.5 Exclusion criteria: pancreatic islet transplant waiting list

Exclusion criteria for pancreatic islet transplantation are:

- Weight >80 kg
- C-peptide response to arginine (5 g IV)—exclude any patient with C-peptide greater or equal to 0.3 ng/mL at 2, 3, 4, 5, 7, and 10 minutes post infusion
- Creatinine clearance <75 mL/min/1.73 m^2
- Serum creatinine >130 umol/L
- 24 hour urine protein estimation >300 mg/day
- Baseline haemoglobin <12 g/dL in women or <13 g/dL in men
- Baseline liver function tests outside of normal range
- Insulin requirement >0.7 IU/kg/day
- HbA1c >108mmol/mol (12%)
- Serum cholesterol >10 mmol/l
- Systemic corticosteroid usage
- Treatment with terfenadine, cisapride, astemizole, pimozide, or ketoconazole (that is not discontinued prior to sirolimus administration)
- A positive pregnancy test or desire to fall pregnant following islet cell transplantation

- Malignant disease other than localised and excised skin squamous cell or basal cell carcinoma
- Liver disease, including any form of active viral hepatitis, portal venous abnormality or cirrhosis
- Chronic pancreatitis
- Significant cardiac disease including ischaemic and valvular heart disease
- Respiratory disease including clinically significant asthma, bronchiectasis or obstructive airways disease
- Any form of chronic infection that could, viewed by the transplant team, pose a mortality risk after transplantation
- Any form of chronic or current acute mental or psychiatric illness that could jeopardise patient safety and adherence to medication in the peri- and post-transplantation period
- Allergy to intravenous contrast agents, sirolimus, tacrolimus or anti-thymocyte globulin
- Any other disease that in the opinion of the investigator may pose a significant risk to survival or adherence post transplantation.

8.2.6 Retransplantation

SPK retransplantation is technically possible, particularly where an early graft thrombosis has occurred and the pancreas has been removed. Even late failure of both organs might be considered for retransplantation if standard inclusion/exclusion criteria are met. The decision would then have to be made whether to remove both failed organs prior to relisting or at the time of retransplantation.

8.3 Waiting list management

8.3.1 Solid organ pancreas waiting list

Potential transplant recipients are ranked for transplantation according to their referral date and eGFR level. Each solid organ pancreas transplant unit allocates organs to the patient who has been waiting the longest, provided they are suitable and ready for transplantation. Patients are enrolled into OrganMatch by the transplant unit which will enable them to be matched with potential deceased organ donors.

Waiting time is calculated from the date of referral if eGFR is already ≤25 ml/min. Alternatively, if eGFR >25 ml/min at referral, waiting time only starts once the eGFR is consistently ≤25 mL/min.

Transplantation is only allowed once eGFR is consistently ≤15 ml/min or dialysis has commenced. Of note, because of the typical 2-3 year waiting period, most recipients are transplanted after dialysis has commenced.

Dialysis time itself does not lead to any prioritisation on the waiting list. Although it has been previously shown that more than 12 months pre transplant dialysis detrimentally affects the subsequent pancreas graft survival. However, patients who are highly sensitised to HLA antigens (>75% mPRA) and on dialysis, will be flagged as National Priority and are prioritised nationally in the Kidney Pancreas matching algorithm (see Appendix N). Currently, the logistics of distance make it difficult to include highly sensitised patients from New Zealand in this arrangement.

8.3.2 Islet waiting list

Each islet transplant programme allocates islets to the blood group-matched patient who has been waiting for the longest time on the islet transplant list and is deemed suitable and ready for the islet preparation made available for transplantation. Patients on the waiting list who require a second islet transplant will take priority over those waiting for a first transplant.

Where donor a pancreas meets the appropriate criteria for both solid organ and islet transplantation, it is first offered for solid organ transplantation. If the pancreas is not accepted by the national pancreas transplant units for this purpose, then the pancreas can be offered to the national islet transplant units.

8.3.3 Urgent patients

There is no urgent classification for either solid pancreas or islet transplant candidates.

8.3.4 Histocompatibility Assessment

Each recipient must undergo a series of tests performed at the state Tissue Typing laboratories. These include:

- HLA typing using molecular technique such as Next Generation Sequencing (NGS) at the following HLA loci: A, B, C, DRB1, DQB1, DQA1, DPB1, DPA1
- HLA antibody screening using Luminex single antigen beads. This screening must have occurred within 120 days to be included in matching. It is optimal that all waitlisted patients are screened every 3 months.

These tests will be used in the histocompatibility assessment by the Tissue Typing labs and in consultation with the clinical unit to assign unacceptable antigens. These assigned unacceptable antigens can assist in excluding a waitlisted patient from incompatible donor offers. Additional comprehensive information is available within the National Histocompatibility Guidelines: https://tsanz.com.au/storage/Guidelines/TSANZ_NationalHistocompatibilityAssessmentGuidelineForSolidOrganTransplantation_Final.pdf

8.4 Donor assessment

8.4.1 Donor information and testing

Table 8.1: Donor information required and donor suitability criteria for solid pancreas donation

1. Blood group	ABO compatibility (absolute requirement)
2. Body weight	>25 kg, ideally <100 kg and BMI < 30 kg/m^2
3. Height	No specific requirements
4. Age	Ideally 5 to 55 years old
5. Abdominal girth	No specific requirements
6. Anatomical information	No past or current evidence of acute pancreatitis No evidence of pancreatic or duodenal trauma (may be considered for islets) No evidence of significant fat infiltration of pancreas at laparotomy
7. History of donor haemodynamic status	Inotrope use, blood pressure
8. Laboratory tests	Donor HLA typing is required to perform Virtual XM and Donor Specific Antibody assessments with potential recipients. General organ donor criteria for viral studies: HIV, HBsAg, hepatitis C, CMV Electrolytes, glucose Amylase and/or lipase
9. Medication use	Current use of insulin, dextrose and steroids. Use of inotropes
10. Medical history	No known diabetes mellitus or insulin dependence (prior to admission to hospital) No history of alcoholism or chronic pancreatitis

Table 8.2: Donor information required and donor suitability criteria for islet cell donation

1. Blood group	ABO compatibility (absolute requirement)
2. Donor type	DNDD only
3. Body weight	>25 kg and ideally <150 kg
4. Height	No specific requirements
5. Age	3 – 65 years*
6. Abdominal girth	No specific requirements
7. History of donor haemodynamic status	Current use of insulin, dextrose, steroids, inotropes, blood pressure Any hypoxia or down time
8. Laboratory tests	Donor HLA typing is required to perform Virtual XM and Donor Specific Antibody assessments with potential recipients. General organ donor criteria for viral studies: HIV, HBsAg, hepatitis C, CMV Electrolytes, glucose Amylase and/or lipase
9. Medication use	Current use of insulin, dextrose and steroids

* Regardless of age, if a donor is accepted for heart, lung, liver and/or kidney donation, then the donor may be accepted for pancreatic islets

8.4.2 Donor suitability criteria

Donor suitability criteria are listed in Table 8.1 and Table 8.2. Similar to the selection process for other organs, donor suitability criteria for pancreas transplantation are based on factors that may adversely impact the success of the procedure,[22-26] as well as factors related to recipient safety (e.g. infection risk or transmission of malignancy). DNDD and DCDD donors are suitable for solid organ pancreas transplantation (usually SPK transplantation), although thrombosis rates are higher from DCDD compared with DNDD organs. Within DNDD organs, thrombosis rates are higher in donors over 35 years of age. Currently, islet yields from DCDD donors are insufficient for transplantation, hence these donors are only considered at present for solid organ pancreas donation (in the case of paediatric donors, only DNDD donors are suitable for pancreas donation – see Chapter 11). Suitability criteria for pancreas donation from DCDDs are given in Table 8.3: Extended suitability criteria for pancreas donation after circulatory death.[24,27]

Table 8.3: Extended suitability criteria for pancreas donation after circulatory determination of death[24,27]

Criteria	Comments
Suitable DCDD organ donor	
Age up to 45 years	
No known diabetes mellitus or insulin dependence	
No known pancreatic trauma	May be considered for separate islets
No history of alcoholism or chronic pancreatitis	
Maximum ischaemic time from withdrawal of treatment to organ perfusion <30 min	
Ideally the liver is also deemed suitable for transplantation	Expected to correlate with good pancreatic integrity

8.4.3 Organ retrieval

Due to the small number of pancreas transplant units, geographic considerations as well as availability of local expertise need to be taken into account in the process of pancreas retrieval. In some cases the accepting transplant team (the national pancreas transplant unit) will perform the retrieval. Where circumstances make it possible and/or favourable for the local teams to be involved in the process of retrieval and delivery, this will also be considered. Pancreas donations in Western Australia, Queensland and South Australia may involve the local teams, avoiding the need for the staff from the pancreas units to travel interstate for the retrieval process. This process is greatly appreciated by the pancreas transplant units.

8.5 Allocation

8.5.1 General allocation principles

Organ allocation and distribution currently follow processes that have been established over several years based on referral patterns of recipients and geographical considerations regarding retrieval teams and acceptable ischaemic times. The allocation process for pancreas and islet transplantation is reviewed on an ongoing basis.

As stated above (Section 8.3.1), organs are allocated to the blood group identical patient with the longest waiting time who is a suitable recipient and is currently active on the waiting list. In OrganMatch , the kidney/ pancreas and pancreas algorithm is used to determine the potential list of recipients from which the transplant units will select the most suitable recipient (Appendix N). Occasionally allocation may deviate from this general rule if, for example, the donor is very small and the intended recipient is very large, or vice versa. Similarly, where the donor is DCDD or higher-risk—necessitating a short cold ischaemia time—and the recipient cannot reach the transplant unit in time, an alternative recipient may have to be chosen.

Very rarely, a patient on the waiting list who is at risk of death from either hypos or lack of dialysis access may be given priority irrespective of waiting time. There is no official definition of an urgent category for this type of pancreas transplant within Australia and New Zealand.

Patients on the waiting lists are reviewed annually by the pancreas transplantation teams, either by a transplant physician or transplant surgeon. Normally this occurs at an interstate clinic, but occasionally will necessitate the patient travelling to the transplant centre where they are listed.

8.5.2 Organ sharing and rotation

Donor pancreata arising in New Zealand are initially offered to the Auckland National Pancreas Transplant Unit. If the Auckland Unit is unable to use the organs (e.g. no suitable recipient currently listed, lack of availability of appropriate surgeons for either the retrieval or transplant procedure) then the Australian Pancreas Transplant Units (Westmead, Monash, Royal Adelaide) may receive the offer. For logistical reasons it would be rare for this to happen.

In Australia, organs will initially be considered for sensitised recipients that are listed nationally. If there are no suitable recipients, then organs will be allocated using established geographic patterns of referral as follows:

Jurisdiction of donor hospital	Location of Pancreas Transplant Unit
NSW, ACT, QLD, WA	NSW
VIC/TAS	VIC
SA/NT	SA
NZ	NZ

Donor pancreata arising in New South Wales, Australian Capital Territory, Queensland and Western Australia are initially offered to the Westmead National Pancreas Transplant Unit for consideration for simultaneous kidney and pancreas transplantation. If the Westmead Unit is unable to use the organs (e.g. no suitable recipient currently listed, lack of availability of appropriate surgeons for either the retrieval or transplant procedure due to simultaneous pancreas donor or transplant) then the Monash and Royal Adelaide Units will receive the offer, followed by the islet units (Westmead followed by Victoria/South Australia).

Donor pancreata arising in Victoria or Tasmania are initially offered to the Monash National Pancreas Transplant Unit for consideration for simultaneous kidney and pancreas transplantation. If the Monash Unit is unable to use the organs (e.g. no suitable recipient currently listed, lack of availability of appropriate surgeons for either retrieval or transplant procedure) then the Westmead and Royal Adelaide Units will receive the offer, followed by the the islet units (Victoria/South Australia and Westmead).

Donor pancreata from South Australia and Northern Territory will initially be offered to the Royal Adelaide Unit for consideration for simultaneous kidney and pancreas transplantation. If the Royal Adelaide is unable to use the organs (e.g. no suitable recipient currently listed, lack of availability of appropriate surgeons for either retrieval or transplant procedure) then Westmead and Monash will receive the offers on rotation. When all centres decline the pancreas for solid transplant, the pancreas is offered back to Royal Adelaide for islet transplantation, followed by Victoria and New South Wales.

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9 Intestine

9.1 Preamble

Intestinal transplantation remains challenging and controversial because of the complexity of the intestinal failure patient, the effectiveness of parenteral nutrition (PN), and the risks associated with transplanting the intestine.

The gut is a highly complex, highly immunogenic organ, and is exposed to the external environment of chemicals, parasites, viruses and bacteria. There is a poorly understood symbiotic relationship between the gut and the intestinal flora, which encompass many trillion bacteria. The gut 'microbiota' and the intestinal immune system have a complex relationship that includes tolerance to the native flora. It is therefore not surprising that, following transplantation, the intestine is prone to rejection, loss of the mucosal barrier, and subsequent systemic infection.

Several medical advancements preceded and permitted the development of intestinal transplantation in patients who have intestinal failure. The introduction of PN in the 1970s was followed by the development of intestinal rehabilitation and subsequent remedial intestinal surgery. The concept of a specialised service to manage intestinal failure and rehabilitation is more recent.[1]

While the role of intestinal transplantation in the complex management of intestinal failure is still evolving, PN remains the primary therapy for both adults and children with intestinal failure.

It is estimated that approximately 300-350 patients in Australia are currently PN dependent, corresponding to a prevalence of approximately 11 per million population.[2] Most patients on PN are stable, and consideration for transplantation is currently limited to those who have no chance of intestinal recovery and have potential life-threatening PN-related complications.

As short-term patient and graft survival have increased, attention has turned to improving the long-term outcomes of intestinal transplantation. Long-term survival must be factored into any decision to transplant an individual patient where survival on PN may approximate or exceed that of intestinal transplantation. The improved outcomes of intestinal transplantation and the potential for long-term survival raises the possibility of considering intestinal transplantation for stable patients who have a poor quality of life or — in high-risk patients — before the development of life-threatening PN-related complications.

Management of intestinal failure patients in dedicated centres with multidisciplinary teams has been associated with improved survival and fewer complications.[3–5] Given the small number of patients who might be considered intestinal transplant candidates in Australia and New Zealand, and the fact that they are scattered over a large area, it has been recommended that there should be a single intestinal transplant program supported by organised intestinal rehabilitation programs across the two countries.[6]

Types of intestinal transplantation

Intestinal transplantation incorporates several transplant procedures, and can range in complexity from an isolated intestinal graft to replacement of the entire abdominal cavity including stomach, duodenum, pancreas, small intestine, liver and possibly colon. Kidney transplantation may also be contemplated. In patients who lack abdominal domain or have a severely compromised abdominal wall, a full thickness abdominal wall transplant can also be considered in addition to the intestinal transplant.

The decision for an individual patient as to which organs to replace can be difficult. Intestinal failure associated liver disease (IFALD) is common, and liver function is important in determining whether the liver should also be replaced. Advanced fibrosis, cirrhosis or severe cholestasis and the presence of portal hypertension mandate the liver should be included in the transplantation procedure.

In surgical practice, the graft options centre around isolated intestinal replacement versus the need to include the liver. A multivisceral graft includes the liver, stomach, duodenum, pancreas and small intestine, whereas a modified multivisceral graft does not include the liver.[7–9] The multivisceral graft can also include the spleen and colon. The factors that determine the choice of graft 'cluster' include the aetiology of the intestinal failure and the functional state of the liver and gastric motility. The type of graft is tailored to the individual patient. Organs that are functioning will not be replaced.

9.2 Parenteral Nutrition

There is a medical preference for enteric feeding, if at all possible, because of the reduced risk of systemic infection, venous thrombosis and liver dysfunction in comparison with PN. However, PN remains the nutritional mainstay for patients who cannot eat or whose gastrointestinal tract cannot support enteral nutrition sufficient to meet the metabolic demands of the patient. The great majority of patients will have short-term surgical or medical conditions with no intention that PN will be used long-term, and an intestine that will allow them to return to full enteral feeding once their condition is resolved.

In patients with irreversible intestinal failure PN remains the gold standard for treatment. The five- and ten-year survival for children receiving total parenteral nutrition (TPN) is 89% and 81% respectively; the five- and ten-year survival for adults receiving TPN is 70% and 55% respectively.[10]

However, long-term PN can result in life-threatening complications. Intestinal transplantation has usually been reserved for patients who develop the following problems:[11–13]

The development of IFALD—this can occur in up to half of all TPN patients and is associated with a dramatic reduction in patient survival.[13] IFALD can result in advanced fibrosis or cirrhosis or severe cholestasis. Portal hypertension may develop, manifested by splenomegaly, thrombocytopenia, gastro-oesophageal varices or stomal bleeding. Liver biochemistry often is a poor indicator of the extent of liver injury, so liver biopsy and/or non-invasive assessment of liver fibrosis are important considerations in the longer-term management of these patients.

Central line access failure—as evidenced by central venous thrombosis of two or more central veins, pulmonary embolism, superior vena cava syndrome or chronic venous insufficiency.

Severe sepsis—usually secondary to catheter-related blood stream infections that require hospitalisation, or a single episode of line-related fungemia, septic shock or acute respiratory distress syndrome.

Severe dehydration—frequent episodes of severe dehydration despite intravenous fluid supplementation in addition to TPN.

PN in Australia and New Zealand

PN is widely available in Australia and New Zealand. However, there is little coordination, particularly with the adult PN services.

A distinction should be made between hospitals able to offer PN and those that have a formal intestinal failure/intestinal rehabilitation service. There is a dedicated paediatric intestinal failure service at the Royal Children's Hospital in Melbourne and the Starship Children's Hospital in Auckland, and more recently an adult intestinal failure and rehabilitation service at Austin Health in Victoria. Intestinal failure, particularly in adults, is often treated ad hoc, largely due to the low incidence of gastrointestinal tract pathology and the wide geographic distribution of the few affected patients.

9.3 Intestinal transplantation in Australia

Intestinal transplantation is an emerging therapy in Australia and New Zealand. The low prevalence of intestinal failure across the two countries suggests a need for a single bi-national adult and paediatric transplant centre, as transplantation may be indicated in only four or five patients per year across Australia and New Zealand.

An intestinal transplantation program was established at Austin Health I and Royal Children's Hospital in Melbourne in 2010.[11,14] The first intestinal transplant (liver-intestine) was performed in 2010.[15] A total of 20 intestinal transplants have been performed as of April 2026 (14 adult transplants and 6 paediatric transplants) and there is currently an active waiting list of children and adults.

The intestinal transplantation program is not nationally funded, therefore the funding for transplantation of an individual patient is negotiated on an ad hoc basis with each referring state and New Zealand. This often adds considerably to the time taken to assess the patient, complete their work-up, and activate them on the waiting list.

A single bi-national intestinal transplantation service would ideally be supported by a limited network of intestinal rehabilitation centres that would act as a referral base for intestinal failure patients. Management of patients post-transplantation would likely be done at an existing liver transplant centre with expertise in the management of immunosuppression.

9.4 Recipient eligibility

Intestinal failure occurs when intestinal absorption of fluid and nutrients becomes inadequate and life can only be sustained by the use of intravenous PN and fluids. The access line and long-term access can become life-threatening issues, particularly due to the risk of infection and large vein thrombosis.

Approximately 70% of intestinal failure in both adults and children is due to anatomical short gut. However, there are multiple other causes, which are summarised in Table 9.1.

Table 9.1: Causes of intestinal failure

Anatomical short gut	Dysmotility	Enterocyte failure	Tumours
Congenital malrotation Necrotizing enterocolitis Trauma Volvulus Gastroschisis Atresia Thrombosis/ischaemia Crohn's disease	Pseudo obstruction Aganglionosis	Microvillous inclusion Tufting enteropathy Autoimmune enteropathy	Familial adenomatous polyposis Inflammatory pseudo tumour Desmoid

Quality of life is impaired to some degree for many patients with intestinal failure, and to a severe degree for a minority. Survival requires daily intervention. This burden is compounded by the inability to eat and the enormous social dysfunction that this entails. Hospitalisation can become frequent and costly, both financially and psychologically. Patient survival is precarious, and the social impairment and psychopathology of a severe chronic disease are common.

The following anatomical combinations can be associated with full enteral recovery, and hence aggressive attempts at intestinal rehabilitation should be undertaken before intestinal transplantation is considered:[16]

- Residual small intestine of >100 cm with a stoma (no colon in continuity)
- Small intestine >60 cm with jejunocolonic anastomosis (part of the colon in continuity)
- Small intestine >30 cm, including the ileum and ICV, in continuity with the entire colon.

The recent clinical use of the glucagon-like peptide-2 analogue teduglutide has revolutionised intestinal failure management and has enabled many patients to either reduce PN dependence or be able to completely wean off PN. This will hopefully allow some patients to avoid intestinal transplantation in the future.[17]

Patients with the following are more likely to remain dependent on PN and hence may ultimately become candidates for transplantation:

- Gut length—very short jejunum, no ileum, no ileocecal valve (ICV), no colon
- Mucosal disease
- Motility disorders
- Abdominal wall defects
- Radiation enteritis
- Age—children may do worse on PN
- High-grade intestinal obstruction
- Long duration of PN feeding (>2 years)
- A post-absorptive plasma citrulline level <20 µmol/L (half of normal adult value).

9.4.1 Inclusion criteria

It is important to realise that only a small proportion of patients with intestinal failure on PN will be referred for transplantation and subsequently accepted and transplanted. Intestinal transplantation is a recognised treatment for patients with intestinal failure but will usually not be considered as an option for stable patients who are coping well with PN. Instead, intestinal transplantation is currently considered only for patients with known irreversible intestinal failure who have life threatening complications of PN or fluid management or have significant limitations to their quality of life that have become life-threatening. This so-called "PN failure" has been defined in the USA as one or more of the following:[12]

- Impending or overt liver failure due to IFALD
- Thrombosis of two or more central veins
- Two or more episodes per year of catheter-related blood stream infections
- A single episode of line-related fungemia, septic shock or acute respiratory distress syndrome
- Frequent episodes of severe dehydration despite intravenous supplementation in addition to PN.

In addition to the criteria above, there is a small group of patients who have aggressive, locally destructive abdominal desmoid tumours, who may be eligible for intestinal transplantation in the absence of PN failure.[18]

There is debate about who should remain on long-term PN and regarding the ability to predict success of intestinal rehabilitation in an individual patient. The ability to predict rehabilitation success or failure may facilitate early consideration of intestinal transplantation before the onset of life-threatening complications.

9.4.2 Exclusion criteria

Exclusion criteria overlap with those listed for liver transplantation (see Chapter 6). In summary, contraindications to intestinal transplantation include:[19]

- Potential for intestinal recovery
- Severe wasting and cachexia
- Drug dependence considered likely to impair survival
- Primary or metastatic cancer (with exception of desmoid tumours)
- Ongoing or recurrent infections that are not responding to treatment
- Significant cardiac or pulmonary pathology
- Demonstrated patient non-compliance or significant psychiatric or social risk
- Potential complications from immunosuppressive therapy that are unacceptable to the patient
- Total loss of central line access.

9.4.3 Referral for intestinal transplantation

At any instant, 10 – 25% of adults and children on long-term PN may have one of the complications listed in Section 9.4.1 that are an indication for intestinal transplantation. It is therefore estimated that fewer than 10 patients per year in Australia and New Zealand would be considered for intestinal transplantation.

However, determining whether a patient should be transplanted is often difficult. Early referral is preferred as it allows sufficient time to assess the patient, modify treatment and consider the need for transplantation.

In patients for whom loss of central venous access is an indication, referral should be made prior to the patient losing all access as central venous access is necessary to survive the transplant operation, as well as for adequate postoperative care.

9.4.4 Assessment and acceptance

While there is no specific upper age limit for intestinal transplantation, most potential recipients are likely to be under 50 years of age. Patient adherence to medical treatment is critical to success. A stable social and psychological history is mandatory because of the intensity of the pre- and post-operative procedures and the ongoing medical risks.

Most patients will have undergone multiple abdominal operations that add to the operative risk. The abdominal cavity may be contracted and small with limited space in which to place a new graft.

A detailed assessment of the venous anatomy is mandatory. Thrombosis of the major vessels is common due to the prolonged intravenous access associated with PN. This may include complete thrombosis of the innominate or jugular veins, the superior vena cava and inferior vena cava. Vein mapping is essential to enable planning of the operation and anaesthetic access. In some patients who have lost major veins and where current intravenous access may be via direct atrial or lumbar caval lines, lack of access may preclude transplantation.

Co-morbidities are common in intestinal failure patients and will influence the decision to proceed with transplantation. End-stage kidney disease is frequent, often due to long-term hydration issues and occasionally due to renal oxalosis as a complication of short bowel syndrome. In this case, combined kidney and intestinal transplantation may be considered.

Sensitisation and antibody status are critical to the success of intestinal transplantation. Preformed HLA antibodies in the potential recipient make donor matching difficult and often impossible. Currently there are attempts to moderate donor specific antibodies (DSAs) in recipients with high titre and high panel reactive antibodies (PRA).

Assessment for intestinal transplantation may take several months; therefore, early referral is recommended. This duration reflects the time required to thoroughly evaluate the patient and their response to various therapies, including surgical interventions, with the aim of avoiding transplantation where possible.

9.4.5 Retransplantation

Re-transplantation is possible but has a high failure rate when compared to primary transplantation.[20] This is largely due to immunologic factors, which make rejection of the second transplant more likely, the presence of sepsis associated with failure of the primary graft, and other organ system failures. Liver-inclusive intestinal retransplantation offers a better long-term outcome when compared to liver-free retransplantation.[21]

9.5 Donor assessment

The selection of appropriate deceased donors is critical to success of intestinal transplantation. In general, only stable donors who meet the criteria described below would be considered for intestinal transplantation. Most of the criteria for liver donor suitability also apply to intestinal donation (see Chapter 6).

The "ideal intestinal donor" is quite uncommon; hence interstate and New Zealand donors will be considered for all potential recipients. An ideal donor would be <50 years of age and donate via the DNDD pathway. Donors between 50 and 60 years of age will be considered if other factors are favourable.

Recipients must be ABO-compatible with the donor. Therefore, O universal donors can be considered for A, AB, or B recipients. The EBV and CMV status of the donor will also influence recipient selection because of the morbidity caused to naive recipients who develop a primary viral infection after transplantation.

In terms of technical factors affecting donor suitability, the gut is sensitive to ischaemia and hypotension therefore intestinal donors must have limited inotrope exposure, low volume or no blood transfusion and stable

haemodynamics. The intestine does not tolerate cold storage and should be transplanted in the shortest possible time frame, ideally in under six hours. Irreversible intestinal damage has been observed after approximately five hours of cold ischemia.[22] Due to previous abdominal surgery, the recipient explant operation may take several hours and this will need to be factored into the timing of the donor retrieval. Unlike other solid organs there is currently no clinically available machine perfusion for the intestine.

The state of the donor liver will affect the decision to accept the intestine for transplantation. Further, the retrieving surgeon's opinion of the intestine at the time of surgery and after perfusion is critical to the decision that the transplant should proceed.

Donors and recipients need to be size-matched because of the limited abdominal space. Donors should be between 50% and 100% of recipient weight. Due to a lack of size-matched organs for paediatric recipients, reduced size intestine with or without liver transplantation has been performed elsewhere. It is not anticipated that this will occur at the Melbourne unit in the near future.

An isolated intestine can be retrieved as part of the retrieval of other abdominal organs. Intestinal donation will not interfere with simultaneous liver, whole organ pancreas or kidney retrieval.

9.5.1 Tissue typing and cross match

The gut is highly immunogenic and, like the kidney, is sensitive to the presence of circulating donor-specific HLA antibodies. It has become clear that donor-specific HLA antibodies (DSAs) are implicated in medium-long term intestinal allograft dysfunction and graft loss.[23,24]

Intestinal transplantation will only be performed upon the review of a virtual crossmatch. The difficulty in finding a suitable donor for a given recipient can be predicted during the work-up stage by the assessment of recipient DSAs. Recipients with multiple and high-level DSAs will have a high PRA and a high chance of an incompatible crossmatch with most donors. Additional comprehensive information is available within the National Histocompatibility Guidelines: https://tsanz.com.au/storage/Guidelines/TSANZ_NationalHistocompatibilityAssessmentGuidelineForSolidOrganTransplantation_Final.pdf

Although Luminex technology allows for 'virtual' crossmatching, a physical crossmatch can be requested for urgent listings where there has been insufficient time for antibody testing. This must be factored into the donation process and may delay organ retrieval, especially if the donor is in a regional hospital and the donor's blood needs to be transported to the state tissue-typing laboratory.

9.6 Allocation

Competition between recipients is unlikely to be a problem during allocation because of the small number of patients on the intestinal transplant waiting list and the specific requirements of each recipient. ABO matching, DSA status, crossmatch results, size-matching and the availability of organs will usually point towards a single recipient.

There is currently no accepted method of ranking wait-listed patients in the context of intestinal transplantation. MELD score is not suitable for intestinal transplantation patients, who may have relatively mild liver disease.

If multiple patients are listed, they will be ranked on clinical criteria based on physician assessment. This will prioritise patients at greatest risk of dying on the waiting list and consider those likely to have the best post-transplant outcomes. If two recipients are otherwise both well matched, the treating physicians will allocate the donor organs to the recipient assessed to be in the greatest need (i.e. the sickest patient).

The prioritisation system assesses the different risk factors for death, including liver failure, recurrent sepsis, fluid issues and loss of vascular access. International experience has demonstrated that patients who require a liver-intestine transplant have the highest waiting list mortality of all potential solid organ transplant recipients.[25] For this reason, in December 2012 the Liver and Intestinal Transplant Committee (LITAC) approved a new urgent list category (Category 2c) for all patients awaiting intestinal transplantation who also require liver transplantation. (See Section 6.3.3). Further, the Renal Transplant Advisory Committee (RTAC) has endorsed the allocation of a kidney (if required) to accompany the intestine (and other abdominal organs as necessary), including interstate donors. Individual patient approval will be obtained from RTAC given the infrequent need for this to occur.

The active intestinal/multivisceral transplantation waiting list for both adults and children is reviewed regularly and circulated weekly to all liver transplant units in Australia and New Zealand.

With time, it is anticipated that transplant activity will increase and allocation criteria may need to be reviewed accordingly.

9.7 Multi-visceral intestinal allocation versus liver-pancreas allocation

An isolated intestinal graft will not interfere with the retrieval and transplantation of other organs and can be retrieved concurrently. Patients who undergo a multivisceral intestinal transplant may need an organ that would otherwise be allocated to a patient on the liver, pancreas or kidney waiting list. There is no simple way of making this allocation decision between the potential recipients competing for the same organs. Allocation will take account of the competing needs of non-intestinal transplant candidates waiting for organs such as liver and pancreas that may be wanted for the intestinal recipient. A suitable multivisceral intestinal graft may be waived because there is a potential liver recipient who will die without urgent transplantation (e.g. a Category 1 listed liver recipient—see Table 6.2).

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10 Vascularised composite allotransplantation

10.1 Preamble

Vascularised composite allotransplantation (VCA) is the transplantation of a vascularised body part containing multiple tissue types as an anatomical/structural unit. VCA is fundamentally more similar to organ transplantation than to tissue transplantation, and is recognised as such by the United States Department of Health and Human Services, and by the European Parliament.[1] Body parts that meet the definition of VCA include limbs, face, larynx and abdominal wall.

As this is such a new field, protocols for assessing recipient and donor eligibility for VCA are currently developed and applied at the institutional level. Efforts are underway to generate standard international guidelines for recipient and donor eligibility for VCA, with a particular focus on developing standardised psychosocial assessment tools (the 'Chauvet protocol').[2] However, these efforts are limited by the small number of VCA transplants that have been performed to date worldwide, and hence the small size and heterogeneity of the available cohort from which to draw evidence-based guidelines. As the practice of VCA transplantation matures, the capacity to generate internationally standardised, evidence-based guidelines will increase.

10.2 Recipient eligibility criteria: hand transplantation

Criteria for recipient eligibility for VCA have a number of unique considerations compared to other forms of transplantation:

- The recipient will experience both positive and negative changes to body image: the graft—and therefore rejection—is visible
- Risk of death or return to dialysis are not factors motivating adherence to immunosuppression
- VCA transplantation may decrease rather than increase life expectancy—the goal is not to extend life, but to increase quality of life
- The recipient is required to comply with lengthy and intensive rehabilitation to achieve function from their transplant, and may initially experience *increased* disability and/or a decrement in quality of life; for some patients, the only gain will be with respect to body image—there may be no functional gain. All patients should be advised of the potential risk of a worse outcome, including the possibility of graft explant.

10.2.1 Inclusion and exclusion criteria

Table 10.1: Inclusion and exclusion criteria for hand transplantation

Inclusion criteria	Exclusion criteria
• Bilateral loss of hands/forearm or unilateral loss with significant contralateral dysfunction as a result of trauma/illness >1 year ago • Patient aged 18 years or older • Psychologically well and stable, including the ability to form a therapeutic alliance with the transplant team* • Able to understand the complexity of the procedure, as well as the risks, benefits and alternatives, and able to communicate their informed decision • A reasonable post-transplant life expectancy, defined as an 80% likelihood of surviving for at least five years after transplantation	• Significant uncorrected chronic comorbid disease, e.g. cardiovascular, respiratory or kidney disease, which results in undue risk from anaesthetic or immunosuppression • Active chronic infection • Active malignancy or one with high five-year likelihood of recurrence • Congenital abnormalities of limbs • Proximal amputation and/or proximal neuromuscular dysfunction • Inability to comply with long term, complex medical and rehabilitative therapy • Untreated/active psychiatric illness • Active cigarette smoking • Active drug or alcohol abuse/addition • Pregnancy

* "Ability to form a therapeutic alliance" refers to an ability to work cooperatively with the transplantation team throughout work-up, transplantation and follow-up.

A criterion that requires further discussion before inclusion in local protocols is a requirement that the patient have tried and failed with prosthetics. Financing of prosthetics in Australia means that access is an issue; however, there would likely be value to the potential recipient in being assessed for and trialling basic prosthetics to gain an understanding of what the sensation of the transplant will be like.

10.2.2 Assessment and acceptance

As for other solid organ transplantation, potential VCA recipient evaluation includes the major criteria of preoperative surgical suitability, infectious disease screening and malignancy screening. There are additional assessments specific to VCA and the patient assessments required in the case of hand transplantation are listed in Table 10.2.

Table 10.2: Patient assessments required prior to listing for hand transplantation

VCA-specific assessment	Non VCA-specific criteria
• Hand surgeon assessment of suitability of proximal stump for transplant based on anticipated outcome • Immunology physician review • Anaesthetic review • Psychological review • EMG for proximal muscle condition • Prosthetics assessment • Imaging: — Xray — CT angiography — MRI and MR angiography — MRI • Preoperative Functional assessment: — DASH score — Michigan Hand Score — Jebsen assessment	• Preoperative investigation • FBE, coagulation profile • ABO serology • Donor specific antibody • Renal function – U+ E/Cr, GFR estimation, urinalysis • Liver function tests • Infectious disease serology – HIV antigen, HTLV I and II antibody, HIV I and II antibody, hepatitis C virus, hepatitis B core antibody, Hep B Surface Ag, syphilis, cytomegalovirus, herpes simplex virus, Toxoplasmosis and varicella-zoster antibody • Pulmonary function tests, chest x-ray • ECG and Echocardiogram • Dental consult • Sinus imaging if indicated

10.2.3 Retransplantation

There is currently no intention to exclude candidates on the basis of prior VCA transplant. The reasons for the loss of the prior graft would be considered as part of the psychological evaluation and assessment of ability to comply with therapy. Self-inflicted trauma is also not a contraindication to VCA transplantation: provided candidates are deemed to be currently psychologically well and stable and meet all other criteria, then they are eligible for VCA transplantation.

10.2.4 Criteria for activation on waiting list

As for other solid organ transplant procedures, the decision to activate a recipient for a VCA is based on agreement between all of the teams involved (surgical, medical and psychological). Given the ethical and health implications for the patient of a negative transplant outcome, a robust approach to risk minimisation is encouraged.

The recipient consent form developed by the St Vincent's Hospital Melbourne team includes information on the transplant operation, the potential long-term effects of transplantation, and what the recipient should expect from the transplant and the rehabilitation process. Potential recipients are informed of the following:

- Hand transplant does not prolong life, instead benefits are measured in improved quality of life
- Studies so far indicate that the function of the transplanted hand is better than that of prosthetics
- Success of the transplant depends as much on the extensive care following the transplant as it does on the surgery itself—some of these therapies are life-long

- Technical success of the surgery will be apparent in two to three days; by two to three months it is expected that the recipient will be able to make a fist, but it will be at least a year before finer finger moments and sensation to the skin develop
- A hand transplant is not the best option for everyone, and risks include:
  - risks related to the operation (infection, bleeding), those related to the anaesthetic and other post-operative complications which make, rarely, result in death
  - rejection, which in some cases may lead to the hand needing to be surgically removed
  - potential to develop certain infections, cancers, diabetes and heart disease as a consequence of immunosuppressive medications
- Inclusion in the International Hand Transplant Registry (handregistry.com)
- Responsibilities of the recipient include:
  - Daily blood tests for the first 30 days, and weekly skin biopsies
  - Medication adherence
  - Hand physiotherapy
  - Clinic visits
- Considerations of the donor family—in order to protect and maintain the privacy of the donor family, the recipient is requested not to share details of the transplant with the media.

It is further recommended that the consent process incorporate a cooling off period whereby, after the recipient gives their initial consent, the recipient considers their decision for approximately 4 weeks and is then asked to re-consent. This cooling-off period is an important ethical safeguard in the consent process.[3]

10.3 Recipient eligibility criteria: face transplantation

Though Australian recipient eligibility criteria for face transplantation have not yet been developed, other international groups have well-developed protocols. The Brigham and Women's Hospital in Boston has performed multiple partial and full-face transplants since gaining institutional review board approval for the procedure in 2008. The recipient eligibility criteria specified under the protocols of this institution are listed in the Table 10.3 adapted to reflect Australian hand transplant eligibility criteria (see Section 10.2).

10.3.1 Inclusion and exclusion criteria

Table 10.3: Recipient inclusion and exclusion criteria specified under Brigham and Women's Hospital protocols for face transplantation,[4] adapted for the Australian context.

Inclusion criteria (Brigham and Women's)	Exclusion criteria (Brigham and Women's)
• Most difficult or impossible to reconstruct facial defects • Defect comprises >25% of the facial area, and/or involves loss of one of the central facial parts such as eyelids, nose or lips • Outcome of an alternative reconstructive method considered unfavourable or unsatisfactory	• Pregnancy • Active psychiatric illnesses are considered individually • Unable to guarantee adequate coverage of follow-up care and immunosuppression
Inclusion criteria (from hand VCA, Section 10.2.1)	**Exclusion criteria (from hand VCA, Section 10.2.1)**
• Patient aged 18 years or older • Psychologically well and stable, including the ability to form a therapeutic alliance with the transplant team • Able to understand the complexity of the procedure, as well as the risks, benefits and alternatives, and able to communicate their informed decision • A reasonable post-transplant life expectancy, defined as an 80% likelihood of surviving for at least five years after transplantation.	• Significant uncorrected chronic comorbid disease e.g. cardiovascular, respiratory or renal, which results in undue risk from anaesthetic or immunosuppression • Active chronic infection • Active malignancy or one with high five-year likelihood of recurrence • Active cigarette smoking • Active drug or alcohol abuse/addition

10.3.2 Assessment and acceptance

Similarly, Australian protocols for face transplant candidate evaluation have not been developed. The protocols for face VCA candidate evaluation used by Brigham and Women's Hospital provide an example of the steps involved in this process.[4,5]

10.4 Donor Assessment

In terms of donor selection, the requirement for the donor hand or face to be a match both in terms of medical compatibility and aesthetic appearance (skin tone, proportion, age, race, gender) is unique to VCA. Secondly, because VCA is performed on physically healthy but severely disabled individuals, strict criteria are necessary to prevent donor transmission of disease. Approaching the families of potential hand and face donors also requires specialised protocols that account for the sensitivity of the request and a lower willingness to consent to donation. Protocols are also required for the fitting of prostheses to replace the donated allograft post-mortem. Further, cold ischaemia time—and therefore travel time—between retrieval and implantation must be minimal. The length of time that a potential recipient will wait for a suitable donor may therefore be extensive: this is a consideration that must be factored into recipient evaluation and informed consent.

Table 10.4 lists the inclusion and exclusion criteria for hand donation that are currently applied in Australia.

Table 10.4: Inclusion and exclusion criteria for hand donation.

Inclusion criteria	Exclusion criteria
• Age 18 – 65 years • Documented neurological death with hemodynamic stability • Aesthetically and physically matched to recipient gender, skin tone, race, age, and size (within 15% of recipient size) • Compatible with donor—matched for viral status and blood type • The donor should not require excessive vasopressors to maintain blood pressure prior to retrieval	• Untreated sepsis, HIV, active cytomegalovirus, Epstein-Barr virus, active tuberculosis, hepatitis B, hepatitis C, viral encephalitis • Malignancy • Current intravenous drug use • Tattoo within past six months • Systemic or limb-related neuropathies • Extensive arthritis

Australian protocols concerning eligibility for face donation have yet to be developed. The Brigham and Women's Face VCA unit have established criteria that include factors common to hand donation, such as ABO compatibility and age, gender and skin colour match. In addition—again in keeping with hand VCA donor assessment—the presence of active sepsis, active viral infections, tuberculosis and active/recent malignancy are considered contraindications to donor acceptance. Specific to face VCA are the exclusion criteria of congenital craniofacial disorder, facial nerve palsy, a history of significant craniofacial or neck trauma and/or surgery, or a plan by the family to hold an open casket funeral.

10.5 Allocation of VCA organs

Given the low volume of VCA transplantations in Australia, and as yet there are not multiple candidates simultaneously waiting for VCA, an allocation policy has not been developed. The UNOS/OPTN protocol for VCA allocation provides benchmark against which a local policy might be developed in the future. Under the UNOS/OPTN allocation protocol, the host OPO offers VCA organs to candidates with a compatible blood type and similar physical characteristics to the donor. The OPO will first offer VCA organs to candidates that are within the OPO's region, and secondly to candidates that are outside of the OPO's region according to proximity. Proximity of the donor and recipient is a relevant factor in allocation given the importance of short ischaemia time.

In addition to the absolute requirements for blood group compatibility and virtual crossmatch, proposed criteria for allocation include age difference, size (especially bones), colour and texture of the skin, and soft-tissue features.[1] Other factors that may be incorporated into allocation criteria include urgency and waiting time. Given the small size of the potential donor pool, HLA matching will not be feasible.

10.6 Multi-organ transplantation

There should be no impediment to undertaking a quality-of-life-improving VCA at the same time as a life-sustaining solid organ transplant. In this instance, the main ethical challenge of a VCA—that of a potential reduction in life years due to immunosuppression in an otherwise healthy recipient—are mitigated. Multiple VCA transplants (i.e. dual hand transplants) are less commonly undertaken internationally due to the challenging and prolonged recovery period for the patient, and none have yet been undertaken in Australia. For suitable candidates, however, multiple VCA would be considered.

10.7 Emerging Issues

Ethics assessment in VCA transplantation

The ethical complexity of VCA is unlike any other area of transplant medicine. Clinical ethicists are often members of VCA teams, assisting with the development of protocols, policies, procedures, and forms. The VCA clinical ethicist can also be involved in screening potential recipient for matters of ethical relevance, including but not limited to capacity assessment and informed consent, as well as coercion and conflict of interest. VCA does not save lives, but hopes to enhance them (without any guarantees), and the expectations and outcomes of the patient and surgical teams may conflict. It is important to understand these matters, as well as the motivations and motivation level of the potential recipient. The philosophical meaning attached to the hand/face/etc. by the patient must be understood, as well as the values, behaviours and emotions that are linked to these body parts. It is important to detect and resolve moral distress pertaining to the donation and transplant, including donor-related issues such as death and dying, fingerprints and identity, and personhood issues. The involvement of a clinical ethicist may therefore be a part of local VCA transplantation protocols in the future.

Psychosocial evaluation in VCA transplantation

Given that the primary goal of VCA is to improve the psychosocial status and quality of life of the recipient, psychosocial evaluation both before and after transplantation is critical not only to establish patient suitability and identify at-risk patients and those in need of ongoing counselling, but also to assess the success of the transplant itself. Psychosocial evaluation should therefore ideally establish (i) a detailed baseline understanding of the impact of the injury on the patient and the extent to which they have adapted to their disability, (ii) the existence of any demonstrable active or untreated psychiatric or psychological impairment that would preclude VCA transplantation, (iii) patient perceptions of the goals of treatment and their expectations post-transplant (also relevant to informed consent), (iii) requirements for psychosocial support pre- and post-transplantation, and (iv) post-transplant changes in quality of life and other psychosocial outcomes over the longer term. It must be further established that the potential VCA recipient will be able to tolerate the physical and psychological stress of all pre-, peri- and post-operative procedures and rehabilitation involved, while simultaneously coping with media attention, a changed physical appearance and a complex immunosuppression regimen.[5]

Therefore—in addition to the standard pre-transplant evaluation of psychiatric wellbeing, social support, substance use, knowledge of transplantation and predicted compliance—VCA transplantation also requires the assessment of body image, adaptation to the trauma, cognitive preparedness, motivation, expectation of transplant outcomes, and potential for psychological regression of the transplant candidate.[2] The principle concern is the potential for a recipient to psychologically reject or otherwise be unable to cope with the transplant, leading to lower quality of life and potentially to non-adherence to immunosuppression and loss of the graft.

In an effort to move towards standardised psychosocial assessment of candidates for hand transplantation, the Innsbruck Psychological Screening Programme for Reconstructive Transplantation (iRT-PSP) was developed in 2011.[2] This assessment method measures cognitive functioning, affective status, psychosocial adjustment, coping, quality of life and life satisfaction based on a semi-structured interview, standardised psychological screening procedures and ongoing follow-up assessment. The iRT-PSP therefore provides a tool for pre-transplant assessment, post-transplant follow-up ratings, and the identification of needs of psychological/psychiatric treatment. The application of standardised psychosocial assessment tools will, in the future, be a part of the VCA candidate assessment process.

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Part C

Paediatric Donors

11 Paediatric donors

11.1 Paediatric donor suitability

All children who die in intensive care should be considered for potential organ donation.

The overall rate of organ donation in children is similar to that in adults; however, this rate declines below two years of age.[1] This is due to a combination of factors – primarily medical unsuitability and age and weight limits for retrieval and transplantation.

Clarity regarding donor eligibility criteria and allocation protocols is critical to maximising donation opportunities. Particularly in the context of paediatric donation, confidence that a potential donor has a good likelihood of being suitable for transplantation is an important factor in initiating the donation conversation. Work to optimise donor identification in paediatric and neonatal intensive care units is ongoing, and criteria continue to be refined regarding suitability for transplantation of organs from paediatric donors, particularly from the smallest of these donors.

The recommendations below reflect local and international experience and current evidence with respect to paediatric donation and transplantation. However, it is acknowledged that there is a spectrum of experience with respect to the transplantation of organs from small paediatric donors and not all units will feel it is appropriate to consider all donors according to the criteria below. In order to facilitate the pathway for donation and allocation of these organs, transplant units should develop their own protocols for acceptance of paediatric donors, guided by the recommendations below as well as local expertise and other relevant considerations.

11.2 Paediatric kidney donation and allocation

For donors greater than 20kg, kidney allocation should proceed as for adult donors. For donors >10kg to 20kg, standard allocation also applies, although kidneys should be offered en-bloc first, then subsequently as single kidneys.[2,3]

Donors >5kg to 10kg constitute a broad category with varying implications for the complexity of retrieval and transplant surgery, particularly in the case of the smallest donors. Availability of appropriate surgical expertise will influence the utilisation of such donors. Ideally, these organs should be managed in centres with specialist experience in small grafts, where clear protocols exist on how to manage them. Centres should pre-emptively discuss their readiness and capacity to transplant small organs. Centres willing to transplant very small organs may also nominate one or more of their senior transplant physicians and surgeons to act as local experts to provide pre-allocation advice to donation staff.

Donor history should be reviewed at the time of pre-allocation discussion and subsequent organ offer, considering possible indications of inherited paediatric renal disease and/or complications of neonatal/paediatric ICU management. Given the relative lack of experience with retrieval and transplantation of very small organs, donor history and any potential risk factors should be documented and post-transplant outcomes carefully monitored. Regular audit of transplant outcomes associated with the donor criteria below will be important to assess their utility and validity and to build evidence-based criteria for the allocation of very small kidneys.

In addition to routine donor information, offers of very small paediatric donors should be accompanied with the following documented data:

- antenatal factors: normal antenatal morphology scan, absence of oligohydramnios, absence of history of transmissible infection
- gestational age at birth and/or reduced size for gestational age
- renal ultrasound with details of kidney/ ureter/ bladder anatomy and kidney size percentile for age

- presence of extra-renal congenital anomalies or syndrome with likelihood of systemic impact affecting the kidneys
- renal function: creatinine with normal range for age and gestation
- acute illness factors: history of central/ umbilical vascular catheterization +/- thrombosis.

Table 11.1: Recommendations for paediatric kidney donation (SK: single kidney, EB: en-bloc)

Size range	Single kidney (SK) or en-block (EB)	Allocation
>20kg	SK	Standard allocation.
>10-20kg	EB first, then SK in certain cases	Standard allocation with default to offer as EB. Recipient transplanting unit has discretion to opt for SK, in which case second kidney to be offered on as SK.
>5-10kg	EB	Allocation proceeds only after pre-allocation discussion with local experts. Referral should be accompanied by standardised paediatric-specific donor variables. Currently the Royal Prince Alfred and Westmead Hospitals in NSW have protocols for consideration of donors of this age and size range.
<5kg		Currently not considered surgically suitable for organ donation.

11.3 Paediatric liver and intestinal donation and allocation

Paediatric liver transplantation requires appropriate size matching. For very small infants requiring liver transplantation, a suitable donor may therefore include a very small paediatric donor. The lower size limit of potential donors includes neonatal donors.

Table 11.2: Recommendations for paediatric liver and/ or intestinal donation

Age and size range	Allocation
DNDD: < 18 years, No lower limit for age or weight. DCDD: ≥ 3kg and < 18 years will be considered for liver donation. DCDD donors are not suitable for intestinal donation.	Liver donation: Refer to home state liver transplant unit first, if no suitable recipient, refer to other units on rotation. Preferential allocation of a donor liver to recipients requiring combined liver and intestinal transplant, as guided by section 7.2 of the National SOP for Organ Allocation, Organ Rotation and Urgent Listing. Intestinal donation: All referrals to Victorian Liver Transplant Unit.

Paediatric donor livers must first be offered to paediatric recipients (<18 years of age). This is the case for whole liver or for both lobes of a split liver when the potential donor is less than 18 years of age. If there are no suitable paediatric recipients in the home state, it is then offered on national rotation for paediatric recipients.

Paediatric livers will only be considered for an adult recipient in two circumstances:

a. In the event that the paediatric liver rotation has been exhausted, the offer returns to the home state and the home state can allocate to an adult recipient. In the event that the home state do not have a suitable recipient, the liver is offered on the Adult Liver Allocation Rotation – *please see Appendix A of the National SOP for Organ Allocation, Organ Rotation and Urgent Listing.*
b. There is a very sick/dying potential adult recipient in the donor home state. Allocation in this circumstance requires discussion and consensus by the Paediatric Liver Transplant Units Directors (or their delegate).

11.4 Paediatric lung donation and allocation

The recipient criteria are set out by the Nationally Funded Centre (NFC) for Paediatric Lung and Heart-Lung Transplantation and supports lung transplantation for children ≥4 years and >10kg. Reflecting that children this small may have restrictive lung disease and a small chest cavity, smaller paediatric donors may be suitable as per recommendations in Table 11.3.

Table 11.3: Recommendations for paediatric lung donation and allocation

Age and size range	Allocation
<17 years old or <120cm (and in both cases >8kg)	Allocation to Paediatric Lung Transplant The Alfred Bayside Health, both DCDD and DNDD

11.4.1 Paediatric heart-lung blocs and allocation

Infants and children with a variety of medical conditions may require heart-lung transplant (2-3 cases per year). Paediatric donors suitable for these children are rare and such transplants are only performed by the Paediatric Heart-Lung Transplant Centre (i.e. recipients under age 16) at the The Alfred Bayside Health. The prioritisation and allocation of all these smaller donor organs must be considered at the time of referral as a bloc.

Table 11.4: Recommendation for paediatric heart-lung donation

Age and size range	Allocation
< 17 years old and/or ≤ 50 kg	Formal referral of all DNDD donor heart-lung blocs fitting these criteria to the Heart-lung Transplant centre at The Alfred Bayside Health. If the Paediatric centre can't use these organs, then the lungs default back to the home state and national rotation and the heart is offered to the paediatric heart transplant centres as per Appendix O.

11.5 Paediatric heart donation and allocation

Infants and children can derive significant benefit from heart transplantation, with a median post-transplant survival of up to 25 years for infants.[4] Any donor weighing greater than or equal to 3 kg is deemed potentially suitable. For infants with severe heart disease, an early decision on pursuing wait-listing for cardiac transplant vs mechanical support (VAD) is often necessary.[5] An understanding of the size of the donor pool and likely waiting time is critical in informing this decision. Accordingly, it is recommended that all potential donors ≥3kg be formally assessed for heart donation. Discussion with the transplant team to determine if there is a suitable recipient should only be undertaken if this is the express wish of the donor family. A 'paediatric donor heart' is defined as being retrieved from a donor <17 years-old AND/OR 3kg to ≤50kg. The paediatric DNDD heart offering workflow process is outlined in Appendix O.

Paediatric DCDD heart donors weighing < 40kg, located at the Royal Childrens Hospital (RCH) only, may be considered by the RCH Heart Transplant program. All other DCDD donors ≥40kg are to be offered to St Vincents Hospital (SVH), Sydney, for consideration (*N.B* SVH may also consider paediatric recipients waitlisted at the Childrens Hospital Westmead).

Paediatric donors with both heart and lungs suitable for use as a bloc should be referred to the Paediatric Heart Lung Transplant Centre at the Alfred Bayside Health – see 11.4.1 above.

Table 11.5: Recommendations for paediatric heart donation and allocation

Donor pathway and age/size range	Allocation
DNDD <17 years old and/or 3kg to ≤50kg	Please refer to Appendix O
DCDD ≥40 Kg	Offer to St Vincent's Hospital (SVH), Sydney, for consideration (*N.B* SVH may also consider paediatric waitlisted patients at Children's Hospital Westmead)
DCDD < 40 kg*	Offer to RCH Paediatric heart transplant program for consideration

*ONLY donors located at the Royal Children's Hospital (RCH)

11.6 Paediatric pancreas donation and allocation

Paediatric DNDD donors >25kg are suitable for pancreatic donation. These should initially be offered for solid organ donation and, if not allocated, then offered for islet donation.

Paediatric DCDD donors are not currently suitable for pancreas donation.

Table 11.6: Recommendations for paediatric pancreas donation

Age and size range	Allocation
>25kg	DNDD suitable for solid organ or islet donation.

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Appendices

Appendix A

TSANZ Advisory Committees & Working Groups, terms of reference

The TSANZ Advisory Committees and Working Groups represent the interests and views of their organ-specific special interest group in Australia and New Zealand. The Working Groups are informal networks whereas the Advisory Committees have a more structured work process. There is some variation in the constituency and mode of operation of the individual groups, but the areas listed below are a set of 'minimum requirements' for each Advisory Committee.

Each Advisory Committee acts as the peak body for the organ group it represents. It is broadly representative of the individuals, units and states taking part in the given transplantation area, and has the capacity to formulate clinical standards and policies in this area. Some Advisory Committees hold two face-to-face meetings each year, whereas others meet once during the TSANZ Annual Scientific Meeting. Additional teleconferences are held as required throughout the year. Decisions are normally made by consensus, but when consensus cannot be reached decisions are made by vote.

The Chair of each Advisory Committee reports to the TSANZ Board on a regular basis via the Chair of the Advisory Committees and Working Groups.

Key functions of the Advisory Committee are to:

- Act as the peak body for their special interest group in areas of recipient eligibility, donor organ retrieval, allocation and standards of practice
- Formulate standards of practice and conduct regular audits and reviews (including audits of the interstate exchange of organs and of allocation processes)
- Oversee and regularly review the eligibility criteria and allocation algorithms for their organ group
- Provide a forum for discussion of new or emerging therapies or practices in their field of transplantation
- Provide advice to TSANZ Board on current, new or emerging therapies or practices in their field of transplantation, engaging relevant stakeholders in the process
- Regularly review the information that they make available on the TSANZ website for accuracy and current applicability.

The terms of reference of the Advisory Committees oblige them to foster sound governance by having:

- Auditable and transparent processes and operation.
- A process for effective engagement with their constituencies
- Consumer and community representation as required of any peak body
- Documented processes for election of members and the Chair, including specification of tenure.

Any change to standards or policies initiated by the Advisory Committees undergoes a process of consultation that involves endorsement by TSANZ Board and OTA.

Appendix B

Donor age and weight requirements by jurisdiction

The tables below should be used in conjunction with the recommended donor assessment of medical suitability outlined in these TSANZ Clinical Guidelines.

Table B1: DNDD Pathway

Organ	NSW/ACT	QLD	VIC/TAS	SA	WA	NT	NZ	TSANZ Clinical Guidelines
Heart	≥3 kg – ≤65 years							≥3 kg – ≤65 years
Lung	≥8 kg – ≤75 years							≥8 kg – ≤75 years
Liver	Nil Limit	Nil Limit	≤85 years	≤80 years	≤85 years	≤80 years	Nil Limit	Not specified
Split Liver	≤50 years							Not specified
Pancreas	5 – ≤55 years ≥25 kg – <100 kg *N.B SA home state donor: up to 60 years*							5–55 years old >25 kg – <100 kg BMI ≤30
Pancreas Islets	>25 kg – 65 years AND <150 kg							3–65 years >25 kg – <150 kg
Kidneys	≥5 kg – ≤85 years							3 months up to 85 years
Stomach/ Intestine	≤55 years							Ideal donor <50 years, donors between 50–60 will be considered

Table B2: DCDD Pathway

Organ	NSW/ACT	QLD	VIC/TAS	SA	WA	NT	NZ	TSANZ Clinical Guidelines
Heart	≤55 years							≤55 years
Lung	≥8kg – ≤75 years							≥8 kg – ≤75 years
Liver	≥3 kg – ≤60 years	≤70 years	≤75 years	<45 years	≤70 years	<40 years	Nil Limit	≥3 kg
Pancreas	≥25 kg – ≤45 years	N/A	≥25 kg – ≤45 years	8–55 years (BMI <30)	N/A	8–55 years (BMI <30)	N/A	Up to 45 years
Pancreas Islets	>20 kg – ≤35 years *For research only*							Currently, islet yields from DCDD donors are insufficient for transplantation
Kidneys	≥5 kg – ≤75 years							3 months up to 75 years

Appendix C

Kidney allocation algorithms

National Allocation formula

Match level	Description	Criteria		Base score
1	Very highly sensitised	**1a**	mPRA ≥99.7	99 700 000
	ABO compatible matches allowed	**1b**	mPRA ≥99	99 000 000
		1c	mPRA ≥98	98 000 000
		1d	mPRA ≥97	97 000 000
		1e	mPRA ≥96	96 000 000
		1f	mPRA ≥95	95 000 000
National Urgent	ABO compatible matches allowed	Recipient National urgency >0		90 000 000
2	HLA matching with EPTS restriction	**2a**	0 mismatches at HLA-A or HLA-B and EPTS ≤25	89 000 000
	Prioritises good HLA matches for low EPTS recipients	**2b**	1 mismatch at HLA-A or HLA-B and EPTS ≤25	88 000 000
	Recipients must be matched at HLA-DRB1 and ABO matched	**2c**	2 mismatches at HLA-A or HLA-B and EPTS ≤25	87 000 000
		2d	0 mismatches at HLA-A or HLA-B and EPTS ≤60	86 000 000
3	HLA matching and highly sensitised	**3a**	0 mismatches at HLA-A or HLA-B or HLA-DRB1 and mPRA >80	79 000 000
		3b	1 mismatch at HLA-A or HLA-B or HLA-DRB1 and mPRA >80	78 000 000
		3c	2 mismatch at HLA-A or HLA-B or HLA-DRB1 and mPRA >80	77 000 000
	Centre credit difference (interstate pay-backs)	**3d**	Matched at HLA-DRB1, 1 mismatch at HLA-A or HLA-B, mPRA ≤80 and centre credit difference ≤-3	76 000 000
	Restricted to EPTS-KDPI difference of <50 points	**3e**	Matched at HLA-DRB1, 2 mismatch at HLA-A or HLA-B, mPRA ≤80 and centre credit difference ≤-6	75 000 000
		3f	mPRA >80 and centre credit difference ≤-9	74 000 000
		3g	Centre credit difference <-20	73 000 000

Other parameters	Bonus points added	
Paediatric	**0-17 years**	250 000
	18 years	218 750
	19 years	187 500
	20 years	156 250
	21 years	125 000
	22 years	93 750
	23 years	62 500
	24 years	31 250
Donor centre = patient centre	50	
Recipient Centre credit	1000 + recipient centre credit	
Recipient and Donor are HLA DRB1 homozygote	500 000 (except level **3g**)	
Waiting time (on dialysis)	Number of months x 1	

State Allocation

- Allocation initially matched with a restriction applied (EPTS-KDPI difference ≤50), then unrestricted matching is applied.
- If a KDPI max is specified in OrganMatch, it will be applied to all Levels of State Allocation.
- A maximum KDPI value of 20 is applied to kidneys retrieved from donors <18 years.

Level	Description	Details	Base Score
State Urgent	State Urgency Index >0	Urgency index added to base score	60 000 000

Level	Description	Details		Restricted base score	Unrestricted base score
State HLA-matching	HLA mismatches A/B/DRB1	**1a**	0 0 0	49 000 000	39 000 000
		1b	1 0 0 or 0 1 0	48 000 000	38 000 000
		1c	1 1 0	47 000 000	37 000 000
		1d	0 0 1	46 000 000	36 000 000
		1e	2 0 0 or 0 2 0	45 000 000	35 000 000
		1f	1 0 1 or 0 1 1	44 000 000	34 000 000
		1g	2 1 0 or 1 2 0	43 000 000	33 000 000
State Waiting	Months on dialysis	Number of months x 1		40 000 000	30 000 000

Additional bonuses applied at the State Level:

- Paediatric bonus of 10 000 000 for restricted algorithms – **state HLA-matching**. With age tapering scores as follows:

  Points = 10,000,000 – ((10,000,000/ (25-17)) *(age – 17))

Age (years)	Points
0–17	10 000 000
18	8 750 000
19	7 500 000
20	6 250 000
21	5 000 000
22	3 750 000
23	2 500 000
24	1 250 000

- Paediatric bonus of 100 000 for restricted algorithms – **state waiting**. With age tapering scores as follows:

  Points = 100,000 – ((100,000/ (25-17)) *(age – 17))

Age (years)	Points
0–17	100 000
18	87 500
19	75 000
20	62 500
21	50 000
22	37 500
23	25 000
24	12 500

- Recipient and donor are HLA DRB1 homozygous – bonus 500 000 to state HLA-matching algorithm only.

In the event that more than one patient has the same score, the ranking of the patients with identical scores is randomised.

Interstate Utilisation Algorithm

In rare situations there may not be enough patients in a given state to be able to accept the available kidneys. Most often this occurs if the donor has a rarer blood group, such as AB. If there are not enough patients to receive the kidneys locally, the interstate utilisation algorithm is run. This list incorporates patients from across the country, to ensure that the kidneys do not go to waste.

Kidneys that are offered via the interstate utilisation algorithm and eventually accepted at offer rank 20 or higher are excluded from the calculation of the centre credit balance.

Level	Description	Details		Restricted base score	Unrestricted base score
State HLA	HLA mismatches	**1a**	0 0 0	19 000 000	9 000 000
	A/B/DRB1	**1b**	1 0 0 or 0 1 0	18 000 000	8 000 000
		1c	1 1 0	17 000 000	7 000 000
		1d	0 0 1	16 000 000	6 000 000
		1e	2 0 0 or 0 2 0	15 000 000	5 000 000
		1f	1 0 1 or 0 1 1	14 000 000	4 000 000
		1g	2 1 0 or 1 2 0	13 000 000	3 000 000
State Waiting	Months on dialysis	Number of months x 1		10 000 000	0

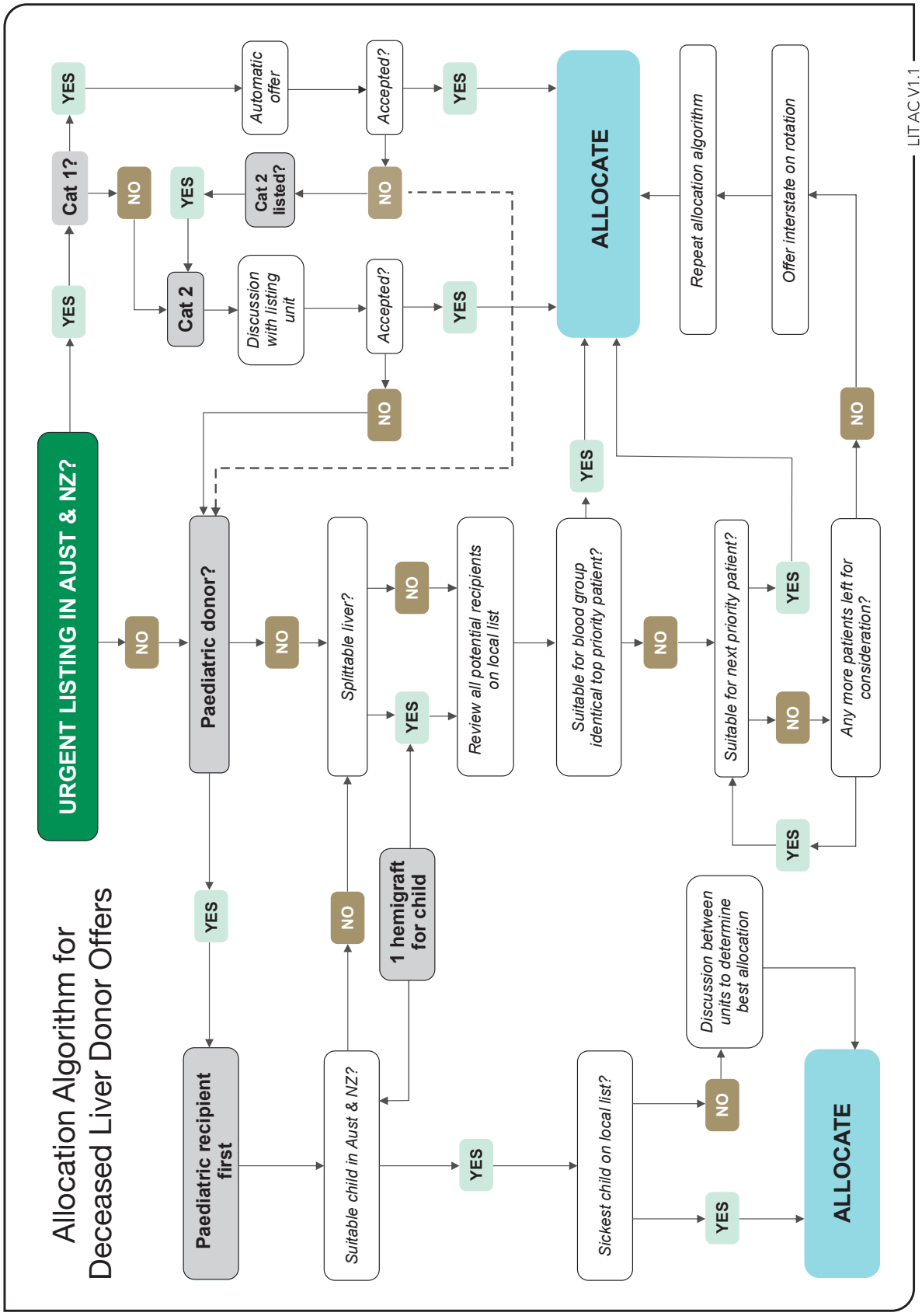
ABO selection rules

The ABO selection rules determine the acceptable organ matches, as shown:

Algorithm	Level	Donor ABO type	Patient ABO type
National	Level 1	A	A
		A	AB
		B	B
		B	AB
		AB	AB
		O	O
		O	A
		O	B
		O	AB
National	Level 2 and Level 3	A	A
		B	B
		AB	AB
		O	O
State	NSW	A	A
	WA	A	AB
	VIC	B	B
	SA	B	AB
	QLD	AB	AB
		O	O

Appendix D

Liver donor allocation flow diagram



Appendix E

Guidelines for lung donor bronchoscopy & CT chest

Purpose

The purpose of this supplementary guideline is to provide guidance to Donation Specialist Coordinators in arranging additional diagnostic investigations of bronchoscopy and CT chest in potential lung donors.

The guidelines described below were last reviewed in March 2023. The guidance document is intended to be used by all clinicians who may request or perform a donor bronchoscopy and/or CT Chest. The guidelines should be viewed only as recommendations. They do not establish legally enforceable responsibilities.

Mention of specific products or equipment in this document does not represent an endorsement of such products or equipment by the Lung Advisory Committee nor does it necessarily represent preference for those products or equipment over similar competitive products or equipment. It is incumbent on the reader who intends to use any information, forms or procedures contained in this document to evaluate such materials for use in the light of operational requirements associated with their facility.

Lung Donor Bronchoscopy

Rationale

- 50% expected to be abnormal in lung donors with findings including mucous/foreign aspirated material/ blood clot plugging, bronchial infection and rarely, endobronchial mass
- Opportunity for acquisition of microbiological specimens to enhance antibiotic regimens early post-transplant.

Most requests for bronchoscopy will be for when the donor is in ICU, before the retrieval team arrives for donor organ evaluation and retrieval.

Indications

- X ray evidence of segmental or lobar collapse
- Significant burden of secretions on ETT suctioning
- Assessment of pulmonary infiltrates especially if unilateral
- History of aspiration or foreign body inhalation
- Donors with unexpectedly low PO_2 (at the guidance of the requesting transplant physician)

Method/technique

- Local anaesthesia is required in DCDD donors
- Visualisation of :
  - site of ETT
  - airway anatomy to assess for variations including right upper lobe tracheal bronchus
  - extent of airway inflammation and vascularity site and extent of secretions, clot, aspirated material, foreign bodies and tumours
- Airway toilet to remove secretions. Small volume aliquots of 5-20ml N/Saline inserted and aspirated via suction: send for urgent microbiology: m/c/s, fungal culture, and AFB.

CT Chest

Rationale

The plain chest radiograph has a relatively low sensitivity compared with CT imaging in the detection of lung abnormalities in potential lung donors. Whilst CT scans are not considered routine in the work up of a lung donor, indications in either the standard or marginal donor may include:

Indications

- Clarification of anomalies suggested on a CXR especially in donors with >20 pack year history of smoking where exclusion of lung malignancy or emphysema is of particular concern
- Donors with history of penetrating or blunt trauma to assess for diaphragmatic tears, lung lacerations, extent of pneumothorax, pulmonary contusions and other infiltrates
- Donor history of aspiration or infection to assess for extent of consolidation as CXR may underestimate structural abnormalities (this may be of particular interest if only single lung donation is being considered)
- All lung donors >70 years of age due to increased incidence of lung pathology- including subtle emphysema, lung nodules and airway calcification
- All lung donors who test positive for SARS-CoV-2 on PCR from the upper respiratory tract – to assess for any sequelae of COVID-19.

A CT scan of the chest performed on admission for a lung donor will generally suffice. A formal report from a radiologist is ideal although not always practical. Representative images of lung windows from the upper, mid and lower sections of the thorax should be de-identified and uploaded to the OrganMatch Donor Chart.

Method/technique

CT chest (without contrast) to define lung parenchyma and airway anatomy – contrast may be required to outline mediastinal and vascular structures although potential nephrotoxicity needs to be considered.

Appendix F

National notification for lung transplantation

Preamble

The National Notification Lung Transplantation process described below is adapted from the TSANZ-OTA National Standard Operating Procedure – Organ Allocation, Organ Rotation, Urgent Listing.

Indications

- Patient survival estimated to be days to weeks without transplantation as a result of or due to development of:
  - Requirement for ECMO
  - New or worsening respiratory failure needing high flow oxygen, non-invasive ventilation, or mechanical ventilation
  - Rapid deterioration as indicated by, but not limited to a significant rise in partial pressure of carbon dioxide, marked reduction in functional capacity, acute irreversible fall in lung function parameters or refractory right heart failure.
- Highly sensitised patient with high Panel Reactive Antibody or high titre anti-HLA antibodies, in order to enhance their overall exposure to a larger donor pool. Consideration should be given to initiate national notification for patients who are excluded from OrganMatch algorithm matching based on their unacceptable antigens.
- Unusual technical requirements – size extremes (small TLC) where size-matched organ availability is limited.

NB: These are for general guidance only rather than an automatic trigger for national notification, with institutional factors, prognosis and predicted outcome post transplantation influencing decision making.

National notification procedures

a. National notification for lung transplantation is at the discretion of the Lung Transplant Unit Director. It is the responsibility of the Lung Transplant Director (or their delegate) to notify all other Lung Transplant Units. Updating the recipients OrganMatch enrolment must occur to ensure appropriate identification and matching. The listing can be viewed within OrganMatch by the donation and transplant clinicians as required.

b. A notification from one state is not binding on other states. A national notification does not override lung allocation standard procedures.

c. The donation coordinator will be informed by the home state lung transplant unit at the time of offering the lungs if the home state will waiver the offer for a patient on the national notification list.

d. In this circumstance, the 'Logistics – offer waived for urgent or national notification' can be selected in OrganMatch.

e. In the event the lungs are not accepted for the national notification patient, the lungs are offered back to the home state.

f. A patient listed for national notification will remain active for four weeks. If a patient remains on national notification beyond four weeks, re-notification of all Lung Transplant units is required, along with the urgent relisting date in the OrganMatch enrolment.

Review

The operation of the national notification list will be subject to annual audit by the Lung Transplant Advisory Committee (LTAC) and be listed as a standing agenda item at LTAC meetings.

Appendix G

Heart matching algorithm

Match Level	Description	Criteria	Base Scrore	Additional Points
1	Heart Paediatric	Donor age < 17 years old and/or ≤ 50 kg Recipient < 17 years old and listed at one of the paediatric heart transplant centres	5 000 000	5 000 000
2	National Urgent Flag	Patient is listed as Urgent	5 000 000	2 000 000
3	Standard	All active recipients ready for matching	5 000 000	
		Home state		1 000 000
		Blood group compatibility		See blood group table

ABO compatibility rules

The following table show the compatible ABO groups. Additional points are added to the score for compatibility. This assists with the final sort order.

Algorithm	Donor ABO type	Patient ABO type	Score
Heart	A	A	100,000
	A	AB	70,000
	B	B	100,000
	B	AB	70,000
	AB	AB	100,000
	O	O	100,000
	O	A	70,000
	O	B	40,000
	O	AB	10,000

Appendix H

Transplant Units – Australia and New Zealand

Currently recognised transplant units

			Heart	Renal	Lung	Liver	Pancreas*
NSW	1	St Vincent's Hospital Sydney	●	●	●		
	2	The Children's Hospital at Westmead	●	●		●	
	3	Prince of Wales Hospital		●			
	4	Sydney Children's Hospital		●			
	5	John Hunter Hospital		●			
	6	Liverpool Hospital		●			
	7	Royal North Shore Hospital		●			
	8	Royal Prince Alfred Hospital		●		●	
	9	Westmead Hospital		●			●

			Heart	Renal	Lung	Liver	Pancreas*
VIC	10	The Alfred Bayside Health	●	●	●		
	11	The Royal Melbourne Hospital		●			
	12	The Royal Children's Hospital	●	●		●	
	13	Austin Hospital		●		●	
	14	Monash Medical Centre		●			●
	15	Monash Children's Hospital		●			
	16	St Vincent's Hospital Melbourne		●			
QLD	17	The Prince Charles Hospital	●		●		
	18	Princess Alexandra Hospital		●		●	
	19	QLD Children's Hospital		●		●	
	20	North Queensland Kidney Transplant Unit		●			
SA	21	Royal Adelaide Hospital		●			●
	22	Women's and Children's Hospital		●			
	23	Flinders Medical Centre				●	
WA	24	Fiona Stanley Hospital	●	●	●		
	25	Sir Charles Gardiner Hospital		●		●	
	26	Perth Children's Hospital		●			
NZ	27	Auckland City Hospital	●	●	●	●	●
	28	Wellington Hospital		●			
	29	Christchurch Hospital		●			
	30	Starship Children's Hospital#				●	

*Simultaneous pancreas and kidney transplant unit – defined as a clinical service of a state public hospital that actually performs the relevant transplant procedure.

#Transplants are performed at Auckland City Hospital, but patients are transferred to Starship for post-operative care.

Clinical islet separation facilities

A clinical islet separation facility is defined as a clinical facility of a state public hospital that actually separates islets from human pancreata under a Human Research Ethics Committee (HREC)-approved protocol and has the required regulatory approval/licensing.

NSW	Westmead Islet Laboratory
VIC	St Vincent's Institute of Medical Research

Clinical islet transplantation and infusion units

A clinical islet transplant unit is defined as a clinical service of a state public hospital that actually performs the relevant transplant procedure under HREC-approved protocols

NSW	Australian National Pancreas Transplant Unit, Westmead Hospital
SA	The Royal Adelaide Hospital
VIC	St Vincent's Hospital Melbourne
NZ	New Zealand National Pancreas Transplant Unit, Auckland City Hospital

Research islet separation facilities

A research islet facility is defined as a state public hospital or research institute that actually separates islets from human pancreata for research under a HREC-approved protocol with whatever regulatory approval/licensing is required

NSW	Westmead Islet Laboratory
SA	The Royal Adelaide Hospital
VIC	St Vincent's Institute of Medical Research

Intestinal transplantation units

VIC	The Austin and the Royal Children's Hospital

Vascularised composite allograft units

VIC	St Vincent's Hospital Melbourne

Appendix I

Summary of recommendations for infectious disease screening in deceased donors

Abbreviated infectious disease screening recommendations by pathogen. The recommendations below should be used in conjunction with the detailed explanations of these recommendations provided in Chapter 2.

Pathogen	Distribution/ endemic areas/high-risk groups	Screening recommendations	Utilisation
Viruses			
Coronavirus (SARS- CoV-2)	Worldwide	Lower respiratory tract SARS-CoV-2 PCR for lung donors	Donation can proceed from non-lung donors with positive SARS-CoV-2 PCR provided the transplanting organ has not been damaged by the infection. Lung transplantation from SARS-CoV-2 PCR positive donor can be considered on a case-by-case basis with recipient informed consent.
Cytomegalovirus (CMV)	Worldwide; >50% prevalence in the Australian adult population	Anti-CMV (IgG) recommended for all donors, with prospective results preferable where possible	Accept, irrespective of CMV serostatus. If donor is CMV+ve, suitable prophylaxis and post-transplant monitoring of the recipient are required.
Epstein-Barr virus (EBV)	Worldwide; >90% prevalence in the Australian adult population	Anti-EBV (IgG) recommended for all donors, with prospective results preferable where possible	Accept, irrespective of EBV serostatus. If donor is seropositive and recipient is seronegative, post-transplant virological monitoring is suggested.
Hepatitis B virus (HBV)	Worldwide, with high prevalence (>50% HBcAb +ve) in Asia, South Pacific, sub-Saharan Africa and the Middle East	HBsAg, HBcAb, HBsAb should be performed for all donors, with results required prior to transplantation proceeding; HBV-NAT is recommended for all donors, with results required prospectively wherever logistically feasible	HBV-NAT +ve OR HBsAg +ve: Organs may be transplanted in HBV+ve recipients. Transplantation to non-infected recipients may be considered on a case-by-case basis, with antiviral prophylaxis. If proceeding, also test for HDV. HBcAb+ve/HBsAg-ve: HBV transmission may occur in naïve liver recipients: ideally allocate livers to HBV-infected recipients or recipients with an immune response to vaccination and provide HBV prophylaxis.
Hepatitis C virus (HCV)	Worldwide, with prevalence >3% in many African and Middle Eastern countries (Egypt >15%) Highest prevalence in ANZ among IVDU and the prison population.	Anti-HCV should be performed for all donors, with results required prior to transplantation proceeding; HCV-NAT is recommended for all donors, with results required prospectively wherever logistically feasible	HCV-NAT +ve: Transplantation should be considered for all recipients. HCV-negative recipients should provide informed consent and a plan for post-transplant antiviral treatment and monitoring should be followed. Anti-HCV +ve/HCV-NAT –ve: Transplantation should be considered for all recipients. Represents spontaneous clearance of virus or successful treatment. HCV transmission is unlikely. Donor is classified as increased viral risk; recipient post-transplant monitoring is required.

Pathogen	Distribution/ endemic areas/high-risk groups	Screening recommendations	Utilisation
Hepatitis D virus (HDV)	High prevalence though with wide local/ regional variation in the Mediterranean, Eastern Europe, Middle East, Pakistan, central and northern Asia, western and central Africa, Amazonian basin, Pacific Islands and Vietnam	In the event of an HBsAg +ve or HBV-NAT +ve donor, the HDV status of the donor should be determined, including HDV RNA and HDV antibody assays	Where there is a risk of HDV transmission, transplantation should be discussed with an infectious diseases physician or hepatologist prior to proceeding.
Herpes simplex virus (HSV)	Worldwide; seroprevalence of 76% (HSV-1) and 12% (HSV-2) in Australian adults	Screening not required where antiviral prophylaxis is routinely administered	Organs can be accepted from donors with latent herpes family infections. Organs from donors with acute herpes viraemia should only be considered with the administration of HSV-active antiviral treatment to the recipient.
Human herpesvirus-8 (HHV-8) or Kaposi's sarcoma – associated herpesvirus	Variable; high prevalence in the Mediterranean, parts of Africa and parts of China	Routine screening is not recommended	Potential donors should not be excluded from donation based on perceived risk of HHV-8. Solid organ transplant recipients should be tested for HHV-8 in the context of a compatible illness.
Human immuno-deficiency virus (HIV)	Worldwide, with highest prevalence in sub-Saharan Africa, Russia, Ukraine, Estonia, Thailand, Papua-New Guinea, Belize, Surinam, Guyana and some Caribbean regions.	All donors should be screened for HIV using an HIV Ag/Ab combination assay, with results required prior to transplantation proceeding; HIV-NAT is recommended for all donors, with results required prospectively wherever logistically feasible	Use of organs from selected donors with an antibody and/or NAT-positive for HIV should be considered for waitlisted recipients with HIV, in consultation with a HIV specialist. Donation of organs from donors with HIV for recipients without HIV is not recommended, except in exceptional circumstances.
Human T-lymphotrophic virus-1 (HTLV-1)	Regions of high endemicity in sub-populations of Japan, sub-Saharan Africa, the Caribbean, South America, the Middle East, and Aboriginal people of central Australia.	HTLV-1/2 screening using serology is recommended for all organ donors, with prospective results preferable where possible	Organs should not be utilised from donors confirmed to have HTLV-1/2. Screening tests can produce false positive results and if timely confirmatory testing is not possible, it is recommended that an infectious diseases physician or microbiologist advise on whether the results predict genuine HTLV infection, which is influenced by the strength of the test (e.g. signal to cut-off ratio) and the pre-test probability of infection. If a donor is retrospectively confirmed to be infected with HTLV-1 and organs are transplanted, monitoring of recipients for infection/disease is recommended.
Influenza	Worldwide; influenza season in ANZ from June to August, affecting 5-10% of the population	If influenza-like illness in the donor is suspected, influenza-specific NAT should be performed (although prospective results are not essential)	The presence of influenza is not a contraindication to the transplantation of non-lung organs. Utilisation of lungs should be considered on a case-by-case basis. Post-transplant influenza treatment for 5-10 days is suggested for all recipients of organs from a donor infected with influenza.

Pathogen	Distribution/ endemic areas/high-risk groups	Screening recommendations	Utilisation
West Nile virus	Variable; seasonal epidemics during late summer in Africa, parts of Europe, the Middle East, North America and west Asia.	Screening of asymptomatic donors is not recommended. Targeted testing using serology and NAT is recommended for donors with compatible symptoms and recent history of travel (<4 weeks) to an endemic country or region with an ongoing outbreak	If a donor is suspected or known to be infected with WNV, an infectious disease specialist should be consulted for advice on testing requirements and whether it is safe to proceed with donation.
Zika virus	Widespread; outbreaks possible wherever there are mosquito vectors, a suitable climate, and intense movement of people.	Screening of asymptomatic donors for Zika virus is not recommended. Zika serology should only be used as a diagnostic test in donors with compatible symptoms and epidemiological risk factors (i.e. history of travel to an endemic area <4 weeks previous)	In the event that a donor tests positive for Zika virus infection, seek advice from an infectious diseases specialist.
Bacteria and other			
Multidrug resistant (MDR) bacteria	Worldwide; risk factors include prolonged ICU stay, prior hospitalisation in a foreign country, vasopressor use, need for cardiopulmonary resuscitation, traumatic injury	No requirement for enhanced microbiological screening over and above standard ICU practice	Organs from donors with positive cultures for MDR bacteria may be considered for transplantation with close recipient follow-up. Transplantation should be carefully considered in the event the organ to be transplanted is itself colonised or the donor is bacteraemic. Discuss with an infectious disease specialist and, if donation proceeds, provide a full treatment course to the recipient.
Mycobacterium tuberculosis	Worldwide; majority of cases in ANZ occur in the overseas born population, most commonly in persons born in India, China, central and south east Asia, Papua New Guinea and Africa. Other risk factors include household/ occupational contact with tuberculosis, incarceration, residence in an aged care facility, homelessness and immunosuppression	Donor testing with microscopy and PCR are recommended where infection is suspected based on epidemiological and clinical factors suggestive of active or latent infection	Donation of organs from donors currently being treated for tuberculosis or with positive test results is not recommended other than in exceptional circumstances after discussion with an infectious diseases physician. Donors with previous active or latent tuberculosis can be considered, taking into account completeness of treatment, antibiotic sensitivities and current evidence of infection in the donor. Discussion with an infectious diseases physician close follow-up of the recipient, and consideration of tuberculosis prophylaxis for the recipient are recommended.
Malaria	Any tropical country is a risk area	Donors who have spent >3 month in an endemic area or have visited an endemic area in the last 12 months (any duration) should be screened for Plasmodium using NAT or serology	If a donor tests positive for malaria by NAT or serology, transplantation may proceed, and the recipients should be treated (and tested) for malaria. If donor testing is negative, recipients should be tested for malaria should a compatible clinical syndrome develop.
Strongyloides stercoralis	Developing countries and central/tropical Australia	All donors should be screened for Strongyloides, (prospective results are not essential)	If the donor tests positive for *Strongyloides*, transplantation may proceed with recipients treated with ivermectin.

Pathogen	Distribution/ endemic areas/high-risk groups	Screening recommendations	Utilisation
Transmissible spongiform encephalopathies (TSE)	Risk factors include family history of CJD, receiving human pituitary-derived hormones prior to 1986, notification from the department of health as being at increased risk of TSE due to risk factor exposure, death from early onset dementia, death from any obscure undiagnosed neurological disorder.	No appropriate screening test exists, exclude on the basis of donor history indicating risk of TSE	Persons at risk of TSE should be excluded from organ donation.
Treponema pallidum (syphilis)	Worldwide	All donors should be screened for *T.pallidum*, with results available prospectively where possible. Donors should be first screened using a treponemal-specific enzyme immunoassay, with confirmation of positive results by a non-treponemal test (e.g. the rapid plasma reagin test)	If primary, latent or tertiary syphilis is detected in the donor, donation may proceed with appropriate prophylactic treatment of the recipient. A donor with secondary syphilis may be bacteraemic with the involvement of many organs, hence caution should be taken if clinical manifestations of secondary syphilis are present.
Trypanosoma cruzi	Mexico, Central and South America	Donors who have spent >3 months in Mexico, Central or South America at any time in their lives should be screened for *T.cruzi* using serology	Donor with known *T.cruzi* infection should be excluded from heart donation. Infection with *T.cruzi* is not a contraindication to the donation of non-cardiac organs, although recipients require close follow-up for 24 months for the appearance of acute infection.

Appendix J

Further resources for assessing risk of donor-derived malignancy

Table J1: Guidelines and web-based resources containing information on donor-derived malignancies

Guideline/resource	Publisher	Contents	URL
NOTIFY Library		Library of documented adverse outcomes associated with the clinical use of human organs, blood, tissues and cells.	notifylibrary.org
Transplantation of Organs from Deceased Donors with Cancer or a History of Cancer. Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO), 2020.	UK Government Department of Health	Recommendations for patients in the UK, based on a review of the UK National Transplant Registry and a review of the literature.	https://www.gov.uk/government/publications/transplantation-of-organs-from-donors-with-a-history-of-cancer
Guide to the Quality and Safety of Organs for Transplantation (9th ed.). Chapter 9: Risk of Transmission of neoplastic diseases.	European Directorate for the Quality of Medicines & Health Care, Council of Europe	Current evidence for assessment of the risk of transplanting organs from donors with a past or present history of malignancies. Grading of risk is provided for an extensive list of malignancies that may be identified in the donor history or be discovered at the time of organ retrieval.	https://www.edqm.eu/en/guide-quality-and-safety-of-organs-for-transplantation

Table J2: Key registries and databases containing information on donor-derived malignancies

Database/registry	Contents	Key references
United Network for Organ Sharing Registry	Incidence of cancer history in donors; rate of malignancy transmission from donors with a known cancer history.	Kauffman et al. Transplantation, 2000; 70(12):1747 Kauffman et al. Transplantation, 2002; 73(4):579 Kauffman et al. Transplantation, 2002; 74(3):358 Kauffman et al. Transplantation, 2007; 84(2):272
Organ Procurement and Transplantation Network/ Disease Transmission Advisory Committee	Reports of confirmed donor-transmitted malignancies	Ison et al. Am J Transplant, 2011; 11(6):1123 Nalesnik et al. Am J Transplant, 2011;11(6):1140 Green et al. Transplantation, 2015; 99(2):282
The Israel Penn International Transplant Tumor Registry	Voluntary reporting of donor malignancy resulting in transmission to one or more recipients	Feng et al. Transplantation, 2002;74(12):1657 Buell et al. Surgery, 2001;130(4):660 Buell et al. Transplantation, 2003;76(2):340 Buell et al. Transplant Proc, 2005;37(2):581
United Kingdom Transplant Registry	Reports of confirmed donor-transmitted malignancies; case series reports of outcomes of transplantation from donors with a history of cancer	Desai et al. Transplantation, 2012;94(12):1200 Desai et al. Br J Surg, 2014; 101(7):768 Watson et al. Am J Transplant, 2010; 10(6):1437
Organización Nacional de Trasplantes Registry (Spain)	Reports of confirmed donor-transmitted malignancies	Garrido et al. Transplantation, 2008;85(8 Suppl):S61
Centro Nazionale Trapianti Registry (Italy)	Incidence of cancer history in donors; outcomes of transplantation from donors with a history of cancer	Venettoni et al. Ann Transplant, 2004;9(2):15 Nanni Costa et al. Transplantation, 2008;85(8S Suppl):52 Taioli et al. Transplantation, 2007;83(1):13 Zucchini et al. Transplantation, 2008;85(8 Suppl):S57 Fiaschetti et al. Transplant Proc, 2012;44(7):1848

MALORY – MALignancy in Organ donors and Recipient safetY (Germany)	Cohort study of 648 recipients of organs from 248 donors with a history of cancer, with recipients followed for 6 years.	Moench et al. Transplantation, 2012; 94(10S):208
Danish Registry	Data linkage study, linking organ donors from a single transplant centre in Denmark to the Danish tumour registry and examining outcomes in recipients over 27 years.	Birkeland et al. Transplantation, 2002;74(10):1409

Appendix K

Family history of cancer and cancer genes

Donor assessment should include a history of genetic testing identifying a cancer predisposition mutation in the donor or their first-degree blood relatives. The presence of such a mutation may indicate an increased risk of occult malignancy in the donor, or an increased risk of cancer developing in the donated organ during the lifetime of the recipient. The level of risk will vary according to the specific gene and the specific organs donated (see Table K1).

Where no specific mutation has been identified in the individual or their family, the interview should also determine if there is a family history of cancer where:

- Multiple cancers have been diagnosed at young age
- There are multiple cases of the same type of cancer or patterns indicative a cancer predisposition syndrome
- Multiple cases of rare cancers

Consideration should be given to investigation of donors with a known cancer predisposition genetic mutation for occult malignancy. The risk of occult malignancy will vary depending on the gene, the age of the donor and previous screening or risk reducing strategies. There are no data to determine the risk of malignancy in transplanted organs from donors with a cancer predisposition gene.

Further advice as to the likelihood of a genetic susceptibility syndrome and the potential risk of malignancy in donated organs may be sought from a familial cancer service. See https://www.genetics.edu.au/genetic-services/cancer-genetics-clinics for services in Australia/New Zealand.

Table K1: Risk of malignancy in known mutation carriers for cancer predisposition genes and affected transplant organs

Gene	Organ at increased risk	Risk in known mutation carriers
TP53	Multiple	>90%
VHL (Von Hippel Lindau Syndrome)	Pancreas, Kidney, Adrenal	80% RCC 10-17% PNET
STK11 (Peutz-Jegher Syndrome)	Pancreas	26% adenocarcinoma
FH (Hereditary Leiomyoma RCC)	Kidney	15% RCC
FLCN (Birt Hogg Dube Syndrome)	Kidney	19% (various types)
APC (familial adenomatous polyposis)	Pancreas, gastrointestinal (stomach, duodenum, small and large bowel)	5%
Mismatch Repair (Lynch Syndrome)	Urothelial tract Pancreas	3% Increased, but <2%
CDKN2A	Pancreas, Skin (melanoma)	Increased, but <2%
BRCA2	Pancreas	Increased, but <2%

Appendix L

Information on Australian and New Zealand cancer registries

Australia

Cancer is a notifiable disease in Australia under the Public Health Act or equivalent in each state and territory. As a result, operational and governance arrangements vary; however, the Australian Association of Cancer Registries encourages a standard approach to cancer data collection and management across Australia.

Each state and territory operates a cancer registry that assembles information about new cases of cancer and cancer deaths. Data are supplied to the registries from a range of sources, such as hospitals, pathology laboratories, radiotherapy centres and the registrars of births, deaths and marriages—though mandated notifiers and the breadth of data collected vary between jurisdictions (Table L1). All registries record location, morphological type, topography, diagnosis date, grade and basis of diagnosis.

The registries are "case-based" data collections: Each piece of information provided to the registry is considered in the context of other information about the same person and used to progressively create a complete picture of tumours for that person. This differs from standard event-based data collections where each episode is coded in isolation. Cases are generally identified by Name, Sex and Date of Birth. In most jurisdictions, this is regularly validated within the jurisdiction against electoral rolls to improve data accuracy and reduce duplicate entries.

The cancer registries' responsibilities are local: they supply information for use by their state or territory for planning of services, estimation of survival rates and treatment evaluation. Cancer data are also available for use in epidemiological studies.

Arrangements exist in some jurisdictions (see Section 2.4.2.6) for DonateLife staff to query the state-based registry (either directly or indirectly) to obtain the history of a potential donor once appropriate consent for donation is obtained from the next of kin. However, information from the registry is limited to those cancers diagnosed or treated within that state or territory and is identified primarily by name and date of birth. In order to obtain a complete history, it is important to ascertain if the donor previously resided in a different state or territory, and/or may have been diagnosed or treated under a different name. Where the potential donor resided in another jurisdiction, contact DonateLife staff in that jurisdiction to proceed with further enquires.

The registries forward an agreed list of data elements to the Australian Institute of Health and Welfare (AIHW) annually to a national repository—the Australian Cancer Database—for national reporting and disease monitoring. National de-duplication and cross-border case resolution is undertaken annually by the AIHW in the preparation of the annual reporting database. Availability of jurisdictional data to the Australian Cancer Database is usually around 1-3 years after diagnosis. This data collection is not available for interrogation to obtain the malignancy history of a potential donor.

Table L1: Data providers to state and territory cancer registries

	NSW*	VIC	QLD	WA	SA	TAS	NT	ACT
Hospitals	Mandated	Mandated	Mandated	Mandated	Mandated	Mandated	Mandated	Mandated
Pathology laboratories	Mandated	Mandated 94% of pathology is available within 6 weeks	Mandated	Mandated	Mandated	Mandated	Mandated	Mandated
Radiation oncology treatment centres	Mandated	Mandated (ROV notifiers) since 2017		Mandated	Mandated	Mandated	Not mandated	Not mandated

Screening programs		Breast and cervical screening programs				Breast and HCC screening programs**	
Residential aged care facilities	Mandated		Mandated			Not mandated	Mandated
Other	Oncology outpatients Cancer care centres Haematology and bone marrow transplant services Forensic medicine Treatment information: chemo & radiotherapy episodes from 2010 onwards			Opthamol-ogists GPs		Not mandated	

* A lot of information is captured on the pathology report, the inpatient notification (surgical) or on the radiotherapy/chemotherapy treatment notification, which may not be explicitly listed in a data field.

** Annual ascertainment with BreastScreen NT and Hepatobiliary Multi-Disciplinary Teams (HCC surveillance)

Table L2: Cancer-specific information available in state and territory cancer registries

Non-melanoma skin cancer								
	NSW*	VIC	QLD	WA	SA	TAS	NT	ACT
		VCR does not capture skin SCC and BCC.[1]		Incidental collection of head and neck coded when received.	Skin BCCs of ano-genital area[2] Skin SCCs of ano-genital area[2] and skin of lip	Machine coded according to ICD-O3 only.	Skin BCCs of ano-genital area[2] Skin SCCs of ano-genital area[2] and skin of lip	
Melanoma of the skin								
	NSW*	VIC	QLD	WA	SA	TAS	NT	ACT
Primary site	✓	✓	✓	✓	✓	✓	✓	✓
Subsite			✓	✓	✓	✓	✓	
Morphology	✓	✓	✓	✓	✓	✓	✓	✓
Differentiation		Grade always 9	✓	✓			✓	
Laterality	✓	✓	✓	✓	✓	✓	✓	✓
Level		✓	✓	✓	✓	✓	✓	

Ulceration		✓	✓		✓		From 20143	
Breslow thickness	✓	✓	✓	✓	✓	✓	✓	✓
Mitotic rate			✓				From 2014[3]	
Regression		✓	✓					
Nodal status		✓	✓				From 2014[3]	
Metastatic status		Stage at diagnosis from 2018 Stage 4 at diagnosis since 2016	✓	✓ (only when identified via path/ death cert)	✓ a category under the 'level of invasion'	✓	From 2014[3]	
Recurrence or progression		✓	✓					
Degree of spread*	✓	TNM stage at diagnosis from 2018				✓	From 2014[3]	✓
Breast cancer								
	NSW*	VIC	QLD	WA	SA	TAS	NT	ACT
Stage at Dx		✓						
Tumour size	✓	✓	✓	✓	✓	✓	✓	✓
Nodal status		✓	✓	✓	✓	✓	✓	
Tumour grade		✓	✓	✓	✓	✓	✓	
Laterality	✓	✓	✓	✓	✓	✓	✓	✓
Degree of spread*	✓					✓	✓	✓
Hormone receptor status		✓	From 2019	Oestrogen receptor status only	Oestrogen receptor status only		From 2014 – PR in notes field; ER and HER2 in specific fields	
Chemotherapy	✓							
Radiotherapy	✓	From 2017						
Colorectal cancer								
	NSW*	VIC	QLD	WA	SA	TAS	NT	ACT
Stage at Dx		✓			✓		From 2014 – If pTNM available	
Tumour size			✓		✓	✓ (resection only)	✓	

Tumour grade		✓	✓	✓	✓	✓	✓	
Degree of spread*	✓					✓	From 2014 – In notes field or in specific field if pTNM available	✓
Prostate cancer								
	NSW*	VIC	QLD	WA	SA	TAS	NT	ACT
Tumour size			✓		✓	✓		
Gleason score		✓	From 2019	✓	✓	✓	From 2014[3]	
ISUP		Grade in ISUP class since 2017				From 2017	From 2014[3]	
Degree of spread*	✓					✓	From 2014[3]	✓
Thyroid cancer								
	NSW*	VIC	QLD	WA	SA	TAS	NT	ACT
Tumour size			✓		✓	✓	✓	
Degree of spread*	✓	Stage 4 at Dx from 2016				✓	From 2014[3]	✓
Bladder cancer								
	NSW*	VIC	QLD	WA	SA	TAS	NT	ACT
Tumour size			✓		✓ but not usually reported on path	✓	✓	
Tumour behaviour		✓ urothelial cell tumours						
Tumour grade		✓	✓		✓	✓	✓	
Degree of spread*	✓	Stage 4 at Dx				✓	From 2014[3]	✓

* A lot of information is captured on the pathology report, the inpatient notification (surgical) or on the radiotherapy/chemotherapy treatment notification, which may not be explicitly listed in a data field.

[1] VCR is receiving some notifications (hospital and Path reports) for SCC and BCC of skin. VCR may provide incomplete data on such cases. Notifications for SCC of skin for C445, C510-C519, C600-C609, C632 (anogenital area) only.

[2] Anogenital area refers BCC/SCC of anus, perineum, perianal area, labia, vulva, penis, or scrotum.

[3] Documented in notes field. Nodal and metastatic status documented in notes field or in specific field if pTNM available.

New Zealand

The New Zealand Cancer Registry (NZCR) captures all primary malignant tumours (invasive and in situ) first diagnosed in New Zealand, excluding squamous and basal cell skin cancers unless they arise in the skin of the genitalia. The NZCR was originally established in 1948, with coverage increasing after the passage of the Cancer Act in 1993. As of March 2023, Organ Donation New Zealand and the NZCR are in the process of establishing a protocol for health professionals to access the registry at the time of donor evaluation.

The NZCR is "case-based", with each piece of information provided to the registry considered in the context of other information about the same person and used to progressively create a complete picture of tumours for that person. Cases are generally identified by Name, Sex, and NHI number. In addition to the data specified in Table L3, the NZCR captures clinical notes – a text field with supplementary information on the cancer registration – from 2001 onwards. The NZCR does not collect treatment information.

Table L3: Cancer-specific information available in the New Zealand Cancer Registry

	Cancer type					
	Breast	Colorectal	Gynaecological	Melanoma	Prostate	Respiratory
Primary site	✓	✓	✓	✓	✓	✓
Morphology	✓	✓	✓	✓	✓	✓
Tumour grade/Differentiation	✓	✓	✓	✓	✓	✓
Laterality	✓		✓			✓
TNM stage at diagnosis	✓	✓	✓	✓	✓	✓
Tumour size	✓	✓	✓	✓	✓	✓
Nodal status	✓	✓	✓	✓	✓	✓
Metastatic status	✓	✓	✓	✓	✓	✓
Multiple tumours flag	✓	✓	✓	✓	✓	✓
Degree of spread	✓	✓	✓	✓	✓	✓
Level of direct spread		✓				
Ulceration				✓		
Breslow thickness				✓		
Mitotic rate				✓		
Hormone receptor status	✓ (ER/PR since 2001, HER2 since 2008)					
Gleason score					✓	
Resection margin	✓			✓		
Recurrence or progression						

Appendix M

Recommendations on the use of organs from donors with CNS tumours

Table M1: Recommendations on the use of organs from donors with central nervous system (CNS) tumours, by risk category. Derived from SaBTO[1] and the 2016 WHO classification of tumours of the central nervous system.[2]

Minimal risk of transmission (<0.1%) – Likely to be acceptable for all organ types and recipients

WHO Grade I and II tumours:

- Pilocytic/ Subependymal giant cell
- Diffuse astrocytoma, IDH-mutant
- Pleomorphic xanthoastrocytoma
- Oligodendroglioma, IDH-mutant & 1p/19q-codeleted
- Oligoastrocytoma
- Subependymoma/ Myxopapillary ependymoma
- Ependymoma
- Choroid plexus/ Atypical choroid plexus papilloma
- Angiocentric glioma
- Chordoid glioma of the third ventricle
- Gangliocytoma
- Ganglioglioma
- Desmoplastic infantile astrocytoma and ganglioglioma
- Dysembryoplastic neuroepithelial tumour
- Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos)
- Central/ Extraventricular neurocytoma
- Cerebellar liponeurocytoma
- Papillary glioneuronal tumour
- Rosette-forming glioneuronal tumour
- Pineocytoma
- Schwannoma
- Neurofibroma
- Perineurioma
- Meningioma/ Atypical meningioma
- Solitary fibrous tumour/Haemangiopericytoma (I or II)
- Haemangioblastoma
- Craniopharyngioma
- Granular cell tumour
- Pituicytoma
- Spindle cell oncocytoma of the adenohypophysis

Low-risk of transmission (0.1% to <2%) – Likely to be acceptable for many organ types and recipients

WHO Grade III and equivalents:

- Anaplastic astrocytoma, IDH-mutant
- Anaplastic oligodendroglioma, IDH-mutant & 1p/19q-codeleted
- Ependymoma, RELA fusion-positive (II or III)
- Anaplastic ependymoma
- Choroid plexus carcinoma
- Anaplastic gangliomyoma
- Pineal parenchymal tumour of intermediate differentiation (II or III)
- Papillary tumour of the pineal region (II or III)
- Malignant peripheral sheath tumour (II, III or IV)
- Anaplastic (malignant) meningioma
- Anaplastic pleomorphic xanthoastrocytoma
- Haemangiopericytoma Grade III

Low- to intermediate-risk of transmission[a] – consider on a case-by-case basis

WHO grade IV tumours and equivalents:

- Glioblastoma
- Diffuse midline glioma, H3K27 M-mutant
- Pineoblastoma
- Medulloblastoma
- Embryonal tumour with multilayered rosettes, C19MC-altered
- CNS embryonal tumour, NOS
- CNS embryonal tumour with rhabdoid features
- Medulloepithelioma
- Ependymoblastoma
- Atypical teratoid/rhabdoid tumour
- Germinoma
- Immature teratoma
- Teratoma with malignant transformation
- Yolk sac tumour
- Embryonal carcinoma
- Non-gestational Choriocarcinoma

Unacceptable risk

- Primary cerebral lymphoma
- All secondary intracranial tumours

[a] Best available evidence suggests that the risk of transmission from donor to recipient in the case of Grade IV CNS tumours is ≤2%

References

1 Transplantation of Organs from Deceased Donors with Cancer or a History of Cancer. Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO), UK Government Department of Health, London, UK, 2014.

2 Louis DN, Ohgaki H, Wiestler OD, Cavenee WK. World Health Organisation Histological Classification of Tumours of the Central Nervous System. International Agency for Research on Cancer, 2016, France

Appendix N

Kidney/Pancreas and Pancreas allocation algorithm

Match Level	Description	Criteria	Base Score	Additional points
1	National Priority	mPRA >75 Commenced Dialysis	80 000 000	
	National Priority Bonus			10 000 000
	Waiting Time			Number of months x 1

Match Level	Description	Criteria	Base Score	Additional points
2	Standard Pancreas Only	mPRA >75 Commenced Dialysis	80 000 000	
	Donor Home state associated Transplant unit *			7 000
	Waiting Time			Number of months x 1

Match Level	Description	Criteria	Base Score	Additional points
3	Standard Kidney/ Pancreas		80 000 000	
	Donor Home state associated Transplant unit *			+5000
	Non home state Kidney/ pancreas recipients			
	Waiting Time			Number of months x 1

*Donor Home state bonus is applied as follows for:

NSW/ACT , WA , QLD donors and recipients listed for Transplant at Westmead Hospital

Victoria and Tasmania donors recipients listed for Transplant at Monash Medical Centre

South Australia and Northern Territory Donors and recipients listed for Transplant at Royal Adelaide Hospital

ABO selection rules

The ABO selection rules determine the acceptable organ matches, as shown:

Algorithm	Donor ABO type	Patient ABO type
National Priority	A	A
	A	AB
	B	B
	B	AB
	AB	AB
	O	O
	O	A
	O	B
	O	AB
Kidney/Pancreas	A	A
	B	B
	B	AB
	AB	AB
	O	O
Pancreas	A	A
	B	B
	B	AB
	AB	AB
	O	O

Appendix O

Paediatric DNDD Heart Offering Principles

Contacts for heart offering

RCH = Royal Children's Hospital, VIC. Heart/Lung Transplant Coordinator on call via the RCH switchboard: 03 9345 5522

CHW = Children's Hospital Westmead, NSW. Call SVH Heart/Lung Transplant Coordinator via on-call mobile: 0416 143 723 specifying offer is for paediatric waitlisted patient.

NZ = Auckland City Hospital. Call Heart/Lung Transplant Coordinator on call via the ACH switchboard: 0011 64 9307 4949.

N.B New Zealand paediatric donor heart offers that are declined by the New Zealand heart transplant unit may also be offered to RCH and then CHW for consideration of paediatric recipients.