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 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 181 routine, and subsequent priority, islet transplants performed in the UK between 1 April 2010 and 31 December 2020 were analysed from the UKTR. Outcome data are reported for routine transplants only.

RESULTS

- 3 In 2021 there were 23 islet transplants performed, of which 7 were SIK. There were 33 patients on the islet transplant list at 31 December 2021, 23 routine (10 SIK) and 10 priority patients.
- 4 One-year graft survival for first routine islet alone grafts is 82% for transplants performed 1 January 2016 to 31 December 2020. There is a significant difference in five-year graft survival for those receiving a routine and priority top-up graft compared with those receiving a routine only graft, 60% and 34%, 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 9 events (IQR 0 48) at time of transplant, to none at one, two, three and five years' post-transplant. Of all routine islet transplants, 90 (82%) 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 49 mmol/mol (IQR 42 58) at one year and 54 (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 100 (83%) patients at one-year post-transplant.
- 7 The median insulin dose, for patients who received routine and priority grafts, fell from 0.51 units/kg (IQR 0.38 – 0.63) at time of transplant to 0.3 units/kg (IQR 0.21 – 0.49) three years post-transplant. Insulin independence at some point in the first-year post-transplant was achieved for 34% of patients overall where reported.

SUMMARY

8 In 2021, the number of islet transplants and patients on the waiting list at the end of the year have increased, although not back to pre-COVID levels. One-year graft survival is 82% for transplants performed between 1 January 2016 and 31 December 2020. 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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March 2022

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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 January 2019 and 31 December 2021 from the UK Transplant Registry (UKTR) are reported, by centre and financial year.
- 11 Between 1 April 2010 and 31 December 2020, there were 181 routine islet transplants performed in the UK. Outcome data on these 181 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 January 2019 to 31 December 2021, 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 December 2020, there were a total of 285 islet transplants performed, 181 (64%) of which were routine (including 23 SIK transplants) and 104 were priority. One patient received only a priority transplant in this time period as their routine transplant was before 1 April 2010.
- For those patients receiving a routine transplant between 1 April 2010 and 31 December 2020, the number of known graft failures at one-year post-transplant is reported in **Table 4**. Of the 181 routine transplants performed, 101 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 30 (30%) patients; 3-6 months for 36 (36%) patients; 6-12 months for 33 (33%) patients and more than one year for two patients who were highly sensitised.

Table 1 UP	able 1 UK islet transplant activity between 1 January 2019 and 31 December 2021, by transplant type and calendar year																				
2019 Total					2020 Total					2021			То	otal							
Centre	ITA	IAK	IAP	IAPK	SIK	Ν	%	ΙΤΑ	IAK	IAP	IAPK	SIK	Ν	%	ITA	IAK	IAP	IAPK	SIK	Ν	%
Bristol Edinburgh King's Manchester Newcastle Oxford Royal Free	0 8 ³ 3 ¹ 0 2 5 0	0 4 0 3 0 0 0	0 0 0 0 0 0	0 0 0 0 0 0 0	0 2 0 5 0 0 0	0 14 3 8 2 5 0	0 44 9 25 6 16 0	0 4 ¹ 1 0 4 1 0	0 0 0 0 0 0	0 0 0 0 0 0	0 0 0 0 0 0 0	0 1 ¹ 0 2 ¹ 0 1 0	0 5 1 2 4 2 0	0 36 7 14 29 14 0	0 7 0 3 1 ¹ 0	0 2 0 1 ¹ 2 0	0 0 0 0 0 0	0 0 0 0 0 0 0	0 3 0 3 ² 0 1 0	0 12 0 4 5 2 0	0 52 0 17 22 9 0
TOTAL ITA = Islet t SIK = Simult 1 Includes 1 [1 2 Includes 2 [1 3 Includes 3 [1]	18 ransplataneou DCD tr DCD tr DCD tr	7 ant alo is islet/ anspla anspla anspla	0 ne IA /kidney nt nts nts	0 «K = Islet	7 after k	32 idney	100 IAP =	10 Islet a	0 after pa	0 ancreas	0 : IAPK	4 = Islet	14 after s	100 simultar	11 neous	5 pancre	0 eas/ kio	0 Iney	7	23	100

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		2	019				2020						2021					
Trancolont		Total			Number of patients				Total		Nun pat	nber of tients			To	otal	Number of patients	
Centre	Routine	Priority	Ν	%	Ν	%	Routine	Priority	Ν	%	Ν	%	Routine	Priority	Ν	%	Ν	%
Bristol	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Edinburgh	9 ²	5	14	44	10	42	2 ¹	3	5	36	5	38	8 ³	4	12	55	9	47
King's	3	0	3	9	3	13	0	1	1	7	1	8	0	0	0	0	0	0
Manchester	64	2	8	25	7	29	2 ²	0	2	14	2	15	3 ³	1	4	18	4	21
Newcastle	1	1	2	6	1	4	3	1	4	29	3	23	4	1	5	23	4	21
Oxford	3	2	5	16	3	13	2 ¹	0	2	14	2	15	2 ¹	0	2	5	2	11
Royal Free	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL	22	10	32	100	24	100	9	5	14	100	13	100	17	6	23	100	19	100
¹ Includes 1 S ² Includes 2 S ³ Includes 3 S ⁴ Includes 5 S	SIK transplan SIK transplan SIK transplan SIK transplan	t ts ts ts																

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	31	December 2	2019		31	December 2	31 December 2021					
-			Т	otal			Т	otal		Total		
l ransplant Centre	Routine	Priority	Ν	%	Routine	Priority	Ν	%	Routine	Priority	Ν	%
Bristol	0	0	0	0	0	0	0	0	0	0	0	(
Edinburgh	1 ¹	2	3	13	4	1	5	25	9 ²	4	13	39
King's	0	1	1	4	0	0	0	0	0	0	0	(
Manchester	10 ⁵	0	10	42	74	0	7	35	7 ³	2	9	27
Newcastle	6	0	6	25	6 ¹	0	6	30	6 ¹	3	9	27
Oxford	2	0	2	8	2	0	2	10	1	1	2	e
Royal Free	2	0	2	8	0	0	0	0	0	0	0	(
TOTAL	21	3	24	100	19	1	20	100	23	10	33	100
¹ Includes 1 S	SIK transplan	t										
² Includes 3 S	SIK transplan	ts										
³ Includes 6 S	SIK transplan	ts										

Table 4One-year graft outcome following routine islet transplant,1 April 2010 to 31 December 2020									
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	66	56	16						
Routine and one priority graft	91	83	4						
Routine and two priority grafts	1	1	0						
SIK routine graft									
Routine only	14	9	2						
Routine and one priority graft	9	7	0						
Routine and two priority grafts	0	0	0						
Total	181	156	22						

Figure 1a One-year graft function by total IEQ per kg recipient body weight for islet alone routine only grafts, 1 April 2010 to 31 December 2020







- 16 One-year graft outcome by total IEQ per kg (IEQx1000/kg) transplanted is presented in Figures 1a and 2a, for the whole time period for islet alone routine only and routine and priority grafts, respectively. Figures 1b and 2b show the data for transplants in the recent time period, January 2016 to 31 December 2020. The median total IEQ per kg transplanted for 12 SIK routine only transplants was 3847.5 (IQR 2651.5 5715) and for nine SIK routine and priority grafts was 7924 (IQR 7015 10045). This was 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 89%, 95% CI (81-94%) for transplants performed between 1 January 2010 and 31 December 2015 and 82%, 95% CI (66-90%) for transplants performed between 1 January 2016 and 31 December 2020. Five year graft survival is 53%, 95% CI (41-64%) for transplants performed between 1 January 2008 and 31 December 2013 and 51%, 95% CI (37-63%) for transplants performed between 1 January 2014 and 31 December 2020.
- 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 34%, 95% CI (21-48%) and for first routine grafts followed by a priority graft is 60%, 95% CI (48-71%). This difference was statistically significant, p<0.0001.</p>
- **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 48%, 95% CI (30-64%) and for routine grafts followed by a priority graft is 64%, 95% CI (51-74%). This difference was not statistically significant, p=0.0692.
- 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 93%, 95% CI (85-97%).
- 21 Of the 23 SIK islet transplants in the 1 April 2010 to 31 December 2020 time period, 22 were the first islet transplant for the patient. Of these 22, follow-up information was available for 18 and the estimated one-year graft survival rate is 89%, 95% CI (62-97%).









Figure 5 Five-year graft survival following first routine islet alone transplantation performed in the UK between 1 April 2008 and 31 December 2020, 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 2020, 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 2020



- 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 110 cases and 72 (65%) patients had a reduced number of events. 90 (82%) patients experienced no severe hypoglycaemic events during the first year following their routine transplant, whilst 20 (18%) patients experienced between one and nine events.
- For the 20 SIK transplants where severe hypoglycaemic events were reported at transplant, the median rate was 1.5 (IQR 0-47) and for the 11 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 120 cases at one-year post-transplant and in 100 (83%) patients a reduction in HbA1c was reported. The proportion of patients with HbA1c of less than 53 mmol/mol was 17% of 151 at time of transplant, 57% of 124 patients at one-year post-transplant, 42% of 79 patients at three years and 37% of 43 patients at five years post-transplant.
- 26 For the 20 SIK transplants where HbA1c was reported at transplant, the median was 67 mmol/mol (IQR 60-77) and for the 10 reported at one-year post-transplant, the median was 57 mmol/mol (IQR 43-70).

PAG(22)xx



Figure 8 Reduction in severe hypoglycaemic events three years post-transplant for Figure 9

Reduction in severe hypoglycaemic events three years post-

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Figure 11 Reduction in HbA1C three years post-transplant for routine and priority grafts, 1 April 2010 – 31 December 2020 (excluding SIK transplants)



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Figure 12 Insulin dose three-years post-transplant for routine only grafts, 1 April 2010 – 31 December 2020 (excluding SIK transplants) Figure 13 Insulin dose three-years post-transplant for routine and priority grafts, 1 April 2010 – 31 December 2020 (excluding SIK transplants)

- 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 106 patients where the difference in insulin dose between transplant and one-year post-transplant could be calculated, 94 (89%) reported a reduction. Of the 119 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 21 SIK transplants where insulin dose was reported at transplant, the median was 0.54 units/kg (IQR 0.35-0.72) and for the 10 reported at one-year post-transplant, the median was 0.38 units/kg (IQR 0.26-0.49).

SUMMARY

- 29 In 2021, the number of islet transplants and patients on the waiting list at the end of the year have increased, although not back to pre-COVID levels.
- 30 One-year graft survival is 82% for transplants performed between 1 January 2016 and 31 December 2020 and 89% for the earlier cohort between 1 April 2010 and 31 December 2015. Five-year graft survival was 51% overall between 1 April 2008 and 31 December 2020. 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 34%, 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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Table I	Table IIslet graft function at one year post transplant by transplant centre, 1 April 2010 to31 December 2020										
	Graft function at one year following routine transplant in the time period										
Transplant	Routine	Priority transplants		No. with	Graft failure		Priority				
centre	transplants	performed (% of		known	(% of	known	grafts with				
	performed	rout	routine)		outco	ome)	graft failure				
Bristol	3	1	(33)	3	0	(0)	0				
Edinburgh	65	46	(71)	54	4	(7)	2				
King's College	11	7	(64)	8	2	(25)	0				
Manchester	22	12	(55)	19	3	(16)	0				
Newcastle	33	16	(48)	30	3	(10)	0				
Oxford	36	17	(47)	31	9	(29)	2				
Royal Free	11	5	(45)	11	1	(9)	0				
Total	181 ¹	104	(57)	156 ²	22 ³	(14)	4				
 ¹ Includes 23 SI ² Includes 16 SI ³ Includes 2 SIK 	 ¹ Includes 23 SIK transplants: Edinburgh (8), Manchester (13), Newcastle (1), Oxford (1) ² Includes 16 SIK transplants: Edinburgh (5), Manchester (10), 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 December 2020 ¹										
			Annual rate of severe hypoglycaemic events								
	No. of	Median at	Median at	Median at	Median	No. with	Missing ³				
Transplant	routine	registration ²	transplant	one year	reduction	reduced	N (%)				
centre	transplants	(IQ range)	(IQ range)	(IQ range)	(IQ range)	events					
Bristol	3	2 (2 – 3)	3 (2 – 50)	0 (0 – 0)	3 (2 – 50)	3	0 (0)				
Edinburgh	57	50 (20 – 50)	32 (9 – 50)	0 (0 – 0)	31 (8 – 50)	38	13 (23)				
King's College	11	4 (2 – 16)	3 (0 – 16)	0 (0 – 0)	0 (0 – 3)	2	6 (55)				
Manchester	9	5 (1 – 8)	3 (1 – 8)	0 (0 – 0)	3 (1 – 9)	6	1 (11)				
Newcastle	32	10 (5 – 25)	20(2-32)	0(0-1)	19 (1 – 30)	17	10 (31)				
Oxford	35	3(1-4)	0(0-1)	0(0-0)	0(0-2)	5	16 (46)				
Royal Free	11	4 (0 – 8)	0 (0 – 0)	0 (0 – 0)	0 (0 – 0)	1	2 (18)				
Total	158	19 (4 – 50)	8 (0 – 34)	0 (0 – 0)	7 (0 – 37)	72	48 (30)				
¹ Excluding SIK tr	ansplants										

² Only available for 92 observations
 ³ Information missing at either transplant or one-year post-transplant

Table III	Table III Reduction in HbA1c at one-year post transplant, 1 April 2010 to 31 December 2020 ¹											
			HbA1c	mmol/mol								
Transplant centre	No. of routine transplants	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	57	62 (52 – 70)	53 (47 – 62)	5 (0 – 13)	35	10 (18)						
King's College	11	70 (55 – 86)	42 (10 – 45)	26 (9 - 87)	6	5 (45)						
Manchester	9	64 (57 – 75)	45 (43 – 47)	18 (8 – 36)	8	1 (11)						
Newcastle	32	74 (63 – 83)	51 (41 – 58)	17 (13 – 31)	23	8 (25)						
Oxford	35	62 (55 - 69)	48 (41 – 54)	17 (10 – 25)	21	12 (34)						
Royal Free	11	61 (56 – 86)	51 (43 – 57)	4 (0 – 20)	6	2 (18)						
Total	158	64 (55 – 75)	51 (42 – 59)	13 (3 – 21)	100	38 (24)						
¹ Excluding SIK transp	plants		1 1		I	1						

Table IV	Table IVReduction in insulin dose per kg at one-year post transplant,1 April 2010 to 31 December 20201										
Transplant	No. of		Insulin dose/kg								
centre	routine transplants	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	57	0.51 (0.37 – 0.61)	0.25 (0.11 – 0.42)	0.23 (0.12 – 0.33)	21	14 (25)					
King's College	11	0.35 (0.22 - 0.42)	0.13 (0.07 – 0.21)	0.20 (0.15 – 0.27)	3	7 (64)					
Manchester	9	0.52 (0.45 – 0.55)	0.30 (0.23 – 0.38)	0.27 (0.25 – 0.35)	3	2 (22)					
Newcastle	32	0.47 (0.34 – 0.58)	0.31 (0.12 – 0.41)	0.19 (0.04 – 0.28)	5	12 (38)					
Oxford	35	0.45 (0.32 - 0.62)	0.26 (0.12 – 0.38)	0.26 (0.07 – 0.43)	5	14 (40)					
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	158	0.48 (0.33 – 0.60)	0.26 (0.12 – 0.41)	0.23 (0.10 – 0.33)	40	52 (33)					
¹ Excluding SIK tra	ansplants	1	I	I	I I						