

**NHS BLOOD AND TRANSPLANT
ORGAN DONATION AND TRANSPLANTATION DIRECTORATE**

PANCREAS ADVISORY GROUP

ISLET TRANSPLANT ACTIVITY AND OUTCOME
SUMMARY

INTRODUCTION

- 1 Islet transplant data has been collected by NHSBT since the introduction of four transplant and follow-up forms in July 2010. This paper provides basic summaries of transplant activity and outcomes.

DATA

- 2 Islet transplant activity, including simultaneous islet and kidney (SIK) grafts, and end of year transplant list for the last three calendar years were analysed. Data on 239 (150 routine and 89 priority) islet transplants performed in the UK between 1 April 2010 and 31 December 2018 were analysed from the UKTR. Outcome data are reported for all routine transplants.

RESULTS

- 3 In 2019 there were 32 islet transplants performed. There were 24 patients on the islet transplant list at 31 December 2019, 21 routine (10 SIK) and three priority patients.
- 4 One-year graft survival for first routine islet alone grafts is 88% and five-year graft survival is 51%. There is a significant difference in five-year graft survival for those patients receiving a routine and priority top-up graft compared with those receiving a routine only graft, 60% and 33%, respectively, $p < 0.0001$.
- 5 For patients receiving islet alone routine and priority grafts, the median annual rate of severe hypoglycaemic events fell from 10 events (IQR 1 – 43) at time of transplant, to none at one, two and three years' post-transplant. 87 (82%) patients experienced no severe hypoglycaemic events in the first-year post-transplant.
- 6 Median HbA1c fell from 64 mmol/mol (IQR 54 – 75) at time of transplant, to 48 mmol/mol (IQR 42 – 58) at one year and 55 (IQR 47 – 64) three years post-transplant, for patients who received routine and priority grafts. Overall, a reduction in HbA1c was reported for 116 (84%) patients at one-year post-transplant.
- 7 The median insulin dose, for patients who received routine and priority grafts, fell from 0.52 units/kg (IQR 0.36 – 0.63) at time of transplant to 0.3 units/kg (IQR 0.2 – 0.51) three years post-transplant. Insulin dependence at some point in the first-year post-transplant was achieved for 34% of patients overall.

SUMMARY

- 8 In 2019, the number of islet transplants has increased slightly from 2018 and the number on the waiting list at the end of the calendar year has decreased. One-year graft survival is 88%. Reductions in the annual rate of severe hypoglycaemic events, HbA1c and insulin dose at one-year post routine transplant have been reported.

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- 9 Islet transplant data has been collected by NHSBT since the introduction of four transplant and follow-up forms in July 2010. This paper provides basic summaries of transplant activity and outcomes.

DATA

- 10 Recent data on islet transplant activity, including simultaneous islet and kidney (SIK) grafts, and end of year transplant list between 1 January 2017 and 31 December 2019 from the UK Transplant Registry (UKTR) are reported, by centre and calendar year.
- 11 Additionally, data on 239 (150 routine and 89 priority) islet transplants performed in the UK between 1 April 2010 and 31 December 2018 were analysed from the UKTR. Outcome data are reported for all routine transplants. Where outcome data are unavailable from UKTR, data collected by the UKITC clinical research forms have been considered. These data have been provided by the Newcastle research group who collate and maintain the research data base.
- 12 All islet transplant outcome data reported are specific to the routine transplant and one-year centre specific outcomes are presented in the Appendix.

RESULTS

- 13 The number of islet transplants performed by centre for the last three calendar years, 1 January 2017 to 31 December 2019, is shown by transplant type and islet status in **Tables 1** and **2**, respectively. **Table 3** shows the transplant list at the end of the last three calendar years by islet status.
- 14 Between 1 April 2010 and 31 December 2018, there were a total of 239 islet transplants performed, 150 (63%) of which were routine. Of the 89 priority grafts, two were patients receiving a priority graft following a routine graft performed before 1 April 2010 and were excluded from this analysis.
- 15 The number of known graft failures at one-year post-transplant is reported in **Table 4**. Of the 150 routine transplants performed, 86 patients received priority grafts in the time period analysed. The majority of these patients received their first priority graft within six months of their routine graft: 0-3 months for 25 (29%) patients; 3-6 months for 33 (38%) patients; 6-12 months for 26 (30%) patients and more than one year for two patients who were highly sensitised.

Table 1 UK islet transplant activity between 1 January 2017 and 31 December 2019, by transplant type and calendar year

Transplant Centre	2017					Total		2018					Total		2019					Total	
	ITA	IAK	IAP	IAPK	SIK	N	%	ITA	IAK	IAP	IAPK	SIK	N	%	ITA	IAK	IAP	IAPK	SIK	N	%
Bristol	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Edinburgh	11 ²	0	0	0	2	13	48	7	1	0	0	2	10	34	8 ³	4	0	0	2	14	44
King's	0	0	0	0	0	0	0	2	0	0	0	0	2	7	3 ¹	0	0	0	0	3	9
Manchester	2	0	0	0	2 ¹	4	15	1	4 ²	0	0	4 ³	9	31	0	3	0	0	5	8	25
Newcastle	1	0	0	0	0	1	4	3	1	0	0	1	5	17	2	0	0	0	0	2	6
Oxford	9	0	0	0	0	9	33	3	0	0	0	0	3	10	5	0	0	0	0	5	16
Royal Free	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL	23	0	0	0	4	27	100	16	6	0	0	7	29	100	18	7	0	0	7	32	100

ITA = Islet transplant alone IAK = Islet after kidney IAP = Islet after pancreas IAPK = Islet after simultaneous kidney/pancreas SIK = Simultaneous kidney/islet

¹ Includes 1 DCD transplant
² Includes 2 DCD transplants
³ Includes 3 DCD transplants

Table 2 UK islet transplant activity between 1 January 2017 and 31 December 2019, by islet status, number of patients and calendar year

Transplant Centre	2017						2018						2019					
	Routine	Priority	Total		Number of patients		Routine	Priority	Total		Number of patients		Routine	Priority	Total		Number of patients	
			N	%	N	%			N	%	N	%			N	%	N	%
Bristol	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Edinburgh	8 ²	5	13	48	10	48	6 ²	4	10	34	8	35	9 ²	5	14	44	10	42
King's	0	0	0	0	0	0	1	1	2	7	1	4	3	0	3	9	3	13
Manchester	3 ²	1	4	15	4	19	4 ⁴	5	9	31	7	30	6 ⁴	2	8	25	7	29
Newcastle	1	0	1	4	1	5	4 ¹	1	5	17	4	17	1	1	2	6	1	4
Oxford	6	3	9	33	6	29	3	0	3	10	3	13	3	2	5	16	3	13
Royal Free	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL	18	9	27	100	21	100	18	11	29	100	23	100	22	10	32	100	24	100

¹ Includes 1 SIK transplant

² Includes 2 SIK transplants

³ Includes 3 SIK transplants

⁴ Includes 4 SIK transplants

Table 3 UK islet transplant list, 31 December 2017 to 31 December 2019, by islet status and calendar year

Transplant Centre	31 December 2017				31 December 2018				31 December 2019			
	Total				Total				Total			
	Routine	Priority	N	%	Routine	Priority	N	%	Routine	Priority	N	%
Bristol	0	0	0	0	0	0	0	0	0	0	0	0
Edinburgh	7 ¹	1	8	29	3 ¹	1	4	12	1 ¹	2	3	13
King's	1	0	1	4	1	0	1	3	0	1	1	4
Manchester	7 ²	4	11	39	16 ⁴	0	16	48	10 ³	0	10	42
Newcastle	5 ¹	1	6	21	6 ¹	0	6	18	6	0	6	25
Oxford	2	0	2	7	2	2	4	12	2	0	2	8
Royal Free	0	0	0	0	2	0	2	6	2	0	2	8
TOTAL	22	6	28	100	30	3	33	100	21	3	24	100

¹ Includes 1 SIK transplant
² Includes 6 SIK transplants
³ Includes 9 SIK transplants
⁴ Includes 14 SIK transplants

Table 4 One-year graft outcome following routine islet transplant, 1 April 2010 to 31 December 2018

Number of grafts	No. of transplants	No. with known outcome at one year	No. with known graft failure at one year
Islet routine graft			
Routine only	59	53	15
Routine and one priority graft	78	75	2
Routine and two priority grafts	1	1	0
SIK routine graft			
Routine only	5	2	1
Routine and one priority graft	7	6	0
Routine and two priority grafts	0	0	0
Total	150	137	18

Figure 1 One-year graft function by total IEQ per kg recipient body weight for islet alone routine only grafts, 1 April 2010 to 31 December 2018

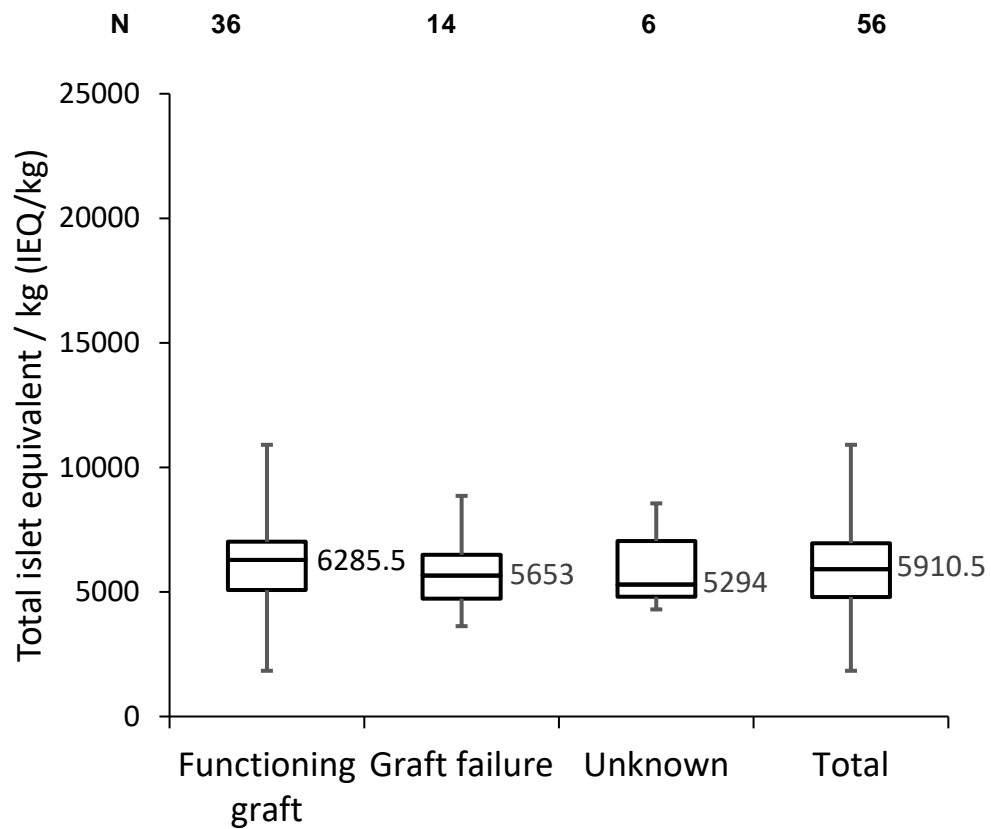
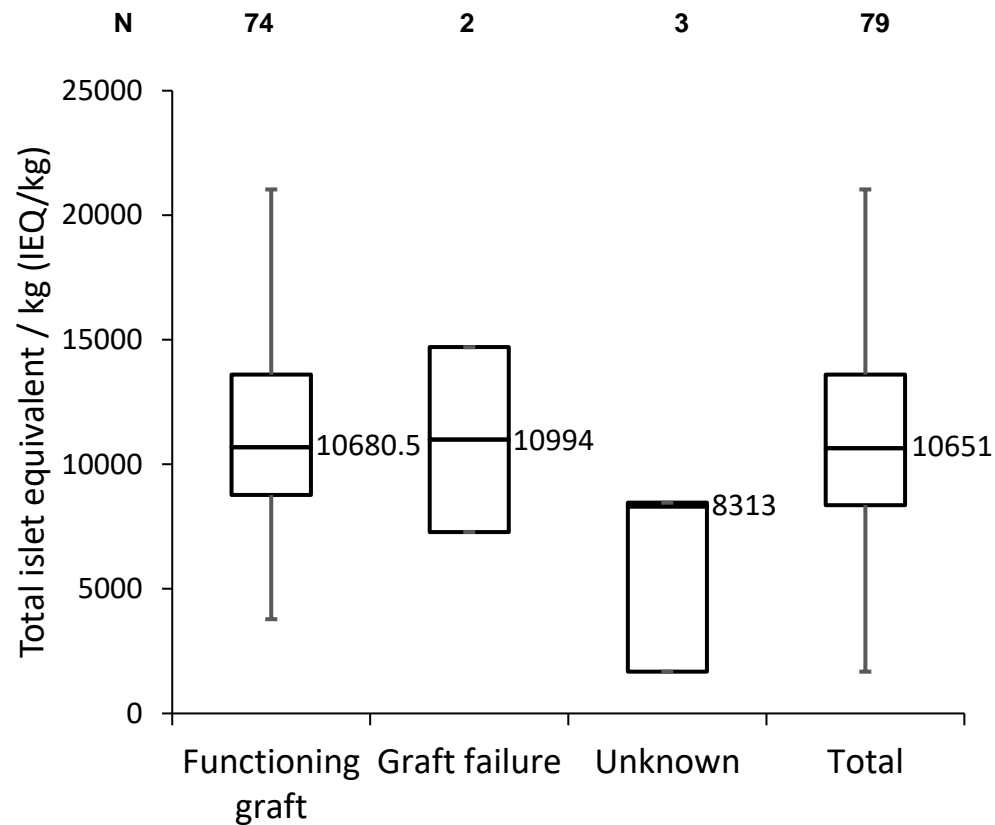


Figure 2 One-year graft function by total IEQ per kg recipient body weight for islet alone routine and priority grafts, 1 April 2010 to 31 December 2018



- 16 One-year graft outcome by total IEQ (IEQx1000/kg) transplanted is presented in **Figure 1** and **Figure 2**, for islet alone routine only and routine and priority grafts, respectively. The median total IEQ transplanted for five SIK routine only transplants was 4101 (IQR 3594 - 4695) and for seven SIK routine and priority grafts was 7924 (IQR 7015 - 10526). This was slightly lower than the median for islet alone transplants in both groups.
- 17 Kaplan-Meier survival plots showing one-year and five-year graft survival after first routine islet alone transplants are presented in **Figure 3** and **Figure 4**, respectively. One year graft survival is 88%, 95% CI (81-93%) and five year graft survival is 51%, 95% CI (40-60%).
- 18 **Figure 5** shows a Kaplan-Meier survival plot of five-year graft survival by type of graft. Estimated five-year graft survival for first routine only grafts is 33%, 95% CI (19-48%) and for first routine grafts followed by a priority graft is 60%, 95% CI (46-72%). This difference was statistically significant, $p < 0.0001$.
- 19 **Figure 6** shows a Kaplan-Meier survival plot of five-year graft survival by type of graft, where the first routine graft was still functioning at one-year post-transplant. Estimated five-year graft survival for routine only grafts is 47%, 95% CI (27-64%) and for routine grafts followed by a priority graft is 63%, 95% CI (48-74%). This difference was not statistically significant, $p = 0.06$.
- 20 **Figure 7** shows a Kaplan-Meier survival plot of five-year patient survival after first routine islet alone transplant. Five year patient survival is 94%, 95% CI (84-98).
- 21 Of the 12 SIK islet transplants in the 1 April 2010 to 31 December 2018 time period, 11 were the first islet transplant for the patient. Of these 11, one year outcome is known for eight patients and seven were functioning and one had failed.

Figure 3 One-year graft survival following first routine islet alone transplantation performed in the UK between 1 April 2010 and 31 December 2018

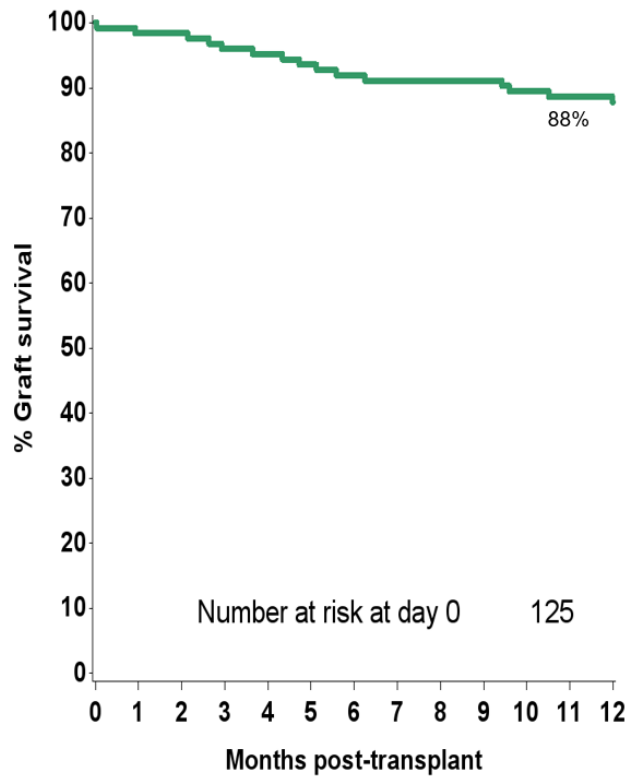


Figure 4 Five-year graft survival following first routine islet alone transplantation performed in the UK between 1 April 2008 and 31 December 2018

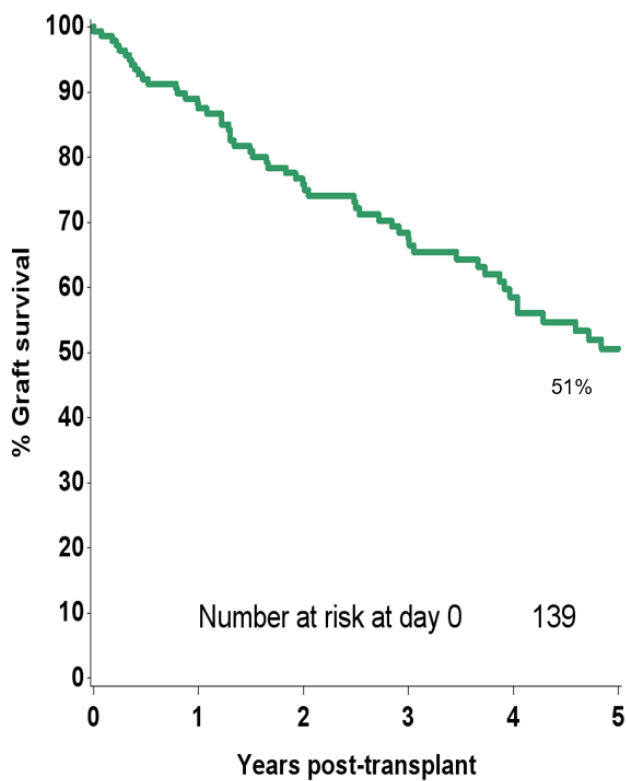


Figure 5 Five-year graft survival following first routine islet alone transplantation performed in the UK between 1 April 2008 and 31 December 2018, by type of graph

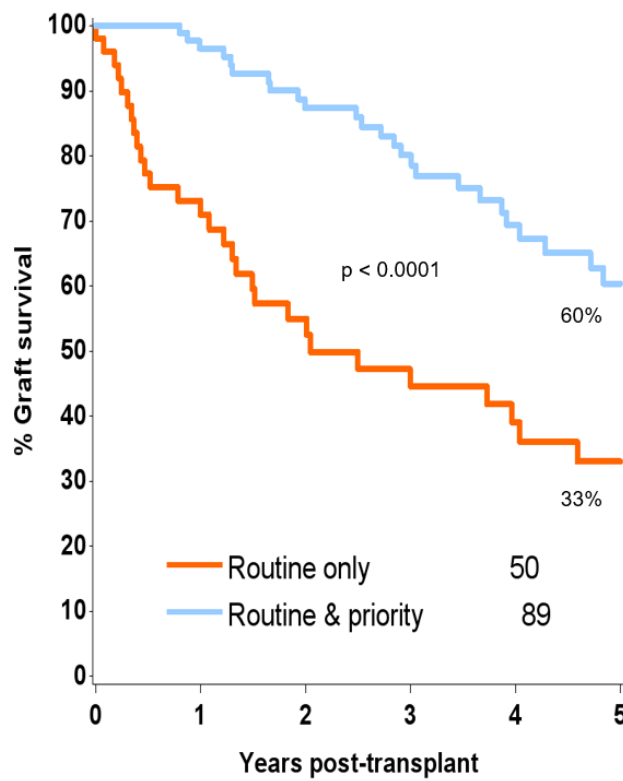


Figure 6 Five-year graft survival following first routine islet alone transplantation where the routine graft was functioning at one year in the UK between 1 April 2008 and 31 December 2018, by type of graph

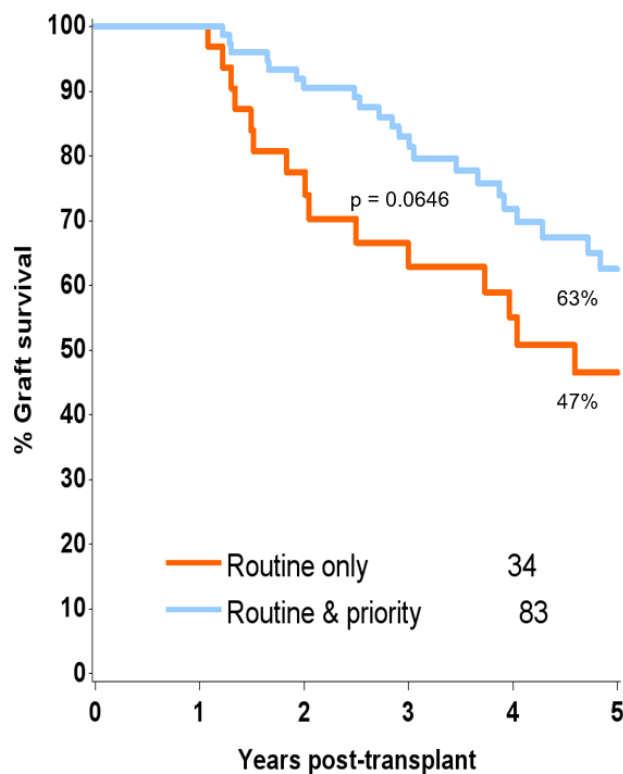
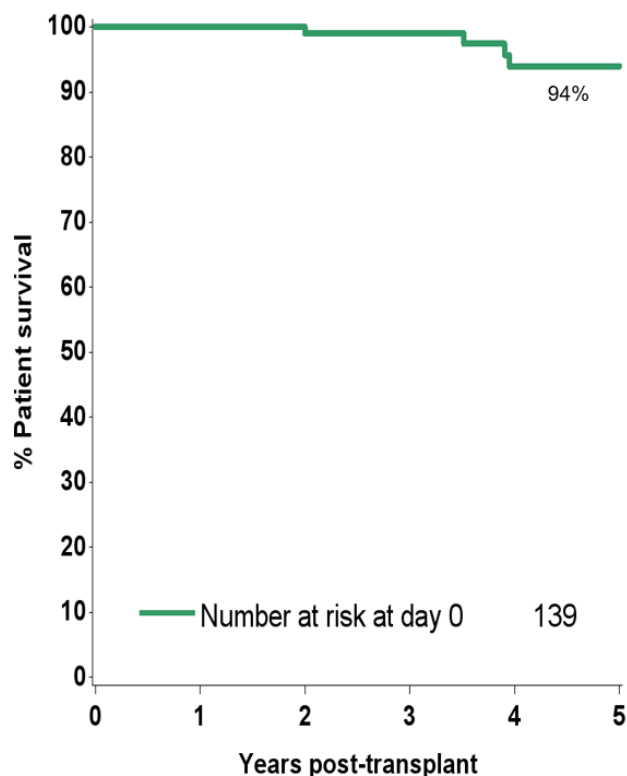


Figure 7 Five-year patient survival following first routine islet alone transplantation performed in the UK between 1 April 2008 and 31 December 2018



- 23 **Figures 8 and 9** show the median rate of severe hypoglycaemic events, excluding SIK transplants, for routine only grafts and for routine and priority grafts, respectively. Overall, at one-year post-transplant data were available in 106 cases and 69 (65%) patients had a reduced number of events. 87 (82%) patients experienced no severe hypoglycaemic events during the first year following their routine transplant, whilst 19 (18%) patients experienced between one and nine events.
- 24 For the 11 SIK transplants where severe hypoglycaemic events were reported at transplant, the median rate was 4 (IQR 0-50) and for the 6 reported at one-year post-transplant, the median rate was 0 (IQR 0-1).
- 25 Median HbA1c is reported in **Figure 10** for routine only grafts and **Figure 11** for routine and priority grafts, excluding SIK transplants. Overall, data were available to calculate the reduction in HbA1c in 113 cases at one-year post-transplant and in 93 (82%) patients a reduction in HbA1c was reported. The proportion of patients with HbA1c of less than 53 mmol/mol was 18% of 136 at time of transplant, 60% of 115 patients at one-year post-transplant, 38% of 72 patients at three years and 38% of 34 patients at five years post-transplant.
- 26 For the 11 SIK transplants where HbA1c was reported at transplant, the median was 69 mmol/mol (IQR 60-77) and for the 5 reported at one-year post-transplant, the median was 43 mmol/mol (IQR 41-55).

Figure 8 Reduction in severe hypoglycaemic events three years post-transplant for routine only grafts, 1 April 2010 – 31 December 2018 (excluding SIK transplants)

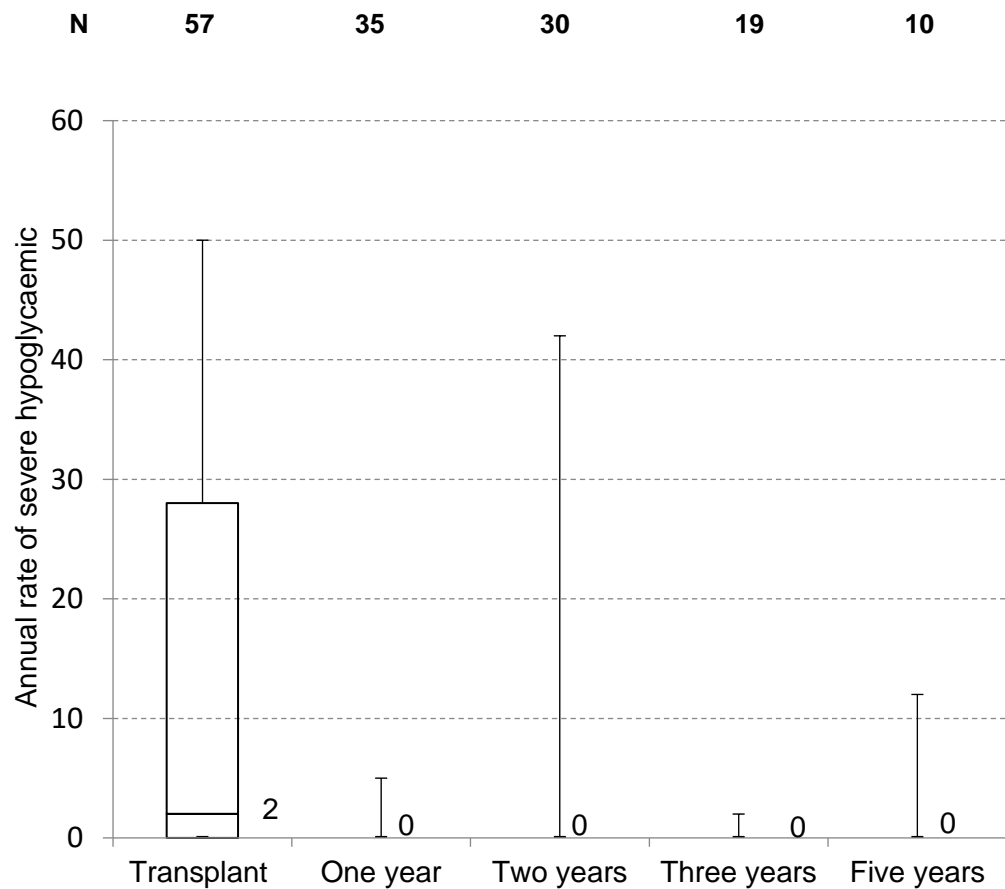


Figure 9 Reduction in severe hypoglycaemic events three years post-transplant for routine and priority grafts, 1 April 2010 – 31 December 2018 (excluding SIK transplants)

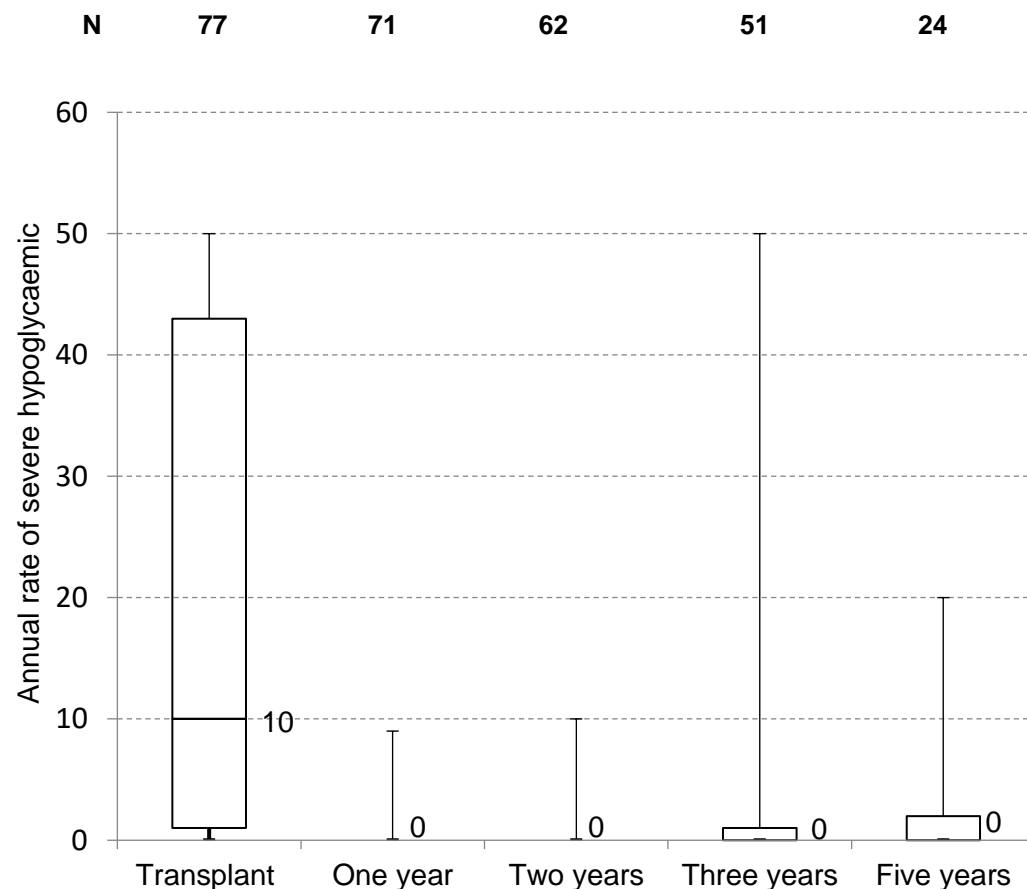


Figure 10 Reduction in HbA1C three years post-transplant for routine only grafts, 1 April 2010 – 31 December 2018 (excluding SIK transplants)

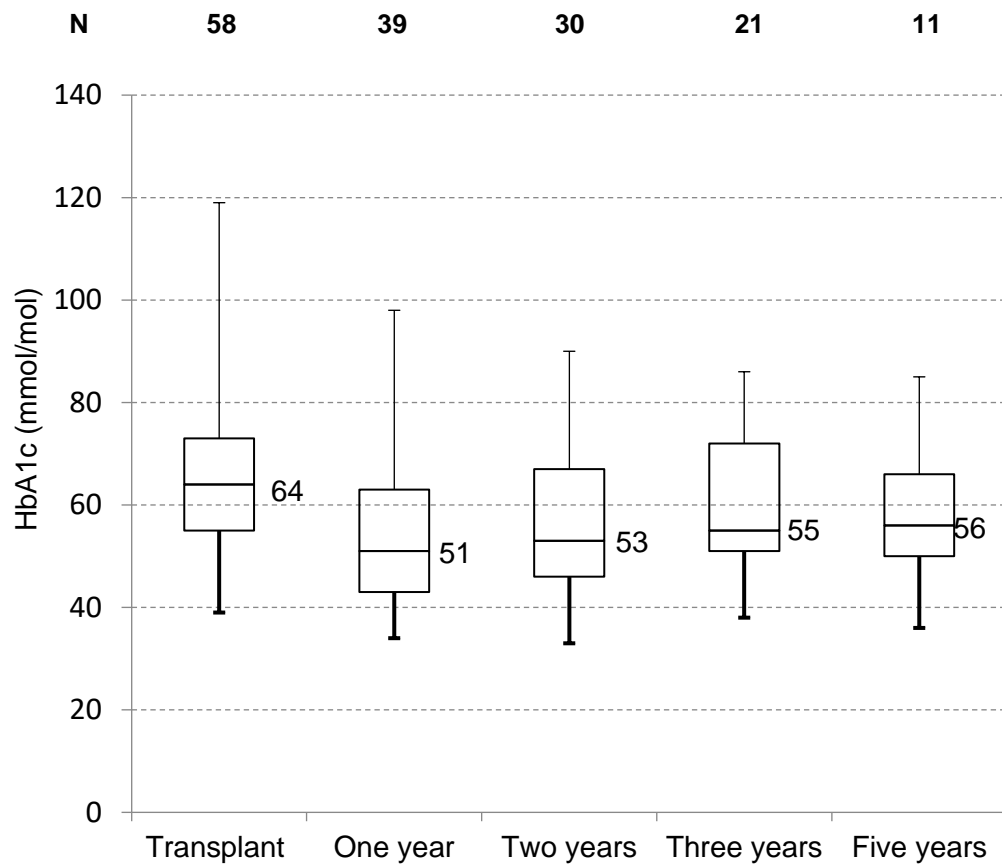


Figure 11 Reduction in HbA1C three years post-transplant for routine and priority grafts, 1 April 2010 – 31 December 2018 (excluding SIK transplants)

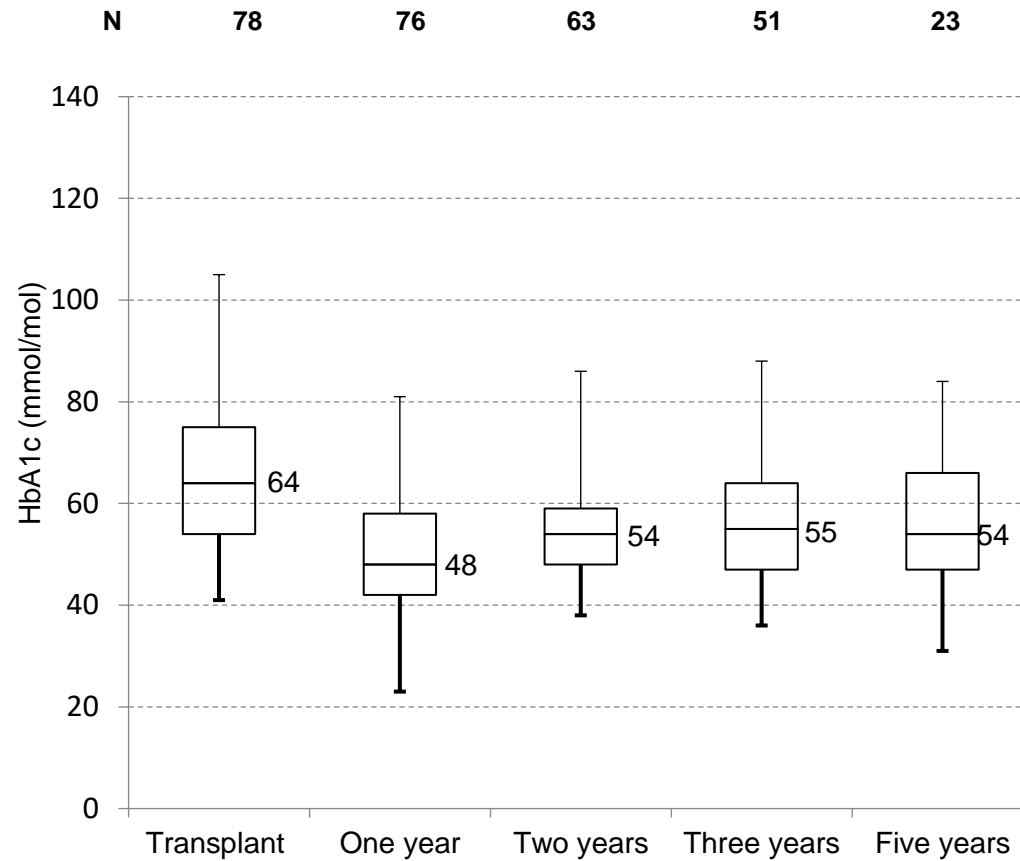


Figure 12 Insulin dose three-years post-transplant for routine only grafts, 1 April 2010 – 31 December 2018 (excluding SIK transplants)

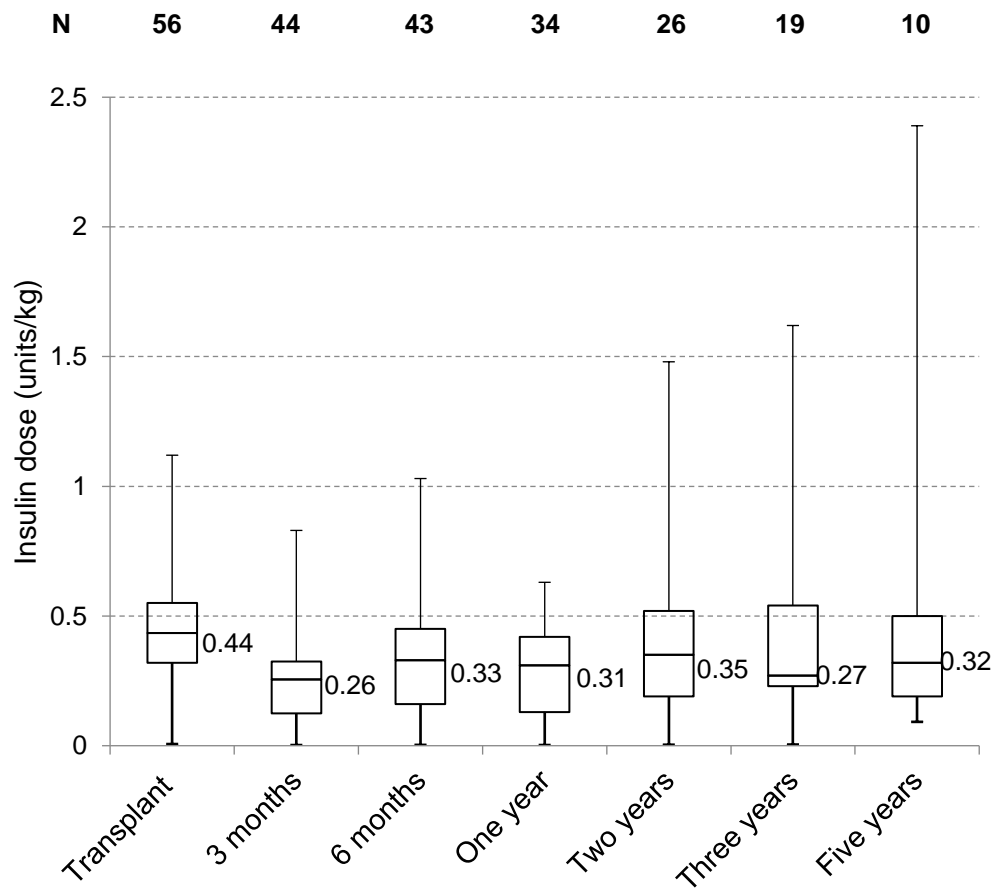
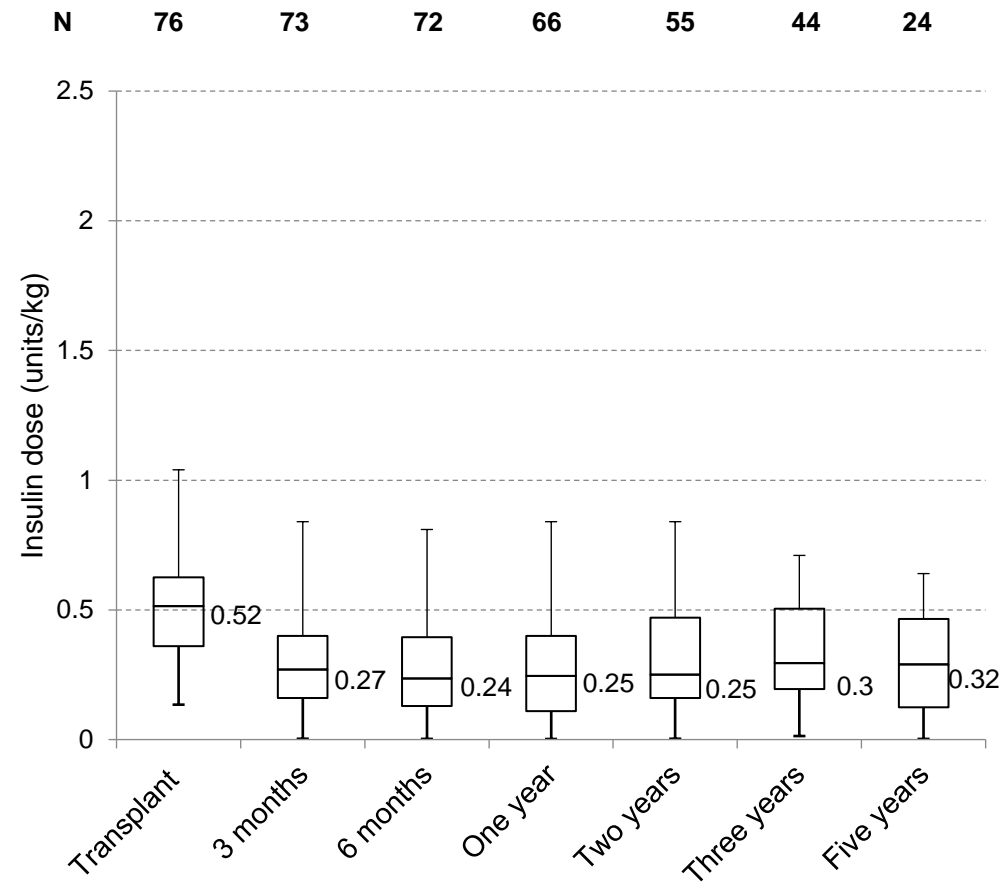


Figure 13 Insulin dose three-years post-transplant for routine and priority grafts, 1 April 2010 – 31 December 2018 (excluding SIK transplants)



- 27 **Figure 12** and **Figure 13** show the median insulin dose for routine only grafts and routine and priority grafts, respectively, excluding SIK transplants. Overall, in 99 patients where the difference in insulin dose between transplant and one-year post-transplant could be calculated, 87 (87%) reported a reduction. Of the 114 patients with insulin independence status reported for the first-year post-transplant, 39 (34%) achieved insulin independence at some point in the year.
- 28 For the 12 SIK transplants where insulin dose was reported at transplant, the median was 0.66 units/kg (IQR 0.45-0.74) and for the 6 reported at one-year post-transplant, the median was 0.27 units/kg (IQR 0.24-0.41).

SUMMARY

- 29 In 2019, the number of islet transplants had increased slightly from 2018. The number on the waiting list at the end of the calendar year has decreased.
- 30 One-year graft survival was 88% and five-year graft survival was 51%. Those patients receiving a routine and a priority top-up graft had significantly better five-year graft survival than those receiving a routine only, 60% and 33%, respectively, $p < 0.0001$. Reductions in the rate of severe hypoglycaemic events, HbA1c and insulin dose at one-year, two years and three years post routine transplant have been reported.

APPENDIX

Transplant centre	Routine transplants	Priority transplants	Graft function at one year		
			No. with known outcome	Graft failure	Priority grafts with graft failure
Bristol	3	1	3	2	0
Edinburgh	54	38	48	2	1
King's College	8	6	8	2	0
Manchester	14	10	14	3	0
Newcastle	29	14	26	8	0
Oxford	31	15	27	1	1
Royal Free	11	5	11	2	0
Total	150¹	89	137²	18³	2

¹ Includes 12 SIK transplants: Edinburgh (5), Manchester (6), Newcastle (1)
² Includes 8 SIK transplants: Edinburgh (2), Manchester (6)
³ Includes 1 SIK transplants: Manchester (1)

Transplant centre	No. of routine transplants	Annual rate of severe hypoglycaemic events					
		Median at registration ² (IQ range)	Median at transplant (IQ range)	Median at one year (IQ range)	Median reduction (IQ range)	No. with reduced events	Missing ³ N (%)
Bristol	3	2 (2 – 3)	3 (2 – 50)	0 (0 – 0)	3 (2 – 50)	3	0 (0)
Edinburgh	49	50 (20 – 50)	32 (9 – 50)	0 (0 – 0)	27 (7 – 50)	37	6 (12)
King's College	8	4 (0 – 16)	1 (0 – 27)	0 (0 – 0)	0 (0 – 3)	2	3 (38)
Manchester	8	5 (5 – 8)	4 (1 – 9)	0 (0 – 0)	3 (1 – 10)	6	1 (13)
Newcastle	28	25 (5 – 25)	21 (2 – 32)	0 (0 – 1)	19 (1 – 29)	15	8 (29)
Oxford	31	2 (1 – 3)	0 (0 – 1)	0 (0 – 0)	0 (0 – 2)	5	12 (39)
Royal Free	11	4 (0 – 8)	0 (0 – 0)	0 (0 – 0)	0 (0 – 0)	1	2 (18)
Total	138	20 (4 – 50)	8 (0 – 34)	0 (0 – 0)	7 (0 – 35)	69	32 (23)

¹ Excluding SIK transplants
² Only available for 75 observations
³ Information missing at either transplant or one-year post-transplant

Transplant centre	No. of routine transplants	HbA1c mmol/mol				No. with lower HbA1c	Missing N (%)
		Median at transplant (IQ range)	Median at one year (IQ range)	Median reduction (IQ range)			
Bristol	3	68 (53 – 70)	56 (33 – 81)	0 (0 – 37)	1	0 (0)	
Edinburgh	49	59 (51 – 67)	53 (45 – 62)	3 (0 – 13)	32	5 (10)	
King's College	8	67 (59 – 86)	44 (42 – 45)	10 (2 – 26)	6	2 (25)	
Manchester	8	64 (56 – 76)	44 (42 – 47)	18 (8 – 36)	7	1 (13)	
Newcastle	28	74 (62 – 86)	50 (41 – 58)	15 (0 – 27)	20	6 (21)	
Oxford	31	62 (55 – 69)	48 (41 – 56)	10 (0 – 21)	21	9 (29)	
Royal Free	11	61 (56 – 86)	51 (43 – 57)	2 (0 – 20)	6	2 (18)	
Total	138	64 (55 – 75)	49 (42 – 59)	9 (0 – 20)	93	25 (18)	

¹ Excluding SIK transplants

Transplant centre	No. of routine transplants	Insulin dose/kg			No. insulin independent at some point	Missing N (%)
		Median at transplant (IQ range)	Median at one year (IQ range)	Median reduction (IQ range)		
Bristol	3	0.42 (0.37 – 0.48)	0.20 (0.12 – 0.47)	0.22 (0.01 – 0.25)	1	0 (0)
Edinburgh	49	0.51 (0.36 – 0.61)	0.25 (0.11 – 0.41)	0.23 (0.13 – 0.33)	20	9 (18)
King's College	8	0.32 (0.21 – 0.39)	0.13 (0.07 – 0.21)	0.20 (0.15 – 0.27)	3	4 (50)
Manchester	8	0.52 (0.40 – 0.54)	0.28 (0.23 – 0.38)	0.27 (0.25 – 0.30)	3	2 (25)
Newcastle	28	0.48 (0.34 – 0.61)	0.36 (0.23 – 0.46)	0.19 (-0.02 – 0.28)	5	10 (36)
Oxford	31	0.45 (0.32 – 0.62)	0.26 (0.12 – 0.38)	0.26 (0.07 – 0.43)	5	11 (35)
Royal Free	11	0.56 (0.40 – 0.80)	0.42 (0.24 – 0.50)	0.14 (0.01 – 0.35)	2	3 (27)
Total	138	0.48 (0.33 – 0.60)	0.26 (0.12 – 0.41)	0.23 (0.10 – 0.32)	39	39 (28)

¹ Excluding SIK transplants