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Australia and New Zealand Islet and Pancreas Transplant Registry Annual Report 2018—Islet Donations, Islet Isolations, and Islet Transplants

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on behalf of the Australian Islet-cell Transplant consortium

Background. This is an excerpt from chapter 4 of the annual registry report from the Australia and New Zealand islet and pancreas transplant registry. The full report is available at http://anziptr.org/reports/. **Methods.** We report data for all allogeneic islet isolation and transplant activity from 2002 to end 2017. Solid organ pancreas transplantation activity is reported separately. New Zealand does not have an islet transplant program. Data analysis was performed using Stata software version 14 (StataCorp, College Station, TX). **Results.** From 2002 to 2017, a total of 104 allogeneic islet transplants were performed in 62 recipients. **Conclusions.** The number of islet transplants performed in Australia was slightly lower in 2017 but continues to increase over time.

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Overview of Islet Transplantation

Islet transplants are a treatment for type 1 diabetics who have hypoglycemic unawareness and/or severe metabolic instability, are sensitive to insulin, but who have minimal or no kidney impairment. Pancreatic islets are isolated from whole donor pancreas organs and are infused into the liver of transplant recipients via the portal vein. Islet transplant recipients generally require more than 1 islet transplant to become insulin-independent.

Data for islet transplant donors and recipients in Australia are still sparse. The islet transplant program started in 2002. There are 2 islet isolation facilities in Australia; St Vincent's Hospital Melbourne in Victoria, and Westmead Hospital in New South Wales. There are 3 active islet transplant centers: the National Pancreas Transplant Unit at Westmead Hospital, St Vincent's Hospital Melbourne, and the Royal Adelaide Hospital. There is no islet transplant program in New Zealand.

We have only reported islet donors and procedures that were intended to be used for an islet transplantation and

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The authors declare no conflicts of interest.

The operation of this registry is legally mandated by the Australian Organ and Tissue Authority (OTA), hence institutional review board approval was not required.

A.C.W. is the registry executive officer. J.H. is the data analyst. P.F.A. is the data interpreter and article editor. W.J.H. is the data interpreter and article editor. T.R. is the data interpreter and article editor. C.D. is the data interpreter and article editor. N.R. is the data interpreter and article editor. D.G. is the data interpreter and article editor. M.L. is the data interpreter and article editor. T.L. is the data interpreter and article editor. P.J.K. is the biostatistics consultant.

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TABLE 1.

Referrals for allogeneic islet transplant during 2017 by state of residence and transplant center they were referred to

State of residence	Westmead New South Wales	St. Vincent's Victoria	Royal Adelaide South Australia	Total
New South Wales	9	0	0	9
Victoria	0	15	0	15
Queensland	1	0	0	1
South Australia	0	0	6	6
Western Australia	1	0	1	2
Tasmania	0	0	0	0
Australian Capital Territory	0	0	0	0
Northern Territory	0	0	0	0
Total	11	15	7	33

not islet isolation procedures that were undertaken for research purposes only. Some donor isolations intended for transplantation did not proceed to transplantation, generally because the pancreas processing failed to meet release criteria, with the major reason being insufficient concentrations of islet cells.

Islet Waiting List Activity

The islet program waiting list is intentionally not long. Table 1 shows the number of patients referred for an islet transplant in 2017 by state of residence and the transplant center they were referred to. Table 2 shows the number of patients accepted onto an islet waiting list during 2017, whereas Table 3 shows the islet waiting list activity over time.

Islet Isolations

Islet isolation procedures follow good manufacturing procedure guidelines as set out by the Australian Therapeutic Goods Administration. The decision to proceed with transplantation is made once release criteria are met. Release criteria establish quality and quantity of the isolation and include absence of bacteria, absence of endotoxin, and a minimum concentration of 4000 IEQ/kg. Isolations occur at 1 of 2 dedicated isolation facilities at Westmead (Sydney) and St. Vincent's Institute (Melbourne). Islet preparations that meet release criteria may be transplanted locally or transported to 1 of the other 2 centers for transplantation, depending on patient and islet characteristics. A summary of islet cell isolation activity by center and year is presented in Table 4.

The donor characteristics of islet cell donor isolations are presented in Table 5. Donor characteristics are influenced in part by the Australian donor pancreas allocation policy

TABLE 2.

Patients accepted onto a waiting list for an allogeneic islet transplant during 2017 by state of residence and transplant center they were referred to

State of residence	Westmead New South Wales	St. Vincent's Victoria	Royal Adelaide South Australia	Total
New South Wales	4	0	0	4
Victoria	0	4	0	4
Queensland	0	0	0	0
South Australia	0	0	3	3
Western Australia	0	0	0	0
Tasmania	0	0	0	0
Australian Capital Territory	0	0	0	0
Northern Territory	0	0	0	0
Total	4	4	3	11

TABLE 3.

Islet waiting list status over time; Westmead Hospital (New South Wales), St Vincent's Hospital (Victoria), Royal Adelaide Hospital (South Australia)

	Patients (n)			
	2017	2016	2015	2014
Waiting list activity				
Active list at beginning of year	15	13	12	7
Added to active list during the year	16	12	8	11
First transplant	10	7	6	9
Second transplant	2	5	4	2
Third transplant	5	0	1	0
Removed from active list during year	10	8	13	11
First transplant	4	3	11	9
Second transplant	3	6	6	4
Third transplant	5	0	1	0
Death while active on list	0	0	0	1
Death within 12 months of removal from list	0	0	0	0
Active waiting list at the end of year	12	15	13	12
Transplants to waiting list				
Recipients	10	1	13	9
Transplants	12	1	16	10
Under consideration but not active on list				
Eligible	8	9	3	4
Delay	5	1	4	1
Withdrawn	1	2	12	11
Long-term follow-up	0	1	0	0
No decision	4	1	0	0
Death	0	0	1	1
Other reasons	4	6	7	3
Referred but declined for islet transplantation				
Not eligible	23	19	8	16

Includes simultaneous islet kidney transplants. Some patients with multiple transplants in the same year were added and removed multiple times.

TABLE 4.

Summary of allogeneic islet cell isolation activity, for all centers in Australia

Activity	2017	2002-2016	Total
Westmead (New South Wales)			
Pancreata donations discarded before isolation	3	3	6
Islet isolations	13	237	250
Islet isolations used for transplant	7	53	60
Islet isolations discarded	6	184	190
Islet recipients	6	33	37
St. Vincent's (Victoria)			
Pancreata donations discarded before isolation	0	4	4
Islet isolations	10	128	138
Islet isolations used for transplant	5	39	44
Islet isolations discarded	5	89	94
Islet recipients	4	24	25

Some recipients with multiple transplants have received islets from both Westmead and St. Vincent's.

TABLE 5.

Donor characteristics for allogeneic islet isolations (all centers)

	Patients (n)		
	2017	2002-2016	Total
Total	23	365	388
Age			
Mean (SD)	41.8 (11.7)	46.3 (13.0)	46.1 (13.0)
0-24	4	28	32
25-34	2	42	44
35-44	5	70	75
45+	12	224	236
Unknown	0	1	1
Sex			
Female	14	157	171
Male	9	205	214
Unknown	0	0	0
BMI, kg/m^2			
Mean (SD)	30.4 (8.0)	28.7 (6.3)	28.8 (6.5)
Underweight (<18.5)	0	3	3
Normal weight (18.5-24)	7	109	116
Overweight (25-29)	5	120	125
Obese (30+)	11	132	143
Unknown	0	1	1
State of residence			
New South Wales	6	119	125
Victoria	10	110	120
Queensland	6	29	35
South Australia	1	69	70
Western Australia	0	15	15
Tasmania	0	13	13
Australian Capital Territory	0	2	2
Northern Territory	0	6	6
Unknown	0	2	2
Donor type			
DBD	23	349	372
DCD	0	16	16
Unknown	0	0	0
Donor mode of death			
Cerebral hypoxia/ischemia	3	47	50
Cerebral infarct	1	21	22
Intracranial hemorrhage	16	163	179
Nonneurological condition	2	41	43
Other neurological condition	1	6	7
Traumatic brain injury	0	33	33
Unknown	0	46	46
Days ventilated before donation			
Mean (SD)	2.9 (1.7)	3.0 (2.3)	3.0 (2.3)
Alcohol consumption			
Current	11	54	65
Former	0	3	3
Never	12	151	163
Unknown	0	157	157
Smoking history			
Current	11	88	99
Former	2	4	6
Never	9	159	168
Unknown	1	114	115
Cultural and ethnic group			
Indigenous Australian	0	1	1
Maori or Pacific Islander	0	1	1
White	15	234	249
North East Asian (Chinese)	0	1	1
South East Asian	1	3	4
South and Central Asian (Indian)	0	1	1
Middle Eastern or North African	0	0	0
Other	0	2	2
Unknown	7	122	129
Blood group			
O	18	187	205
A	2	139	141
B	0	26	26
AB	1	12	13
Unknown	2	1	3
CMV serology			
IgG positive	17	138	155
IgG negative	4	115	119
Unknown	2	72	74

DBD, donor after brain death; DCD, donor after circulatory death; IgG, immunoglobulin G; SD, standard deviation; BMI, body mass index.

which allocates pancreata for both pancreatic islet isolation and for whole pancreas transplantation. This policy is available at https://www.tsanz.com.au/organallocationguidelines/index.asp. Please note that solid organ pancreas transplant activity is also reported by the registry, and an extract is also published for 2017[1] and for 2018.[2]

Donors who provided pancreata that resulted in islet isolations that proceeded to transplantation are summarized in Table 6.

Islet Transplant Recipients

Figure 1 illustrates the number of islet cell transplants in Australia between 2002 and 2017. The transplants were performed in Westmead (58), St Vincent's (29), and Royal Adelaide (17) Hospitals. In 2017, 7 transplants were performed at Westmead, 5 at St Vincent's and none at the Royal Adelaide.

The characteristics of donor and recipient matches according to sex and blood group distributions for all centers are presented in Table 7 and Table 8.

State of residence of recipients receiving an islet transplant in 2017, by the order of their transplant is presented in Table 9.

The states of residence of donors and recipients for each transplantation are shown in Table 10, stratified by the transplant center.

Characteristics of islet recipients over time are shown in Table 11.

The time from activation on the waiting list to first islet transplant for 2002 to 2017 is presented in Figure 2. Data were available for 91 patients added to the waiting list before December 31, 2017, 56 of whom have received at least 1 transplant during this period. However, the date of waitlisting is complete for only 50 patients, 35 of whom received at least 1 transplant as of December 31, 2017. Recipients waited a median of 0.98 years from activation on the waiting

TABLE 6.

Donor characteristics for allogeneic islet isolations which resulted in transplantation in 2017

	Donors (n)		
	Westmead Hospital	St. Vincent's Hospital	Total
Total	7	4	11
Age			
Mean (SD)	40.0 (14.3)	47 (3.7)	42.5 (11.8)
0-24	2	0	2
25-34	1	0	1
35-44	1	1	2
45+	3	3	6
Sex			
Female	3	2	5
Male	4	2	6
BMI kg/m^2			
Mean (SD)	31.2 (16.1)	27.6 (3.1)	29.9 (12.7)
Underweight (<18.5)	1	0	1
Normal weight (18.5-24)	1	1	2
Overweight (25-29)	1	2	3
Obese (30+)	4	1	5
State of residence			
New South Wales	2	0	2
Victoria	2	4	6
Queensland	2	0	2
South Australia	0	0	0
Western Australia	1	0	1
Tasmania	0	0	0
Australian Capital Territory	0	0	0
Northern Territory	0	0	0
Donor type			
DBD	7	4	11
DCD	0	0	0
Donor mode of death			
Cerebral hypoxia/ischemia	0	1	1
Cerebral infarct	1	0	1
Intracranial hemorrhage	4	3	7
Nonneurological condition	2	0	2
Other neurological condition	0	0	0
Traumatic brain injury	0	0	0
Days ventilated before donation			
Mean (SD)	3.3 (1.8)	3.1 (1.7)	3.2 (1.7)
Cold ischemia time, h			
Mean (SD)	8.6 (5.0)	4.9 (1.0)	7.3 (4.3)
Alcohol consumption			
Current	2	4	6
Former	0	0	0
Never	3	0	3
Unknown	2	0	2
Smoking history			
Current	2	4	6
Former	1	0	1
Never	3	0	3
Unknown	1	0	1
Cultural and ethnic group			
Indigenous Australian	0	0	0
Maori or Pacific Islander	0	0	0
White	7	4	11
North East Asian (Chinese)	0	0	0
South East Asian	0	0	0
South and Central Asian (Indian)	0	0	0
Middle Eastern or North African	0	0	0
Other	0	0	0
Blood group			
O	7	0	7
A	0	4	4
B	0	0	0
AB	0	0	0
CMV serology			
IgG positive	5	2	7
IgG negative	2	2	4

SD, standard deviation; BMI, body mass index; DBD, donor after brain death; DCD, donor after circulatory death; IgG, immunoglobulin G.

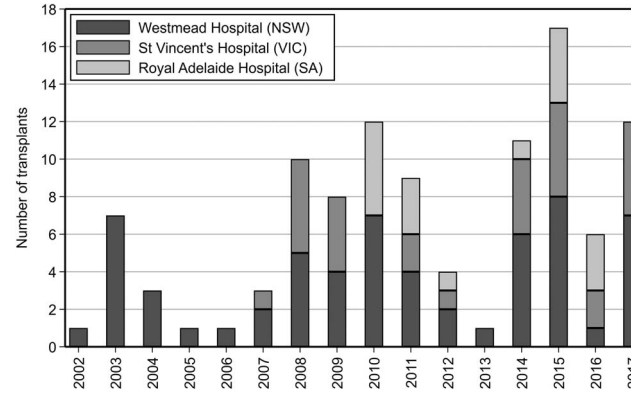

FIGURE 1. Allogeneic islet transplant activity 2002 to 2017, by transplanting center.

list to receiving their first transplant (interquartile range, 0.62-2.18 years).

The time from first to second islet transplant for 2002 to 2017, truncated at 5 years, is presented in Figure 3. Recipients waited a median of 0.80 years from first transplant to receiving a second transplant (interquartile range, 0.32-13.63 years).

The time from second to third islet transplant for 2002 to 2017, truncated at 5 years, is presented in Figure 4. The median time from second transplant to third transplant has not yet been reached (25th percentile, 1.33 years), likely due to many recipients not requiring a third transplant.

TABLE 7.

Cross tabulation of recipient and donor sex, 2002-2017

	Donor sex		
Recipient sex	Female	Male	Total
Female	29	41	70
Male	14	20	34
Total	46	63	104

This includes 60 isolations at Westmead, and 44 isolations at St. Vincent's only. Recipients could receive more than 1 transplant and therefore may be duplicated in numbers.

TABLE 8.

Cross tabulation of recipient and donor blood groups, 2002-2017, for allogeneic islet transplants undertaken in Australia

	Donor blood group				
Recipient blood group	O	A	B	AB	Total
O	32	0	0	0	32
A	15	35	0	0	50
B	3	0	8	0	11
AB	0	4	1	4	9
Unknown	2	0	0	0	2
Total	52	39	9	4	104

This includes 60 isolations at Westmead, and 44 isolations at St. Vincent's only. Recipients could receive more than 1 transplant and therefore may be duplicated in numbers.

TABLE 9.

Allogeneic islet transplant recipients by state of residence and number of transplants received (all centers, 2017)

Recipient state of residence	1st	2nd	3rd	Total
New South Wales	3	3	1	7
Victoria	1	0	3	4
Queensland	0	0	0	0
South Australia	0	0	0	0
Western Australia	0	0	0	0
Tasmania	0	0	0	0
Australian Capital Territory	0	0	0	0
Northern Territory	0	0	0	0
Unknown	0	0	1	1
Total	4	3	5	12

The distribution of C-peptide measurements over time after first islet infusion is presented in Figure 5. The normal range for a nondiabetic person in the fasting state is approximately 0.7 to 1.9 ng/mL.

The impact of hypoglycemia on an individual can be gauged by a symptom score to measure frequency, severity and degree of unawareness of hypoglycemia experienced by diabetics. The Edmonton hyposcore is a numeric score based on day to day measurements of blood glucose by an individual with diabetes over a 4-week period. The higher the HYPO score, the worse the impact of hypoglycemia for an

TABLE 11.

Characteristics of allogeneic islet cell transplant recipients in Australia by year of first transplant

	Patients (n)		
	2017	2002-2016	Total
Total	4	58	62
Age, y			
Mean (SD)	48.3 (10.8)	58.7 (11.0)	54.5 (11.6)
0-24	0	0	0
25-34	0	1	1
35-44	1	5	6
45+	3	0	3
Unknown	0	52	52
Sex			
Female	2	41	43
Male	2	17	19
State of residence			
New South Wales	3	21	24
Victoria	1	14	15
Queensland	0	1	1
South Australia	0	13	13
Western Australia	0	0	0
Tasmania	0	1	1
Australian Capital Territory	0	0	0
Northern Territory	0	0	0
Unknown	0	8	8
Blood group			
O	1	11	12
A	3	15	18
B	0	3	3
AB	0	2	2
Unknown	0	27	27
No. transplants per recipient			
1	3	14	17
2	1	24	25
3	0	20	20
Wait time from listing to first transplant, y			
0-1	3	20	23
1-2	0	3	3
2+	1	4	5
Unknown	0	31	31
Insulin-independent posttransplant			
Yes	0	18	18
No	4	40	44

Insulin independence defined as being free from insulin use for 14 or more consecutive days. SD, standard deviation.

TABLE 10.

Cross-tabulation of allogeneic islet donor and recipient state of residence 2002-2017

	Donor state of residence								
Recipient state of residence	New South Wales	Victoria	Queensland	South Australia	Western Australia	Tasmania	Australian Capital Territory	Northern Territory	Total
New South Australia	16	9	2	4	0	0	0	0	31
Victoria	0	21	2	5	0	2	0	1	31
Queensland	5	2	1	0	0	0	0	0	8
South Australia	5	7	1	9	1	2	0	0	25
Western Australia	3	0	2	1	0	0	0	0	6
Tasmania	0	0	1	1	0	0	0	0	2
Australian Capital Territory	0	0	0	1	0	0	0	0	1
Northern Territory	0	0	0	0	0	0	0	0	0
Total	29	39	9	21	1	4	0	1	104

This includes 58 recipients at Westmead, 29 recipients at Melbourne, and 17 recipients at Royal Adelaide. Recipients could receive more than 1 transplant and therefore may be duplicated in numbers.

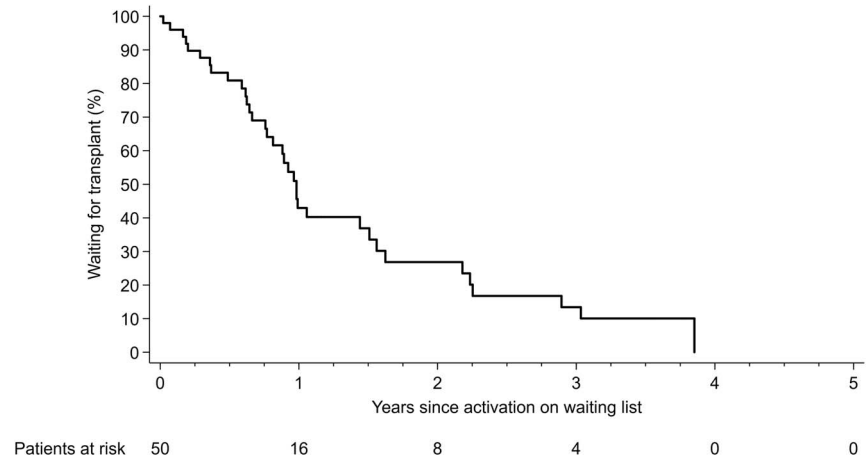

FIGURE 2. Time from activation on a waiting list to first allogeneic islet transplant.

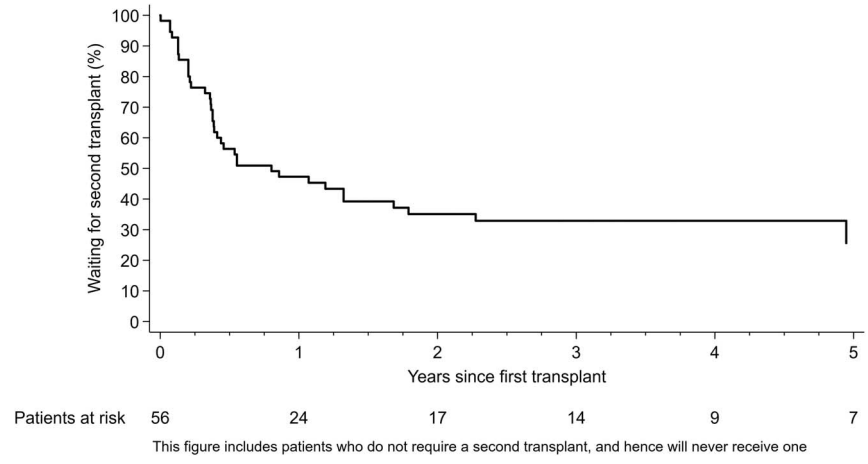

FIGURE 3. Time from first to second allogeneic islet transplant.

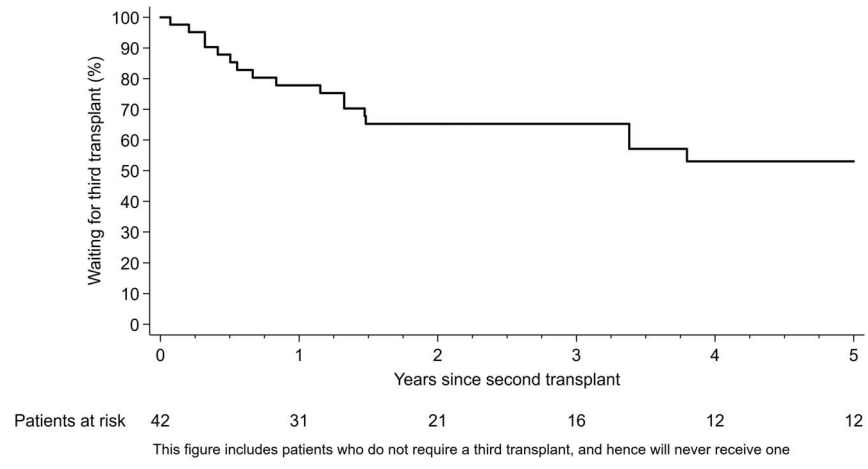

FIGURE 4. Time from second to third allogeneic islet transplant.

individual. The full HYPO score scale is presented in the article by Ryan et al (Diabetes 2004;53:955-962).

The distribution of HYPO score measurements over time after first islet infusion (but before second islet infusion) is presented in Figure 6; the distribution of HYPO score measurements over time after second islet infusion (but before third islet infusion) is presented in Figure 7, and the distribution of HYPO score measurements over time after third islet infusion is presented in Figure 8.

The distribution of glycosylated hemoglobin A1c (HbA1c) measurements over time after first islet infusion (but before second islet infusion) is presented in Figure 9, the distribution of HbA1c measurements over time after second islet infusion (but before third islet infusion) is presented in Figure 10, and

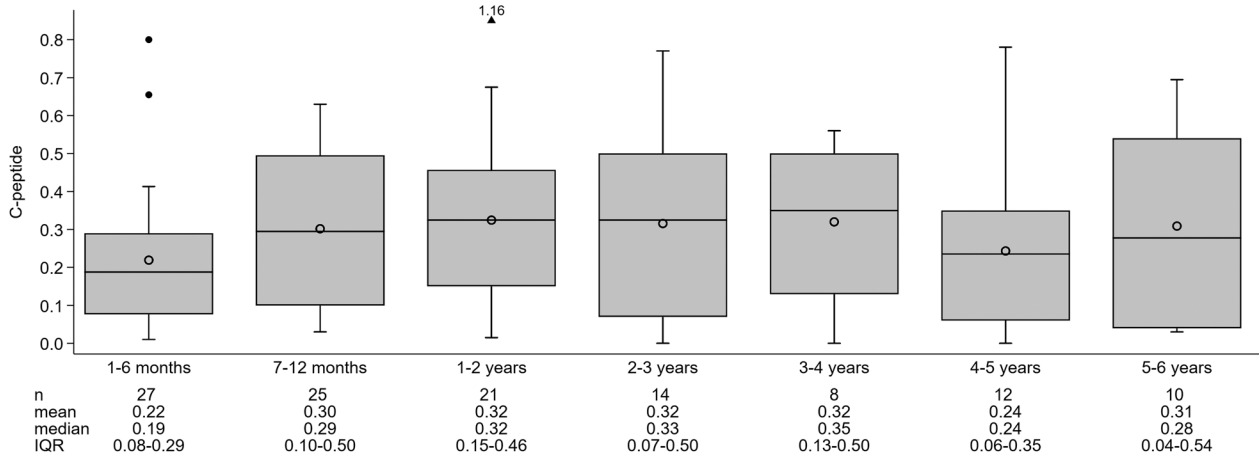

FIGURE 5. Posttransplant distribution of C-peptide over time after at least 1 allogeneic islet infusion.

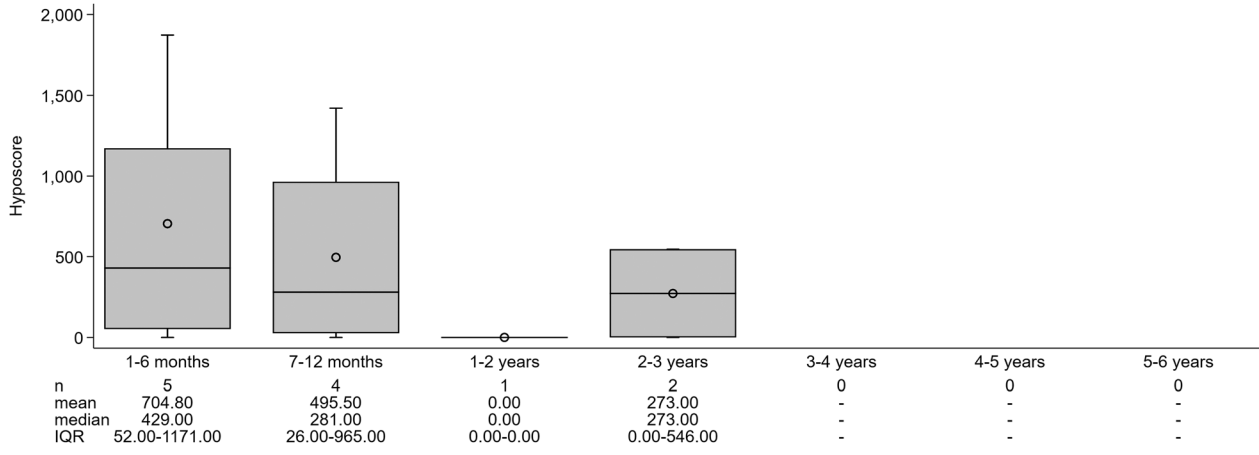

FIGURE 6. Posttransplant distribution of HYPO score over time since first allogeneic islet infusion.

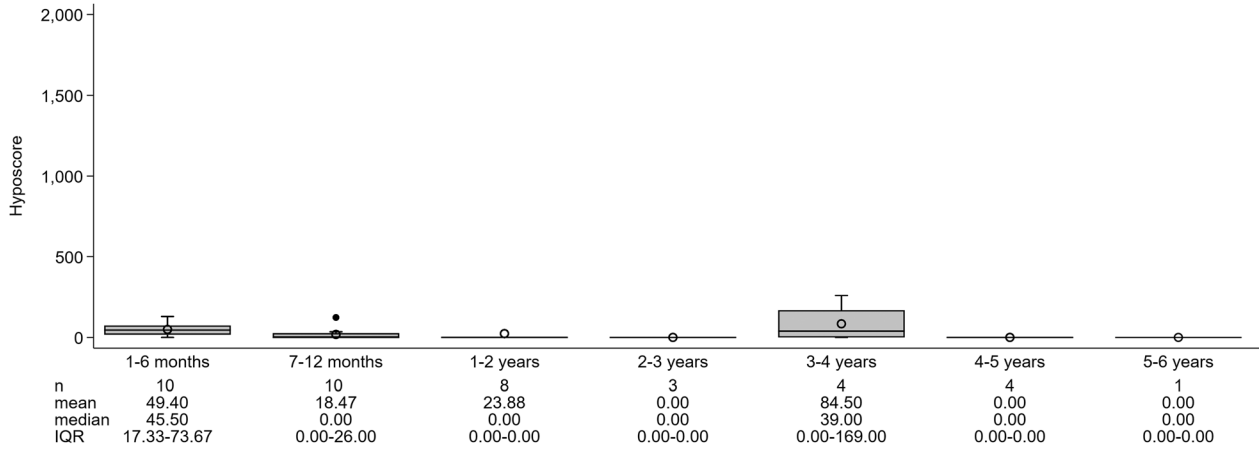

FIGURE 7. Posttransplant distribution of HYPO score over time since second allogeneic islet infusion.

the distribution of HbA1c measurements over time third first islet infusion is presented in Figure 11.

Insulin independence is defined as a person being free from insulin use for at least 14 days. Current registry data is incomplete, but shows there are at least 18 patients who have achieved insulin independence; 1 patient after their first transplant, 9 patients after their second transplant, and 8 patients after their third transplant. The duration of insulin independence from the time insulin was first ceased for 2002 to 2017 is presented in Figure 12.

The Future: Reporting Islet Transplant Activity and the ANZIPTR Registry

The ANZIPTR registry is a clinical quality registry, reporting annually, on pancreas and islet transplant activity

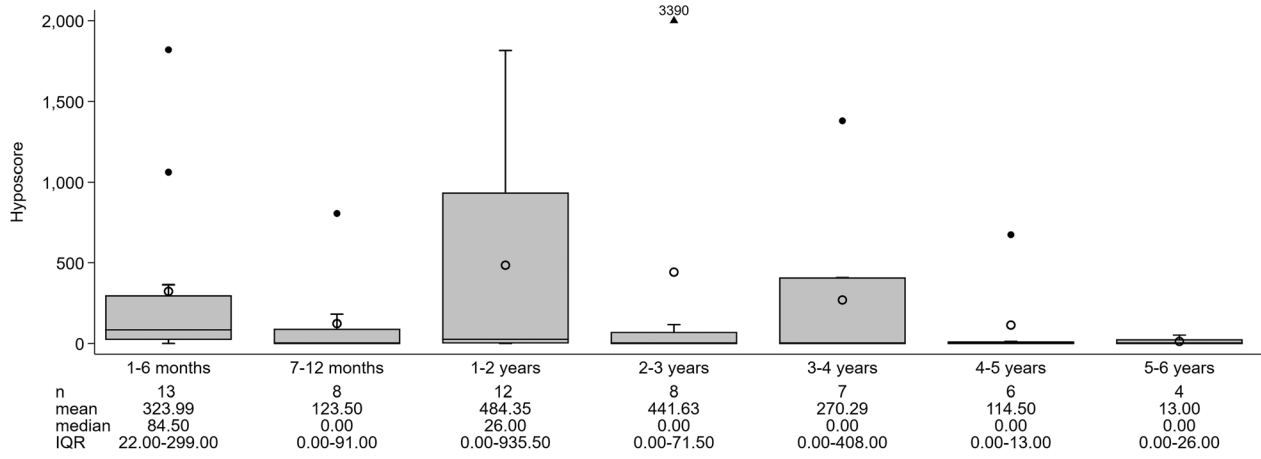

FIGURE 8. Posttransplant distribution of HYPO score over time since third allogeneic islet infusion.

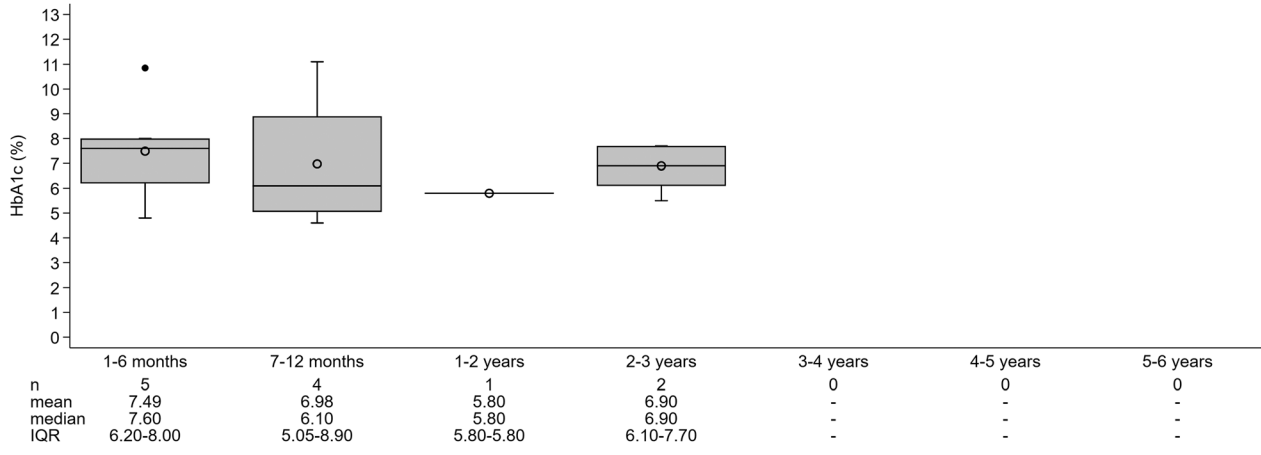

FIGURE 9. Posttransplant distribution of hemoglobin A1c (HbA1c; %) over time since first allogeneic islet infusion.

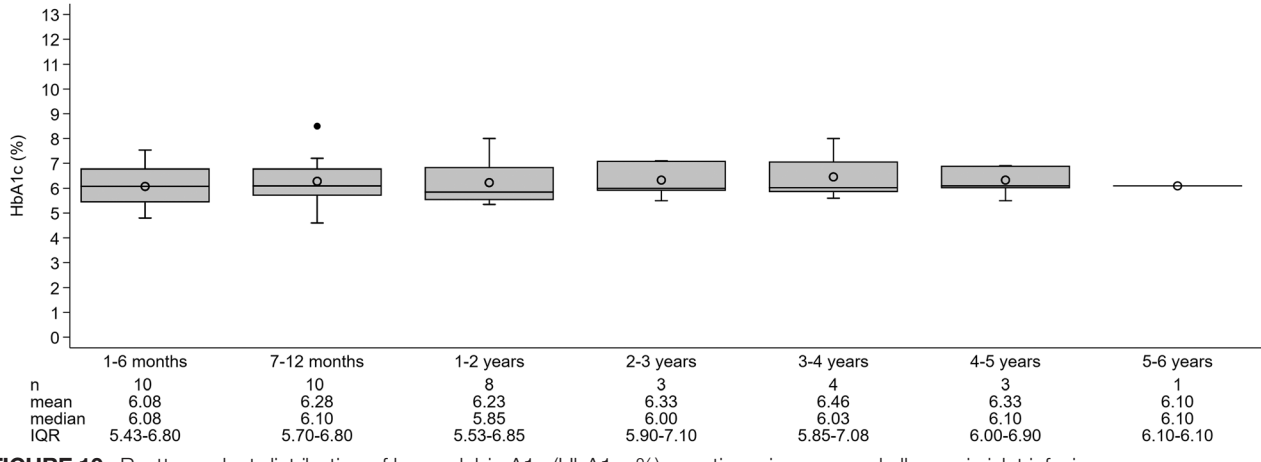

FIGURE 10. Posttransplant distribution of hemoglobin A1c (HbA1c; %) over time since second allogeneic islet infusion.

in Australia and New Zealand. To learn more about the ANZIPTR registry and to see full annual reports since 2005, please see http://anziptr.org.

It is important to note that registry data seeks to be both inclusive and population based, and that data are collected in real time. The data on which this report is based were data-locked in March 2018. However, the database is dynamic, with regular data interrogation and cleaning, as part of the reporting process, and so this report may not entirely reflect that data today. Changes and corrections are also made as the data are used, when any omissions or errors are identified, and clarification is sought from the contributing center. We constantly work to include more informative analyses and to improve data quality.

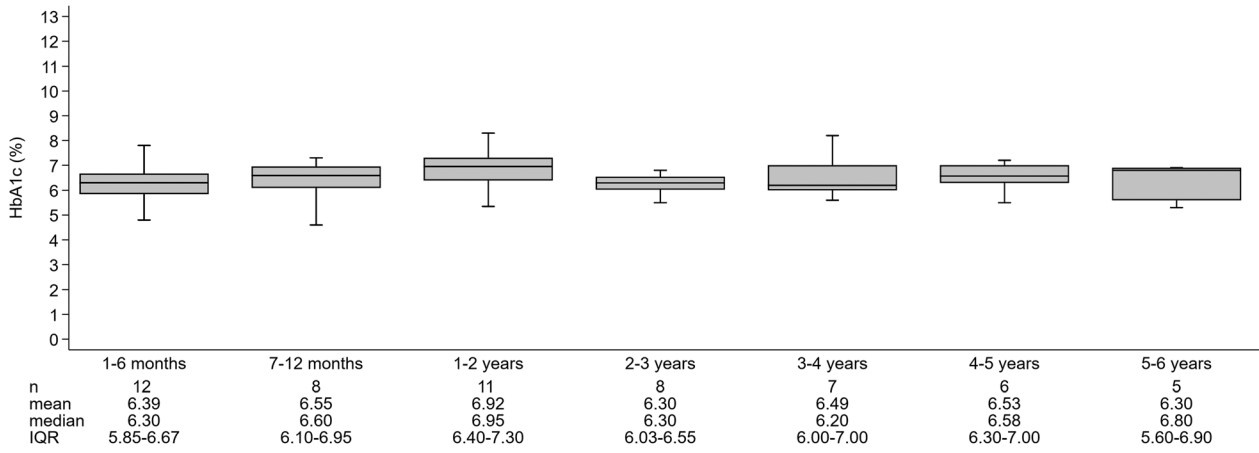

FIGURE 11. Posttransplant distribution of hemoglobin A1c (HbA1c; %) over time since third allogeneic islet infusion.

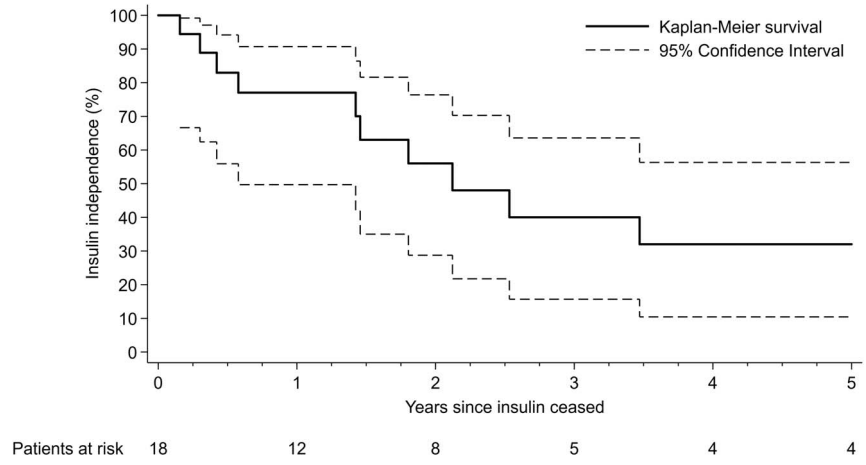

FIGURE 12. Posttransplant duration of insulin independence from time first ceased.

Islet transplantation in Australia is still developing, and so the numbers of recipients are small. Given the small numbers of recipients contributing data, please interpret results with caution, and in knowledge that random variability may be substantial with small sample sizes.

Future reports will endeavor to include more and longer-term outcome data and to include separate analyses on the small number of people undergoing kidney-with-islet procedures in Australia.

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