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ORIGINAL ARTICLE

Cancer transmissions and non-transmissions from solid organ transplantation in an Australian cohort of deceased and living organ donors

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SUMMARY

Evidence on cancer transmission from organ transplantation is poor. We sought to identify cases of cancer transmission or non-transmission from transplantation in an Australian cohort of donors and recipients. We included NSW solid organ deceased donors 2000–2012 and living donors 2004–2012 in a retrospective cohort using linked data from the NSW Biovigilance Register (SAFEBOD). Central Cancer Registry (CCR) data 1972–2013 provided a minimum one-year post-transplant follow-up. We identified cancers in donors and recipients. For each donor-recipient pair, the transmission was judged likely, possible, unlikely, or excluded using categorization from international guidelines. In our analysis, transmissions included those judged likely, while those judged possible, unlikely, or excluded were non-transmissions. In our cohort, there were 2502 recipients and 1431 donors (715 deceased, 716 living). There were 2544 transplant procedures, including 1828 (72%) deceased and 716 (28%) living donor transplants. Among 1431 donors, 38 (3%) had past or current cancer and they donated to 68 recipients (median 6.7-year follow-up). There were 64 (94%) non-transmissions, and 4 (6%) transmissions from two living and two deceased donors (all kidney cancers discovered during organ recovery). Donor transmitted cancers are rare, and selected donors with a past or current cancer may be safe for transplantation.

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Introduction

Organ transplantation is a life-saving treatment for many people with end-stage organ failure. In Australia, people with end-stage kidney disease have a five-year survival of approximately 50% when treated with dialysis [1,2], compared with 90% for those who receive a kidney transplant [3]. Five-year post-transplant survival is also high after liver transplant (80%) [4], heart transplant (80%) [5], and lung transplant (70%) [5]. Despite

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the clear benefits of transplantation, safety risks must also be carefully considered including the potential for donor to recipient transmission of infectious disease or cancer. Cancer transmission is of particular concern because it may be fatal for the recipient [6], and many potential donors with a history of cancer are therefore declined for transplantation. Recipients and transplant clinicians face a delicate trade-off between maximizing organ donation opportunities and minimizing the risk of transmission [7].

The Transplantation Society of Australia and New Zealand (TSANZ) has published clinical guidelines for organ transplantation from deceased donors [8]. These guidelines provide an overview of the evidence surrounding the risk of cancer transmission by cancer site and are similar to guidelines in the UK [9], Europe [10], and the United States [11]. However, the quality of evidence available for estimating cancer transmission risks is poor [12]. Relatively few donors with a known history of cancer are accepted for donation [13]. Those who are accepted are highly selected, hence cancer transmission is a rare occurrence [14,15]. Indeed, the recommendations for donors with a central nervous system (CNS) tumor, for instance, are ultimately based on studies with no observed transmissions [16,17].

The Safety and Biovigilance in Organ Donation (SAFEBOD) Public Health Register was established in New South Wales (NSW) in 2018, with one of its aims to identify cases of donor to recipient cancer transmission and non-transmission [18]. New South Wales is the largest Australian state with approximately 8.1 million people [19], and it is demographically representative of the entire country. We sought to use the SAFEBOD register to investigate cancer transmissions and non-transmissions in a cohort of donors and recipients over a 13-year period.

Methods

Study cohort

We performed a retrospective cohort study of solid organ donors and recipients linked to health records using data from the NSW Biovigilance Public Health Register (SAFEBOD). Records were linked probabilistically using personal identifiers such as name, date of birth, and address. SAFEBOD was initiated under the NSW Public Health Act 2010 and was approved by the University of Sydney Human Research Ethics Committee (project number 2016/758). Further details of the SAFEBOD study linkage have been published previously [18].

Our study population included all solid organ transplants performed in NSW from deceased (January 01, 2000, to December 31, 2012) and living (January 01, 2004, to December 31, 2012) donors. We had complete follow-up data for living donors, recipients, and transplant outcomes until December 31, 2016. Linked data from the population-based NSW Central Cancer Registry (CCR) are lagged by approximately 5 years; hence, data are only available until the end of 2013 despite linkage for SAFEBOD being performed in 2018. We therefore chose December 31, 2012, as the end of our study period to ensure at least one year of post-transplant follow-up for cancer was available for all participants. We excluded transplants where either the donor or recipient had a non-NSW postcode at transplant, since cancers diagnosed across state boundaries may not always be notified to the NSW CCR.

Identifying cancers

In Australia, all cancer diagnoses must be notified to the relevant state or territory cancer registry under statute. Cancers are classified using both the International Statistical Classification of Diseases for Oncology 3rd Edition (ICD-O) [20] and the International Statistical Classification of Diseases and Related Health Problems Tenth Revision Australian Modification (ICD-10-AM) [21]. We considered any donor or recipient tumor that was notifiable to the CCR to be a cancer. This included all malignant and in situ tumors but excluded non-melanoma skin cancers which are not notifiable [22].

We assigned each cancer a site based on its ICD-O code reported in the CCR. Other cancer details such as diagnosis date and level of spread were primarily based on CCR; however, the CCR only includes the highest level of spread within 4 months of diagnosis. Therefore, we also sought further details of any cancers from other SAFEBOD sources including: the Admitted Patient Data Collection (ADPC), death records from the Registry of Births, Deaths, and Marriages (RBDM), the Australian and New Zealand Organ and Tissue Donor Registry (ANZOD), the Australian and New Zealand Dialysis and Transplant Registry (ANZDATA), the Australian and New Zealand Cardiothoracic Organ Transplant Registry (ANZCOTR), and the Australian and New Zealand Liver and Intestine Transplant Registry (ANZLITR).

We documented all donor and recipient cancers from before and after transplant. For living donors, we considered whether cancers diagnosed after transplant may have been present prior to donation. For deceased donors,

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we considered the possibility that cancers discovered during organ recovery may not have been notified to the CCR, despite the statutory notification rules. Although new cancer diagnoses are notifiable even if discovered after death, it is possible that because of administrative confusion these cancers may not have been notified or may have been notified against the recipient rather than the donor (e.g., if a kidney cancer is discovered during organ recovery, resected, and then, the kidney used for transplant). We also considered that some donor cancers may have been undiagnosed at the time of death, so we would only find out about the cancer via a transplant recipient if a transmission occurred (e.g., a metastatic cancer diagnosed in a recipient shortly after transplant may be judged a likely transmission, which implies the donor had cancer prior to donation).

Transmission likelihood

We categorized each transplant procedure (i.e., each donor–recipient pair) by the likelihood that a transmission had occurred (a donor-transmitted cancer), compared with an alternative explanation (e.g., a donor-derived *de novo* cancer arising in the recipient). We used categories likely, possible, unlikely, or excluded, based on international guidelines for investigating the imputability of malignancy transmission [23–25]. We did not include categories for definite or proven transmission because this would require access to more granular case-by-case information than we were able to acquire using linked health data (e.g., detailed pathology reports). The guidelines are subjective since the distinction between donor-derived cancers (i.e., *de novo* cancer in a recipient, arising in donor cells, that was not present at transplantation) and donor-transmitted cancers (i.e., pre-existing cancer transmitted with donor cells at the time of transplantation) is often difficult to discern. Therefore, records for each transplant procedure (donor–recipient pair) were reviewed on a case-by-case basis by two co-authors with expertise in transplant nephrology and cancer epidemiology (ACW and CMV). Any disagreements were resolved with another co-author with expertise in transplant nephrology (MW).

The characteristics considered when evaluating the likelihood of transmission were age, sex, donation pathway (living vs. deceased), donor mode of death, and all cancers before or after transplant for the donor and all recipients of their organs (including date of diagnosis, primary site, level of spread, and source of information within SAFEBOD). Broadly, we considered transmission to be likely if a donor had past or current cancer and the recipient developed metastatic cancer or cancer in the transplanted organ. Transmission was considered possible if there was no reported cancer in the donor, but the recipient developed metastatic cancer or cancer in the transplanted organ shortly after transplantation. Transmission was considered unlikely (but still a possibility) if the recipient developed non-metastatic or late onset cancer that could potentially have originated in the donor, despite a lack of corroborating evidence in any donor records. In all other cases (e.g., recurrence of a recipient's previous cancer, or no cancer), transmission was excluded.

Data analysis

We summarized the donor and recipient characteristics and outcomes of all transmissions and non-transmissions and reported these as proportions of donors and transplant procedures. We also focused on certain donor cancers of particular interest: kidney and brain cancers. Kidney cancers discovered during organ recovery may in some circumstances be resected (where this is thought to be curative) and the kidney used for transplantation. Brain cancers typically occur in younger people who are otherwise relatively healthy compared with the average donor, and certain types of brain cancer are less likely to metastasize and are acceptable for donation under current guidelines [8].

In addition, we also restricted our analysis to donors with any reported past or current cancer. Some donor cancers may only be discovered if a transmission occurs; hence, there may also be donors with cancer that remains undiscovered because it does not result in transmission. To account for this possible bias, we performed sensitivity analyses by further restricting our analysis to donor cancers (i) reported against the donor in any data source, (ii) notified against the donor in the CCR, and (iii) recognized by clinicians at the time of donation.

We defined a transmission as any transplant procedure (donor–recipient pair) where transmission was judged likely, while a non-transmission was any transplant procedure where transmission was judged possible, unlikely, or excluded. In sensitivity analyses, we considered alternative likelihood thresholds for defining transmissions and non-transmissions.

Results

Study cohort

We included 2502 NSW recipients of 1431 NSW donors in our analysis, as health records for interstate donors and recipients were not present in SAFEBOD. These

recipients underwent 2544 transplant procedures, including 1828 (71%) from 715 deceased donors and 716 (29%) from living donors (Fig. 1).

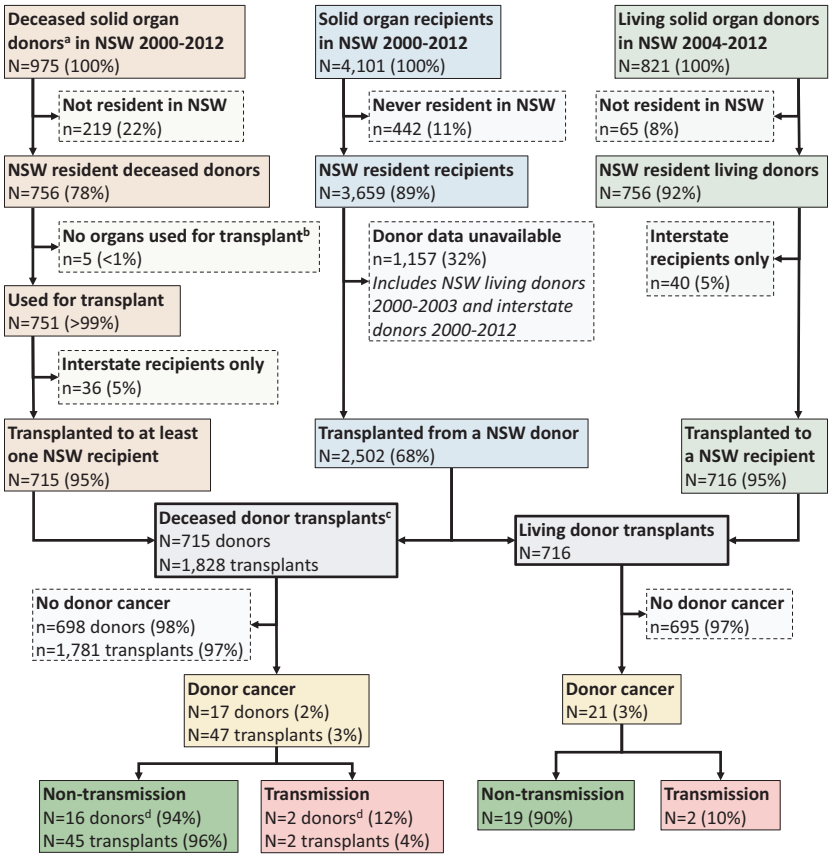
Donor cancers

Among 1431 donors, 38 (3%) had evidence of at least one past or current cancer (43 cancers total). This included 17 (45%) deceased and 21 (55%) living donors who donated to 68 NSW recipients (with a further six interstate recipients excluded from our analysis). The median post-transplant follow-up for recipients was 6.7 years (IQR 4.8–10.3). Of these donors, 38 (100%) had cancer reported against the donor in at least one data source, 33 (87%) had cancer notified against the donor in the CCR, and for 37 (97%) the cancer was recognized by clinicians at the time donation decisions were made. The most common cancers in donors were kidney (n = 14, 37%), brain (n = 7, 18%), prostate (n = 6, 16%), melanoma (n = 4, 11%), breast (n = 3, 8%), and thyroid (n = 3, 8%). Donor cancers are summarized in Table S1.

Summary of transmissions and non-transmissions

Among 68 transplant procedures from 38 donors with past or current cancer, there were four (6%) transmissions from two living and two deceased donors, and 64 (94%) non-transmissions from 19 living and 16 deceased donors (Fig. 1). One deceased donor with two recipients was counted as a transmission to one recipient and a non-transmission to the other recipient. The overall transmission rate was 0.16% of 2544 transplant procedures, and 0.28% of all donors transmitted cancer to at least one recipient. Donor and recipient characteristics of all transmissions and non-transmissions are presented in Table S1.

Our findings were robust to restricting which donor cancers were included, as well as to alternative



[a] *Actual donors (commenced organ recovery)*
[b] *Donor discard rate. Includes organs not recovered, and organs discarded*
[c] *Transplant procedures, which may include multiple transplanted organs*
[d] *Includes one donor with two recipients: one transmission and one non-transmission*

Figure 1 Flowchart of donors and recipients included in the study cohort, and transmissions and non-transmissions.

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likelihood thresholds for defining transmissions and non-transmissions (Table S2). In sensitivity analysis scenarios, the transmission rate ranged from 4%-23%, while the non-transmission rate ranged from 77% to 96%. Even in the most conservative scenario including all transmissions judged likely, possible, or unlikely, transplants from donors with a past or current cancer were much more likely to result in non-transmission (77%) compared with transmission (23%).

Details of kidney cancer transmissions and non-transmissions

All 14 donors with kidney cancer (four deceased, 10 living) had their cancer discovered during organ recovery. These donors donated to 19 NSW recipients, resulting in 15 (79%) non-transmissions and four (21%) transmissions. Details of transmissions and non-transmissions from donors with kidney cancer are summarized for deceased donors in Table 1, and for living donors in Table 2.

The first deceased donor had an adenocarcinoma (not notified to the CCR) resected from one kidney before transplant and donated their other kidney to a different recipient. The resected kidney failed because of adenocarcinoma (ICD-O histology 8310) after 8 months (transmission) and was removed. The recipient was still alive 13 years post-transplant. The other recipient survived 10 years with a functioning transplant (non-transmission).

The second deceased donor had their kidney with adenocarcinoma (not notified to the CCR) discarded but donated their liver and other kidney. The kidney recipient survived 7 years with a functioning transplant (non-transmission), while the liver recipient survived 6 years (non-transmission).

The third deceased donor had cancer resected from one kidney before transplant and also donated their other kidney, liver, and heart. The cancer was reported to be an adenocarcinoma in ANZOD but was notified to the CCR against the recipient at the time of transplant as a renal cell carcinoma (ICD-O 8312). Both the resected kidney and liver recipients were still alive with a functioning transplant after 6 years of follow-up (non-transmissions). The other kidney was lost immediately with the recipient surviving 1 year (non-transmission), while the heart recipient survived 5 years (non-transmission).

The final deceased donor's kidneys were discarded because of an adenocarcinoma discovered during organ recovery, but it was not reported whether this was diagnosed in one or both kidneys. This cancer was not notified to the CCR so no further histology details are available. The donor's lungs were nevertheless donated to a single recipient who developed metastatic adenocarcinoma of uncertain site with lung metastases (ICD-O 8140) 6 months post-transplant and died 1 month later (transmission).

The 10 living donors with kidney cancer all had their cancer resected, and the kidney used for transplant. One donor had a renal cell carcinoma (ICD-O 8312), and their recipient developed metastatic renal cell carcinoma (ICD-O 8312) 3 years post-transplant (transmission). It was not reported whether this was in the native or transplanted kidney, nor whether the cancer was removed with a partial or full nephrectomy. The recipient was still alive 6 years post-transplant. Another donor had adenocarcinoma (ICD-O 8310), and their recipient had renal cell carcinoma (not notified to the CCR) in the transplanted kidney 2 years post-transplant (transmission), which was removed 1 month later. The recipient was still alive 4 years post-transplant. Of the remaining eight donors, five had adenocarcinoma (ICD-O 8310), one had renal cell carcinoma (ICD-O 8312), one had chromophobe cell renal carcinoma (ICD-O 8317), and one had papillary adenocarcinoma (ICD-O 8260). The eight recipients of these donor were all non-transmissions, with two recipients surviving 1 and 4 years respectively, and six recipients still alive after a median 5 years post-transplant follow-up (IQR 4.4-6.3).

Details of brain cancer non-transmissions

There were seven donors with brain cancer, including six deceased donors whose terminal hospital admission was related to brain cancer diagnosed up to a year prior to donation, and one living donor with a brain cancer diagnosed 17 years prior. The six deceased donors with current brain cancer included four with glioblastoma (grade 4), one with oligodendroglioma (grade 2), and one with glioma (unknown grade). All were accepted for donation in accordance with current guidelines [8]. They donated to 25 NSW recipients, and all 25 (100%) were non-transmissions. Details of these non-transmissions are summarized in Table 3.

The living donor with glioma (unknown grade) also had a renal cell carcinoma (ICD-O 8312) discovered during organ recovery. The tumor was resected before transplant, but despite this the transplant resulted in a transmission (described above). We counted this as a kidney cancer transmission; hence, there were no brain cancer transmissions in our study.

Table 1. Cancer transmissions and non-transmissions in NSW 2000–2012 from deceased donors with kidney cancer.

Donor							Recipient					
#	Year	Path	Age	Sex	Cancer type(s)	Diagnosis*	#	Organ(s)	Age	Sex	Transmission	Recipient outcome, at end of follow-up (December 31, 2016)
1	2003	DBD	55+	M	Adenocarcinoma†	Recovery	1	Single kidney	25–34	M	Likely	Kidney tumor resected before transplant. Transplant failed because of cancer after 8 months (not in the CCR). Still alive
							2	Single kidney	45–54	F	Non-transmission	Died because of myocardial infarction after 10 years with functioning transplant
2	2008	DBD	55+	M	Adenocarcinoma†	Recovery	1	Single kidney	55–64	M	Non-transmission	Tumor found in right kidney during organ recovery, discarded, and left kidney transplanted. Died because of cardiogenic shock after 7 years with functioning transplant
							2	Whole liver	55–64	M	Non-transmission	Died with transplant failure because of fungal sepsis after 6 years
3	2010	DBD	35–54	F	Renal cell carcinoma‡	Recovery	1	Single kidney	45–54	F	Unlikely	Kidney tumor resected before transplant. Kidney cancer reported in the CCR against the recipient at time of transplant, with no evidence of recurrence. Alive with functioning transplant
							2	Single kidney	45–54	F	Non-transmission	Transplant failed because of immediate rejection, died 1 year later
							3	Whole liver	55–64	F	Non-transmission	Alive with functioning transplant
							4	Heart	55–64	F	Non-transmission	Non-melanoma skin cancer reported after 2 years (not notifiable). Died with transplant failure because of cancer 3 years later
4	2011	DCD	55+	M	Adenocarcinoma†	Recovery	1	Double lung	65–74	F	Likely	Donor kidneys discarded because of kidney cancer found during organ recovery. Metastatic cancer of uncertain site (bone, lung, and liver metastases) diagnosed after 6 months. Died because of cancer 1 month later with functioning transplant

CCR, central cancer registry; DBD, donation after brainstem death; DCD, donation after circulatory death.

Each row represents an individual recipient. Recipients with the same donor are grouped together with alternating white/shaded background.

*When cancer was first diagnosed in the donor (years prior, during a deceased donor's terminal hospital admission, during a living donor's workup, or during organ recovery).

†Cancer not notified to the CCR.

‡Cancer notified to the CCR against the recipient.

Table 2. Cancer transmissions and non-transmissions in NSW 2000-2012 from living donors with kidney cancer.

Donor						Recipient					
#	Year	Age	Sex	Cancer type(s)	Diagnosis*	#	Organ(s)	Age	Sex	Transmission	Recipient outcome, at end of follow-up (December 31, 2016)
5	2006	35–54	F	Renal cell carcinoma	Recovery	1	Single kidney	45–54	M	Non-transmission	Kidney tumor resected before transplant. Alive with functioning transplant
6	2010	35–54	F	Renal cell carcinoma Glioma	Recovery 17 years	1	Single kidney	65–74	M	Likely	Kidney tumor resected before transplant. Metastatic kidney cancer diagnosed after 3 years (not reported if native or transplanted kidney). Alive with functioning transplant
7	2010	55+	F	Papillary adenocarcinoma Breast† (m)	Recovery 1 year	1	Single kidney	65–74	M	Non-transmission	Kidney tumor resected before transplant. Transplant failed because of BK virus nephropathy after 1 year, still alive
8	2011	55+	F	Adenocarcinoma	Recovery	1	Single kidney	55–64	M	Non-transmission	Kidney tumor resected before transplant. Alive with functioning transplant
9	2011	55+	M	Adenocarcinoma	Recovery	1	Single kidney	65–74	F	Unlikely	Kidney tumor resected before transplant. Donor metastatic lung cancer reported 3 years after transplant (not in the CCR). Donor died because of cancer 2 years later. Recipient metastatic liver cancer reported after 4 years (not in the CCR, pre-transplant history of non-melanoma skin cancer). Recipient died because of cancer 2 months later with functioning transplant
10	2011	55+	M	Chromophobe cell renal carcinoma Melanoma Prostate	Recovery Work-up 2 years	1	Single kidney	65–74	M	Non-transmission	Kidney tumor resected before transplant. Alive with functioning transplant
11	2012	55+	F	Adenocarcinoma	Recovery	1	Single kidney	55–64	M	Non-transmission	Kidney tumor resected before transplant. Transplant failed because of acute rejection after 1 year, died 5 months later
12	2012	35–54	M	Adenocarcinoma	Recovery	1	Single kidney	65–74	F	Non-transmission	Kidney tumor resected before transplant. Non-melanoma skin cancer reported after 11 months (not notifiable). Alive with functioning transplant
13	2012	55+	M	Adenocarcinoma	Recovery	1	Single kidney	65–74	M	Likely	Kidney tumor resected before transplant. Cancer in transplanted kidney reported after 2 years (not in the CCR). Transplant failed because of cancer 1 month later, still alive
14	2012	35–54	F	Adenocarcinoma	Recovery	1	Single kidney	65–74	M	Non-transmission	Kidney tumor resected before transplant. Alive with functioning transplant

CCR, central cancer registry; (m), metastases.

*When cancer was first diagnosed in the donor (years prior, during donor workup, or during organ recovery).

†Uncertain if recognized by clinicians at time of donation.

Table 3. Cancer transmissions and non-transmissions in NSW 2000–2012 from deceased donors with brain cancer.

Donor							Recipient					
#	Year	Path	Age	Sex	Cancer type(s)	Diagnosis*	#	Organ(s)	Age	Sex	Transmission	Recipient outcome, at end of follow-up (December 31, 2016)
15	2000	DBD	15–34	F	Glioblastoma	Admission	1	SPK	–	–	Unknown	Interstate recipient
							2	Single kidney	–	–	Unknown	Interstate recipient
							3	Whole liver	35–44	F	Non-transmission	Alive with functioning transplant
							4	Double lung	15–24	F	Non-transmission	Alive with functioning transplant
16	2000	DBD	55+	F	Glioblastoma	Admission	1	Single kidney	25–34	M	Non-transmission	Died because of ischemic heart disease after 16 years with functioning transplant
							2	Single kidney	45–54	M	Non-transmission	Non-melanoma skin cancer reported after 4 years (not notifiable). Alive with functioning transplant
							3	Whole liver	65–74	F	Non-transmission	Non-melanoma skin cancer reported after 9 years (not notifiable). Alive with functioning transplant
							4	Double lung	55–64	F	Non-transmission	Non-melanoma skin cancer reported after 12 years (not notifiable). Died because of septicemia 3 years later with functioning transplant
17	2004	DBD	35–54	F	Oligodendroglioma	1 year	1	SPK	25–34	F	Non-transmission	Kidney failed because of chronic allograft nephropathy after 8 years. Pancreas failed because of acute rejection 23 months later. Still alive
							2	Single kidney	45–54	M	Non-transmission	Alive with functioning transplant
							3	Whole liver	55–64	F	Non-transmission	Died with transplant failure because of acute rejection after 2 years
							4	Double lung	25–34	F	Non-transmission	Died with transplant failure because of bronchiolitis obliterans after 2 years
18	2007	DBD	35–54	F	Glioblastoma	Admission	1	Single kidney	25–34	M	Non-transmission	Died with transplant failure because of withdrawal from immunosuppressants after 7 years
							2	Single kidney	55–64	M	Non-transmission	Non-melanoma skin cancer reported after 2 years (not notifiable). Alive with functioning transplant
							3	Whole liver	25–34	F	Non-transmission	Died with transplant failure because of perforated duodenal ulcer after 2 years
							4	Double lung	25–34	F	Non-transmission	Alive with functioning transplant
							5	Heart	65–74	M	Non-transmission	Non-melanoma skin cancer reported after 20 months (not notifiable). Alive with functioning transplant

Table 3. Continued.

Donor							Recipient					
#	Year	Path	Age	Sex	Cancer type(s)	Diagnosis*	#	Organ(s)	Age	Sex	Transmission	Recipient outcome, at end of follow-up (December 31, 2016)
19	2007	DBD	15–34	F	Glioblastoma	Admission	1	Single kidney	65–74	M	Non-transmission	Non-melanoma skin cancer reported after 2 years (not notifiable). Alive with functioning transplant
							2	Single kidney	55–64	M	Non-transmission	Alive with functioning transplant
							3	Whole liver	55–64	M	Non-transmission	Metastatic throat cancer reported after 6 years (not in the CCR). Died because of cancer 4 months later with functioning transplant
							4	Double lung	45–54	M	Non-transmission	Died because of respiratory failure after 1 year
							5	Heart	45–54	F	Non-transmission	Non-melanoma skin cancer reported after 7 months (not notifiable). Alive with functioning transplant
20	2009	DBD	15–34	M	Glioma	Admission	1	Single kidney	45–54	F	Non-transmission	Alive with functioning transplant
							2	Single kidney	55–64	M	Non-transmission	Alive with functioning transplant
							3	Split liver	45–54	F	Non-transmission	Alive with functioning transplant
							4	Split liver	0–4	F	Non-transmission	Alive with functioning transplant
							5	Double lung	35–44	M	Non-transmission	Prostate cancer diagnosed after 2 years. Died because of respiratory failure 3 years later

CCR, central cancer registry; DBD, donation after brainstem death; SPK, simultaneous pancreas-kidney transplant.

Each row represents an individual recipient. Recipients with the same donor are grouped together with alternating white/shaded background.

*When cancer was first diagnosed in the donor (years prior, or during a deceased donor's terminal hospital admission).

Details of other cancer non-transmissions

There were six donors (three deceased, three living) with current or past prostate cancer who donated to nine recipients (median post-transplant follow-up 6.5 years, IQR 5.0–12.5), all of which were non-transmissions. This included a living donor with chromophobe cell renal carcinoma discovered during organ recovery (described previously), as well as a deceased donor who had metastatic prostate cancer with regional spread 11 years prior to donation whose two kidney transplant recipients were still alive with a functioning transplant 4 years post-transplant.

There were four donors (two deceased, two living) with current or past melanoma who donated to five recipients (median post-transplant follow-up 5.4 years, IQR 5.0–5.4), all of which were also non-transmissions. This included the same living donor with chromophobe cell renal carcinoma and prostate cancer described previously. These melanomas were all recognized at time of donation; one living donor had an in-situ melanoma discovered during donor work-up, one deceased donor had a 0.13 mm Breslow thickness melanoma removed 2 years prior, and the thickness of the remaining two melanomas was not reported.

There were two living donors with breast cancer diagnosed 4 and 6 years prior to donation whose kidney recipients were still alive with a functioning transplant 9 years and 5 years post-transplant, respectively (non-transmissions). In addition, one female living donor with kidney cancer described above also had a metastatic breast cancer diagnosed 1 year prior to donation. It is unclear whether clinicians were unaware of the donor's cancer history, or whether they recognized the cancer and considered the risk of transmission to the male recipient acceptable. Fortunately, this was a non-transmission. The recipient's kidney failed because of BK virus nephropathy 1 year post-transplant, but the recipient was still alive 6 years post-transplant.

There were two living donors with thyroid cancer diagnosed 6 and 18 years prior to donation. One kidney failed 2 years post-transplant because of focal sclerosing glomerulonephritis, but the recipient was still alive 12 years post-transplant (non-transmission). The other recipient was still alive with a functioning transplant 9 years post-transplant (non-transmission). Additionally, one deceased donor had metastatic thyroid cancer diagnosed 34 years prior to donation that was not recognized by clinicians at the time of transplant. The single kidney recipient died 1 month post-transplant because of acute myocardial infarction; hence, this was considered a non-transmission.

Discussion

We analyzed an observational cohort of transplant procedures between NSW donors and recipients during 2000-2012 and identified cases of cancer transmissions and non-transmission. Overall, cancer transmissions were rare (0.16% of transplant procedures). Even among transplants from donors with past or current cancer, non-transmission (94%) was much more common than transmission (6%). In cases where transmissions occurred, recipient outcomes were variable.

Our study's main strength is that we have identified cancer transmissions and non-transmissions using data linkage to a population-based cancer registry and other administrative health records to supplement transplant registry records. Previous population-wide studies of donors and recipients have demonstrated a very low risk of cancer transmission. One study from the US reported transmission rates of 0.012% among transplant procedures and 0.025% among donors [14], while another study in the UK reported slightly higher rates of 0.05% among transplant procedures and 0.1% among donors [15]. However, these studies relied only on cancers reported to transplant registries (not cancer registries), and without access to donor records some donor-transmitted cancers may not have been recognized. This may explain why their transmission rates are lower than our observed rates.

Recipient outcomes from donor kidneys with a tumor discovered during organ recovery that is resected before transplant (restored kidney transplant) have been studied previously. For small renal cell carcinomas, guidelines suggest the risk of transmission after tumor resection is minimal (<0.1%) for tumors ≤1 cm, or low (0.1–2%) for tumors 1–2.5 cm [8]. A 2018 systematic review found no cancer recurrences after 5 years post-transplant follow-up of 107 patients from 17 studies [26]. One included study noted a cancer recurrence 9 years post-transplant; however, it was not reported whether this was donor-transmitted or donor-derived [27]. This contrasts with our study, in which we observed three transmissions in 16 recipients from 12 donors with resected kidney tumors. While previous studies only monitored recipients of resected kidneys, we also included recipients of other organs, as well as recipients of donors whose tumor-affected kidney was discarded rather than resected. This accounted for one additional transmission to a double lung recipient.

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Previous studies have also focused on transmission rates from specific cancers, with CNS tumors of particular interest because of a theoretical risk of transmission. We did not find any cases of transmission of a CNS tumor, which aligns with earlier findings in Australia [16] and the UK [17]. This is despite some brain malignancies (e.g., glioblastoma) being considered intermediate (2–10%) risk of transmission in TSANZ and other guidelines [8,9,11,28].

This study benefited from a linked dataset with complete population coverage, which provides confidence that most transmissible cancers have been captured. Our use of other SAFEBOD datasets to supplement the CCR (such as hospitalizations and transplant registries) ensures that all transmissions have been included. In fact, we found several donor cancers that were not notified to the CCR and would have been missed had we relied on CCR data alone.

Nevertheless, some donor cancers may have been missed if they were diagnosed interstate, prior to 1972, or in a living donor post-transplant and after 2013. This means non-transmissions may have been underestimated. Similarly, we could not ascertain transmissions to recipients out of state or diagnosed after 2013. Additionally, nearly all donor cancers in our cohort were recognized by clinicians at the time they were accepted for donation. These donors have been carefully selected for transplantation in a risk-averse clinical setting; hence, our observed transmission rate is likely an underestimate of the risk of transmission from a donor with past or current cancer. Only one donor in our cohort had a cancer that was not known to clinicians at the time of donation (a thyroid cancer notified to the CCR 34 years prior).

Our reliance on population cancer registry and administrative datasets meant that clinical and histopathological information was not available for interrogation. We were unable to ascertain the size or grade of most cancers we identified, which limited our ability to make clinical recommendations for individual donor cancers. Instead, we have relied on data extracted from original pathology reports by trained coders at the NSW CCR, and our findings remain relevant at the population level.

These results support safe use of carefully selected donors with a past or current cancer for transplantation. We have added to the evidence base which could inform further development and refinement of guidelines for organ donation from donors with a past or current cancer [8]. Considering the variability in recipient outcomes following cancer transmission, our findings encourage incorporating patient preferences into decisions to accept or decline an offered organ to ensure the risks of accepting a transplant from a donor with cancer are balanced against the risks of remaining on an organ waiting list. Future work will build on these findings to evaluate the economic costs and benefits of increasing organ donation through accepting more donors with a risk of cancer transmission.

Conclusions

Overall, cancer transmission via organ transplantation is rare. Kidney cancers discovered during organ recovery posed the greatest risk of transmission, but non-transmission was nevertheless the most likely outcome. Donors with a past or current cancer who are carefully screened may be safe for transplantation.

Authorship

JAH: participated in research design, writing of the paper, performance of the research, and data analysis. CMV: participated in performance of the research and writing of the paper. MW: participated in performance of the research and writing of the paper. KMJW: participated in writing of the paper. PJK: participated in research design, performance of the research, and writing of the paper. NDLM: participated in research design and writing of the paper. BMR: participated in research design and writing of the paper. KW: participated in research design and writing of the paper. ACW: participated in research design, performance of the research, and writing of the paper.

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Conflict of interest

The authors of this manuscript have no conflicts of interest to disclose

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Data availability statement

The data that support the findings of this study are available from the NSW Ministry of Health. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the authors with the permission of the NSW Ministry of Health.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Cancer transmissions and non-transmissions from NSW organ transplant procedures 2000–2012, sorted by cancer site, donation pathway, and year of transplantation.

Table S2. Number of donors with cancer, transplant procedures, transmissions, and non-transmissions in each sensitivity analysis scenario.

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