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Australia and New Zealand Islet and Pancreas Transplant Registry Annual Report 2019: Islet Donations, Islet Isolations, and Islet Transplants

Angela C. Webster, PhD,^{1,2} James A. Hedley, MBIostat,² Patricia F. Anderson, MN,¹ Wayne J. Hawthorne, PhD,^{1,3} Toni Radford, DipN,⁴ Chris Drogemuller, PhD,^{4,5} Natasha Rogers, PhD,^{1,3} David Goodman, PhD,^{6,7} Melissa H. Lee, MBBS,^{7,8} Thomas Loudovaris, PhD,⁹ and Patrick J. Kelly, PhD,² on behalf of the Australian Islet-cell Transplant consortium

OVERVIEW OF ISLET TRANSPLANTATION

Islet transplants are a treatment for patients with type 1 diabetes who have hypoglycemic unawareness and/or severe metabolic instability and are sensitive to insulin,

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¹ Centre for Transplant and Renal Research, Westmead Hospital, NSW, Australia.

² Sydney School of Public Health, Faculty of Health and Medicine, University of Sydney, NSW, Australia.

³ Westmead Clinical School, Faculty of Health and Medicine, University of Sydney, NSW, Australia.

⁴ Central Northern Adelaide Renal and Transplantation Service (CNARTS), The Royal Adelaide Hospital, SA, Australia.

⁵ Department of Medicine, Faculty of Health and Medical Sciences, University of Adelaide, SA, Australia.

⁶ Department of Nephrology, St Vincent's Hospital Melbourne, Vic, Australia.

⁷ Department of Medicine, St Vincent's Hospital Melbourne, University of Melbourne, Vic, Australia.

⁸ Department of Endocrinology and Diabetes, St Vincent's Hospital Melbourne, Vic, Australia.

⁹ St Vincent's Institute of Medical Research, St Vincent's Hospital Melbourne, Vic, Australia.

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

Correspondence: Angela C. Webster, PhD, Centre for Transplant and Renal Research, Australia and New Zealand Islet and Pancreas Transplant Registry, Westmead, NSW 2145, Australia. (angela.webster@sydney.edu.au).

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but who have minimal or no kidney impairment. Whole donor pancreas organs are processed aiming to produce a concentrate of islet cells >4000 islet equivalent numbers/kg in a volume of <9 mL. Islet transplant recipients generally require >1 islet transplant to become insulin independent.

Data for islet transplant donors and recipients in Australia are still sparse.¹ 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. This report contains information about allogeneic islet transplants (ie, islets from a deceased donor).

In this year's report, we have added as much data as we have available on the islet program in Australia to date and expanded description to capture the waiting list for islet transplants, donor, and recipient characteristics. We have only reported islet donors and procedures that were intended to be used for an islet transplantation and not islet isolation procedures that were undertaken only for research purposes. Some donor isolations intended for transplantation did not proceed to transplantation, generally because the pancreas processing failed set release criteria, with the major reason being insufficient concentration 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 2018 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 2018, whereas Table 3 shows the islet waiting list activity over time.

ISLET ISOLATIONS

Sometimes when pancreas donations are processed for islet transplantation, the resulting islets do not meet transplant release criteria. The decision to proceed with

TABLE 1.**Referrals for allogenic islet transplant during 2018 by state of residence and transplant center**

State of residence	Westmead	St Vincent's	Royal Adelaide	Total
New South Wales	9	0	0	9
Victoria	0	14	0	14
Queensland	3	0	0	3
Western Australia	1	0	0	1
South Australia	0	0	2	2
Tasmania	0	0	0	0
Australian Capital Territory	0	0	0	0
Northern Territory	0	0	0	0

TABLE 2.**Patients accepted onto a waiting list for an allogenic islet transplant during 2018 by state of residence and transplant center**

State of residence	Westmead	St Vincent's	Royal Adelaide	Total
New South Wales	9	0	0	9
Victoria	0	5	0	5
Queensland	3	0	0	3
Western Australia	1	0	0	1
South Australia	0	0	2	2
Tasmania	0	0	0	0
Australian Capital Territory	0	0	0	0
Northern Territory	0	0	0	0

TABLE 3.**Islet waiting list status over time: Westmead Hospital (NSW), St Vincent's Hospital (VIC), and Royal Adelaide Hospital (SA)**

	Patients (n)			
	2018	2017	2016	2015
Waiting list activity				
Active list at beginning of y	14	8	3	6
Added to active list during the y	14	17	16	17
First transplant	10	11	9	13
Second transplant	6	4	8	7
Third transplant	0	3	0	1
Removed from active list during y	10	10	10	19
First transplant	8	5	4	16
Second transplant	6	4	8	7
Third transplant	0	3	0	1
Death while active on list	0	0	0	0
Death within 12 mo of removal from list	0	0	0	0
Active waiting list at the end of y	16	14	8	3
Transplants to waiting list				
Recipients	10	10	10	19
Transplants	14	12	12	24
Under consideration but not active on list	10	1	1	1
Referred but declined for islet transplantation	0	0	0	0

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

NSW, New South Wales; SA, South Australia; VIC, Victoria.

TABLE 4.**Summary of allogenic islet cell isolation activity, for all centers in Australia**

Activity	2018	2002–2017	Total
Westmead (New South Wales)			
Pancreata donations discarded before isolation	0	9	9
Islet isolations			
Islet isolations used for transplant	6	48	54
Islet isolations discarded	5	176	181
Islet recipients	5	28	30
St Vincent's (Victoria)			
Pancreata donations discarded before isolation	2	57	59
Islet isolations			
Islet isolations used for transplant	8	44	52
Islet isolations discarded	8	146	154
Islet recipients	6	24	30

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

transplantation is made once release testing is complete and the quality and quantity of islet cells is known. Islet isolation procedures follow good manufacturing procedure guidelines as set out by the Australian Therapeutic Goods Administration. Isolations occur at 1 of 2 dedicated isolation facilities at Westmead (Sydney) and St Vincent's Institute (Melbourne), both associated with their respective local hospitals Westmead and St Vincent's Hospital. Occasionally preparations are sent between Melbourne and Sydney; however, Royal Adelaide Hospital has no islet isolation facility and is dependent on islets from either Westmead or St Vincent's Institute, with the latter being the main provider of islets. A summary of islet cell isolation activity by center and year in presented in Table 4.

TABLE 5.**Donor characteristics for allogenic islet isolations (all centers)**

	Donors (n)		
	2018	2002–2017	Total
Total	29	389	418
Age			
Mean (SD)	50.7 (10.1)	46.1 (13.0)	46.4 (12.9)
0–24	0	33	33
25–34	3	45	48
35–44	4	73	77
45+	22	237	259
Not reported	0	1	1
Sex			
Female	15	168	183
Male	14	218	232
BMI, kg/m ²			
Mean (SD)	27.7 (4.8)	28.8 (6.5)	28.7 (6.4)
Underweight (<18.5)	0	3	3
Normal weight (18.5–24)	13	123	136
Overweight (25–29)	8	130	138
Obese (30+)	8	132	140
Not reported	0	1	1

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TABLE 5. (Continued)

	Donors (n)		
	2018	2002–2017	Total
State of residence			
New South Wales	9	125	134
Victoria	8	120	128
Queensland	2	35	37
Western Australia	2	37	39
South Australia	3	49	52
Tasmania	2	13	15
Australian Capital Territory	3	2	5
Northern Territory	0	5	5
Not reported	0	3	3
Donor type			
Brain dead (DBD)	2	249	251
Circulatory death (DCD)	16	140	156
Donor mode of death			
Cerebral hypoxia/ischemia	8	50	58
Cerebral infarct	3	21	24
Intracranial hemorrhage	14	166	180
Non-neurological condition	1	33	34
Other neurological condition	0	12	12
Traumatic brain injury	2	35	37
Not reported	1	64	65
Days ventilated before donation			
Mean (SD)	3.4 (1.9)	2.9 (2.3)	2.9 (2.3)
Alcohol consumption			
Never	8	35	43
Former	0	5	5
Current	16	208	224
Not reported	5	141	146
Smoking history			
Never	13	87	100
Former	2	19	21
Current	14	174	188
Not reported	0	109	109
Cultural and ethnic group			
Indigenous Australian or Torres Strait Islander	0	1	1
Maori or Pacific Islander	0	1	1
White	28	249	277
North East Asian (Chinese)	0	1	1
South East Asian	1	4	5
South and Central Asian (Indian)	0	1	1
Middle Eastern or North African	0	0	0
Other	0	3	3
Not reported	0	129	129
Blood group			
O	16	206	222
A	10	140	150
B	0	26	26
AB	1	11	12
Not reported	2	6	8
Cytomegalovirus serology			
Negative	13	149	162
Positive	15	125	140
Not reported	1	75	76

BMI, body mass index; DBD, donor after brain death; DCD, donor after circulatory death.

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 that

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>.

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 2018. The transplants were performed in Westmead (68), St Vincent's (30), and Royal Adelaide (18) Hospitals. In 2018, 5 transplants were performed at Westmead, 7 at St Vincent's, and 2 at the Royal Adelaide.

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

State of residence of recipients receiving an islet transplant in 2018, 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 2002–2018 is presented in Figure 2. Data were available for 101 patients added to the waiting list before December 31, 2018, 58 of whom have received at least 1 transplant during this period. However, the date of waitlisting is known for only 59 patients, 21 of whom received at least 1 transplant as of December 31, 2018. The median time to first transplant has not yet been reached (25th percentile: 0.99 y).

The time from first to second islet transplant for 2002–2018 is presented in Figure 3. Recipients waited a median of 1.10 y from first transplant to receiving a second transplant (interquartile range: 0.36–13.63 y).

The time from second to third islet transplant for 2002–2018 is presented in Figure 4. The median time from second transplant to third transplant has not yet been reached (25th percentile: 0.84 y), likely due to many recipients not requiring a third transplant.

The distribution of C-peptide measurements over time after first islet infusion (but before second islet infusion) is presented in Figure 5; the distribution of C-peptide measurements over time after second islet infusion (but before third islet infusion) is presented in Figure 6; and the distribution of C-peptide measurements over time after third islet infusion is presented in Figure 7. The normal range for a person without diabetes is approximately 0.7–3.1 ng/mL.

Occurrence of unpredictable hypoglycemia, particularly if frequent, can impact an individual's quality of life. Ryan et al.² proposed a symptom score to measure frequency, severity, and degree of unawareness of hypoglycemia experienced by patients with diabetes. The HYPO score was stratified by the recorded level of glucose and summed points for the type of symptoms experienced, whether the sufferer recognized the impending hypoglycemia, and whether outside help was needed to recognize or treat each episode. A greater number of points were scored when glucagon was administered, or an ambulance called. The higher the HYPO score, the worse the

TABLE 6.
Donor characteristics for allogenic islet isolations which resulted in transplantation in 2018

	Donors (n)		
	Westmead	St Vincent's	Total
Total	6	8	14
Age			
Mean (SD)	45.2 (8.7)	56.8 (6.8)	51.8 (9.5)
0–24	0	0	0
25–34	1	0	1
35–44	1	0	1
45+	4	8	12
Sex			
Female	3	5	8
Male	3	3	6
BMI, kg/m ²			
Mean (SD)	32.0 (6.9)	26.7 (3.1)	29.0 (5.6)
Underweight (<18.5)	0	0	0
Normal weight (18.5–24)	2	3	5
Overweight (25–29)	0	4	4
Obese (30+)	4	1	5
State of residence			
New South Wales	4	2	6
Victoria	0	5	5
Queensland	1	0	1
Western Australia	0	0	0
South Australia	0	1	1
Tasmania	0	0	0
Australian Capital Territory	1	0	1
Northern Territory	0	0	0
Not reported	0	0	0
Donor type			
Brain dead (DBD)	6	8	14
Circulatory death (DCD)	0	0	0
Donor mode of death			
Cerebral hypoxia/ischemia	0	2	2
Cerebral infarct	2	1	3
Intracranial hemorrhage	4	4	8
Non-neurological condition	0	0	0
Other neurological condition	0	0	0
Traumatic brain injury	0	0	0
Not reported	0	1	1
Days ventilated before donation			
Mean (SD)	3.7 (1.8)	3.8 (2.1)	3.8 (1.9)
Alcohol consumption			
Never	1	0	1
Former	0	0	0
Current	5	8	13
Smoking history			
Never	4	4	8
Former	0	0	0
Current	2	4	6
Cultural and ethnic group			
Indigenous Australian or Torres Strait Islander	0	0	0
Maori or Pacific Islander	0	0	0
White	5	8	13
North East Asian (Chinese)	0	0	0
South East Asian	1	0	1
South and Central Asian (Indian)	0	0	0
Middle Eastern or North African	0	0	0
Other	0	0	0

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TABLE 6. (Continued)

	Donors (n)		
	Westmead	St Vincent's	Total
Blood group			
O	4	6	10
A	2	2	4
B	0	0	0
AB	0	0	0
Cytomegalovirus serology			
Negative	3	2	5
Positive	3	5	8
Not reported	0	1	1

BMI, body mass index; DBD, donor after brain death; DCD, donor after circulatory death.

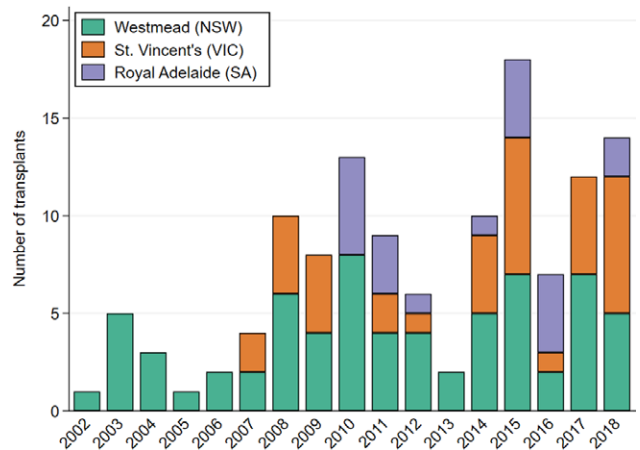


FIGURE 1. Allogenic islet transplant activity 2002–2018, by transplanting center. NSW, New South Wales; SA, South Australia; VIC, Victoria.

TABLE 7.
Cross tabulation of recipient and donor sex, 2002–2018

Recipient sex	Donor sex			Total
	Female	Male	Not reported	
Female	18	20	42	80
Male	3	3	30	36
Total	21	23	72	116

Recipients could receive >1 transplant and therefore may be duplicated in numbers.

TABLE 8.
Cross tabulation of recipient and donor blood groups, 2002–2018, for allogenic islet transplants undertaken in Australia

Recipient blood group	Donor blood group					Total
	O	A	B	AB	Not reported	
O	16	0	0	0	21	37
A	5	13	0	0	41	59
B	3	0	3	0	6	12
AB	0	2	0	1	5	8
Total	24	15	3	1	73	116

Recipients could receive >1 transplant and therefore may be duplicated in numbers.

TABLE 9.**Allogenic islet transplant recipients by state of residence and number of transplants received (all centers, 2018)**

Recipient state of residence	First	Second	Third	Total
New South Wales	1	3	0	4
Victoria	0	0	0	0
Queensland	1	0	0	1
Western Australia	0	0	0	0
South Australia	0	0	0	0
Tasmania	0	0	0	0
Australian Capital Territory	0	0	0	0
Northern Territory	0	0	0	0
Total	2	3	0	5

impact of hypoglycemia for an individual. A HYPO score of 0 equates with no interference in regular life by hypoglycemic episodes. The maximum score per hypoglycemic episode was 198. The distribution of HYPO score measurements over time after first islet infusion (but before second islet infusion) is presented in Figure 8, the distribution of HYPO score measurements over time after second islet infusion (but before third islet infusion) is presented in Figure 9, and the distribution of HYPO score measurements over time after third islet infusion is presented in Figure 10.

The distribution of glycosylated hemoglobin A1c (HbA1c) measurements over time after first islet infusion (but before second islet infusion) is presented in Figure 11; the distribution of HbA1c measurements over time after second islet infusion (but before third islet infusion) is presented in Figure 12; and the distribution of HbA1c measurements over time after third first islet infusion is presented in Figure 13.

Insulin independence is defined as a person being free from insulin use for at least 14 d. There are 20 patients who have achieved insulin independence; 2 patients after their first transplant, 11 patients after their second transplant, and 7 patients after their third transplant. The duration of insulin independence from the time insulin was first ceased for 2002–2018 is presented in Figure 14.

TABLE 11.**Characteristics of allogenic islet cell transplant recipients in Australia by y of first transplant**

	Patients (n)		
	2018	2002–2017	Total
Total	2	55	57
Age			
Mean (SD)	47.5 (20.5)	47.4 (11.4)	47.4 (11.5)
0–24	0	2	2
25–34	1	4	5
35–44	0	14	14
45+	1	35	36
Sex			
Female	0	38	38
Male	2	17	19
State of residence			
New South Wales	1	25	26
Victoria	0	15	15
Queensland	1	1	2
Western Australia	0	4	4
South Australia	0	9	9
Tasmania	0	0	0
Australian Capital Territory	0	1	1
Northern Territory	0	0	0
Blood group			
O	1	19	20
A	1	25	26
B	0	7	7
AB	0	4	4
Number of transplants per recipient			
1	1	14	15
2	1	24	25
3	0	17	17
Wait time from listing to first transplant			
0–1 y	1	14	15
1–2 y	1	2	3
2+ y	0	2	2
Not reported	0	37	37
Insulin independent posttransplant			
Yes	0	20	20
No	2	35	37

Insulin independence defined as being free from insulin use for ≥14 consecutive d.

TABLE 10.**Cross tabulation of allogenic islet donor and recipient state of residence 2002–2018**

Recipient state of residence	Donor state of residence									Total
	NSW	VIC	QLD	WA	SA	TAS	ACT	NT	Not reported	
NSW	0	1	0	0	0	0	0	0	52	53
VIC	0	18	0	1	5	3	0	1	2	30
QLD	0	0	0	0	0	0	0	0	1	1
WA	0	0	0	0	0	0	0	0	8	8
SA	2	7	0	0	4	2	0	0	3	18
TAS	0	0	0	0	0	0	0	0	0	0
ACT	0	0	0	0	0	0	0	0	1	1
NT	0	0	0	0	0	0	0	0	0	0
Total	2	26	0	1	9	5	0	1	67	111

Recipients could receive >1 transplant and therefore may be duplicated in numbers.

ACT, Australian Capital Territory; NSW, New South Wales; NT, Northern Territory; QLD, Queensland; SA, South Australia; TAS, Tasmania; VIC, Victoria; WA, Western Australia.

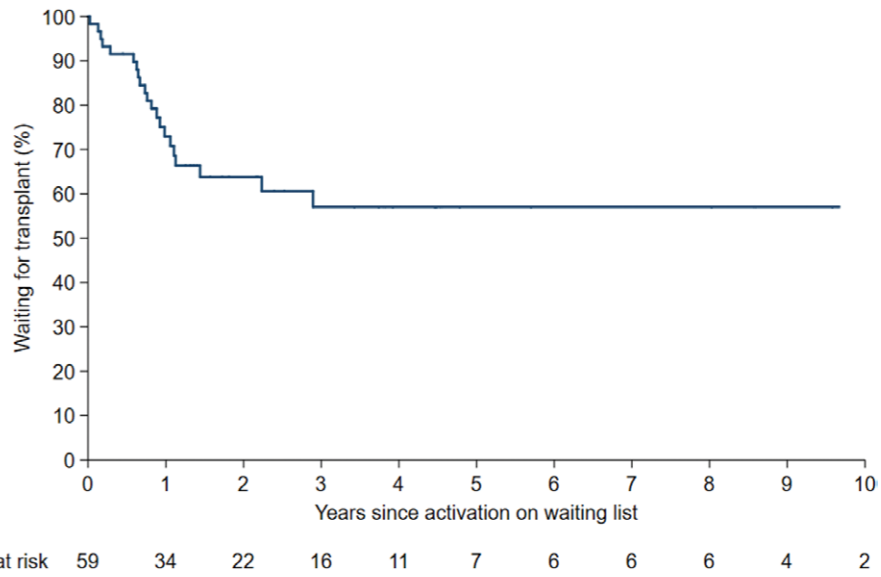


FIGURE 2. Time from activation on a waiting list to first allogenic islet transplant.

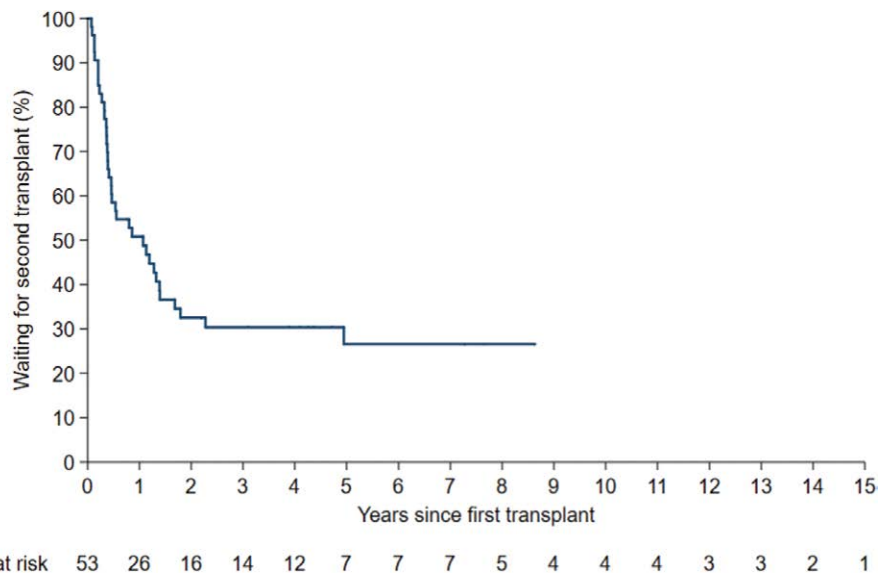


FIGURE 3. Time from first to second allogenic islet transplant. This figure includes some patients who do not require a second transplant and hence will never receive one.

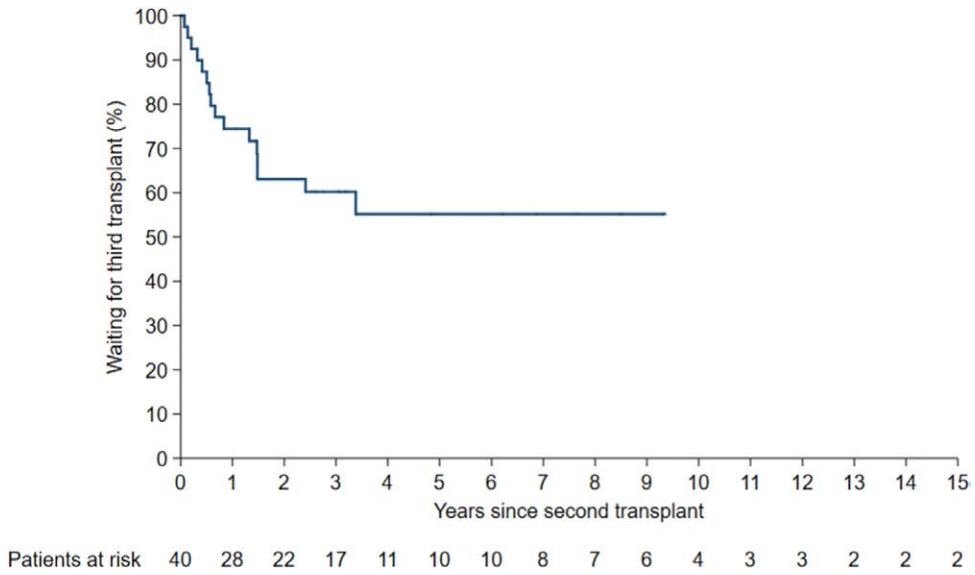


FIGURE 4. Time from second to third allogenic islet transplant. This figure includes some patients who do not require a third transplant and hence will never receive one.

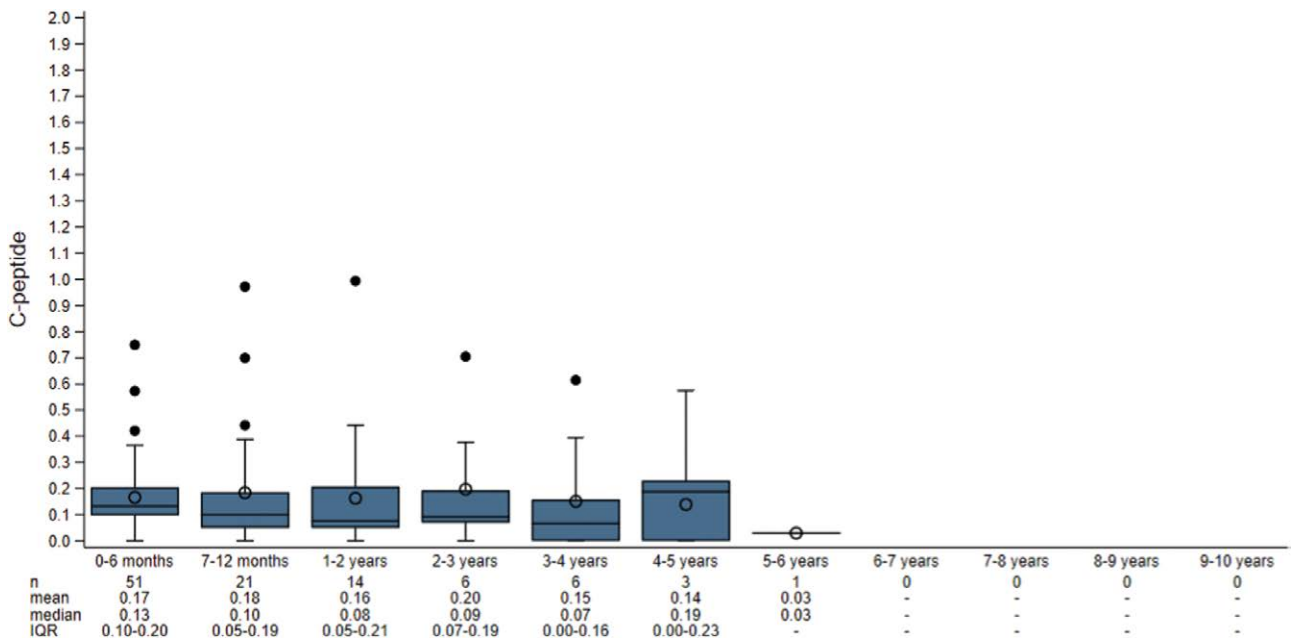


FIGURE 5. Distribution of C-peptide over time since first allogenic islet infusion. IQR, interquartile range.

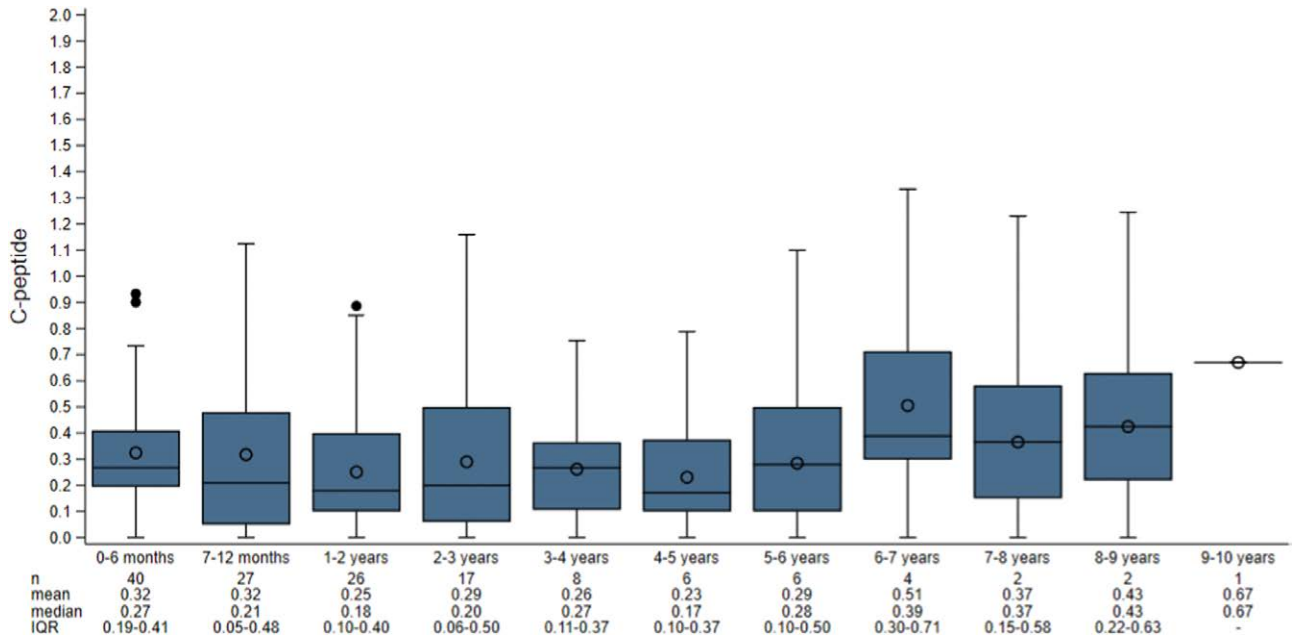


FIGURE 6. Distribution of C-peptide over time since second allogenic islet infusion. IQR, interquartile range.

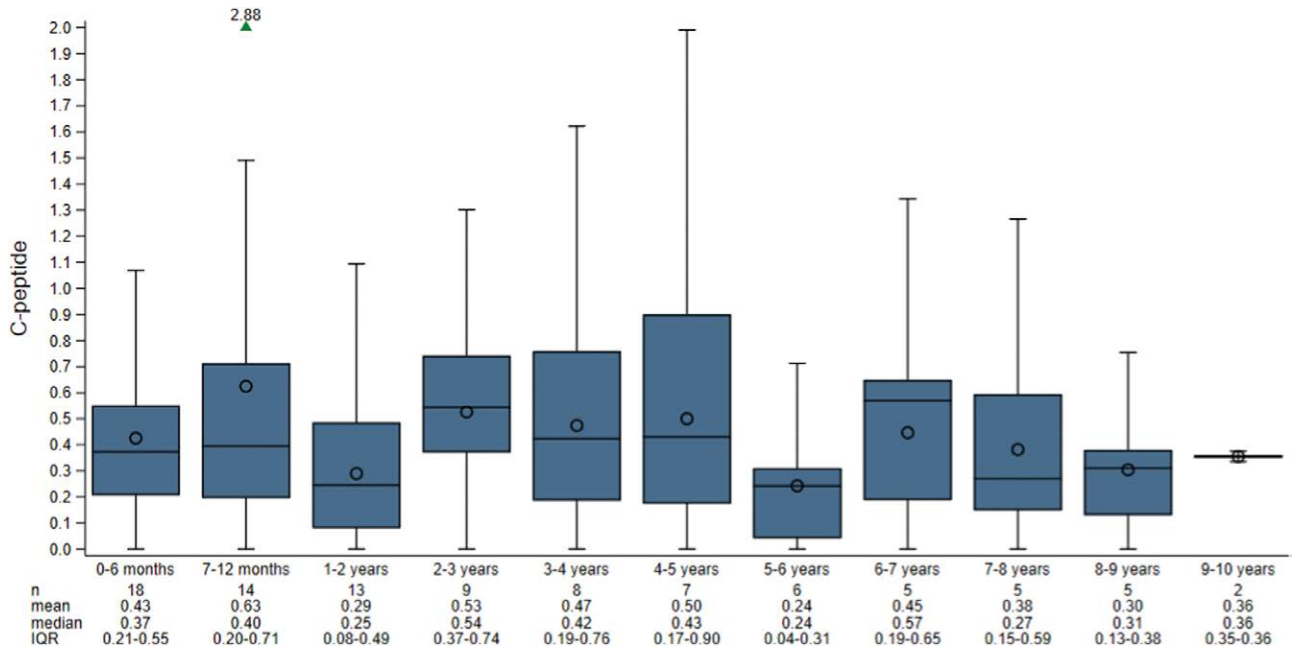


FIGURE 7. Distribution of C-peptide over time since third allogenic islet infusion. IQR, interquartile range.

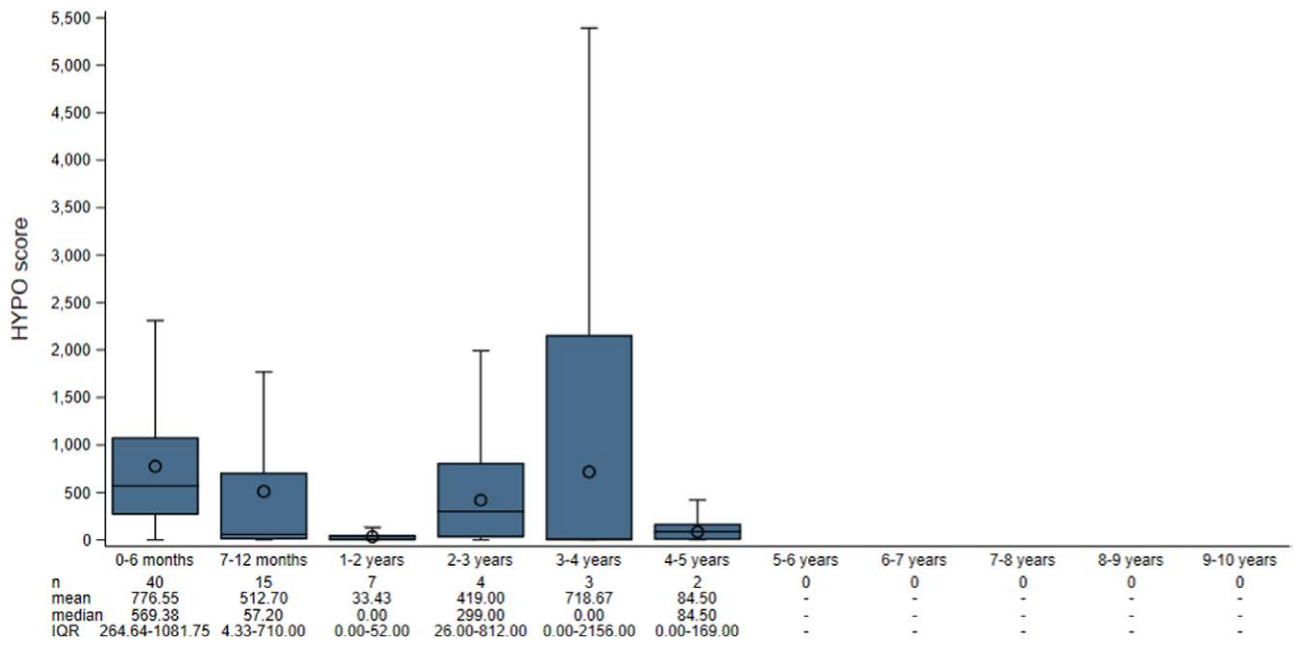


FIGURE 8. Distribution of HYPO score² over time since first allogenic islet infusion. IQR, interquartile range.

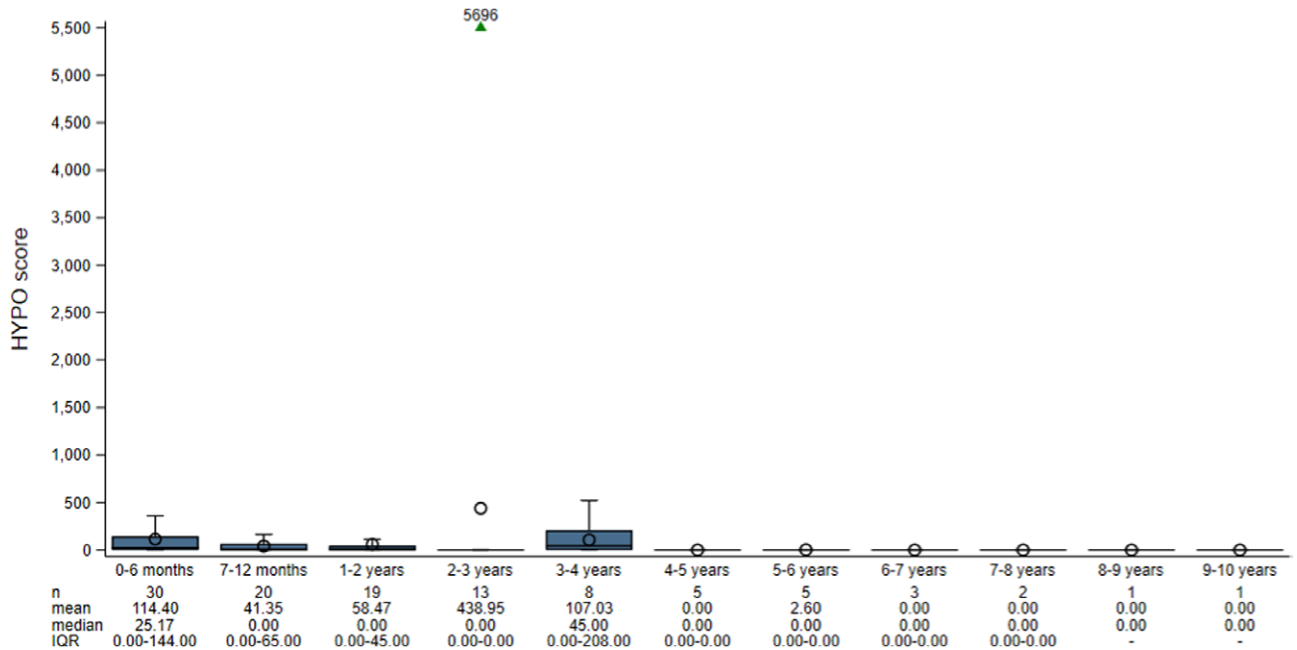


FIGURE 9. Distribution of HYPO score over time since second allogenic islet infusion. IQR, interquartile range.

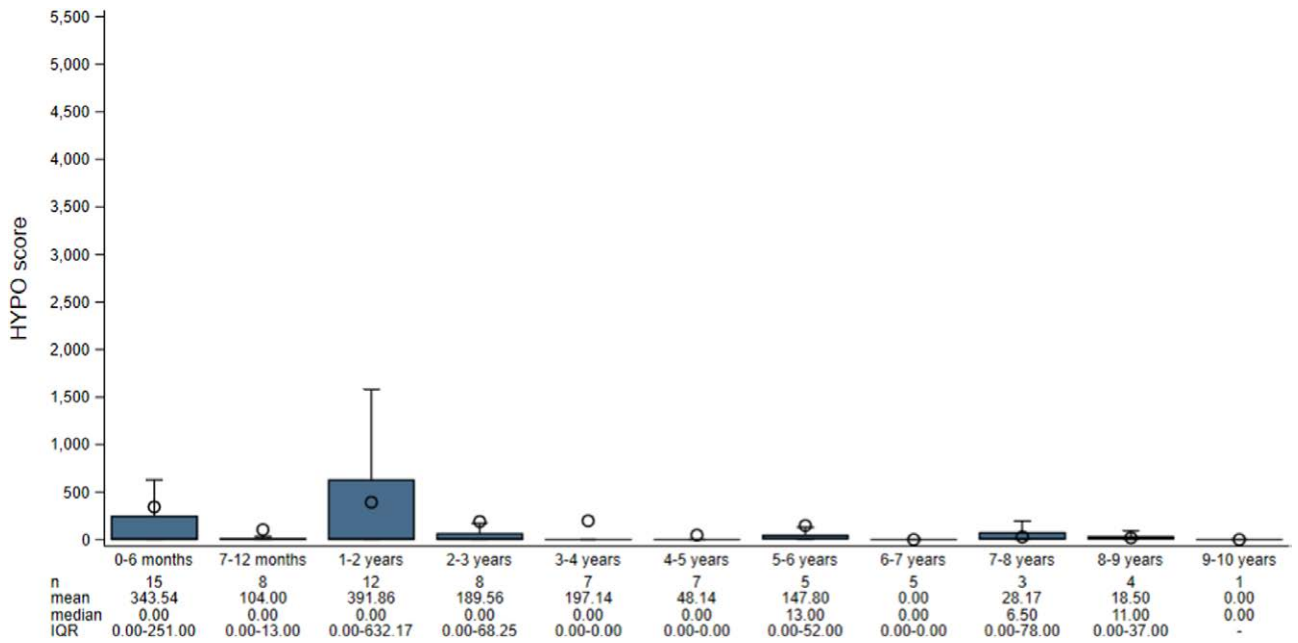


FIGURE 10. Distribution of HYPO score over time since third allogenic islet infusion. IQR, interquartile range.

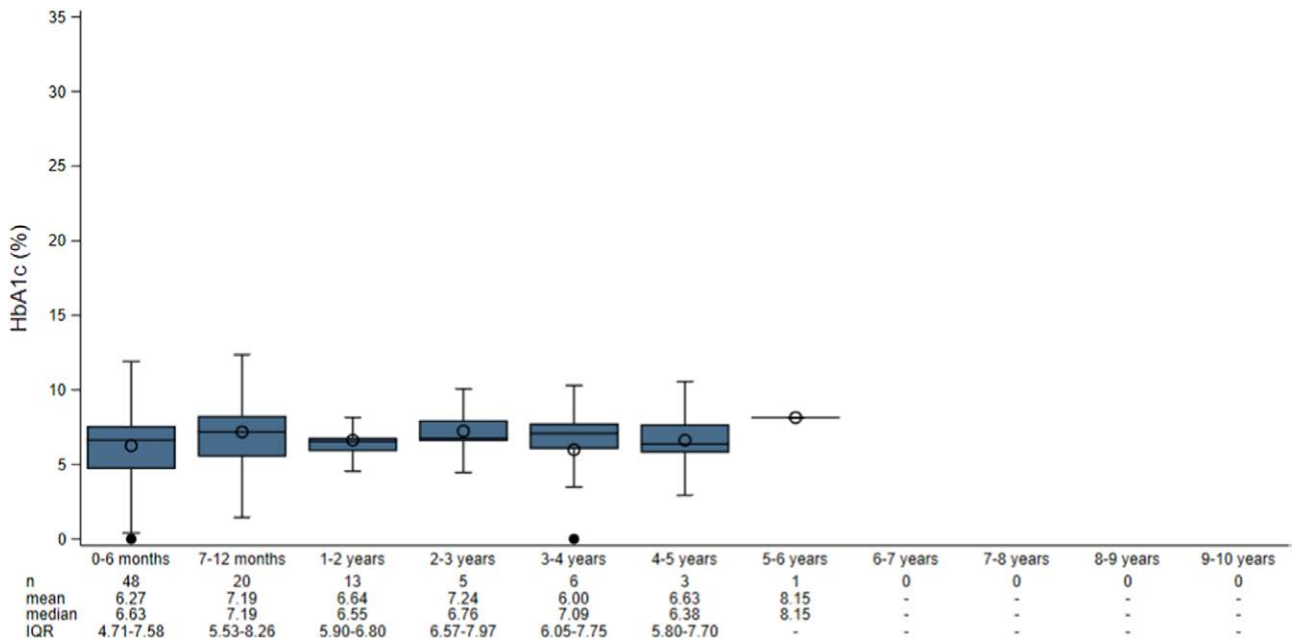


FIGURE 11. Distribution of HbA1c (%) over time since first allogenic islet infusion. HbA1c, glycosylated hemoglobin A1c; IQR, interquartile range.

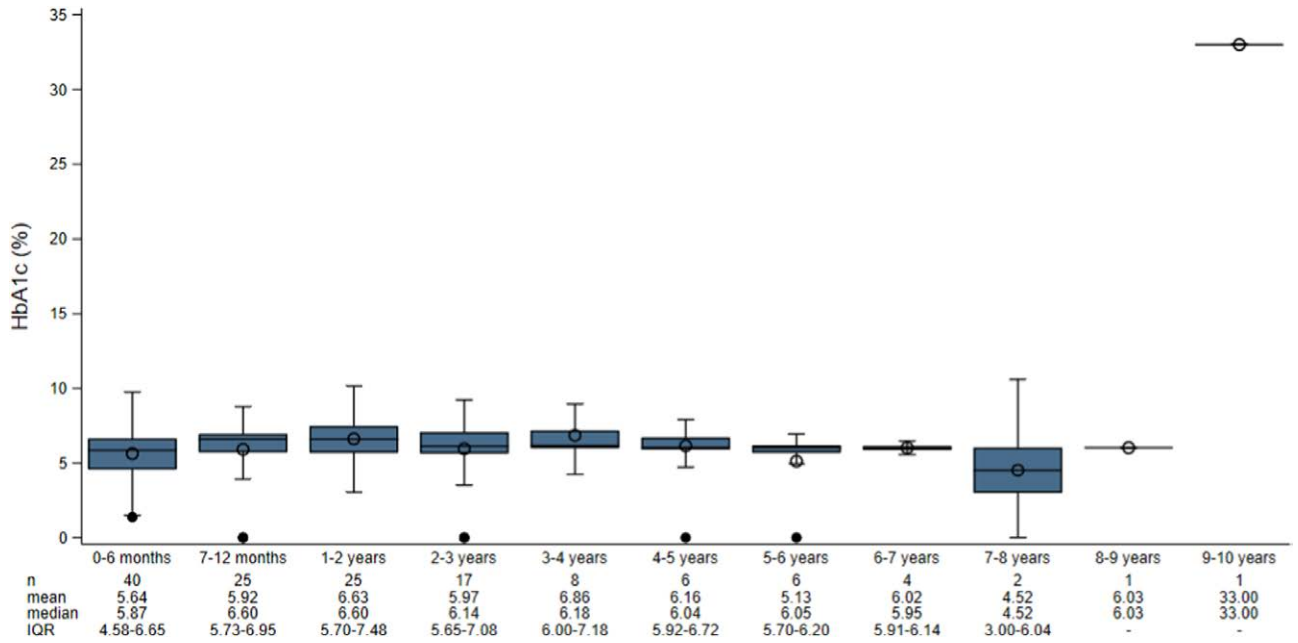


FIGURE 12. Distribution of HbA1c (%) over time since second allogenic islet infusion. HbA1c, glycosylated hemoglobin A1c; IQR, interquartile range.

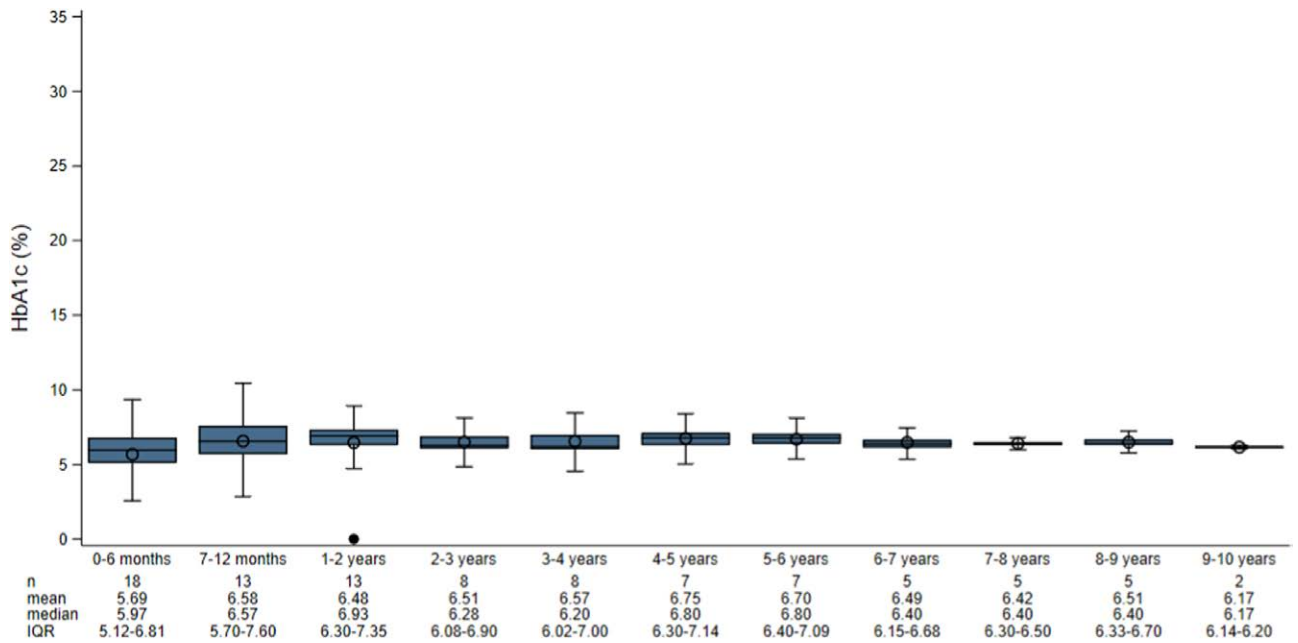


FIGURE 13. Distribution of HbA1c (%) over time since third allogenic islet infusion. HbA1c, glycosylated hemoglobin A1c; IQR, interquartile range.

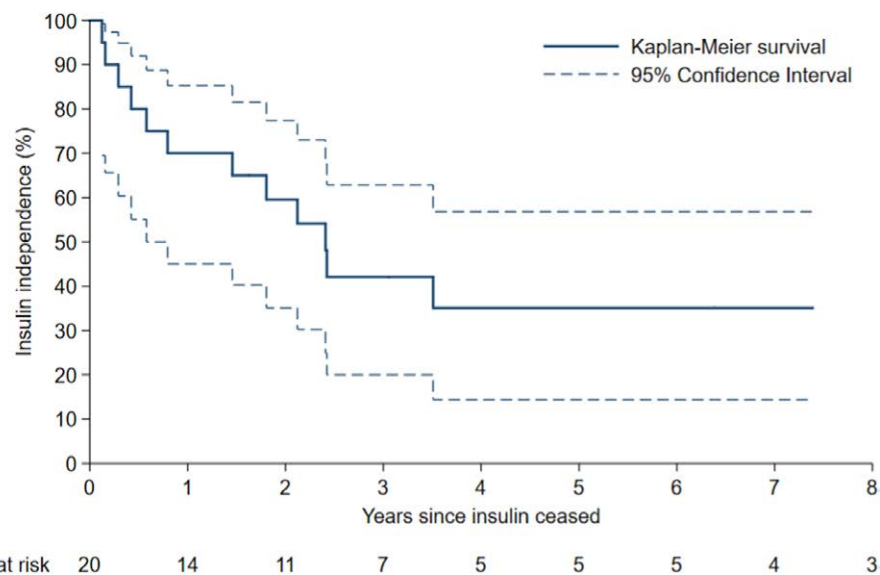


FIGURE 14. Duration of insulin independence from time first ceased.

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