

**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 financial years were analysed. Data on 219 (137 routine and 82 priority) islet transplants performed in the UK where the routine transplant was performed between 1 April 2010 and 31 March 2018 were analysed from the UKTR. Outcome data are reported for all routine transplants.

RESULTS

- 3 In 2018/19 there were 28 islet transplants performed. There were 42 patients on the islet transplant list at 31 March 2019, 36 routine (16 SIK) and six priority.
- 4 One-year graft survival for first routine grafts is 88% and five-year graft survival is 50%. 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, 59% 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 9.5 events (IQR 0.5 – 45.5) at time of transplant, to none at one, two and three years' post-transplant. 84 (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 48 – 63) three years post-transplant, for patients who received routine and priority grafts. Overall, a reduction in HbA1c was reported for 92 (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 0.37 – 0.63) at time of transplant to 0.29 units/kg (IQR 0.21 – 0.52) 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 2018/19, the number of islet transplants has increased slightly from 2017/18 and the number on the waiting list at the end of the financial year has also increased. 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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INTRODUCTION

- 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 April 2016 and 31 March 2019 from the UK Transplant Registry (UKTR) are reported, by centre and financial year.
- 11 Additionally, data on 219 (137 routine and 82 priority) islet transplants performed in the UK where the routine transplant was performed between 1 April 2010 and 31 March 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 has 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 financial years, 1 April 2016 to 31 March 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 financial years by islet status.
- 14 Between 1 April 2010 and 31 March 2018, there were a total of 219 islet transplants performed, 137 (63%) of which were routine. The number of known graft failures at one-year post-transplant is reported in **Table 4**. Of the 137 routine transplants performed, 80 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 22 (28%) patients; 3-6 months for 31 (39%) patients; 6-12 months for 26 (33%) patients and more than one year for one patient who was highly sensitised.
- 15 One-year graft outcome by total IEQ (IEQx1000/kg) transplanted is presented in **Figure 1** and **Figure 2**, for routine only and routine and priority grafts, respectively.

Table 1 UK islet transplant activity between 1 April 2016 and 31 March 2019, by transplant type and financial year

Transplant Centre	2016 - 2017							2017 - 2018							2018 - 2019							
	ITA	IAK	IAP	IAPK	SIK	Total		ITA	IAK	IAP	IAPK	SIK	Total		ITA	IAK	IAP	IAPK	SIK	Total		
						N	%						N	%						N	%	
Bristol	1	0	0	0	0	1	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Edinburgh	16 ²	1	0	0	0	17	50	11	0	0	0	2 ¹	13	50	5	2	0	0	3	10	36	
King's	3	0	0	0	0	3	9	1	0	0	0	0	1	4	2	0	0	0	0	2	7	
Manchester	2	0	0	0	1 ¹	3	9	2	2	0	0	2 ¹	6	23	0	4 ²	0	0	4 ²	8	29	
Newcastle	3	0	0	0	0	3	9	0	0	0	0	0	0	0	3	1	0	0	1	5	18	
Oxford	7 ¹	0	0	0	0	7	21	6	0	0	0	0	6	23	3	0	0	0	0	3	11	
Royal Free	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
TOTAL	32	1	0	0	1	34	100	20	2	0	0	4	26	100	13	7	0	0	8	28	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

Table 2 UK islet transplant activity between 1 April 2016 and 31 March 2019, by islet status, number of patients and financial year

Transplant Centre	2016 - 2017						2017 - 2018						2018 - 2019					
	Routine (SIK)	Priority	Total		Number of patients		Routine (SIK)	Priority	Total		Number of patients		Routine (SIK)	Priority	Total		Number of patients	
			N	%	N	%			N	%	N	%			N	%		
Bristol	0 (0)	1	1	3	1	4	0 (0)	0	0	0	0	0	0	0	0	0	0	0
Edinburgh	9 (0)	8	17	50	11	44	9 (2)	4	13	50	9	47	6 (3)	4	10	36	8	36
King's	2 (0)	1	3	9	2	8	1 (0)	0	1	4	1	5	1 (0)	1	2	7	2	9
Manchester	2 (1)	1	3	9	2	8	3 (2)	3	6	23	4	21	5 (4)	3	8	29	5	23
Newcastle	1 (0)	2	3	9	3	12	0 (0)	0	0	0	0	0	4 (1)	1	5	18	4	18
Oxford	6 (0)	1	7	21	6	24	3 (0)	3	6	23	5	26	3 (0)	0	3	11	3	14
Royal Free	0 (0)	0	0	0	0	0	0 (0)	0	0	0	0	0	0 (0)	0	0	0	0	0
TOTAL	20 (1)	14	34	100	25	100	16 (4)	10	26	100	19	100	19 (8)	9	28	100	22	100

Table 3 UK islet transplant list, 31 March 2017 to 31 March 2019, by islet status and financial year

Transplant Centre	31 March 2017				31 March 2018				31 March 2019			
	Routine (SIK)	Priority	N	%	Routine (SIK)	Priority	N	%	Routine (SIK)	Priority	N	%
Bristol	0 (0)	0	0	0	0 (0)	0	0	0	0 (0)	0	0	0
Edinburgh	8 (2)	0	8	38	5 (2)	3	8	28	6 (0)	2	8	19
King's	0 (0)	0	0	0	1 (0)	0	1	3	2 (0)	0	2	5
Manchester	2 (0)	1	3	14	8 (7)	1	9	31	18 (15)	1	19	45
Newcastle	2 (0)	1	3	14	8 (1)	1	9	31	5 (1)	0	5	12
Oxford	4 (0)	3	7	33	2 (0)	0	2	7	2 (0)	3	5	12
Royal Free	0 (0)	0	0	0	0 (0)	0	0	0	3 (0)	0	3	7
TOTAL	16 (2)	5	21	100	24 (10)	5	29	100	36 (16)	6	42	100

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

Number of grafts	No. of transplants	No. with known outcome at one year	No. with known graft failure at one year
Routine only	57	53	15
Routine and one priority graft	79	74	2
Routine and two priority grafts	1	1	0
Total	137	128	17

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

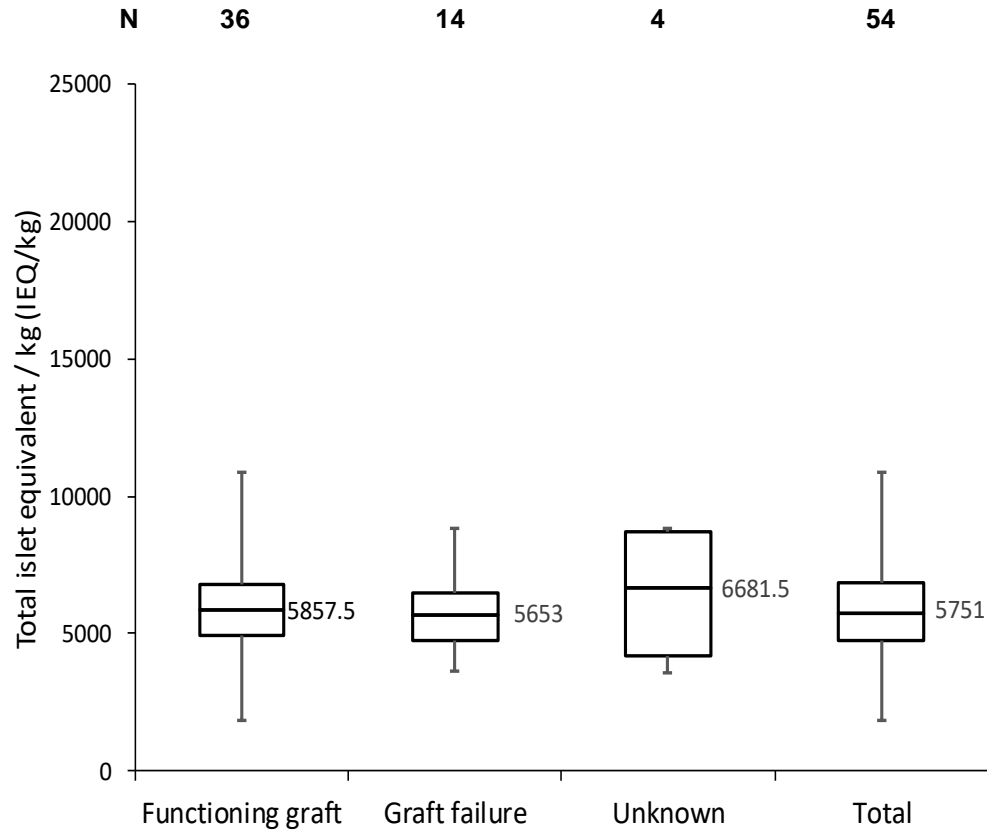
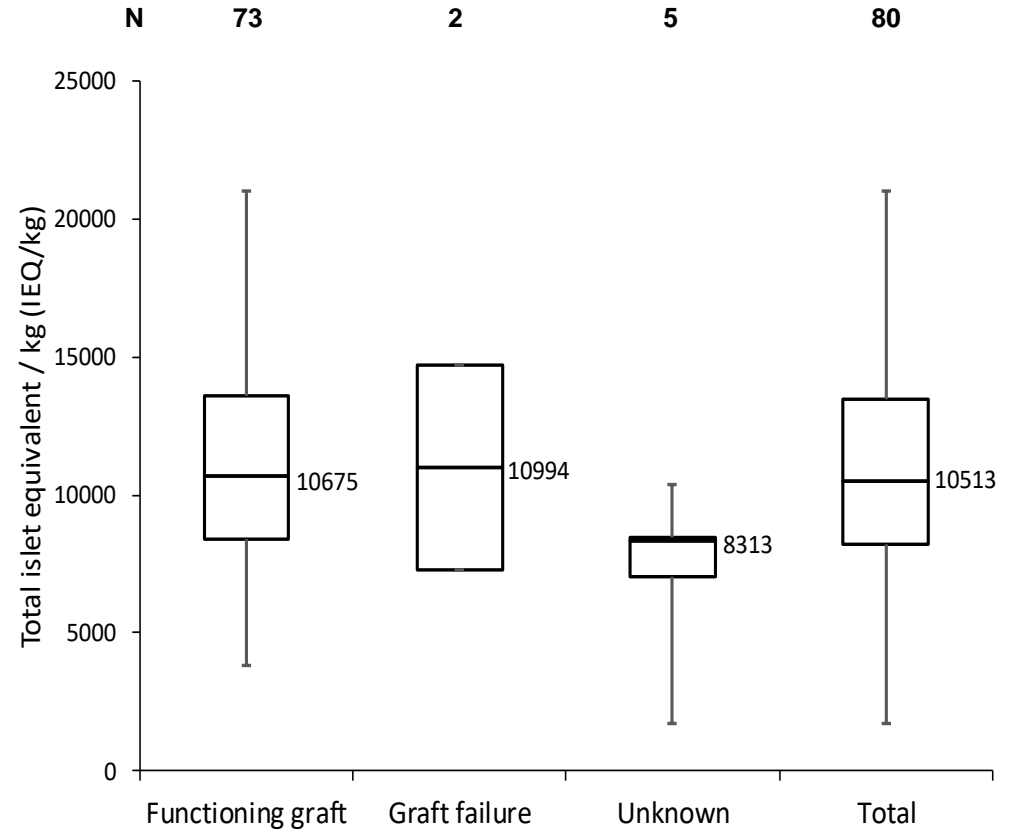


Figure 2 One-year graft function by total IEQ per kg recipient body weight for routine and priority grafts, 1 April 2010 to 31 March 2018



- 16 Kaplan-Meier survival plots showing one-year and five-year graft survival after first routine 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 50%, 95% CI (39-60%).
- 17 **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 59%, 95% CI (45-71%). This difference was statistically significant, $p < 0.0001$.
- 18 **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 61%, 95% CI (46-74%). This difference was not statistically significant, $p > 0.05$.

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

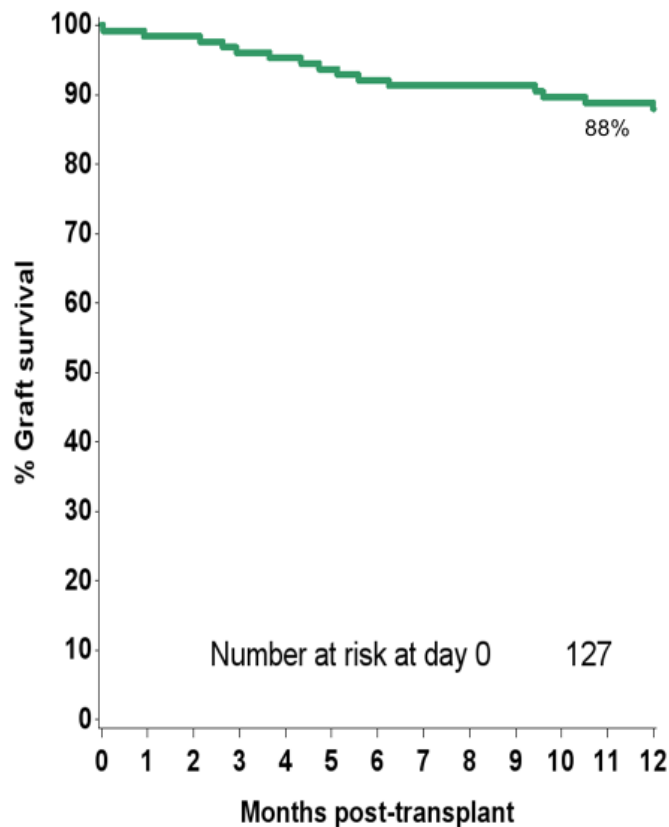


Figure 4 Five-year graft survival following first routine islet transplantation performed in the UK between 1 April 2008 and 31 March 2018

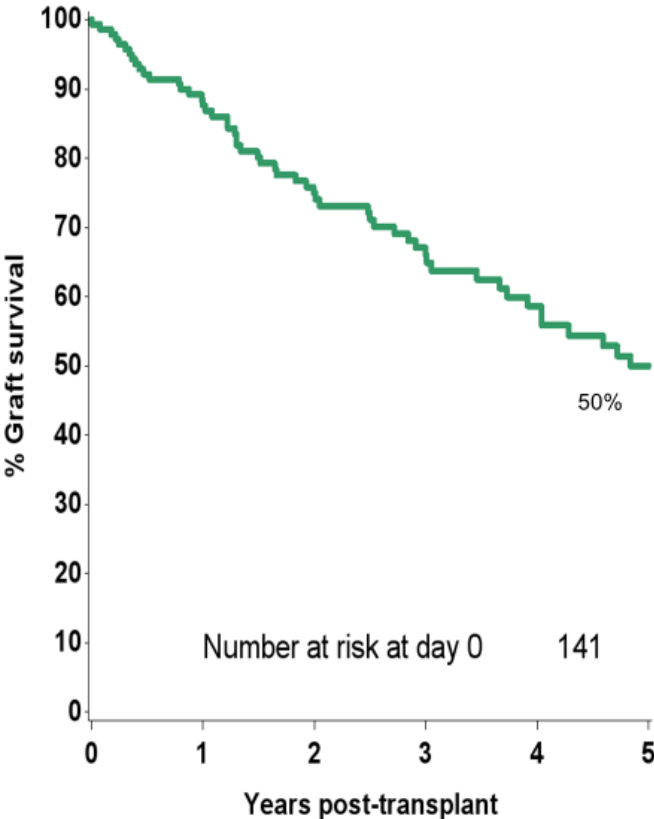


Figure 5 Five-year graft survival following first routine islet transplantation performed in the UK between 1 April 2008 and 31 March 2018, by type of graph

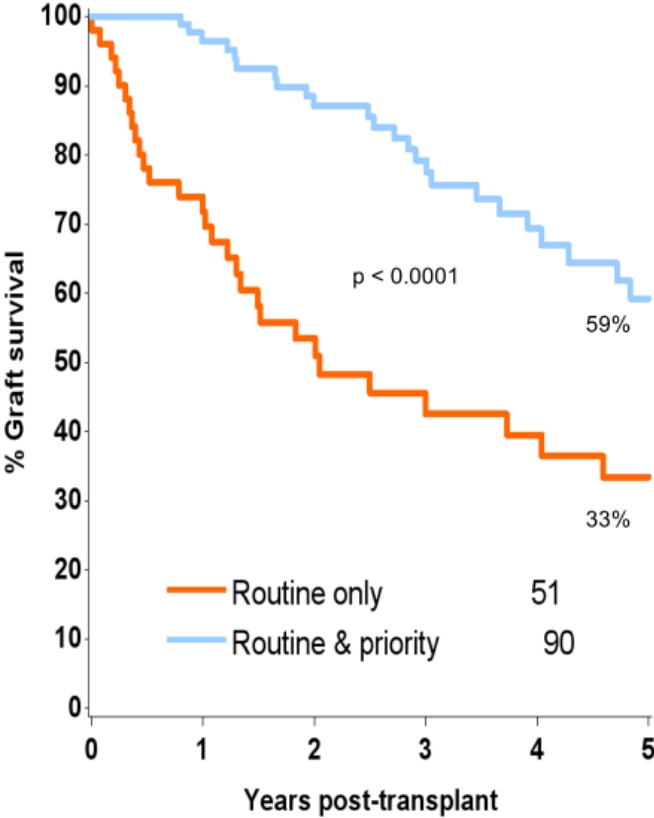
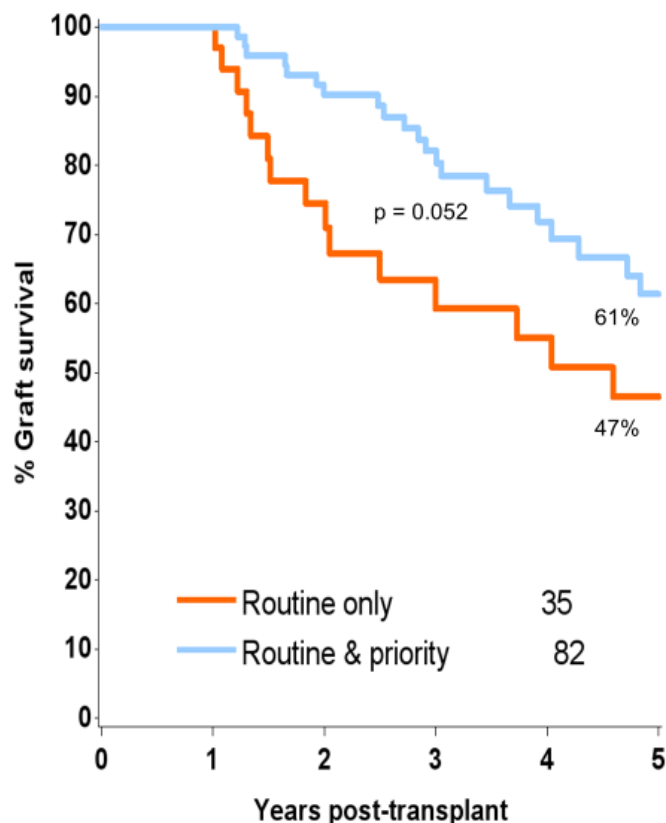


Figure 6 Five-year graft survival following first routine islet transplantation where the routine graft was functioning at one year in the UK between 1 April 2008 and 31 March 2018, by type of graph



- 19 **Figures 7 and 8** 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 103 cases and 66 (64%) patients had a reduced number of events. 84 (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.
- 20 Median HbA1c is reported in **Figure 9** for routine only grafts and **Figure 10** for routine and priority grafts. Overall, data were available to calculate the reduction in HbA1c in 110 cases at one-year post-transplant and in 92 (84%) patients a reduction in HbA1c was reported. The proportion of patients with HbA1c of less than 53 mmol/mol was 18% of 133 at time of transplant, 60% of 113 at one-year post-transplant and 38% of 66 patients at three years post-transplant.
- 21 **Figure 11 and Figure 12** show the median insulin dose for routine only grafts and routine and priority grafts, respectively. Overall, in 86 (90%) patients a reduction in insulin dose between transplant and one-year post-transplant was reported. 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.

Figure 7 Reduction in severe hypoglycaemic events three years post-transplant for routine only grafts, 1 April 2010 – 31 March 2018 (excluding SIK transplants)

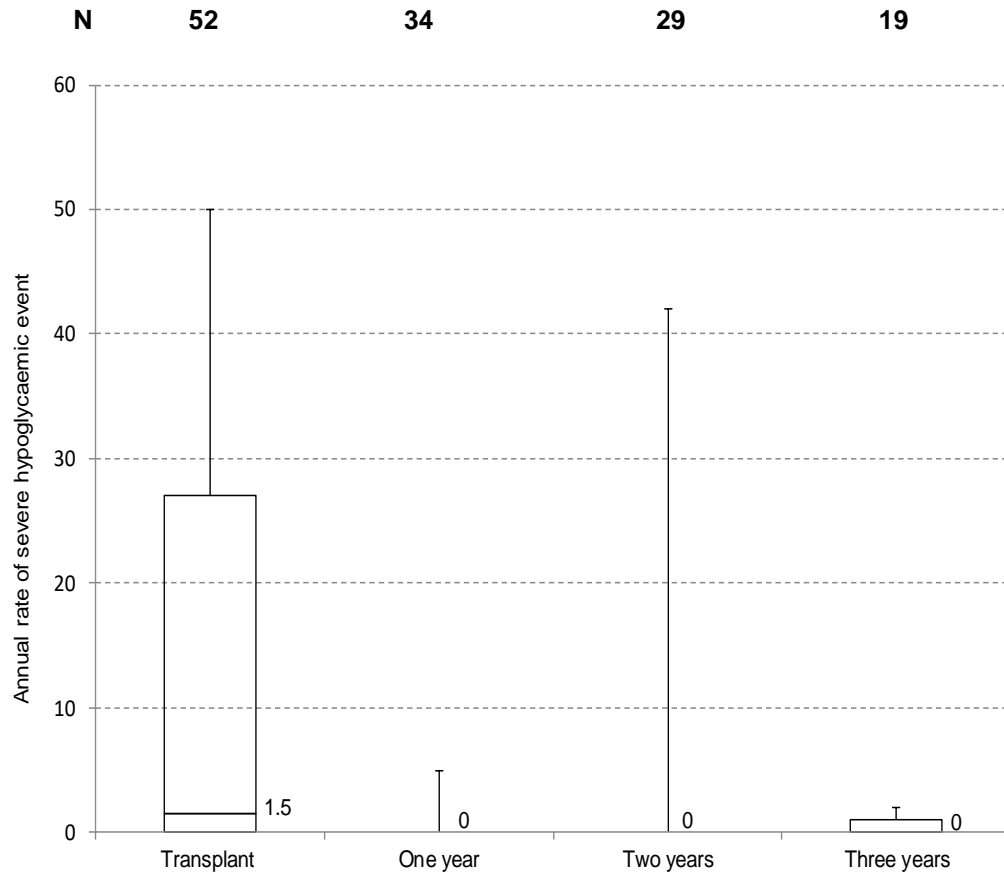


Figure 8 Reduction in severe hypoglycaemic events three years post-transplant for routine and priority grafts, 1 April 2010 – 31 March 2018 (excluding SIK transplants)

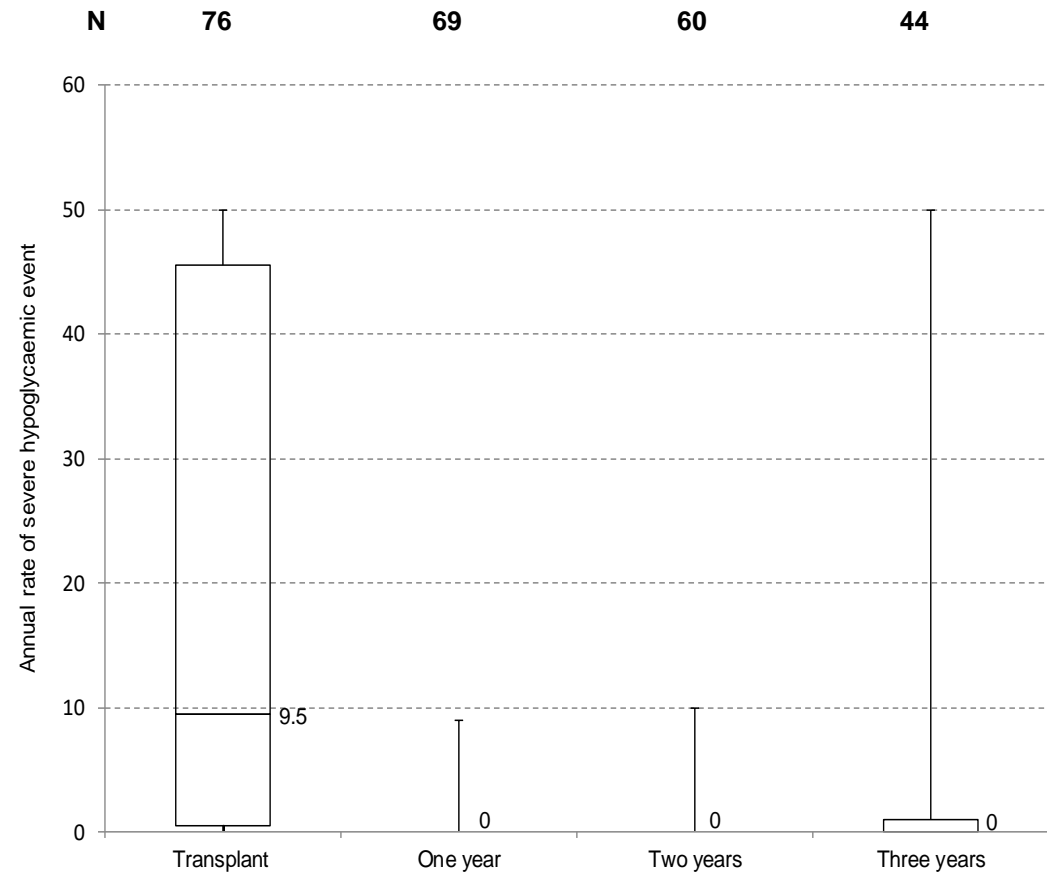


Figure 9 Reduction in HbA1C three years post-transplant for routine only grafts, 1 April 2010 – 31 March 2018

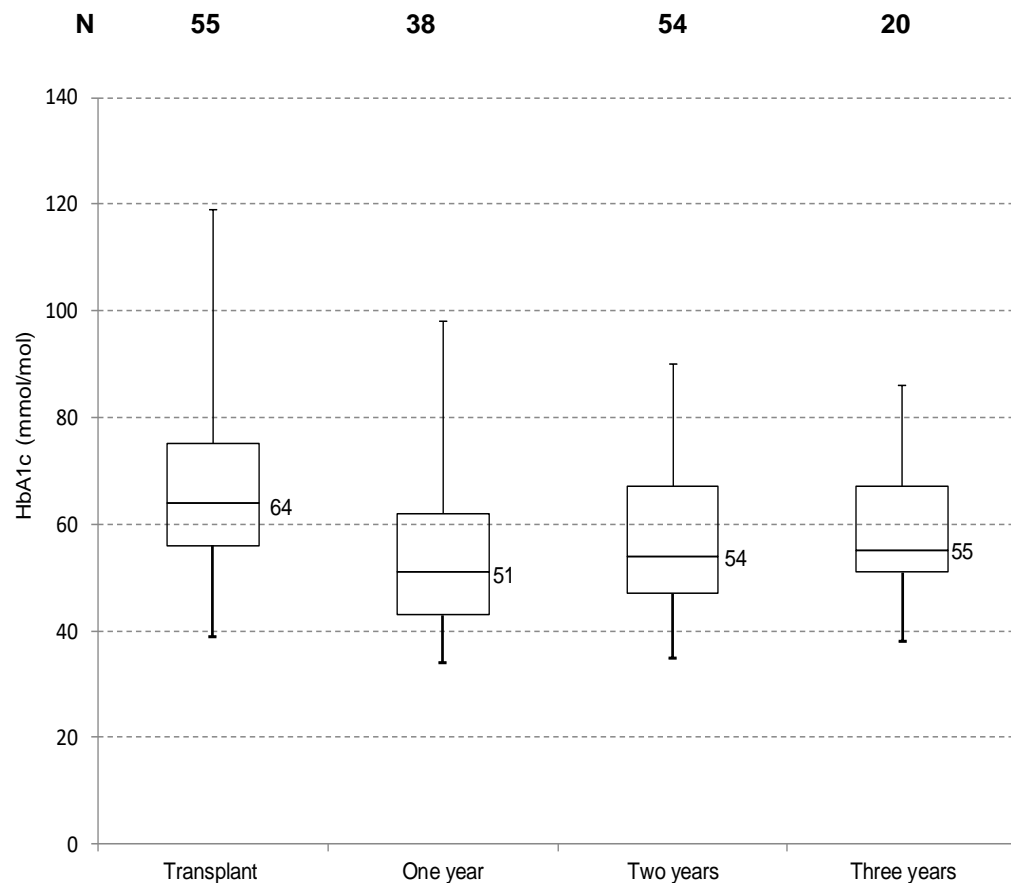


Figure 10 Reduction in HbA1C three years post-transplant for routine and priority grafts, 1 April 2010 – 31 March 2018

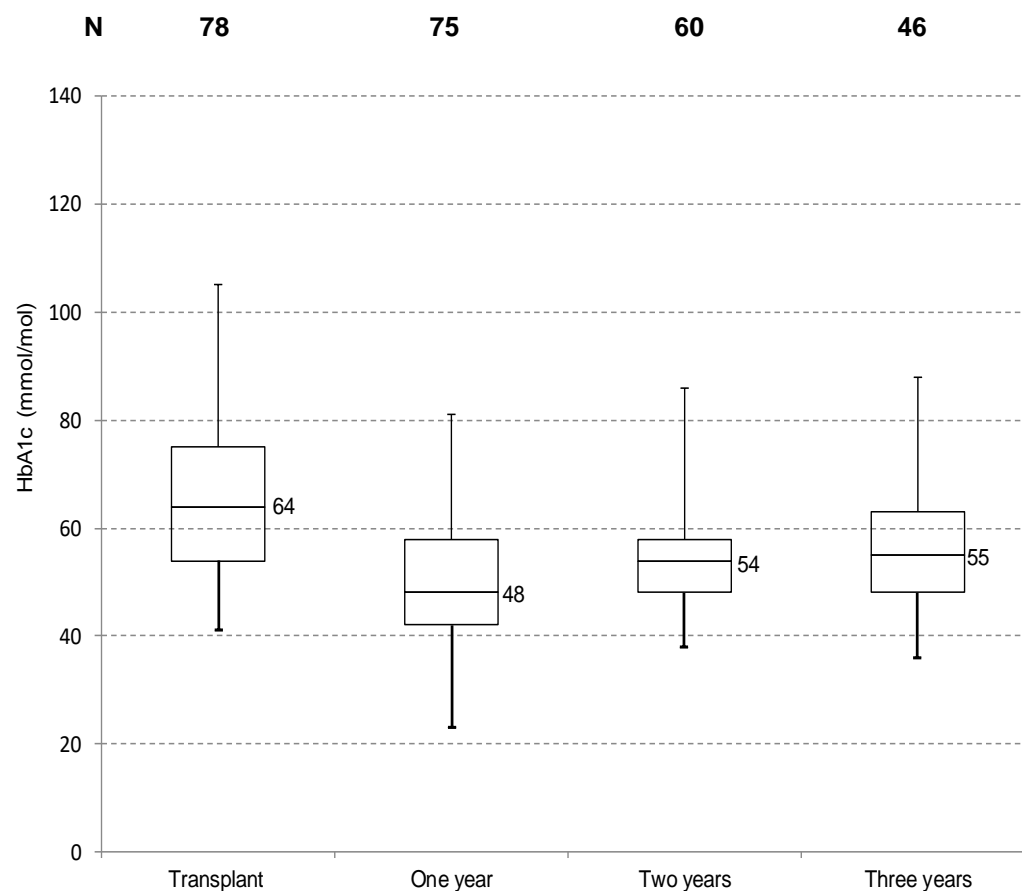


Figure 11 Insulin dose three-years post-transplant for routine only grafts, 1 April 2010 – 31 March 2018

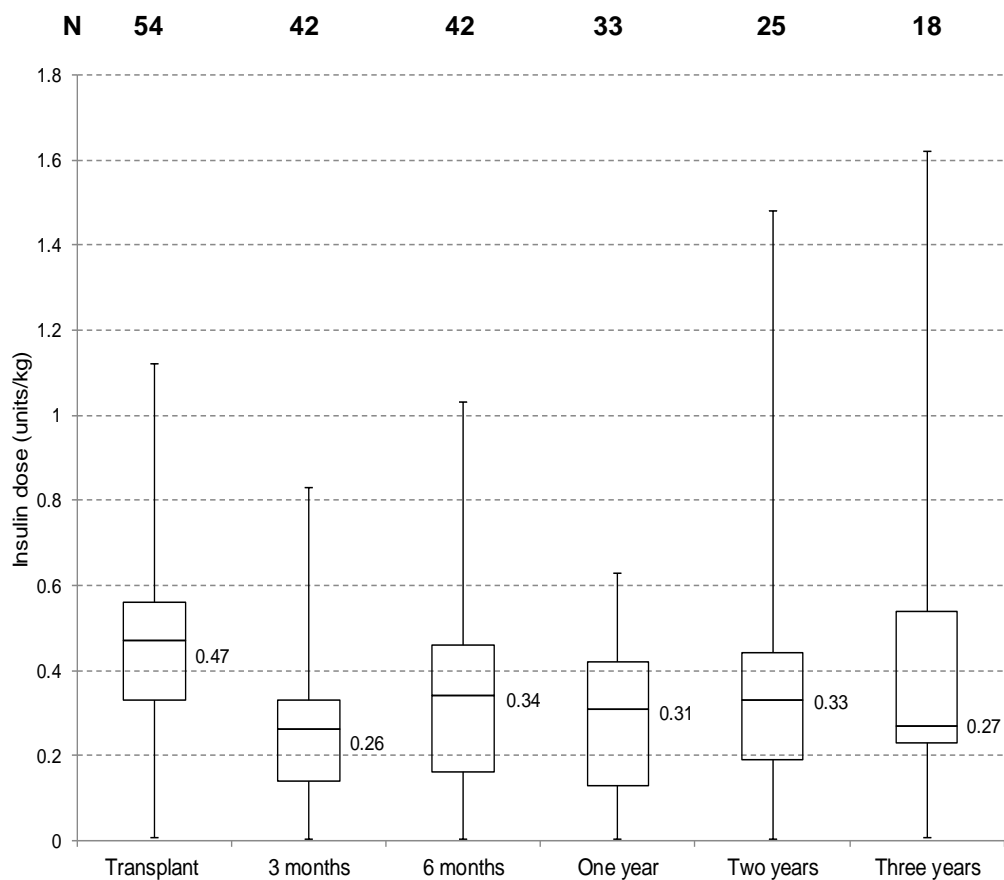
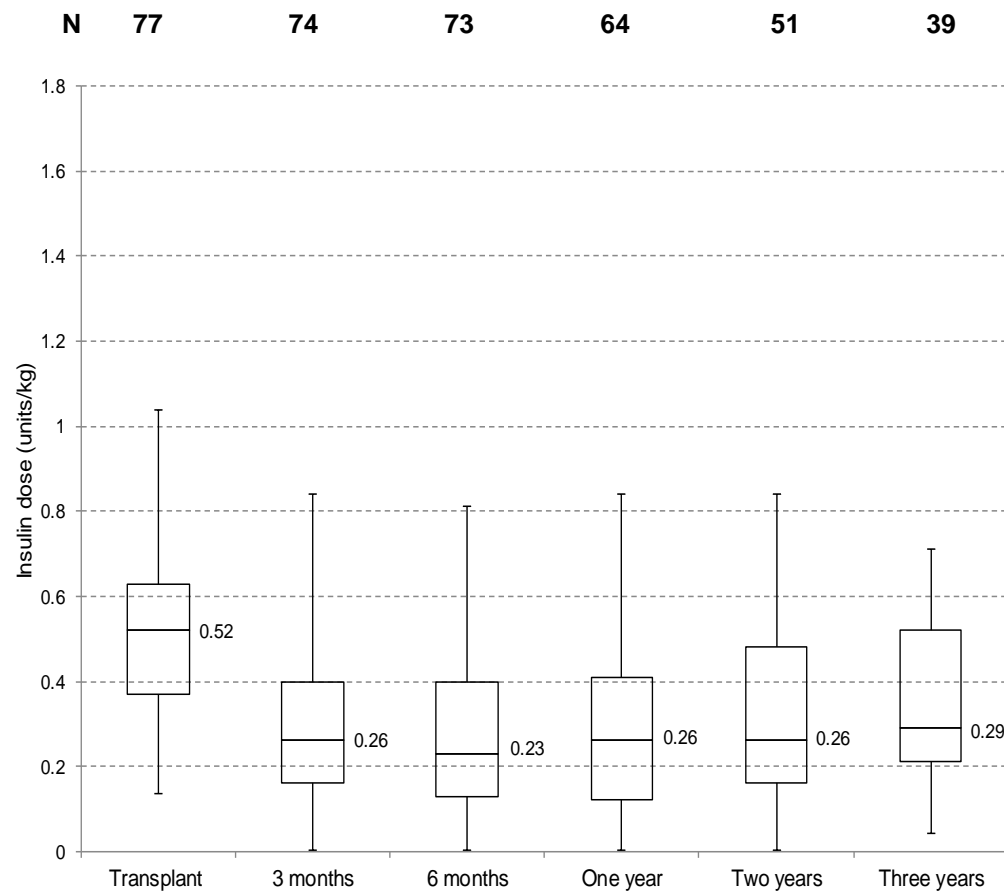


Figure 12 Insulin dose three-years post-transplant for routine and priority grafts, 1 April 2010 – 31 March 2018



SUMMARY

- 22 In 2018/19, the number of islet transplants had increased slightly from 2017/18. The number on the waiting list at the end of the financial year had also increased, in part due to an increase in patients registered for an SIK transplant.
- 23 One-year graft survival was 88% and five-year graft survival was 50%. Those patients receiving a routine and a priority top-up graft had significantly better five-year graft survival than those receiving a routine only, 59% 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.

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July 2019

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	0	0
Edinburgh	50	35	45	2	1
King's College	8	5	8	2	0
Manchester	11	8	10	1	0
Newcastle	25	13	24	3	0
Oxford	29	15	27	8	1
Royal Free	11	5	11	1	0
Total	137	82	128	17	2

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	47	50 (20 – 50)	29 (9 – 50)	0 (0 – 0)	27 (7 – 50)	35	6 (13)
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	25	10 (5 – 25)	20 (2 – 33)	0 (0 – 1)	19 (0 – 30)	14	6 (24)
Oxford	29	2 (1 – 3)	0 (0 – 0)	0 (0 – 0)	0 (0 – 2)	5	10 (34)
Royal Free	11	4 (0 – 8)	0 (0 – 0)	0 (0 – 0)	0 (0 – 0)	1	2 (18)
Total	131	15 (4 – 50)	7 (0 – 34)	0 (0 – 0)	3 (0 – 35)	66	28 (21)

¹ Excluding SIK transplants
² Only available for 70 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)	-3 (-13 – 37)	1	0 (0)	
Edinburgh	50	59 (51 – 68)	53 (46 – 61)	5 (-1 – 13)	31	8 (16)	
King's College	8	67 (59 – 86)	44 (42 – 45)	15 (9 – 33)	6	2 (25)	
Manchester	11	64 (56 – 76)	44 (42 – 47)	22 (9 – 40)	8	3 (27)	
Newcastle	25	77 (67 – 88)	52 (42 – 60)	18 (14 – 33)	19	5 (20)	
Oxford	29	62 (55 – 70)	48 (41 – 56)	17 (10 – 25)	21	9 (24)	
Royal Free	11	61 (56 – 86)	53 (43 – 57)	4 (0 – 20)	6	2 (18)	
Total	137	64 (55 – 75)	50 (42 – 59)	13 (3 – 21)	92	27 (20)	

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	50	0.52 (0.36 – 0.61)	0.30 (0.11 – 0.44)	0.23 (0.14 – 0.32)	19	13 (26)
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	11	0.52 (0.40 – 0.53)	0.29 (0.25 – 0.38)	0.26 (0.24 – 0.27)	4	3 (27)
Newcastle	25	0.51 (0.36 – 0.63)	0.36 (0.18 – 0.47)	0.20 (0.14 – 0.29)	5	9 (36)
Oxford	29	0.47 (0.33 – 0.62)	0.26 (0.12 – 0.38)	0.26 (0.07 – 0.43)	5	9 (31)
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	137	0.48 (0.35 – 0.60)	0.28 (0.12 – 0.42)	0.23 (0.11 – 0.31)	39	41 (30)