NHS BLOOD AND TRANSPLANT

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 156 routine, and subsequent priority, islet transplants performed in the UK between 1 April 2010 and 31 March 2019 were analysed from the UKTR. Outcome data are reported for routine transplants only.

RESULTS

3 In 2019/20 there were 28 islet transplants performed. There were 20 patients on the islet transplant list at 31 March 2020, 18 routine (13 SIK) and two priority patients.

4 One-year graft survival for first routine islet alone grafts is 87% 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 an islet alone routine and a priority graft, the median annual rate of severe hypoglycaemic events fell from 10 events (IQR 0 – 48) at time of transplant, to none at one, two, three and five years' post-transplant. 89 (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 – 63) at three years post-transplant, for patients who received a routine and a priority graft. Overall, a reduction in HbA1c was reported for 96 (83%) 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 0.18 – 0.52) three years post-transplant. Insulin independence at some point in the first-year post-transplant was achieved for 34% of patients overall.

SUMMARY

8 In 2019/20, the number of islet transplants was the same as in 2018/19 and the number on the waiting list at the end of the financial year has halved, although this was as a consequence of the COVID-19 pandemic. One-year graft survival is 87%. 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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Statistics and Clinical Studies **September 2020**

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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 2017 and 31 March 2020 from the UK Transplant Registry (UKTR) are reported, by centre and financial year.

11 Between 1 April 2010 and 31 March 2019, there were 156 routine islet transplants performed in the UK. Outcome data on these 156 routine, and any subsequent priority, islet transplants have been analysed from the UKTR. Outcome data are reported for routine transplants only. 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 financial years, 1 April 2017 to 31 March 2020, 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 2019, there were a total of 247 islet transplants performed, 156 (63%) of which were routine and 91 were priority.

15 For those patients receiving a routine transplant between 1 April 2010 and 31 March 2019, the number of known graft failures at one-year post-transplant is reported in **Table 4**. Of the 156 routine transplants performed, 89 patients subsequently received a priority graft. The majority of these patients received their first priority graft within six months of their routine graft: 0-3 months for 27 (30%) patients; 3-6 months for 33 (37%) patients; 6-12 months for 27 (30%) patients and more than one year for two patients who were highly sensitised.

Table 1 UK islet transplant activity between 1 April 2017 and 31 March 2020, by transplant type and financial year

	2017 - 2018							2018 - 2019							2019 - 2020						
						Total							Total							Total	
Transplant Centre	**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[1]	0	0	0	2	**13**	**50**	5	2	0	0	3	**10**	**36**	9[3]	3	0	0	1	**13**	**46**
King's	1	0	0	0	0	**1**	**4**	2	0	0	0	0	**2**	**7**	2[1]	0	0	0	0	**2**	**7**
Manchester	2	2	0	0	2[1]	**6**	**23**	0	4[2]	0	0	4[2]	**8**	**29**	0	1	0	0	4	**5**	**18**
Newcastle	0	0	0	0	0	**0**	**0**	3	1	0	0	1	**5**	**18**	4	0	0	0	0	**4**	**14**
Oxford	6	0	0	0	0	**6**	**23**	3	0	0	0	0	**3**	**11**	4	0	0	0	0	**4**	**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**	**2**	**0**	**0**	**4**	**26**	**100**	**13**	**7**	**0**	**0**	**8**	**28**	**100**	**19**	**4**	**0**	**0**	**5**	**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
[3] Includes 4 DCD transplants

Table 2 UK islet transplant activity between 1 April 2017 and 31 March 2020, by islet status, number of patients and financial year

Transplant Centre	2017 - 2018						2018 - 2019						2019 - 2020					
			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	0	0	**0**	**0**	**0**	**0**	0	0	**0**	**0**	**0**	**0**	0	0	**0**	**0**	**0**	**0**
Edinburgh	9[2]	4	**13**	**50**	**9**	**47**	6[3]	4	**10**	**36**	**8**	**36**	7[1]	6	**13**	**46**	**8**	**38**
King's	1	0	**1**	**4**	**1**	**5**	1	1	**2**	**7**	**2**	**9**	2	0	**2**	**7**	**2**	**10**
Manchester	3[2]	3	**6**	**23**	**4**	**21**	5[4]	3	**8**	**29**	**5**	**23**	4[4]	1	**5**	**18**	**5**	**24**
Newcastle	0	0	**0**	**0**	**0**	**0**	4[1]	1	**5**	**18**	**4**	**18**	3	1	**4**	**14**	**3**	**14**
Oxford	3	3	**6**	**23**	**5**	**26**	3	0	**3**	**11**	**3**	**14**	2	2	**4**	**14**	**3**	**14**
Royal Free	0	0	**0**	**0**	**0**	**0**	0	0	**0**	**0**	**0**	**0**	0	0	**0**	**0**	**0**	**0**
TOTAL	**16**	**10**	**26**	**100**	**19**	**100**	**19**	**9**	**28**	**100**	**22**	**100**	**18**	**10**	**28**	**100**	**21**	**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 March 2018 to 31 March 2020, by islet status and financial year

Transplant Centre	31 March 2018		Total		31 March 2019		Total		31 March 2020		Total	
	Routine	Priority	N	%	Routine	Priority	N	%	Routine	Priority	N	%
Bristol	0	0	**0**	**0**	0	0	**0**	**0**	0	0	**0**	**0**
Edinburgh	5[2]	3	**8**	**28**	6	2	**8**	**19**	3[1]	1	**4**	**20**
King's	1	0	**1**	**3**	2	0	**2**	**5**	0	1	**1**	**5**
Manchester	8[3]	1	**9**	**31**	18[5]	1	**19**	**45**	15[4]	0	**15**	**75**
Newcastle	8[1]	1	**9**	**31**	5[1]	0	**5**	**12**	0	0	**0**	**0**
Oxford	2	0	**2**	**7**	2	3	**5**	**12**	0	0	**0**	**0**
Royal Free	0	0	**0**	**0**	3	0	**3**	**7**	0	0	**0**	**0**
TOTAL	**24**	**5**	**29**	**100**	**36**	**6**	**42**	**100**	**18**	**2**	**20**	**100**

[1] Includes 1 SIK transplant
[2] Includes 2 SIK transplants
[3] Includes 7 SIK transplants
[4] Includes 12 SIK transplants
[5] Includes 15 SIK transplants

Table 4 One-year graft outcome following routine islet transplant, 1 April 2010 to 31 March 2019

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	60	54	16
Routine and one priority graft	81	77	2
Routine and two priority grafts	1	1	0
SIK routine graft			
Routine only	7	5	2
Routine and one priority graft	7	6	0
Routine and two priority grafts	0	0	0
Total	**156**	**143**	**20**

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 March 2019

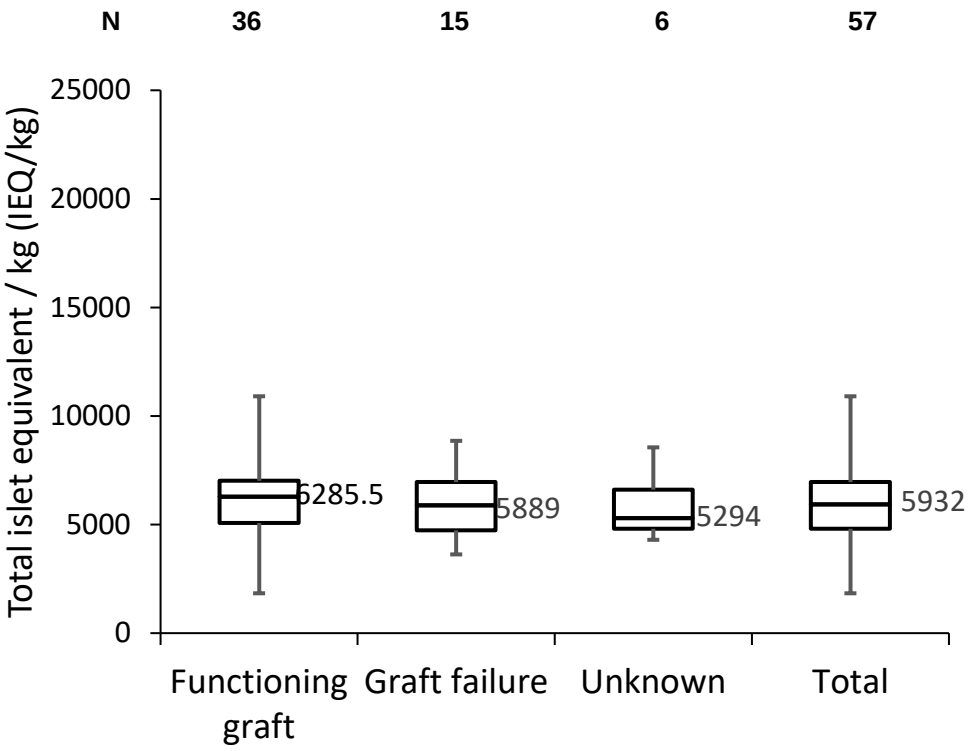
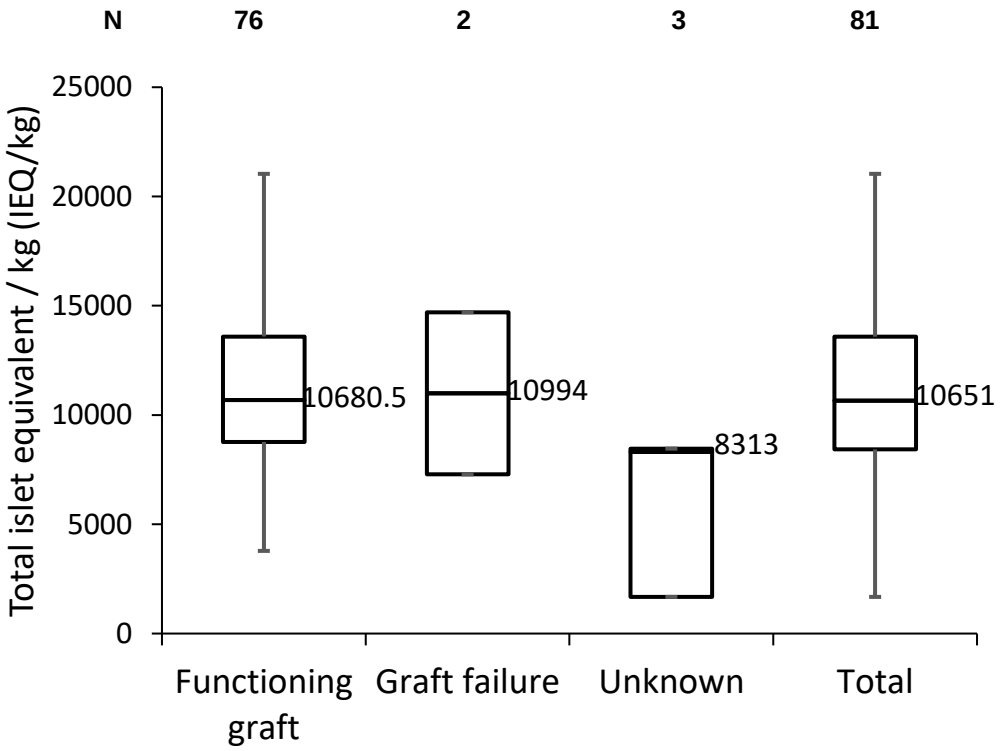


Figure 2 One-year graft function by total IEQ per kg recipient body weight for islet alone routine and priority grafts, 1 April 2010 to 31 March 2019



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 seven SIK routine only transplants was 3594 (IQR 2579 - 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 87%, 95% CI (80-92%) and five year graft survival is 51%, 95% CI (41-60%).

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 (19-47%) and for first routine grafts followed by a priority graft is 60%, 95% CI (47-71%). 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 (28-64%) and for routine grafts followed by a priority graft is 63%, 95% CI (49-74%). This difference was not statistically significant, $p=0.07$.

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 (86-98%).

21 Of the 14 SIK islet transplants in the 1 April 2010 to 31 March 2019 time period, 13 were the first islet transplant for the patient. Of these 13, one year outcome is known for 10 patients and eight were functioning and two had failed.

Figure 3 **One-year graft survival following first routine islet alone transplantation performed in the UK between 1 April 2010 and 31 March 2019**

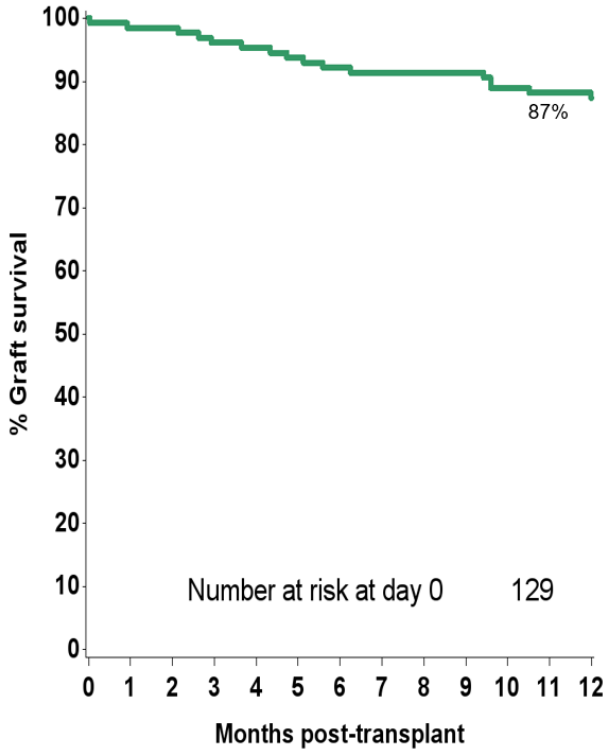


Figure 4 **Five-year graft survival following first routine islet alone transplantation performed in the UK between 1 April 2008 and 31 March 2019**

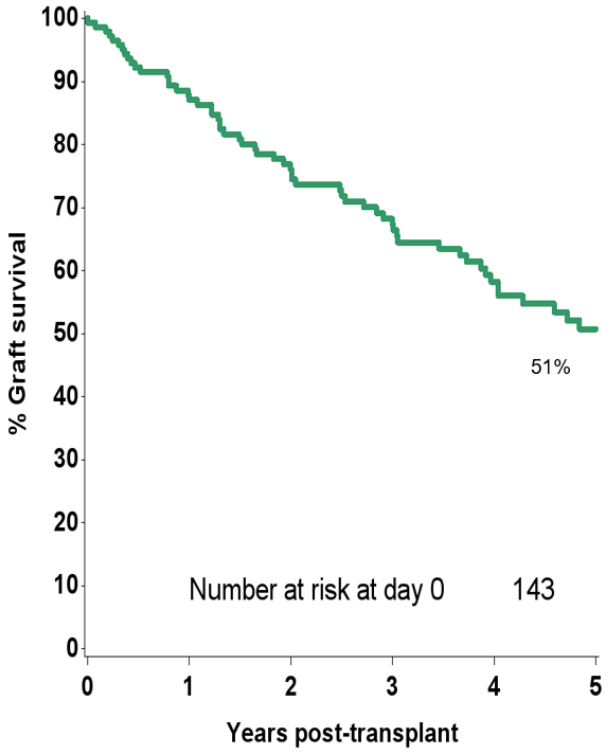


Figure 5 **Five-year graft survival following first routine islet alone transplantation performed in the UK between 1 April 2008 and 31 March 2019, by type of graph**

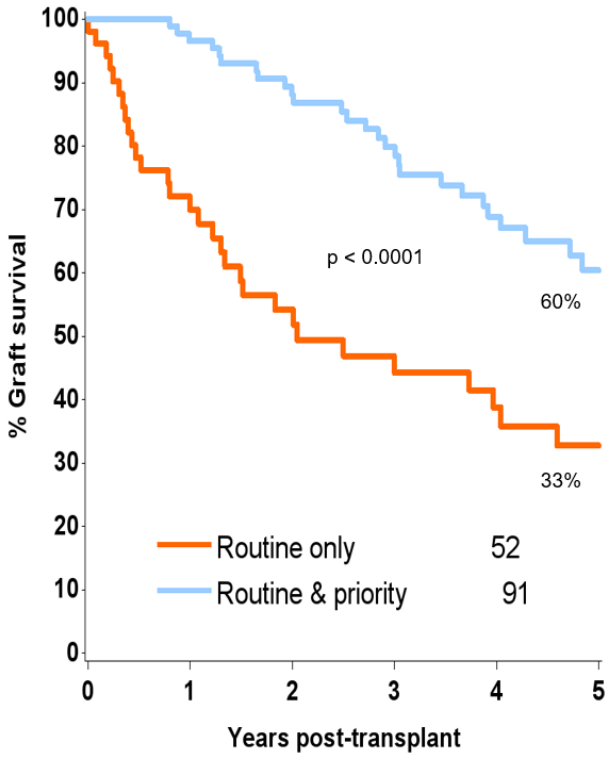


Figure 6 **Five-year graft survival following first routine islet alone transplantation where the routine graft was functioning at one year in the UK between 1 April 2008 and 31 March 2019, by type of graph**

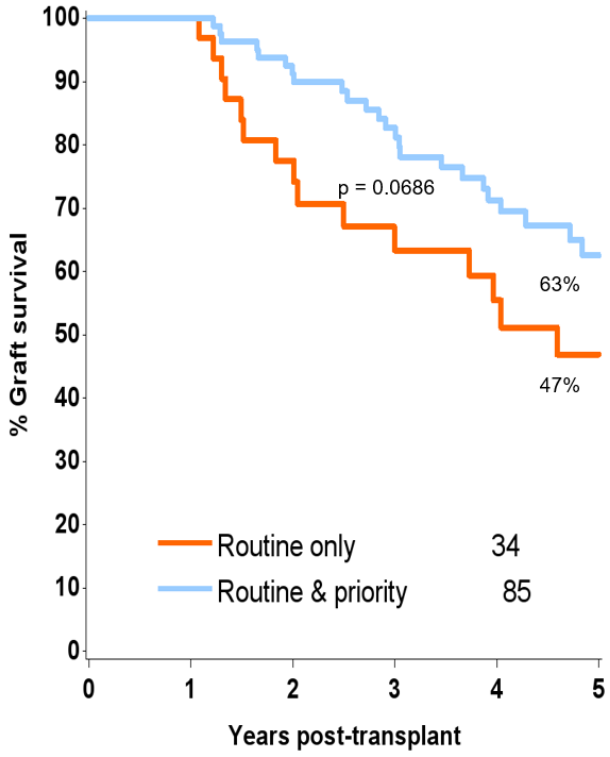
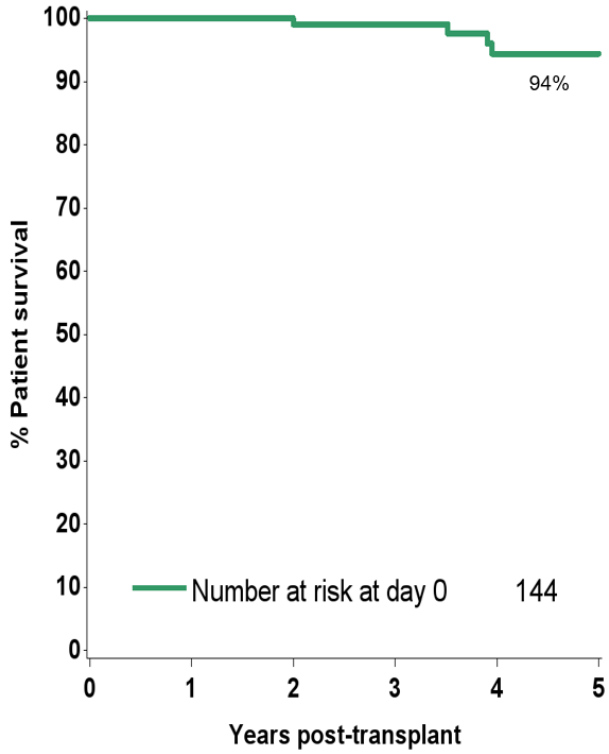


Figure 7 **Five-year patient survival following first routine islet alone transplantation performed in the UK between 1 April 2008 and 31 March 2019**



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 108 cases and 70 (65%) patients had a reduced number of events. 89 (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 13 SIK transplants where severe hypoglycaemic events were reported at transplant, the median rate was 4 (IQR 0-50) and for the 7 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 116 cases at one-year post-transplant and in 96 (83%) patients a reduction in HbA1c was reported. The proportion of patients with HbA1c of less than 53 mmol/mol was 18% of 139 at time of transplant, 58% of 118 patients at one-year post-transplant, 39% of 75 patients at three years and 37% of 35 patients at five years post-transplant.

26 For the 13 SIK transplants where HbA1c was reported at transplant, the median was 69 mmol/mol (IQR 60-76) and for the 6 reported at one-year post-transplant, the median was 49 mmol/mol (IQR 41-70).

Figure 8 **Reduction in severe hypoglycaemic events three years post-transplant for routine only grafts, 1 April 2010 – 31 March 2019 (excluding SIK transplants)**

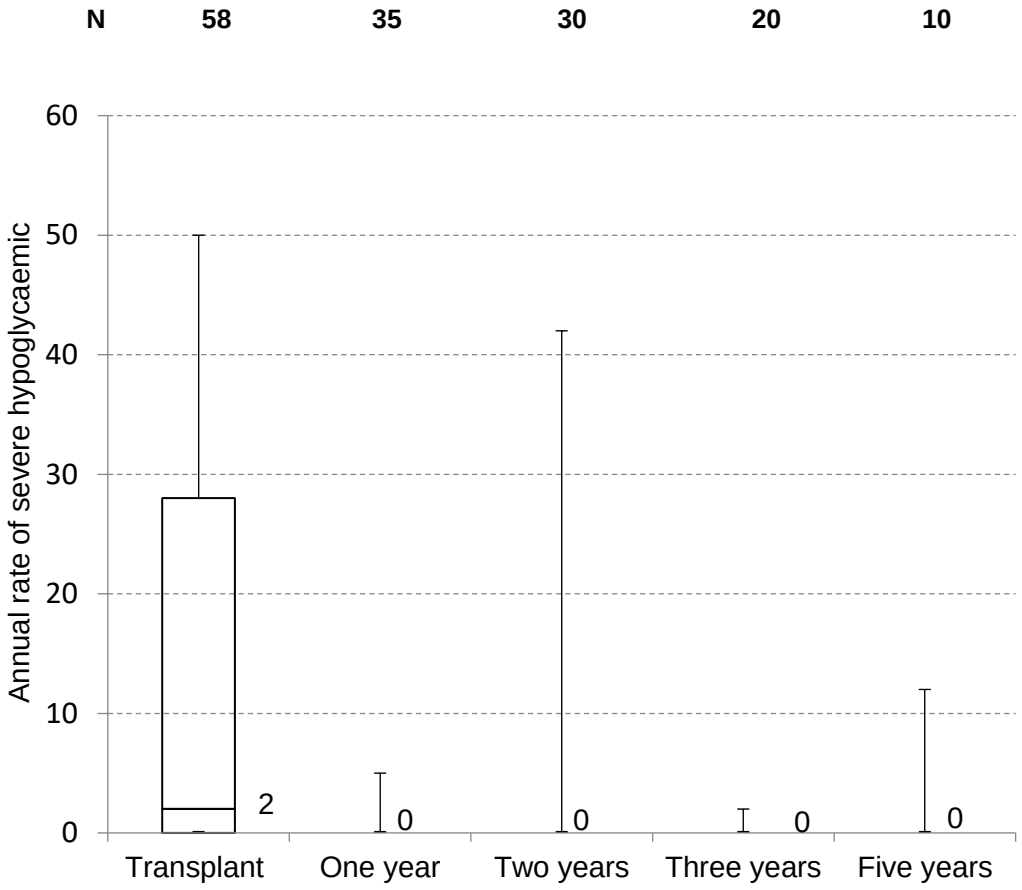


Figure 9 **Reduction in severe hypoglycaemic events three years post-transplant for routine and priority grafts, 1 April 2010 – 31 March 2019 (excluding SIK transplants)**

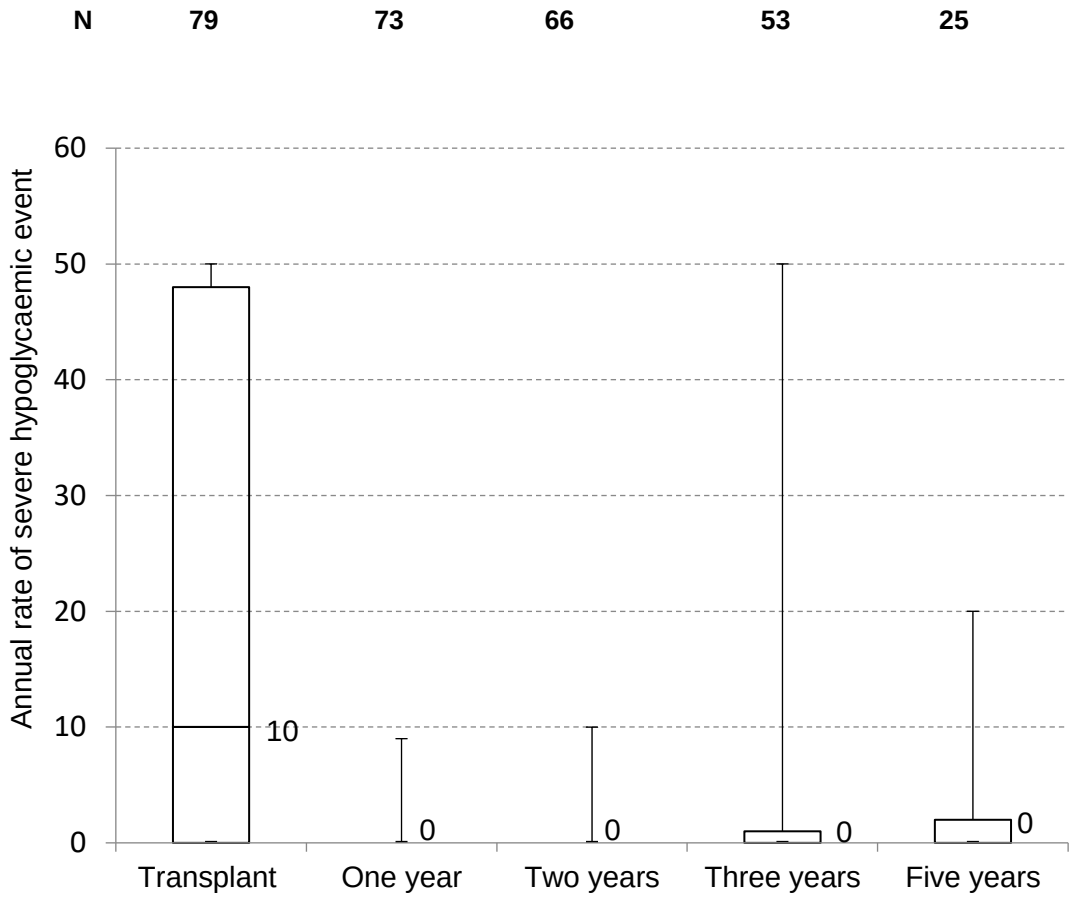


Figure 10 Reduction in HbA1C three years post-transplant for routine only grafts, 1 April 2010 – 31 March 2019 (excluding SIK transplants)

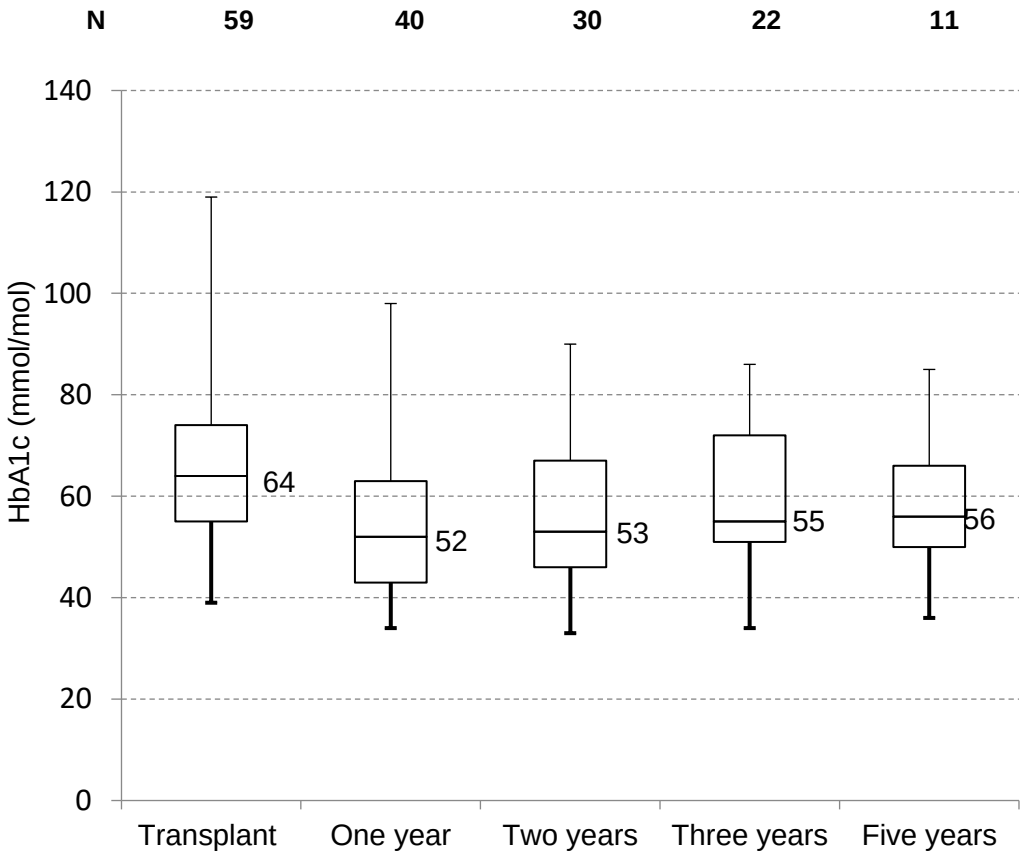


Figure 11 Reduction in HbA1C three years post-transplant for routine and priority grafts, 1 April 2010 – 31 March 2019 (excluding SIK transplants)

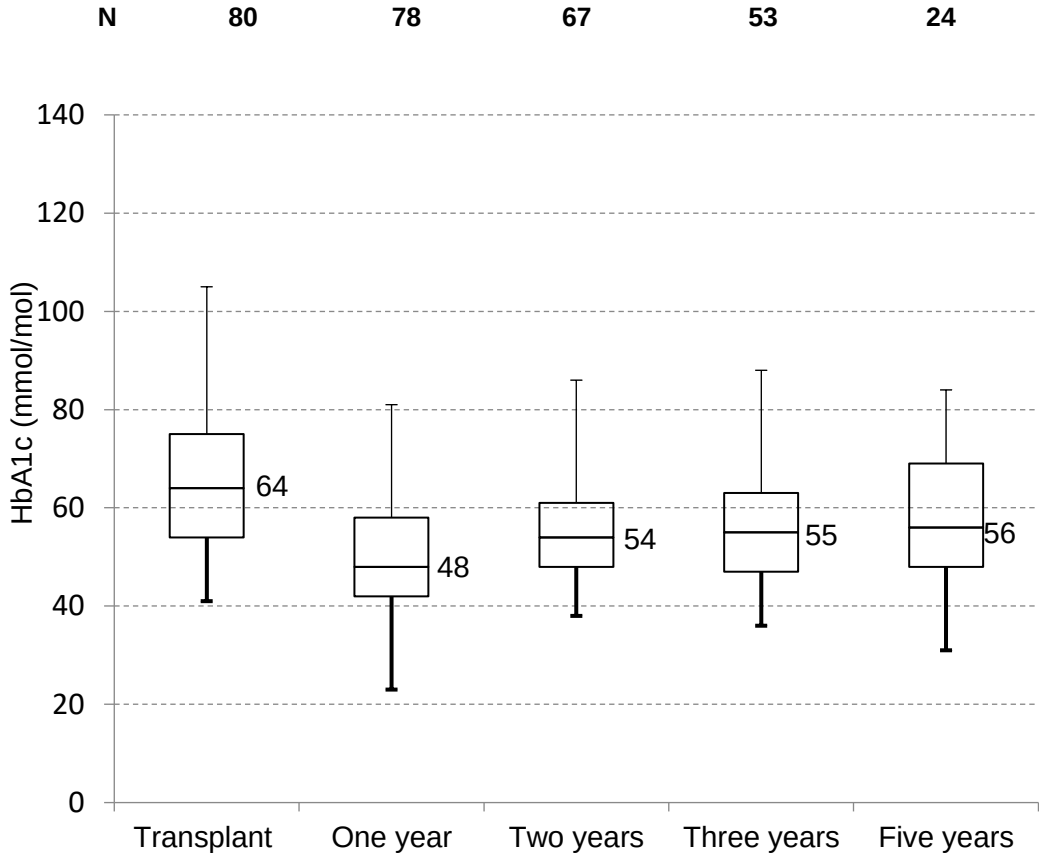


Figure 12 **Insulin dose three-years post-transplant for routine only grafts, 1 April 2010 – 31 March 2019 (excluding SIK transplants)**

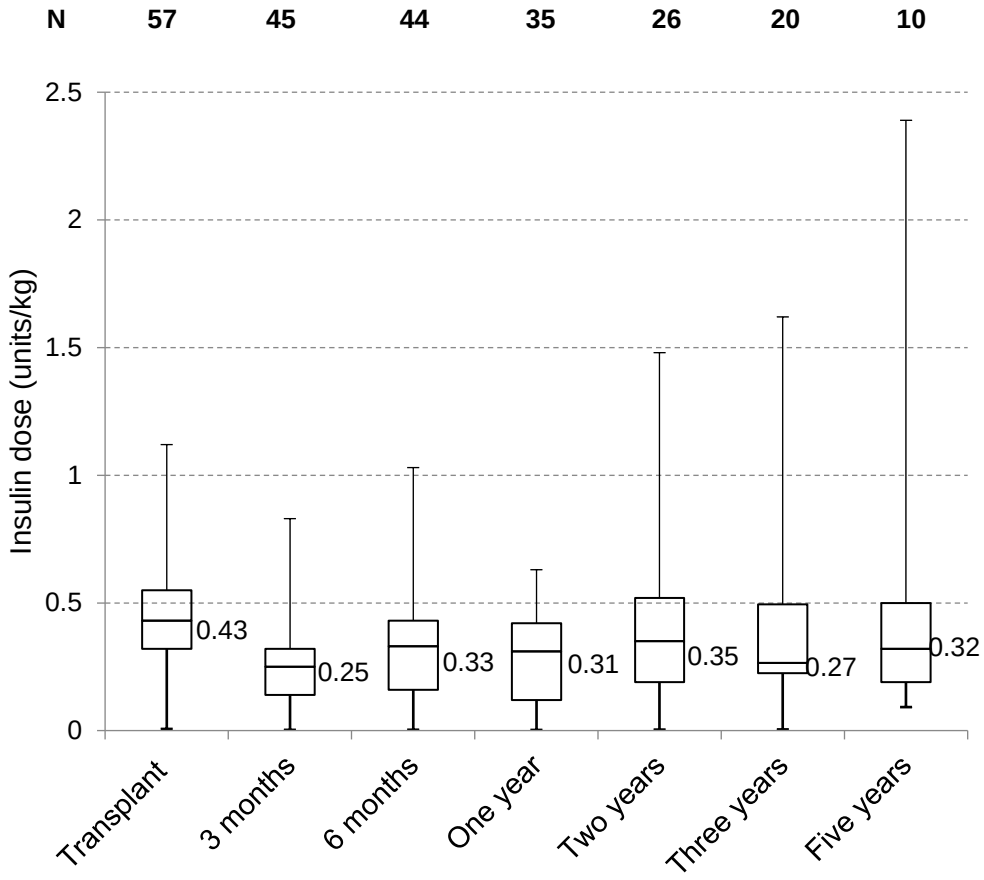
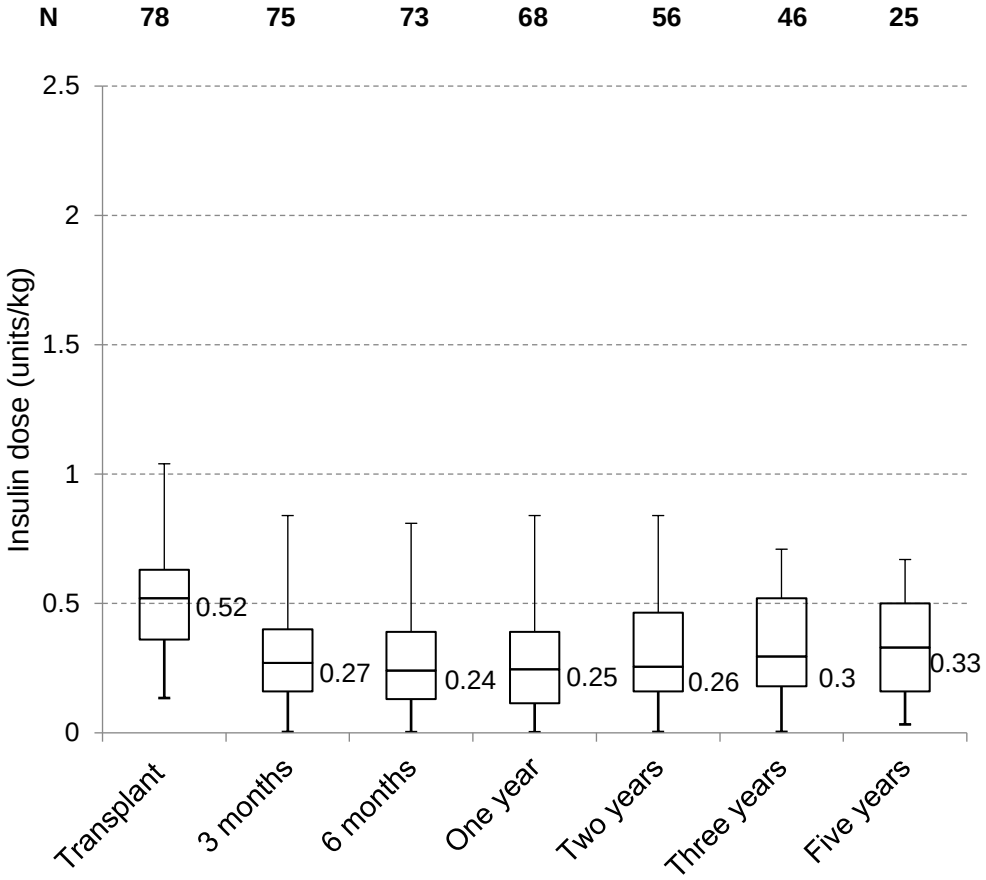


Figure 13 **Insulin dose three-years post-transplant for routine and priority grafts, 1 April 2010 – 31 March 2019 (excluding SIK transplants)**



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 102 patients where the difference in insulin dose between transplant and one-year post-transplant could be calculated, 90 (88%) reported a reduction. Of the 117 patients with insulin independence status reported for the first-year post-transplant, 40 (34%) achieved insulin independence at some point in the year.

28 For the 14 SIK transplants where insulin dose was reported at transplant, the median was 0.66 units/kg (IQR 0.41-0.76) 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 2019/20, the number of islet transplants was the same as in 2018/19 and the number on the waiting list at the end of the financial year has halved, although this was as a consequence of the COVID-19 pandemic.

30 One-year graft survival was 87% 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.

Joseph Parsons
Statistics and Clinical Studies **September 2020**

APPENDIX

Table I **Islet graft function at one year post transplant by transplant centre, 1 April 2010 to 31 March 2019**

Transplant centre	Routine transplants performed	Priority transplants performed	Graft function at one year following routine transplant in the time period		
			No. with known outcome	Graft failure	Priority grafts with graft failure
Bristol	3	1	3	0	0
Edinburgh	56	39	51	3	1
King's College	9	6	8	2	0
Manchester	16	11	16	3	0
Newcastle	29	14	27	3	0
Oxford	32	15	27	8	1
Royal Free	11	5	11	1	0
Total	**156[1]**	**91**	**143[2]**	**20[3]**	**2**

[1] Includes 14 SIK transplants: Edinburgh (6), Manchester (7), Newcastle (1)

[2] Includes 11 SIK transplants: Edinburgh (3), Manchester (7), Newcastle (1)

[3] Includes 2 SIK transplants: Manchester (2)

Table II **Reduction in annual rate of severe hypoglycaemic events at one-year post transplant, 1 April 2010 to 31 March 2019[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	50	50 (22 – 50)	34 (9 – 50)	0 (0 – 0)	31 (8 – 50)	38	6 (12)
King's College	9	4 (0 – 16)	2 (0 – 16)	0 (0 – 0)	0 (0 – 3)	2	4 (44)
Manchester	9	5 (1 – 8)	3 (1 – 8)	0 (0 – 0)	3 (1 – 9)	6	1 (11)
Newcastle	28	25 (5 – 25)	21 (2 – 32)	0 (0 – 1)	19 (1 – 29)	15	8 (29)
Oxford	32	3 (1 – 4)	0 (0 – 1)	0 (0 – 0)	0 (0 – 2)	5	13 (41)
Royal Free	11	4 (0 – 8)	0 (0 – 0)	0 (0 – 0)	0 (0 – 0)	1	2 (18)
Total	**142**	**22 (4 – 50)**	**8 (0 – 34)**	0 (0 – 0)	**7 (0 – 36)**	**70**	**34 (24)**

[1] Excluding SIK transplants

[2] Only available for 78 observations

[3] Information missing at either transplant or one-year post-transplant

Table III **Reduction in HbA1c at one-year post transplant, 1 April 2010 to 31 March 2019[1]**

Transplant centre	No. of routine transplants	HbA1c mmol/mol				
		Median at transplant (IQ range)	Median at one year (IQ range)	Median reduction (IQ range)	No. with lower HbA1c	Missing N (%)
Bristol	3	68 (53 – 70)	56 (33 – 81)	0 (0 – 37)	1	0 (0)
Edinburgh	50	60 (51 – 68)	53 (46 – 62)	5 (0 – 13)	34	4 (8)
King's College	9	70 (64 – 86)	44 (42 – 45)	15 (9 – 33)	6	3 (33)
Manchester	9	64 (57 – 75)	45 (43 – 47)	18 (8 – 36)	8	1 (11)
Newcastle	28	74 (62 – 86)	50 (41 – 58)	17 (13 – 31)	20	6 (21)
Oxford	32	62 (55 – 69)	48 (41 – 56)	17 (10 – 25)	21	10 (31)
Royal Free	11	61 (56 – 86)	51 (43 – 57)	4 (0 – 20)	6	2 (18)
Total	**142**	**64 (55 – 75)**	**51 (42 – 59)**	**12 (3 – 21)**	**96**	**26 (18)**

[1] Excluding SIK transplants

Table IV **Reduction in insulin dose per kg at one-year post transplant, 1 April 2010 to 31 March 2019[1]**

Transplant centre	No. of routine transplants	Insulin dose/kg				
		Median at transplant (IQ range)	Median at one year (IQ range)	Median reduction (IQ range)	No. insulin independent at some point	Missing N (%)
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)	0.23 (0.10 – 0.38)	0.23 (0.12 – 0.33)	21	8 (16)
King's College	9	0.28 (0.22 – 0.38)	0.13 (0.07 – 0.21)	0.20 (0.15 – 0.27)	3	5 (55)
Manchester	9	0.52 (0.45 – 0.55)	0.30 (0.23 – 0.38)	0.27 (0.25 – 0.35)	3	2 (22)
Newcastle	28	0.48 (0.34 – 0.61)	0.36 (0.23 – 0.46)	0.19 (-0.02 – 0.28)	5	10 (36)
Oxford	32	0.45 (0.32 – 0.62)	0.26 (0.12 – 0.38)	0.26 (0.07 – 0.43)	5	12 (38)
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	**142**	**0.48 (0.33 – 0.60)**	**0.26 (0.12 – 0.41)**	**0.23 (0.10 – 0.32)**	**40**	**40 (28)**

[1] Excluding SIK transplants