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# Title: Transmission and non-transmission of melanoma from deceased solid organ donors to transplant recipients: risks and missed opportunities

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## Authorship:

BR coordinated the linkage program for generation of data, designed and conducted the analysis, interpreted data for the work, and drafted the manuscript. JH, ND and PK, advised on data analysis, and reviewed the manuscript for intellectual content. EC, CMV and JFT contributed to the interpretation of data, critically reviewed the manuscript, and provided essential intellectual content. KW and ACW conceived of the overarching study, oversaw data analysis and interpretation, and provided direction and critical review of the manuscript.

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## Abbreviations:

| | |
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| AJCC | American Joint Committee on Cancer |
| CCR | Central Cancer Registry |
| DNA | Deoxyribonuclease |
| DTAC | Disease Transmission Advisory Committee |
| HLA | Human Leukocyte Antigen |
| ICD-10-AM | International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification |
| ICD-O-3 | International Classification of Diseases for Oncology, 3rd Edition |
| IQR | Inter-quartile range |
| NOS | Not otherwise specified |
| NSW | New South Wales |
| OPTN | Organ Procurement and Transplantation Network |
| ORCHARD | Organ Donor Referral Characteristics Study |
| PCR | Polymerase chain reaction |
| RBDM | Registry of Births, Deaths and Marriages |
| SAFEBOD | Safety and Biovigilance in Organ Donation study |
| SabTO | Advisory Committee on the Safety of Blood, Tissues and Organs |
| UNOS | United Network for Organ Sharing |
| TSANZ | Transplantation Society of Australia and New Zealand |

## Abstract:

Background: Biovigilance concerns are in tension with the need to increase organ donation. Cancer transmission-risk from donor to recipient may be overestimated, as non-transmission events are rarely reported. We sought to estimate melanoma transmission-risk in deceased organ donation and identify missed opportunities for donation in an Australian cohort with high melanoma prevalence. Methods: We used a population-based approach and linked deceased organ donors, transplant recipients and potential donors forgone, 2010-2018, with the Central Cancer Registry (CCR), 1976-2018. We identified melanomas using ICD-O-3 classification, assessed probability of transmission, and compared suspected melanoma history in potential donors forgone with melanoma notifications in the CCR. Results: There were 9/993 donors with melanoma in CCR; 4 in-situ low-risk and 5 invasive high-to-unacceptable risk. Four were unrecognised prior to donation. Of 16 transplant recipients at risk, we found 0/14 transmission events (2 recipients had insufficient follow-up). Of 35/3,588 potential donors forgone for melanoma risk alone, 17 were otherwise suitable for donation; 6/35 had no melanoma in CCR, 2/35 had in-situ melanomas and 9/35 had thin invasive melanomas (localised, ≤0.8mm thickness). Conclusions: Our findings contribute to current evidence that suggests donors with melanomas of low metastatic potential may provide opportunity to safely increase organ donation and so access to transplantation.

# 1. Introduction

The need for solid organ transplantation continues to outweigh donor supply and increasing equitable access to organ donation remains a global priority[1]. Potential transmission of malignancy from donor to recipient is a constant concern influencing donor suitability decisions. Current classification systems for assessment of the risk of donor malignancy transmission have evolved from reports of transmission events in recipients to national donation and transplant surveillance agencies and are biased towards transmission events[2]. Contemporary studies have highlighted the need to incorporate non-transmission events in estimates of cancer transmission risk and recommend re-evaluation of classification systems that may inappropriately preclude transplantation due to overestimation of the absolute risk of cancer transmission[3-5].

Current clinical guidelines for donation recommend that donors with a history of invasive melanoma be rejected due to well-documented reports of poor recipient outcomes and a perceived high-risk of transmission (>10%)[2,6,7]. Conversely, non-invasive "in-situ" melanomas are classified as having minimal (<0.1%) transmission risk, and donors are acceptable in most circumstances. Melanoma transmission is a rare event, 0.22 per 10,000 transplants, but is the second most common cancer transmission in solid organ transplantation, representing 17% of all cancer transmissions in kidney transplant recipients and 9% in liver transplant recipients[8-10]. The rarity of events contributes to uncertainty around estimates of melanoma transmission in organ donation and transplantation. Several reviews that combine case reports and small series of transmission events estimate melanoma transmission occurs in 63-100% of recipients of donors with melanoma[9,11-13]. Comparatively, estimates derived from biovigilance registry studies that assess reports of potential

transmission events for probable and proven events, give a lower transmission risk of 18-50%[5,8,14,15]. Four cases of melanoma non-transmission have been reported, suggesting that organs from some donors with a history of melanoma may be suitable for donation[5,16]. These prior studies describe devastating outcomes for recipients with transmitted melanoma but provide insufficient details of the donor's melanomas to understand or stratify transmission risk.

The risk of recurrence and metastasis in patients with thin invasive melanomas (<0.8mm Breslow thickness) with no lymph node involvement is <10% in the Australian general population [17]. A recent systematic review indicated that in transplant recipients the risk of melanoma recurrence was 10-12% when the majority of recipients had previously had thin (<1.0mm) primary melanomas and more than 5 years had elapsed since diagnosis and treatment[18]. In recipients with a history of melanoma, the recommended wait-time in US Guidelines between cancer diagnosis and transplant eligibility is reduced to 1 year in recipients with American Joint Committee on Cancer (AJCC) Stage IA, IB and IIA melanomas compared to over 5 years for more advanced stages[19]. Combined, these considerations warrant the investigation of melanoma transmission risk in organ donation by melanoma stage, treatment and recurrence-free interval.

Medical assessment for deceased organ donor referral is a time-sensitive process. In New South Wales, Australia, potential donor suitability is assessed by donation coordinators and transplant clinicians with donor medical suitability expertise. Once medical suitability is determined and consent from next of kin is obtained, a national allocation algorithm generates a ranked order of potential recipients, and a clinician at a transplanting unit accepts or declines the donor organ offer for a specific patient. Obtaining a comprehensive medical

history for a potential donor often relies on incomplete information, such as information provided by next-of-kin or other proxy, as detailed past medical records may not be available. The prevalence of melanoma in Australia is high, and a melanoma history is of particular concern due to the evidence of long potential dormancy of metastatic melanoma[20 21]. Self-reporting of familial melanoma history is poor, and may be more inaccurate when reported in the stressful circumstances of end-of-life discussions[22]. If a history of melanoma is suspected, the burden of proof lies with organ donation services to uncover pathology reports from any available sources, and there may be limited opportunity to verify collated information[23]. In this context of information uncertainty, significant clinical risk-aversion remains to accepting any potential donors with a melanoma history, regardless of staging, [12,23]. However, in situations where the donor's melanoma is assessed as having a low risk of transmission, the risks of potential transmission needs to be weighed against the life-sustaining or life-saving benefits of transplantation, and the potential harms of remaining on the transplant waiting list[24].

Incorrect estimates of melanoma transmission risk during medical assessment for deceased organ donation may lead to missed opportunities in organ donation (where risk is overestimated) or harm to potential or actual recipients (where risk is underestimated)[25]. Real-time access to melanoma histopathological staging, such as records held by cancer registries, could complement donor medical assessment records. This may provide better estimates of transmission risk, supporting decisions to safely increase deceased organ donation. Thus, in this study we sought to 1) estimate the transmission risk of melanoma from deceased organ donors to transplant recipients and 2) identify missed opportunities for donation in potential donors foregone due to misclassification of melanoma transmission risk in a setting of one of the highest melanoma prevalence countries globally.

## 2. Materials and methods

### *2.1 Data linkage and study cohort*

We used data from the Australian Safety and Biovigilance in Organ Donation (SAFEBOD) study cohort. SAFEBOD uses linked health administrative and national transplant datasets to establish better estimates of disease transmission risk in solid organ donation and transplantation[26]. We included deceased organ donors with a history of melanoma and their corresponding solid organ transplant recipients resident in the state of NSW, 2010-2018 (Figure 1). We also investigated potential deceased donors referred for consideration of organ donation that were forgone due to their melanoma history and the perceived transmission risk to any potential recipients,2010-2018. Records were obtained from the Organ Referral Characterisation Database (ORCHARD). ORCHARD holds consent, clinical and procedural information on all potential deceased donors referred for consideration to the NSW Organ and Tissue Donation Service[27]. Person records were linked to the NSW Central Cancer Registry (CCR) 1972-2018 to identify cancer notifications in deceased organ donors, transplant recipients and potential donors forgone. The NSW Central Cancer Registry (CCR) receives mandatory reports of all incident cancers diagnosed in New South Wales, with near 100% coverage for all NSW residents[28]. Fact and cause of death were ascertained from the NSW Registry of Births, Deaths, and Marriages (RBDM) Death Registrations, 1985-2020. We excluded potential donors forgone who were considered for deceased organ donation who did not have next of kin consent to donation, as under these circumstances any donation is extremely unlikely.

Melanomas were identified in CCR notifications using the International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) four-digit morphology codes "8720-8790" and

included both in-situ and invasive melanomas[29]. Melanomas were categorised by transmission risk as per current guidelines where risk is stratified[2,7]. Briefly, in-situ melanomas are classified as having minimal transmission risk (<0.01%), where donors are likely to be acceptable for all organ types and recipients. Invasive cutaneous melanoma T1-T4 are classified as having a high (>10%) to unacceptable risk of transmission, with donors acceptable in exceptional circumstances. Potential donors with nodal or distant metastatic melanoma are classified as having an unacceptable transmission risk, where use of organs is not recommended in any circumstance. This study was approved by the University of Sydney Human Research Ethics Committee (HREC 2016/758).

### *2.2 Classification of melanoma transmission*

To investigate melanoma transmission, we identified deceased organ donors with a melanoma notification in the CCR and described the post-transplant outcomes of their corresponding transplant recipients. Deceased organ donor and transplant recipient pairs were assessed for the probability of melanoma transmission case-by-case. Probability of transmission was determined using criteria informed by international guidelines (Supplementary Table 1)[2,8,30]. Briefly, recipient cases were categorised as "Excluded" when there was no evidence of melanoma in the recipient or clear evidence of an alternative cause for the recipient's melanoma; "Possible" where evidence of an alternative cause was indeterminate; "Probable" when there was clear evidence of the same melanoma (histology) in the recipient and donor or evidence of melanoma in multiple recipients from the same donor; and "Proven" when there was clear evidence of the same melanoma in the donor and more than one recipient and no evidence of an alternative cause. Cases were designated "Not Assessable" when recipients had less than 6 months of follow-up post-transplant. Each case was reviewed by at least two investigators (BR, JH, CV) and an independent clinical advisor

with expertise in melanoma (JT). Where discrepancies arose, decisions were discussed and made by consensus.

### *2.4 Assessment of melanoma transmission risk in potential donors*

Potential donors may be foregone for multiple reasons. We identified the subset of potential donors who were foregone due only to their melanoma transmission risk. The perceived risk implied by their melanoma history was obtained from ORCHARD. We investigated date of diagnosis, degree of spread and Breslow thickness recorded in any corresponding CCR melanoma record to assess transmission risk. Missed opportunities for donation were considered as potential donors foregone because of (i) a suspected melanoma transmission risk with no verified records of a melanoma in the CCR, or (ii) where the CCR records showed that these melanomas were of similar profile to those in deceased organ donors that had proceeded to donation, and where recipients had not had any subsequent melanoma transmission events. To assess the misclassification of melanoma transmission risk in potential donors forgone for other reasons, we investigated the agreement between melanoma history identified during donor medical assessment from ORCHARD records and verified melanoma case records in the CCR.

### *2.5 Statistical analysis:*

Demographic and clinical characteristics were summarised for deceased organ donors and potential donors forgone using counts and proportions. Median and interquartile age was reported for time-to-event variables. Transplant recipients were followed-up from first transplant to date of death or 31 December 2018. Age at transplantation and post-transplant

outcomes of recipients of deceased organ donors with and without melanoma were compared. Knowledge of a melanoma history prior to donation was then cross-tabulated against probability of melanoma transmission to create four categories; the donor was known to have melanoma during medical assessment for donation and 1) did (known transmission) or 2) did not (known non-transmission) transmit to the recipient; and the donor was not known to have melanoma during medical assessment for donation but did in fact have a melanoma record and 3) did (unknown transmission) or 4) did not (unknown non-transmission) transmit to the recipient. The proportion of Probable/Proven melanoma transmissions within the total number of recipients of donors with a melanoma history was reported, stratified by the transmission risk categories specified in Transplantation Society of Australia and New Zealand guidelines[31], cancer stage and organ type. Transplantation Society of Australia and New Zealand risk categories reflect The Advisory Committee on the Safety of Blood, Tissues and Organs and United Network for Organ Sharing, Organ Procurement and Transplantation Network guidelines that classify risk by probability of future transmission. Briefly, cancers with <0.1% transmission risk are classified as "Minimal"; 0.1 to 2% risk as "Low; 2 to <10% risk as "Intermediate" and >10% risk as "High". Melanoma transmission risk within total number of recipients transplanted 2010-2018 was estimated, per 1,000 persons and Wilson score interval was used to calculate 95% confidence intervals (95%CI). Suspected and verified melanomas in potential donors forgone were cross-tabulated against the recorded reason that donation did not proceed. Melanoma characteristics were compared between deceased organ donors and potential donors foregone due to melanoma transmission risk, to identify any inconsistencies in clinical decisions about medical suitability for donation.

## 3. Results:

### *3.1 Data-linkage and participant characteristics:*

Of 5,667 potential donors referred for consideration for deceased organ donation during 2010-2018, 4,581 had consent obtained from next of kin. Of these, there were 993 deceased organ donors and 3,588 potential organ donors forgone (Figure 1).

Overall, deceased organ donors were younger (52 years; IQR 36-63) compared to potential donors forgone (65 years; IQR 51-75) (Table 1). There was a lower proportion of deceased organ donors with melanoma in CCR (1%) than potential donors forgone (3%). The median time from first melanoma diagnosis to donation was longer in deceased organ donors (7.8 years; IQR 2.4-14.7) than potential donors forgone (6.2 years; IQR 1.8-12.8).

### *3.3 Melanoma transmissions in deceased organ donation:*

There were nine deceased organ donors with a record of melanoma in CCR. Of the nine donors with melanoma, four (50%) had in-situ melanoma, three had invasive melanomas localised to the site of origin, of which two (23%) had a Breslow thickness <0.8mm, and one had melanoma of unknown thickness and degree of spread (Table 2). One donor had two recorded melanomas, a melanoma in-situ and one invasive melanoma localised to the site of origin with <0.8mm thickness. A melanoma history was not suspected in four of these cases prior to donation, but they had melanoma recorded as present in the CCR.

These nine donors donated to 16 transplant recipients: 12 kidneys, three livers and one lung. There was no clear evidence of melanoma transmission between donor and recipient pairs (Table 3). Of the 16 transplant recipients from donors with melanoma, two developed cancer post-transplant. Melanoma transmission was excluded in these two recipients as the cancers were primary cancers, not melanoma (non-small cell carcinoma of the lung and clear cell carcinoma of the kidney). Four recipients died from non-melanoma related causes; non-

rheumatic aortic valve disorder (ICD-10-AM, I35), lung cancer (ICD-10-AM, C43.4), polyneuropathy (ICD-10-AM, G62.9) and transplant-related complications. There was insufficient follow-up time to assess the probability of transmission in two recipients. In total, 0/9 (95%CI 0 , 0.29) deceased organ donors with a history of melanoma and 0/14 (95%CI 0 , 0.22) recipients at risk who had over 6 months of follow-up developed Probable/Proven melanoma transmission. Overall, there were 0/993 Probable/Proven melanoma transmissions in recipients transplanted over the 8-year period: a transmission rate of 0 per 1,000 (95%CI 0 , 3.9 per 1,000) recipients.

### *3.4 Melanoma in potential donors forgone and missed opportunities for donation*

There were 3,588 potential donors forgone of whom, 35 were deemed not medically suitable due to their melanoma risk alone. Of these 35, 6 had no verified melanoma notification in the CCR and 29 had a total of 30 melanoma notifications (Table 2). Of these 29, two melanomas were in-situ (within the same donor) and nine were localised to the site of origin and had a Breslow thickness of <0.8mm. Combined, a total of 11/35 (31%) potential donors forgone and declined for donation due to melanoma risk alone had melanomas of low transmission risk.

Of the 3,553 potential donors that were deemed not medical suitability for other non-melanoma reasons, 22 were suspected to have a history of melanoma. Of these 22, 8 had no verified melanoma notification in the CCR. Of the remaining 14 with melanoma notification, 6 were in-situ and 3 were localised to the site of origin and had a Breslow thickness of ≤0.8mm. Reasons potential donors were deemed medically unsuitable are described in Supplementary Table 2.

The overall agreement between melanoma history suspected during medical assessment and melanoma notification in the CCR was poor (Supplementary table 3). There were a further 61/3,553 potential donors forgone who were not suspected of a melanoma history and had a melanoma notification in the CCR.

## 4. Discussion:

We found no evidence of melanoma transmission in solid organ transplant recipients from donors with early-stage melanomas, whether known or unknown prior to donation. Melanomas in these donors were in-situ, localised and ≤0.8mm in Breslow thickness, and >0.8mm with over 10 years cancer free. We also demonstrated that the accuracy of a melanoma history in potential donors referred for consideration was poor. Access to and consideration of cancer notifications in real-time could have improved the accuracy of melanoma transmission risk assessment prior to donation decisions and delivered several additional donors, without compromising safety.

Our findings are in contrast with current Australian and New Zealand guidelines that classify melanomas (not in-situ) localised to the site of origin, ≤0.8mm in Breslow thickness, with assumed curative surgery [T1/N0/M0] as having a high risk (≥10%) of transmission, with their use recommended only in exceptional circumstances, such as where the recipient faces an imminent threat to life[6,7,32]. We found that donors with early-stage melanomas (localised to the site of origin, ≤0.8mm in Breslow thickness, with assumed curative surgery [T1/N0/M0]) did not transmit to their recipients. We are not the first to report non-transmission in organs from donors with minimally-invasive melanomas. Kauffman et al (2000) first reported no transmission of invasive melanoma, but the authors still classified melanoma as at high-risk of transmission due to previous reports and their small case

numbers[16]. Melanoma non-transmission was similarly reported by the UK Transplant Registry in 2014, where organs from two donors with superficial spreading melanoma, diagnosed at least 8 years before donation, did not transmit the cancer[5]. These authors estimated that the use of donors with cancers misclassified as having a high-risk of transmission would have provided an additional 7.1 years survival at 10 years post-transplant per recipient.

Our work provides evidence of recipient outcomes with over 24-months of follow-up post-transplant[8]. Importantly, the organ recipients from donors with melanoma in our cohort were limited to kidney and liver recipients. There was one double lung transplant recipient who had insufficient follow-up time for assessment of probability of transmission. There is some evidence to suggest that organs with lower anti-tumour immune surveillance and defence, such as the lung and liver, are more susceptible to transmission of malignancy[33]. Early detection of melanoma transmission is essential for effective management and improved survival of transplant recipients with donor-derived melanomas[9]. If melanoma does develop, confirmation of donor origin can be established by PCR-based DNA analysis, HLA typing or immunohistochemistry[34]. In cases of donor-derived metastatic melanoma, the successful use of check-point inhibitors in kidney transplant recipients has been reported[35,36].

Our findings are in line with contemporary estimates of melanoma transmission in countries with a lower melanoma incidence; approximately 0.22 per 10,000 of all solid organ transplant recipients[8]. Melanoma incidence is increasing in Australia, but between 1996-2006, the majority (63%) of melanomas diagnosed were thin (<1.0mm)[37]. This would suggest that when a history of melanoma is not suspected, it is likely that any incident melanoma has a low-risk of transmission.

We found that clinical decision-making during donor assessment was inconsistent, suggesting significant risk aversion to use of donors with low-risk melanomas. Two potential donors were foregone due to a history of melanoma despite records in CCR describing in-situ melanomas which have a minimal (<0.1%) risk of transmission, likely acceptable for all organ types and recipients[7]. A further nine had melanomas localised to the site of origin, with a Breslow thickness of <0.8mm. Combined, a total of 11/58 (19%) potential donors forgone for donation because of melanoma risk alone, had melanomas of low transmission risk and could have donated with reasonable safety. Their use may have been declined due to limited or absent pathology information available when clinical decisions for donation were made. Real-time access to cancer registry records is now available during donor assessment in NSW, including diagnosis date, staging and thickness, which should assist in the medical assessment of deceased organ donors under consideration for donation and reduce the burden of proof for donor coordinators[23]. Furthermore, potential donors with high-risk melanomas could be more easily identified and forgone early in the assessment process, to minimise donor coordinator workload.

Lastly, we limited our estimates of donor gains to potential donors forgone because of melanoma transmission risk alone, which may have underestimated potential donor gains. There were 89 potential donors where next of kin had given consent for donation to proceed, that had suspected or verified melanomas that were recorded as being declined for other reasons, but where melanoma may have been a deciding factor and could have been a source of further donor gains, if information on their pathology had been readily available. Furthermore, the rate of melanoma in potential donors (3%) is less than the national melanoma prevalence (5.8%) [38], which may suggest a bias against the referral of potential

deceased organ donors with a history of melanoma. The incidence of melanoma is increasing globally[39]. Based on 2020 rates in Australia, it is estimated that the burden from melanoma will increase to 510,000 new cases (a roughly 50% increase) and to 96,000 deaths (a 68% increase) by 2040[20].

There were limitations to our study. Solid organ donor selection processes vary between international programs, potentially limiting the direct generalisability of our findings. In other programs it is often decided that potential donors are ineligible prior to any medical assessment or consideration by pre-retrieval teams. It is hard to know whether potential donors with melanoma history are foregone in these settings. The small number of recipients of donors with a history of melanoma is a study limitation, however this limitation is shared by all studies investigating melanoma transmission in organ donation and transplantation, contributing to the uncertainty around transmission risk. Here, we have been able to provide evidence of non-transmission based on melanoma staging using registries and data linkage with comprehensive donor evaluations. As a state-based study, we could not capture melanoma notifications to cancer registries for recipients residing in other states; however, this was limited to two recipients (one liver, one kidney) of donor organs from a donor who also gave to NSW recipients. We were also unable to obtain details of donor melanoma treatment or curative surgery. Such information may be useful in the confirmation of melanoma transmission risk.

In conclusion, we found that some potential donors with a history of melanoma could be suitable for organ donation after due consideration of the melanoma pathology. Melanomas considered at low-risk of metastasis (in-situ melanomas, thin invasive melanomas ≤0.8mm in Breslow thickness) may have an acceptably low risk of transmission in kidney transplantation

and could also be suitable for liver recipients. Clinical guidelines for the assessment of deceased donors with cancer should consider unknown non-transmission events to better reflect the stratified risk of melanoma transmission based on staging. Access to and consideration of cancer notifications in real time could improve the accuracy of transmission risk assessment prior to donation. Consideration of our evidence could support more consistent decisions for donors with low-risk melanomas, potentially increasing the donor pool and access to transplantation.

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## Data availability statement:

Summary level data may be available to researchers upon request and subject to ethical, governance, and data custodian approvals.

## Figure legends:

**Figure 1: Participant flowchart of patients referred for consideration for deceased organ donation, 2010-2018.** Individuals referred for consideration for organ donation were assessed for medical suitability, including a suspicion of history of or current melanoma, prior to donation. Potential donors forgone because of their suspected melanoma transmission risk during donor assessment were checked for verified notifications of melanoma, including in-situ melanoma, in the NSW CCR. Similarly, deceased organ donors were checked for verified notifications of melanoma and checked against whether a melanoma history was suspected during medical assessment. Deceased donor's referral records were sourced from the Organ Donor Referral Characteristics Database (ORCHARD), 2010-2018. Verified cancer records were sourced from the NSW Central Cancer Registry, 1972-2018.

## Supporting information statement:

Additional information may be found in the Supporting Information section.

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## Tables and Figures:

**Table 1. Characteristics of deceased organ donors and, potential donors foregone after deemed not medically suitable for organ donation, 2010-2018**

| Characteristic | Donor type | | Total |
|---|---|---|---|
| | Deceased donor[b] | Potential donor foregone[a] | |
| | N (%) | N (%) | N |
| TOTAL | 993 | 3,588 | 4,581 |
| Median age (years, IQR) | 52 (36-63) | 65 (51-75) | 62 (48-73) |
| Median time from first melanoma diagnosis to donation (years, IQR) | 7.8 (2.4-14.7) | 6.2 (1.8-12.8) | 6.2 (2.0-12.9) |
| Body mass index (kg/m$^2$) | 25 (23-29) | 27 (23-31) | 26 (23-30) |
| Melanoma record in CCR | 9 (1) | 111 (3) | 119 |
| Sex | | | |
| Female | 457(46) | 1,408 (39) | 1,865 |
| Male | 536 (54) | 2,180 (61) | 2,716 |

| | | | |
|---|---|---|---|
| Year of referral/donation | | | |
| 2010-2014 | 445 (45) | 1,281 (36) | 1,726 |
| 2015-2018 | 548 (56) | 2,307 (64) | 2,855 |
| Cause of death | | | |
| Certain infectious and parasitic diseases (A00-B99) | 5 (1) | 113 (3) | 118 |
| Neoplasms (C00-D49) | 11 (1) | 298 (8) | 309 |
| Diseases of the blood and immune mechanism (D50-D89) | 4 (<1) | 31 (1) | 35 |
| Endocrine, nutritional and metabolic diseases (E00-E89) | 12 (1) | 98 (3) | 110 |
| Diseases of the nervous system (G00-G99) | 57 (6) | 170 (5) | 227 |
| Diseases of the circulatory system (I00-I99) | 483 (49) | 1478 (41) | 1,961 |
| Diseases of the respiratory system (J00-J99) | 48 (5) | 229 (6) | 277 |
| Diseases of the digestive system (K00-K99) | 6 (1) | 226 (6) | 232 |
| Diseases arising from pregnancy and congenital abnormalities (O00-Q99) | 13 (1) | 69 (2) | 82 |
| External causes including, injury and poisoning (S00-T98, U50-U73, U90, V00-Y98) | 342 (34) | 582 (16) | 924 |
| Other | 12 (1) | 294 (8) | 306 |
| Ethnicity | | | |
| European | 848 (85) | 1652 (46) | 2,500 |

| | | | |
|---|---|---|---|
| Indigenous peoples | 39 (4) | 183 (5) | 222 |
| Asian | 70 (7) | 206 (6) | 276 |
| Africa and Middle East | 13 (1) | 31 (1) | 44 |
| Unknown | 23 | 1,516 | 1,539 |

Footnote: a. Includes eight potential donors that were previously transplant recipients. Abbreviations: CCR, Central Cancer Registry; IQR, Inter-quartile range

**Table 2. Degree of spread and Breslow thickness of melanomas in deceased organ donors with a history of melanoma, potential donors forgone for melanoma transmission risk, and potential donors suspected of melanoma but forgone for other reasons.**

| Donor type | Breslow thickness category (mm) | | | | | | |
|---|---|---|---|---|---|---|---|
| Degree of spread | Not measurable | ≤ 0.80 | 0.81-2.0 | 2.1-4.0 | ≥ 4.1 | Un-known | Total |
| **Deceased organ donors[a]** | | | | | | | |
| In-situ | 4 | 0 | 0 | 0 | 0 | 0 | 3 |
| Localised to site of origin | 0 | 3 | 0 | 0 | 0 | 1 | 4 |
| Unknown | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| **Total** | **4** | **3** | **0** | **0** | **0** | **2** | **9** |
| **Potential donors foregone for melanoma transmission risk alone[b]** | | | | | | | |
| No melanoma | 6 | 0 | 0 | 0 | 0 | 0 | 6 |
| In-situ | 2 | 0 | 0 | 0 | 0 | 0 | 2 |
| Localised to site of origin | 0 | 9 | 7 | 1 | 1 | 2 | 20 |
| Regional spread, adjacent organs | 0 | 0 | 1 | 0 | 1 | 0 | 2 |
| Regional spread, regional lymph nodes | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| Distant metastases | 0 | 0 | 0 | 1 | 0 | 1 | 2 |
| Unknown | 0 | 0 | 0 | 0 | 0 | 2 | 2 |
| **Total** | **8** | **9** | **8** | **2** | **3** | **5** | **35** |
| **Potential donors foregone for other reasons[c]** | | | | | | | |
| No melanoma | 8 | 0 | 0 | 0 | 0 | 0 | 8 |
| In-situ | 6 | 0 | 0 | 0 | 0 | 0 | 6 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Localised to site of origin | 0 | 3 | 3 | 1 | 0 | 0 | 7 |
| Regional spread, adjacent organs | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Regional spread, regional lymph nodes | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Distant metastases | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Unknown | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Total** | **14** | **3** | **3** | **1** | **0** | **0** | **22** |

Footnote: Where donors had more than 1 melanoma record, the higher risk melanoma was reported; a. includes 1 deceased donor with 1 in-situ melanoma and 1 localised melanoma; b. includes 1 potential donor forgone with 2 in-situ melanomas. Melanoma characteristics were sourced from the NSW Central Cancer Registry.

**Table 3: Proportion of probable/proven melanoma transmissions in solid organ transplant recipients of deceased organ donors with a history of melanoma**

| Melanoma transmission risk category[a] | Cancer type | Total donors with melanoma history | Donors with P/P transmission[b] ÷ Total donors with melanoma history | Total recipients from donors with melanoma | Recipients with P/P transmission[b] ÷ Total recipients from donors at risk[c] | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | kidney | liver | lung | total |
| Minimal (<0.1%) | In-situ cutaneous melanoma | 4 | 0/3 | 7 | 0/6 | 0/1 | | 0/7 |
| | **TOTAL IN-SITU** | **4** | **0/3** | **7** | **0/6** | **0/1** | | **0/7** |
| Low (0.1 - <2%) | - | | | | | | | |
| Intermediate (2% to <10%) | - | | | | | | | |
| High (≥10%) | Cutaneous melanoma ≤0.8mm (T1/N0/M0) completely resected | 3 | 0/3 | 5 | 0/3 | [0/1][c] | [0/1][c] | 0/3 |
| | Cutaneous melanoma >0.8mm (T2-T4/N0/M0) with >10 years cancer free | 1 | 0/1 | 2 | 0/1 | 0/1 | | 0/2 |
| | Cutaneous melanoma T2-T4 with ≤10 years cancer free | | | | | | | |
| Unacceptable | Cutaneous melanoma with nodal involvement or metastasis | | | | | | | |
| | Unknown thickness and behaviour | 1 | 0/1 | 2 | 0/2 | | | 0/2 |
| | **TOTAL INVASIVE** | **5** | **0/5** | **9** | **0/6** | **0/2** | **0/0** | **0/7** |
| **TOTAL** | | **9** | **0/9** | **16** | **0/12** | **0/2** | **0/0** | **0/14** |

**Footnote:** Donor melanomas were identified using ICD-O-3 codes (typography, morphology/stage), Site, Morphology, Degree of spread, Number primary sites, Breslow thickness & Treatment (invasive only). (a) Donor melanomas were categorised based on the current TSANZ transmission risk classification[7] where donors had more than one melanoma, the worst-case scenario was taken. (b) Donors and recipients were assessed for "probable/proven" transmission using criteria adapted from SabTO, DTAC and the WHO NOTIFY project (Supplementary Table 1)[2,6-8]. Recipient cancer post-transplant was identified using ICD-O-3 codes (typography, morphology/stage) and cause of death ascertained from the RBDM using ICD-10-AM codes. (c) Recipients with less than 6-months of follow-up (reported here as 1 lung, 1 liver) were excluded from final transmission risk estimates. Abbreviations: DTAC, Disease Transmission Advisory Committee; ICD-O-3; International Classification of Diseases for Oncology, 3rd edition; ICD-10-AM, International Classification of Diseases, 10th Edition, Australian Modification; RBDM, Registry of Births, Deaths and Marriages; SabTO, Advisory Committee on the Safety of Blood, Tissues and Organs; TSANZ, Transplantation Society of Australia and New Zealand.

**Supplementary Table 1. Criteria to assess probability of melanoma transmission in deceased organ donation**

| Probability of transmission grade | Transmission criteria |
|---|---|
| Excluded | Suspected transmissions fulfil at least one of the following conditions;<br>- Clear evidence of an alternative cause; or<br>- Laboratory evidence that the recipient had a tumour before the application of organs. |
| Possible | Suspected transmission and at least one of the following;<br>- Laboratory evidence of the tumour in a single recipient; or<br>- Evidence is indeterminate to attribute the tumour to the donation process or alternative cause. |
| Probable | The following conditions are met;<br>- Suspected transmission, and<br>- Laboratory evidence of the tumour in a single recipient;<br>And at least one of the following conditions are met;<br>- Laboratory evidence of the same tumour in other recipients; or<br>- Laboratory evidence of the same tumour in the donor (if there is pre-transplant evidence it must indicate these recipients were negative for the tumour before transplant). |
| Proven | All the following conditions are met;<br>- Suspected transmission;<br>- Laboratory evidence of the tumour in a recipient;<br>- Laboratory evidence of the same tumour in other recipients ( if multiple recipients); and<br>- Laboratory evidence of the same tumour in the donor (if there is pre-transplant evidence it must indicate these recipients were negative for the tumour before transplant). |
| Not Assessable | Insufficient information (e.g. follow-up time) to assess probability |

**Supplementary Table 2. Reasons deemed not medically suitable for organ donation in potential donors suspected of melanoma but forgone for other non-melanoma reasons.**

| Not Medically Suitable Reason | Total |
|---|---|
| Cancer | 0 |
| Donor age | 2 |
| No suitable organs for transplant | 3 |
| Current infection | 0 |
| Failed Supportive treatment[a] | 3 |
| Brain death considered unlikely[b] | 6 |
| Did not die in timeframe[c] | 2 |
| Not reported | 6 |
| **Total** | **22** |

Reasons not medically suitable were provided by the Organ and Tissue Donation Service. All patients at end of life and intensive care and emergency department settings are referred for consideration for organ donation. Patients must meet certain criteria for neurological (brain death) or circulatory death[TSANZ 2023] before organ donation can take place. Patients who do not meet these criteria because they a) were not able to be maintained on a mechanical ventilator, b) were unlikely to meet criteria for neurological death or, c) death did not occur within 30-90 minutes of withdrawal of cardio-respiratory supportive treatment.

**Supplementary Table 3. Suspected vs verified melanoma in potential donors forgone**

| Melanoma suspected at referral | Melanoma notification in Central Cancer Register | | |
|---|---|---|---|
| | Yes | No | Total |
| Yes | 43 | 14 | 57 |
| No | 61 | 3,470 | 3,531 |
| TOTAL | 104 | 3,484 | 3,588 |

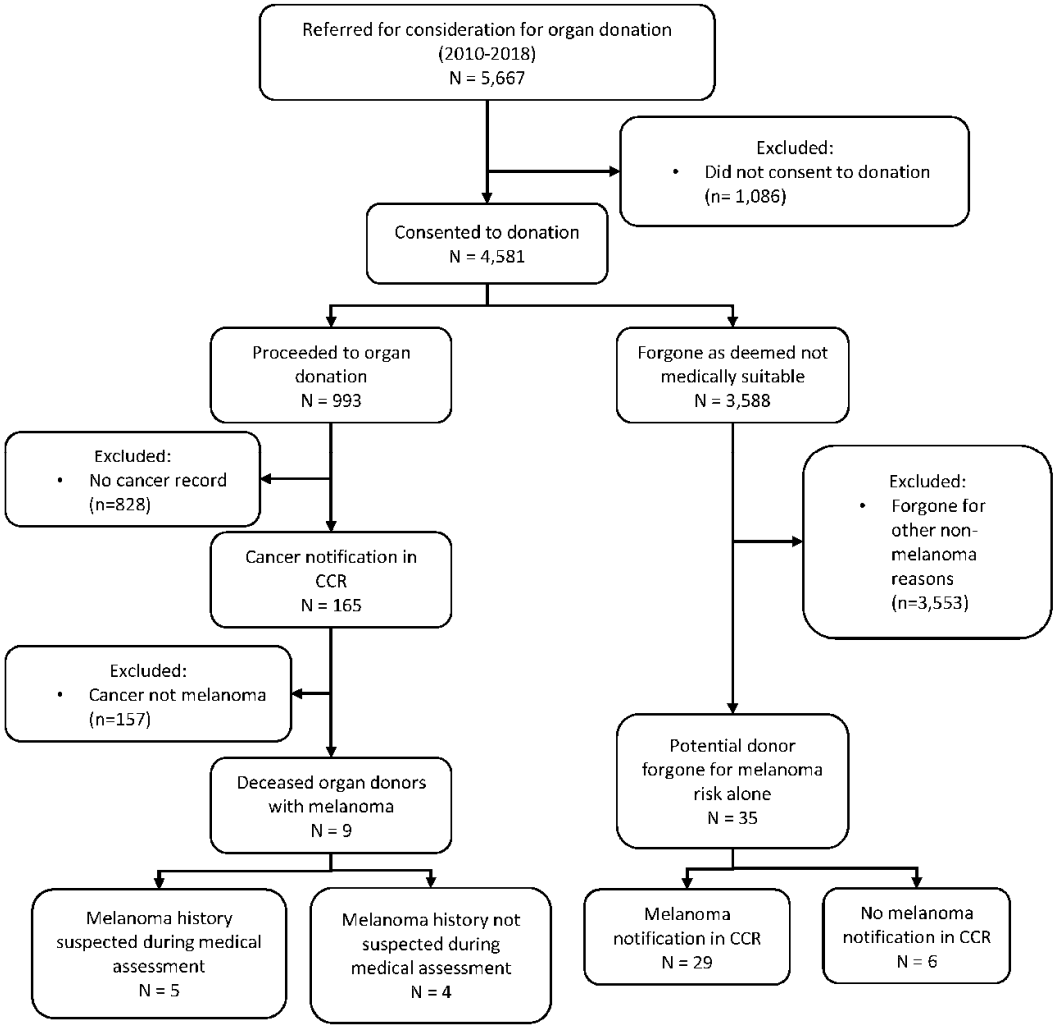


**Figure 1: Participant flowchart of patients referred for consideration for deceased organ donation, 2010-2018.** Individuals referred for consideration for organ donation were assessed for medical suitability, including a suspicion of history of or current melanoma, prior to donation. Potential donors forgone because of their suspected melanoma transmission risk during donor assessment were checked for verified notifications of melanoma, including in-situ melanoma, in the NSW CCR. Similarly, deceased organ donors were checked for

verified notifications of melanoma and checked against whether a melanoma history was suspected during medical assessment. Deceased donor's referral records were sourced from the Organ Donor Referral Characteristics Database (ORCHARD), 2010-2018. Verified cancer records were sourced from the NSW Central Cancer Registry, 1972-2018.