

**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 and end of year transplant list for the last three financial years were analysed. Data on 192 (121 routine and 71 priority) islet transplants performed in the UK where the routine transplant was performed between 1 April 2010 and 31 March 2017 were analysed from the UKTR. Outcome data are reported for all routine transplants.

RESULTS

- 3 In 2017/18 there were 26 islet transplants performed, compared to 34 in 2016/17. The number of patients on the islet transplant list at 31 March 2018 was 29, 24 routine and five priority, compared with 21 in 2016/17.
- 4 Kaplan-Meier estimated one-year graft survival for routine grafts between 1 April 2010 – 31 March 2017 is 88%, 95% CI (81 – 93). Kaplan-Meier estimated five-year graft survival, where the graft was still functioning at one-year post-transplant, is 44%, 95% CI (24 – 62) for routine only grafts and 60%, 95% CI (42 – 74) for routine grafts followed by a priority graft. This difference was statistically significant, $p=0.02$.
- 5 For patients receiving an islet alone transplant, the median annual rate of severe hypoglycaemic events fell from 5.5 events (IQR 0 - 34) at time of transplant, to none at one, two and three years' post-transplant. 77 (80%) patients experienced no severe hypoglycaemic events in the first-year post-transplant.
- 6 Median HbA1c fell from 64 mmol/mol (IQR 55 – 75) at time of transplant, to 51 mmol/mol (IQR 42 – 59) at one year and 54 (IQR 47 – 64) three years post-transplant. Reduction in HbA1c was reported for 85 (84%) patients at one-year post-transplant.
- 7 The median insulin dose fell from 0.49 units/kg (IQR 0.35 – 0.60) at time of transplant to 0.28 units/kg three years post-transplant. Insulin dependence at some point in the first-year post-transplant was achieved for 31% of patients.

SUMMARY

- 8 In 2017/18, the number of islet transplants had slightly decreased from 2016/17 and the number on the waiting list at the end of the financial year had increased. One-year graft survival is 88%. Reduction in 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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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 and end of year transplant list between 1 April 2015 and 31 March 2018 from the UK Transplant Registry (UKTR) are reported, by centre and financial year.
- 11 Additionally, data on 192 (121 routine and 71 priority) islet transplants performed in the UK where the routine transplant was performed between 1 April 2010 and 31 March 2017 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. This 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.
- 13 The four key measures of islet transplant outcome are:
- i. Graft function
 - ii. Reduction in HbA1c (mmol/mol)
 - iii. Reduction in annual rate of severe hypoglycaemic events
 - iv. Reduction in insulin dose

All outcomes are reported at one-year, two-years and three-years post routine transplant.

- 14 One-year centre specific outcomes are presented in the Appendix.

RESULTS

- 15 The number of islet transplants performed by centre for the last three financial years, 1 April 2015 to 31 March 2018, 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.
- 16 Between 1 April 2010 and 31 March 2017, there were a total of 192 islet transplants performed, 121 (63%) of which were routine. Of the 121 routine transplants performed, 70 patients received priority grafts in the time period analysed (including 1 patient who required two priority grafts). The majority of

- priority grafts were transplanted within six months of their routine graft. The time to first priority graft ranged from: 0-3 months for 17 patients; 3-6 months for 28 patients; 6-12 months for 24 patients and more than one year for one patient who was highly sensitised.
- 17 The number of known graft failures at one-year post-transplant is reported in **Table 4**. One-year graft function was recorded for 102 (88%) routine transplants. There were 14 reported graft failures within one year.
 - 18 One-year graft outcome by total IEQ (IEQx1000/kg) transplanted is presented in **Figure 1**. Transplants which resulted in graft failure within one year had a lower median IEQ than those which were still functioning at one year, 5957 and 8943 IEQx1000/kg, respectively.
 - 19 Kaplan-Meier survival plots showing one-year and five-year graft survival after routine transplants are presented in **Figure 2** and **Figure 3**, respectively.
 - 20 **Figure 4** shows a Kaplan-Meier survival plot of five-year graft survival by type of graft, where the graft (routine only or routine followed by a priority) was still functioning at one-year post-transplant. Estimated five-year graft survival for routine only grafts is 44%, 95% CI (24 – 62) and for routine grafts followed by a priority graft is 60%, 95% CI (42 – 74). This difference was statistically significant, $p=0.02$.
 - 21 The median rate of severe hypoglycaemic events, excluding simultaneous islet and kidney transplants, is presented in **Figure 5**. The median annual rate fell from 5.5 events (IQ range: 0 to 34) at time of transplant, to none at one, two and three years' post-transplant. At one-year post transplant data were available in 96 cases and 61 patients (64%) had a reduced number of events at one-year post transplant.
 - 22 77 patients, 80%, experienced no severe hypoglycaemic events during the first year following their routine transplant, whilst 19 (20%) patients experienced between one and nine events.
 - 23 Median HbA1c is reported in **Figure 6**. Overall median HbA1c fell from 64 mmol/mol (IQ range: 55 to 75) at time of transplant, to 51 mmol/mol (IQ range: 42 to 59) at one-year post-transplant. The median HbA1c at three years post-transplant was 54 (IQ range: 47 to 64). Data were available to calculate the reduction in HbA1c in 101 cases at one-year post transplant and in 85 patients (84%) a reduction in HbA1c was reported.
 - 24 The proportion of patients with HbA1c of less than 53 mmol/mol was 18% of 118 at time of transplant, 59% of 104 at one-year post-transplant and 42% of 55 patients at three years post-transplant.
 - 25 **Figure 7** shows the median insulin dose at transplant and specific time points post-transplant. The median insulin dose fell from 0.49 units/kg (IQ range: 0.35 to 0.60) at time of transplant to 0.27 units/kg (IQ range: 0.15 to 0.39) at 3 months post-transplant. This reduction in dose remained constant at one year, two years and three years' post-transplant (0.30 units/kg, 0.27 units/kg and 0.28 units/kg respectively). In 79 (89%) patients a reduction in insulin dose between transplant and one-year post-transplant was reported.

- 26 Of the 104 patients with insulin independence status reported for the first-year post-transplant, 32 (31%) achieved insulin independence at some point in the year.

SUMMARY

- 27 In 2017/18, the number of islet transplants had slightly decreased from 2016/17 and the number on the waiting list at the end of the financial year had increased. One-year graft survival is 88%. Reduction in rate of severe hypoglycaemic events, HbA1c and insulin dose at one-year, two years and three years post routine transplant have been reported.

Table 1 UK islet transplant activity between 1 April 2015 and 31 March 2018, by transplant type and financial year

Transplant Centre	2015 - 2016							2016 - 2017							2017 - 2018									
							Total								Total								Total	
	ITA	IAK	IAP	IAPK	SIK	N	%	ITA	IAK	IAP	IAPK	SIK	N	%	ITA	IAK	IAP	IAPK	SIK	N	%			
Bristol	1	0	0	0	0	1	3	1	0	0	0	0	1	3	0	0	0	0	0	0	0	0		
Edinburgh	18 ³	1 ¹	0	0	0	19	61	16 ²	1	0	0	0	17	50	11 ¹	0	0	0	0	2	13	50		
King's	1	0	0	0	0	1	3	3	0	0	0	0	3	9	1	0	0	0	0	0	1	4		
Manchester	0	0	0	1	0	1	3	2	0	0	0	1 ¹	3	9	2	2	0	0	2 ¹	6	23			
Newcastle	7	0	0	0	0	7	23	3	0	0	0	0	3	9	0	0	0	0	0	0	0	0		
Oxford	2	0	0	0	0	2	6	7 ¹	0	0	0	0	7	21	6	0	0	0	0	0	6	23		
Royal Free	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
TOTAL	29	1	0	1	0	31	100	32	1	0	0	1	34	100	20	2	0	0	4	26	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 5 DCD transplants

Table 2 UK islet transplant activity between 1 April 2015 and 31 March 2018, by islet status, number of patients and financial year

Transplant Centre	2015 - 2016						2016 - 2017						2017 - 2018					
			Total		Number of patients				Total		Number of patients				Total		Number of patients	
	Routine	Priority	N	%	N	%	Routine	Priority	N	%	N	%	Routine	Priority	N	%	N	%
Bristol	1	0	1	3	1	4	0	1	1	3	1	4	0	0	0	0	0	0
Edinburgh	10	9	19	61	13	54	9	8	17	50	11	44	9 ¹	4	13	50	9	47
King's	1	0	1	3	1	4	2	1	3	9	2	8	1	0	1	4	1	5
Manchester	0	1	1	3	1	4	2	1	3	9	2	8	3 ¹	3	6	23	4	21
Newcastle	5	2	7	23	6	25	1	2	3	9	3	12	0	0	0	0	0	0
Oxford	1	1	2	6	2	8	6	1	7	21	6	24	3	3	6	23	5	26
Royal Free	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL	18	13	31	100	24	100	20	14	34	100	25	100	16	10	26	100	19	100

¹ Includes 2 SIK transplants

Table 3 UK islet transplant list, 31 March 2016 to 31 March 2018, by islet status and financial year

Transplant Centre	31 March 2016				31 March 2017				31 March 2018			
	Routine	Priority	Total		Routine	Priority	Total		Routine	Priority	Total	
			N	%			N	%			N	%
Bristol	2	1	3	11	0	0	0	0	0	0	0	0
Edinburgh	9	2	11	39	8 ²	0	8	38	5 ²	3	8	28
King's	2	0	2	7	0	0	0	0	1	0	1	3
Manchester	1	1	2	7	2	1	3	14	8 ³	1	9	31
Newcastle	1	4	5	18	2	1	3	14	8 ¹	1	9	31
Oxford	5	0	5	18	4	3	7	33	2	0	2	7
Royal Free	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL	20	8	28	100	16	5	21	100	24	5	29	100

¹ Includes 1 SIK recipient

² Includes 2 SIK recipients

³ Includes 7 SIK recipients

Number of grafts	No. of transplants	No. with known outcome at one year	No. with known graft failure at one year
Routine only	51	48	12
Routine and one priority graft	69	67	2
Routine and two priority grafts	1	1	0
Total	121	116	14

Figure 1 One-year graft function by total IEQ per kg recipient body weight, 1 April 2010 to 31 March 2017

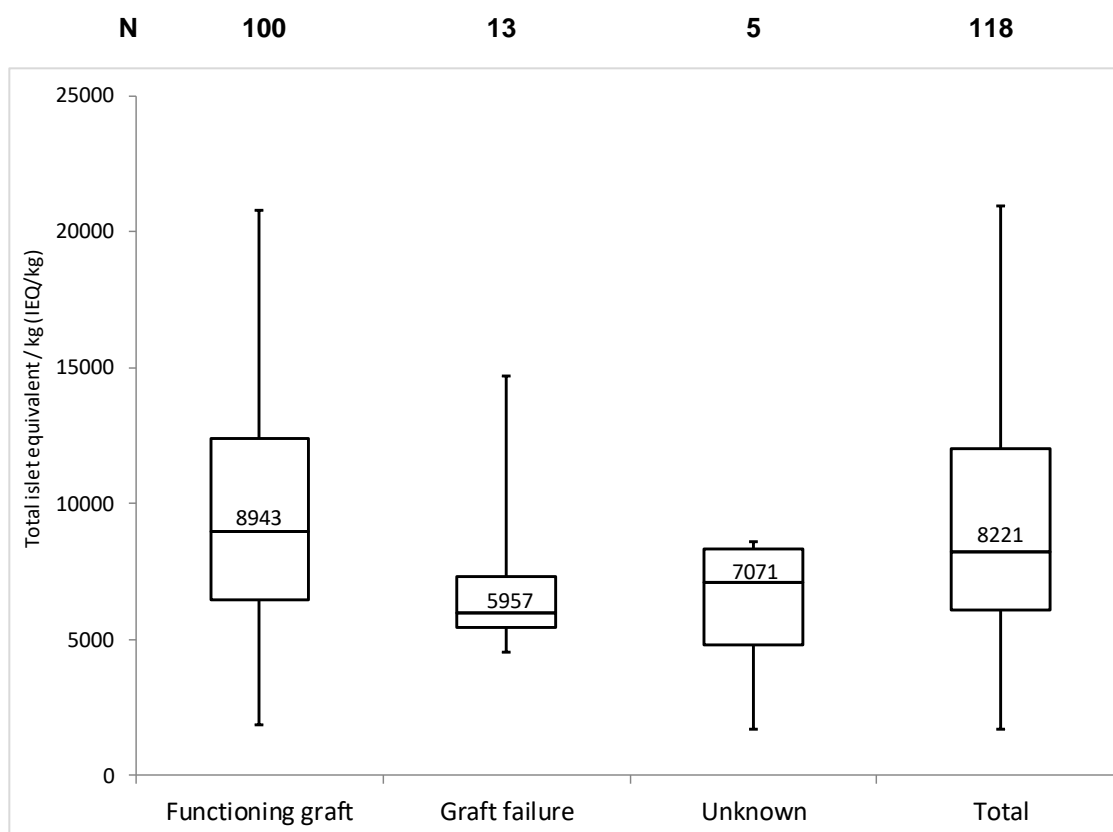


Figure 2 One-year graft survival following routine islet transplantation performed in the UK between 1 April 2010 and 31 March 2017

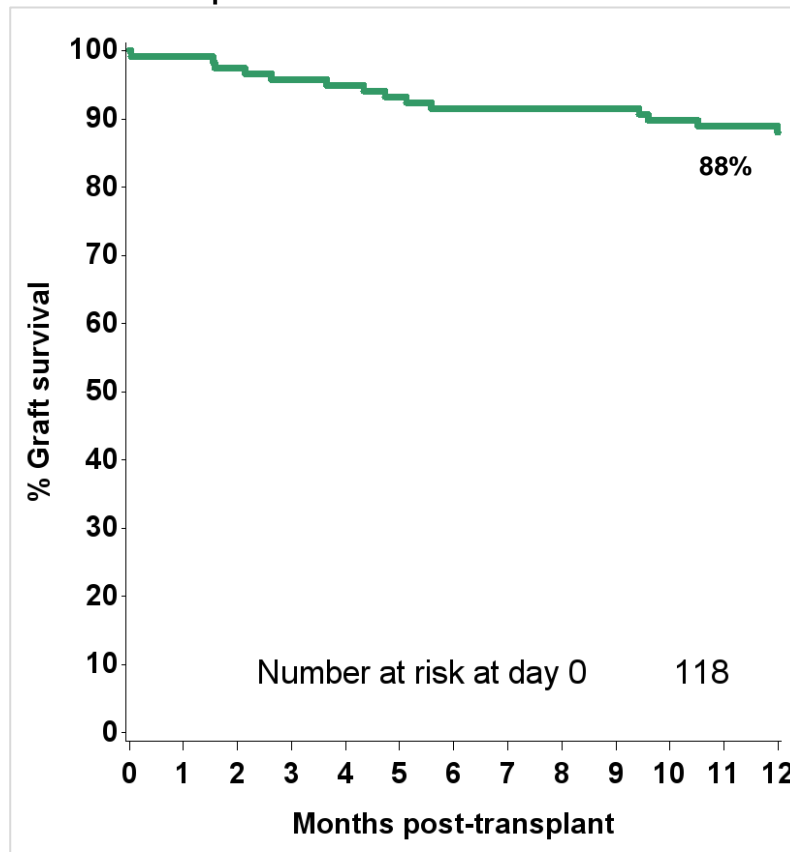


Figure 3 Five-year graft survival following routine islet transplantation performed in the UK between 1 April 2008 and 31 March 2017

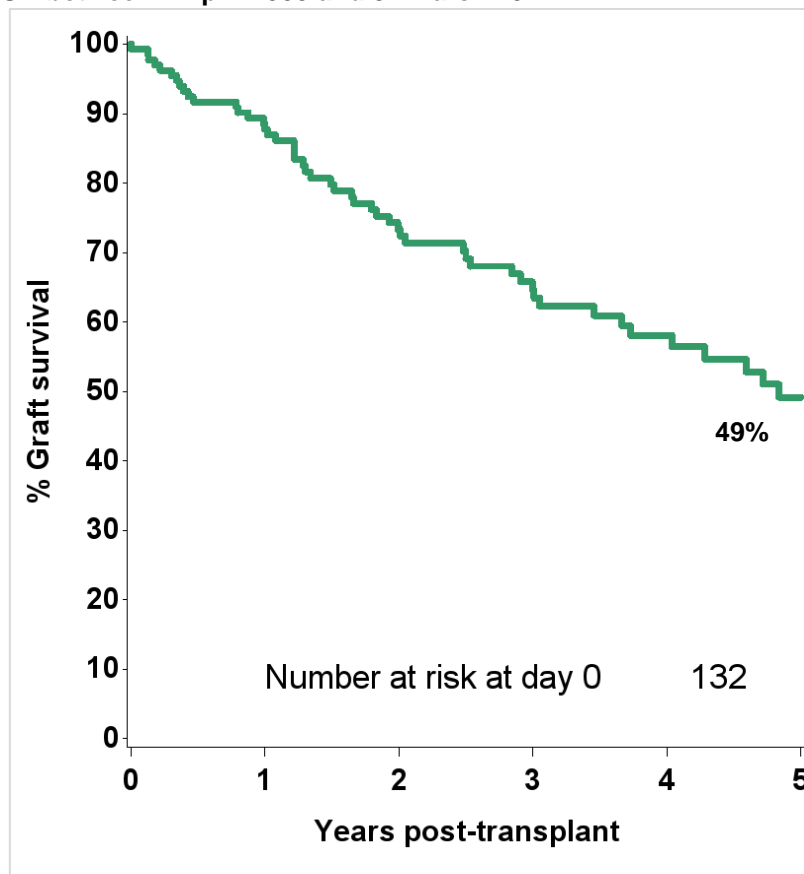


Figure 4 Five-year graft survival following routine islet transplantation performed in the UK between 1 April 2008 and 31 March 2017, by type of graft

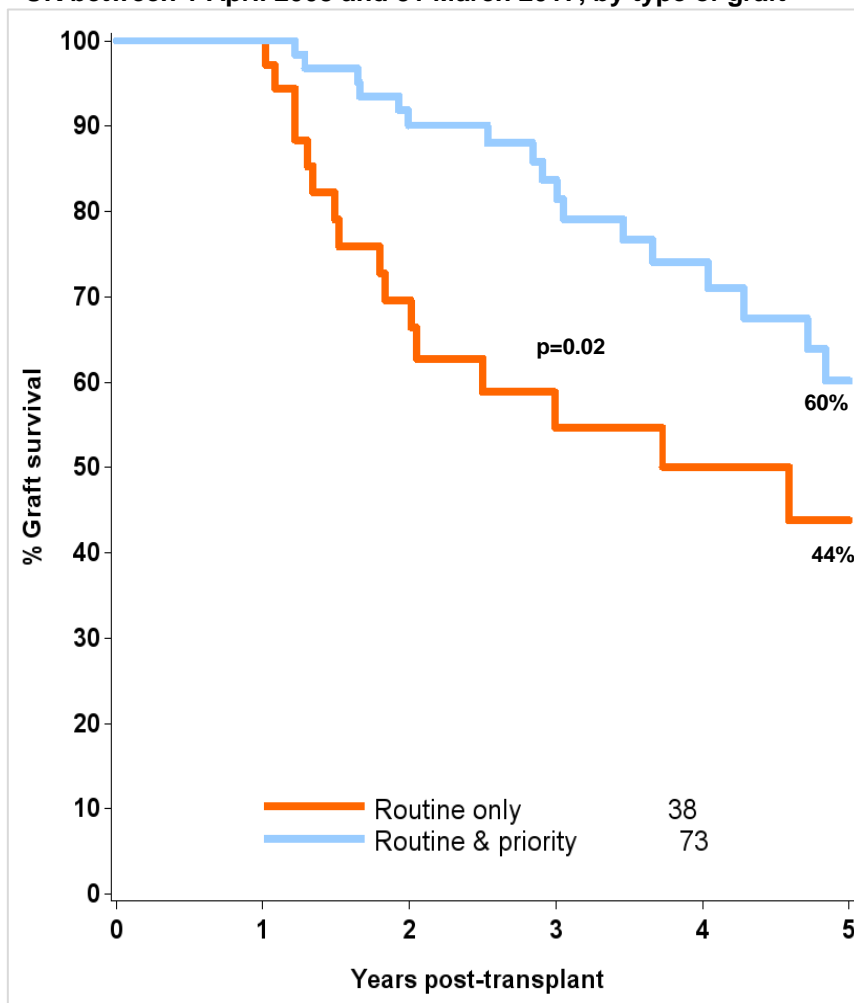


Figure 5 Reduction in severe hypoglycaemic events three years post-transplant, 1 April 2010 – 31 March 2017 (excluding SIK transplants)

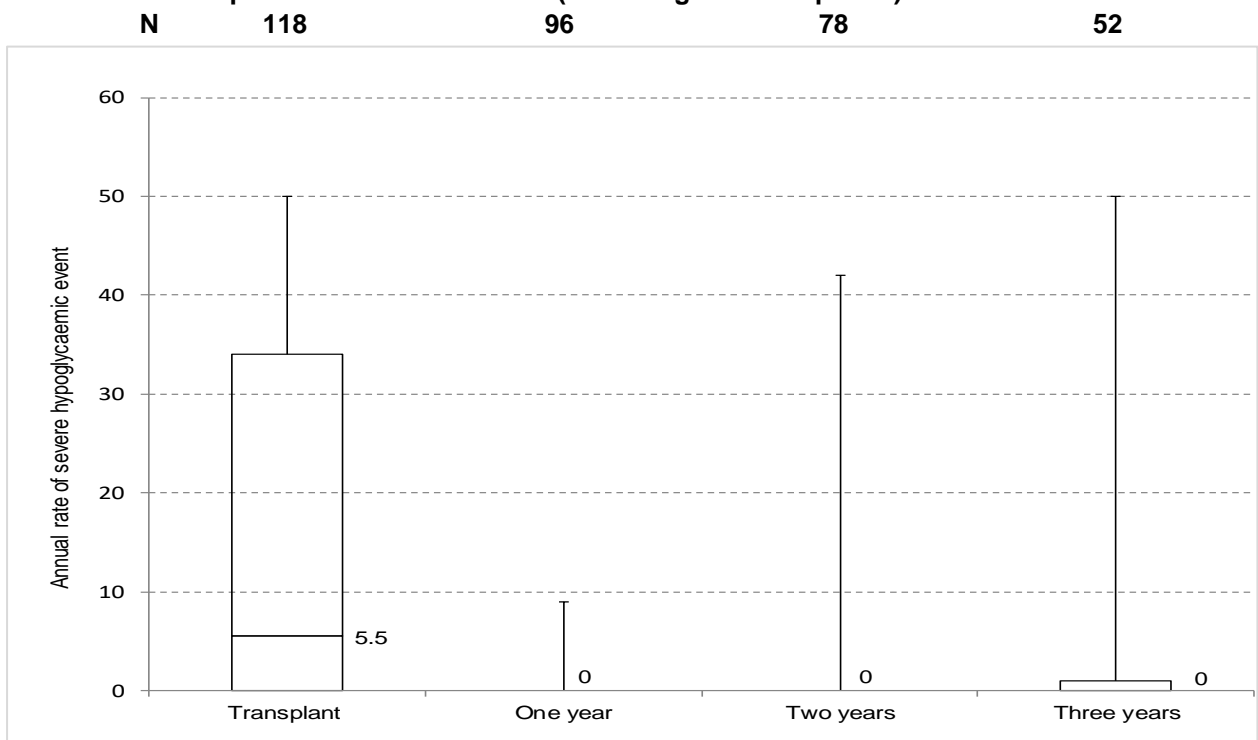


Figure 6 Reduction in HbA1C three years post-transplant, 1 April 2010 – 31 March 2017

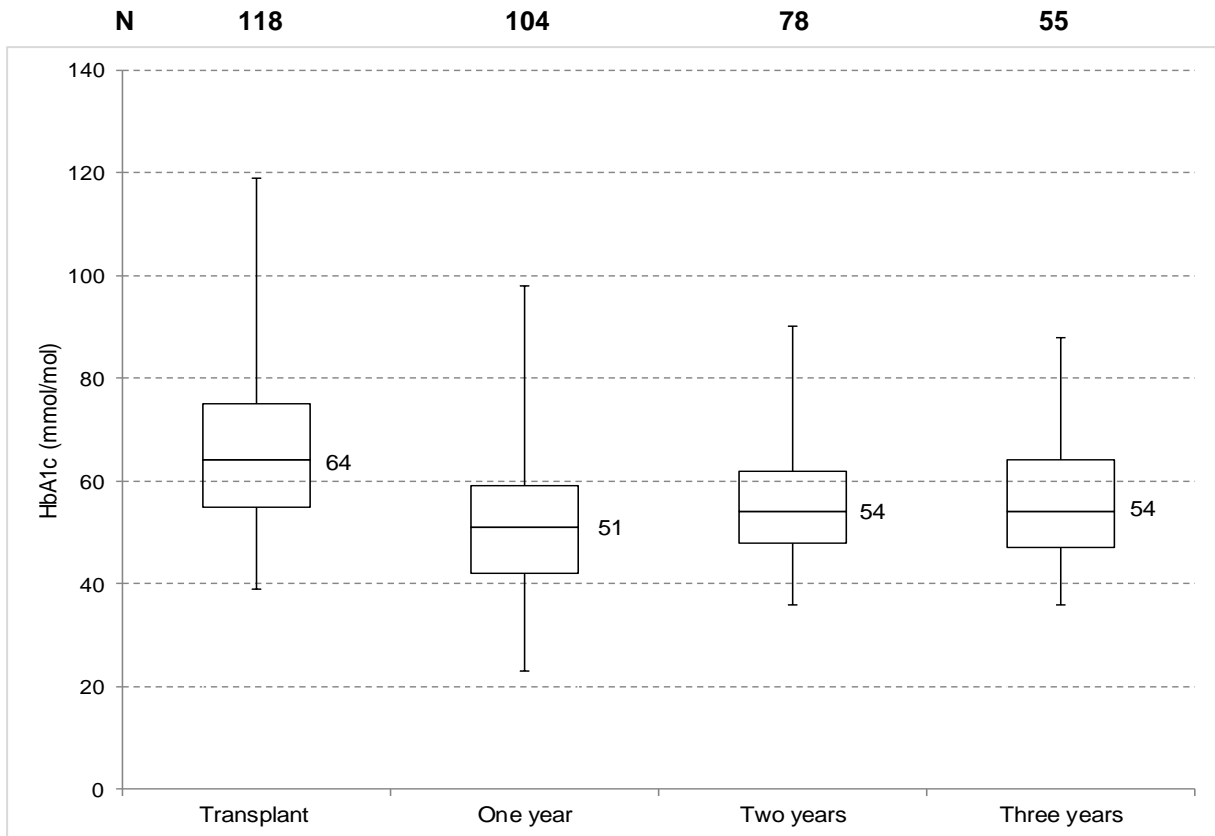
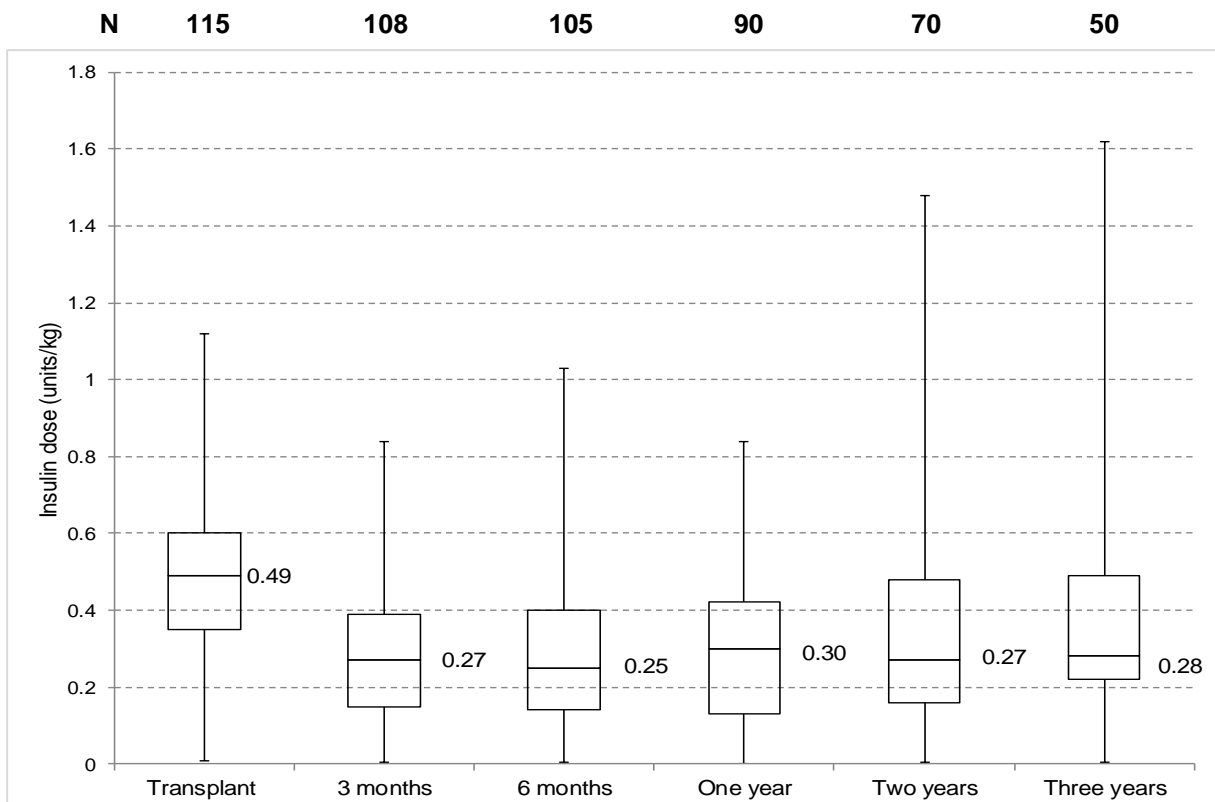


Figure 7 Insulin dose three-years post-transplant, 1 April 2010 – 31 March 2017



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	41	31	40	1	1
King's College	7	4	7	2	0
Manchester	8	5	8	1	0
Newcastle	25	13	24	3	0
Oxford	26	12	24	6	1
Royal Free	11	5	10	1	0
Total	121	71	116	14	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	40	50 (25 – 50)	36(8.5 – 50)	0 (0 – 0)	37 (2 – 50)	31	3 (8)
King's College	7	3 (0 – 4)	2 (0 – 50)	0 (0 – 0)	1.5 (0 – 26.5)	2	3 (43)
Manchester	7	5 (3 – 9)	3 (1 – 10)	0 (0 – 0)	2.5 (1 – 10)	5	1 (13)
Newcastle	25	10 (5 – 25)	20 (2 – 33)	0 (0 – 1)	19 (0 – 30)	14	6 (24)
Oxford	26	1.5 (1 – 2)	0 (0 – 0)	0 (0 – 0)	0 (0 – 2)	5	7 (25)
Royal Free	11	4 (0 – 8)	0 (0 – 0)	0 (0 – 0)	0 (0 – 0)	1	3 (28)
Total	119	20 (4 – 50)	5.5 (0 – 34)	0 (0 – 0)	3 (0 – 39.5)	61	23 (19)

¹ Excluding SIK transplants
² Only available for 59 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	41	59 (53 – 66)	53 (48 – 61)	5 (-3 – 13)	28	3 (7)	
King's College	7	64 (54 – 97)	45 (42 – 45)	11 (9 – 19)	5	2 (29)	
Manchester	8	64 (57 – 77)	43 (42 – 46)	26.5 (14 – 40)	6	2 (25)	
Newcastle	25	77 (67 – 88)	52 (42 – 60)	18 (13.5 – 33)	19	5 (20)	
Oxford	26	62 (55 – 70)	48 (40 – 54)	15 (10 – 25)	20	5 (19)	
Royal Free	11	61 (56 – 86)	53 (42 – 61)	8.5 (1 – 20.5)	6	3 (27)	
Total	121	64 (55 – 75)	51 (42 – 59)	13 (3 – 21)	85	20 (17)	

Transplant centre	No. of routine transplants	Insulin dose/kg			Missing N (%)	Number insulin independent at some point
		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)	0 (0)	1
Edinburgh	41	0.52 (0.36 – 0.60)	0.32 (0.11 – 0.46)	0.21 (0.11 – 0.32)	7 (17)	15
King's College	7	0.35 (0.24 – 0.39)	0.13 (0.07 – 0.21)	0.20 (0.15 – 0.27)	3 (43)	2
Manchester	8	0.53 (0.48 – 0.59)	0.34 (0.25 – 0.38)	0.27 (0.24 – 0.27)	2 (25)	2
Newcastle	25	0.51 (0.36 – 0.63)	0.36 (0.18 – 0.47)	0.20 (0.14 – 0.29)	9 (36)	5
Oxford	26	0.46 (0.33 – 0.62)	0.25 (0.10 – 0.37)	0.26 (0.06 – 0.43)	7 (27)	5
Royal Free	11	0.56 (0.40 – 0.80)	0.44 (0.21 – 0.57)	0.10 (0.00 – 0.46)	4 (36)	2
Total	121	0.49 (0.35 – 0.60)	0.30 (0.13 – 0.42)	0.23 (0.10 – 0.31)	32 (26)	32