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, including 28-day follow-up.

DATA

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 200 routine, and subsequent priority, islet transplants performed in the UK between 1 April 2010 and 31 March 2022 were analysed from the UKTR. Outcome data are reported for routine transplants only.

RESULTS

- In 2022/23 there were 18 islet transplants performed, of which five were SIK. There were 25 patients on the islet transplant list at 31 March 2023, 23 routine (13 SIK) and two priority patients.
- One-year graft survival for first routine islet alone grafts is 83% for transplants performed 1 April 2016 to 31 March 2022. 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, 63% and 39%, respectively p=0.0002.
- 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 47) at time of transplant, to none at one, two, three and five years' post-transplant. Of all routine islet transplants, 109 (85%) experienced no severe hypoglycaemic events in the first-year post-transplant.
- Median HbA1c fell from 64 mmol/mol (IQR 54 75) at time of transplant, to 51 mmol/mol (IQR 42 58) at one year and 55 (IQR 47 64) at three years post-transplant, for patients who received a routine and a priority graft. Overall, a reduction in HbA1c was reported for 105 (83%) patients at one-year post-transplant.
- The median insulin dose, for patients who received routine and priority grafts, fell from 0.52 units/kg (IQR 0.38 0.63) at time of transplant to 0.3 units/kg (IQR 0.17 0.49) three years post-transplant. Insulin independence at some point in the first-year post-transplant was achieved for 35% of patients overall where reported.

SUMMARY

In 2022/23, the number of islet transplants and patients on the waiting list at the end of the financial year have decreased slightly from 2021/22. One-year graft survival is 83% for transplants performed between 1 April 2016 and 31 March 2022. The median annual rate of severe hypoglycaemic events, HbA1c and insulin dose at one-year, two, three and five years post routine transplant are lower than pre-transplant.

ACTION

9 Members are asked to consider whether a maximum number of days post-transplant should be implemented, for data to be reported, on the 28-day form.

Lewis Simmonds
Statistics and Clinical Research

September 2023

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INTRODUCTION

10 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, including 28-day follow-up.

DATA

- Recent data on islet transplant activity, including simultaneous islet and kidney (SIK) grafts, and end of financial year transplant list between 1 April 2020 and 31 March 2023 from the UK Transplant Registry (UKTR) are reported, by centre and financial year.
- 12 Between 1 April 2010 and 31 March 2022 there were 200 routine islet transplants performed in the UK. Outcome data on these 200 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.
- All islet transplant outcome data reported are specific to the routine transplant and one-year centre specific outcomes are presented in the Appendix.

RESULTS

- The number of islet transplants performed by centre for the last three calendar years, 1 April 2020 to 31 March 2023, 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.
- Between 1 April 2010 and 31 March 2022, there were a total of 312 islet transplants performed, 200 (64%) of which were routine (including 31 SIK transplants) and 112 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 March 2022, the number of known graft failures at one-year post-transplant is reported in **Table 4**. Of the 200 routine transplants performed, 110 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 32 (29%) patients; 3-6 months for 39 (35%) patients; 6-12 months for 37 (34%) patients and more than one year for two patients who were highly sensitised.

Table 1 UK islet transplant activity between 1 April 2020 and 31 March 2023, by transplant type and financial year

				2020/21							2021/2	2						2022/23	3			
Transplant								otal Total								Total						
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	3	1	0	0	1 ¹	5	33	8	2 ¹	0	0	3	13	59	5 ²	2	0	0	2 ¹	9	50	
King's	1	0	0	0	0	1	7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Manchester	0	0	0	0	3 ²	3	20	0	1 ¹	0	0	3 ¹	4	18	0	2	0	0	3	5	28	
Newcastle	3	1	0	0	0	4	27	2	1	0	0	0	3	14	3	0	0	0	0	3	17	
Oxford	1	0	0	0	1	2	13	1 ¹	0	0	0	1	2	9	0	1	0	0	0	1	6	
Royal Free	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
TOTAL	8	2	0	0	5	15	100	11	4	0	0	7	22	100	8	5	0	0	5	18	100	

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

¹ Includes 1 DCD transplant ² Includes 2 DCD transplants

Table 2 UK islet transplant activity between 1 April 2020 and 31 March 2023, by islet status, number of patients and financial year

			2020	/21		Ni	. h. a.v. a.f			202	1/22		Marina	han af			202	2/23		Maria	
Transplant	Routi Islet	ne	Priority	Т	otal		nber of tients	Routi Islet	ne	Priority	Т	otal		ber of ients	Routi Islet	ine	Priority	To	otal		nber of tients
Centre	alone	SIK		N	%	N	%	alone	SIK		N	%	N	%	alone	SIK		N	%	N	%
Bristol	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Edinburgh	2	1	2	5	33	4	29	5	3	5	13	59	9	50	3	2	4	9	50	6	43
King's	0	0	1	1	7	1	7	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Manchester	0	3	0	3	20	3	21	0	3	1	4	18	4	22	0	3	2	5	28	5	36
Newcastle	3	0	1	4	27	4	29	2	0	1	3	14	3	17	2	0	1	3	17	2	14
Oxford	1	1	0	2	13	2	14	1	1	0	2	9	2	11	1	0	0	1	6	1	7
Royal Free	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL	6	5	4	15	100	14	100	8	7	7	22	100	18	100	6	5	7	18	100	14	100

Table 3 UK islet transplant list, 31 March 2021 to 31 March 2023, by islet status and financial year 31 March 2021 31 March 2022 31 March 2023 Routine **Priority Priority** Total Routine Priority Total Total Routine **Transplant** Islet Islet Islet SIK Centre alone SIK Ν % alone SIK Ν % alone Ν % Bristol Edinburgh King's 5 Manchester Newcastle Oxford Royal Free **TOTAL**

	t outcome follo o 31 March 2022	wing routine islet trans	plant,
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	71	61	16
Routine and one priority graft	97	95	6
Routine and two priority grafts	1	1	0
SIK routine graft			
Routine only	19	13	3
Routine and one priority graft	12	10	0
Routine and two priority grafts	0	0	0
Total	200	180	25

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 March 2022

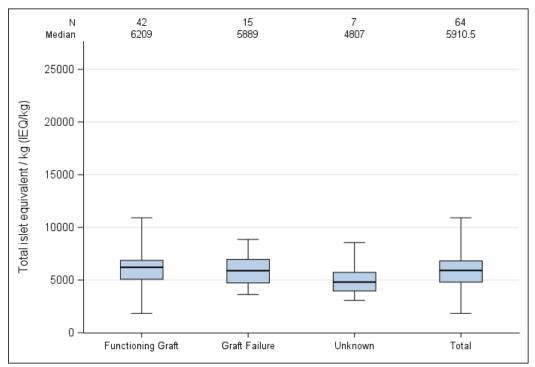


Figure 2a One-year graft function by total IEQ per kg recipient body weight for islet alone routine and priority grafts, 1 April 2010 to 31 March 2022

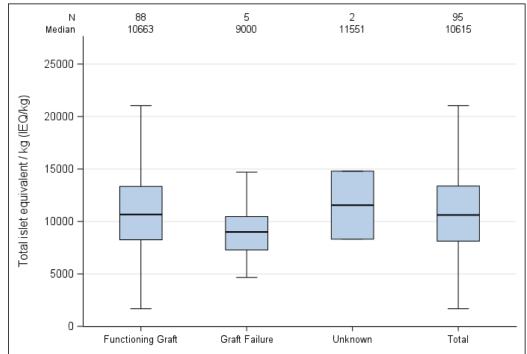


Figure 1b One-year graft function by total IEQ per kg recipient body weight for islet alone routine only grafts, 1 April 2016 to 31 March 2022

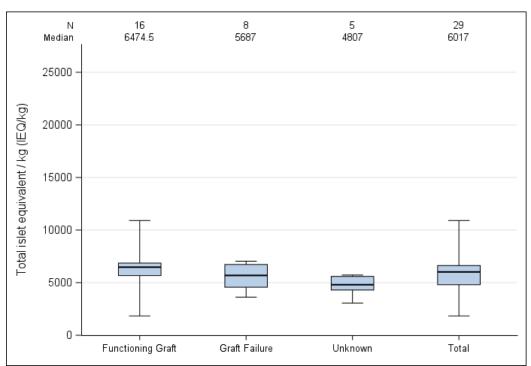
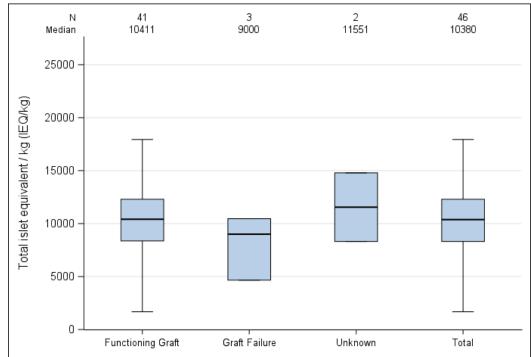


Figure 2b One-year graft function by total IEQ per kg recipient body weight for islet alone routine and priority grafts, 1 April 2016 to 31 March 2022



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- 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, 1 April 2016 to 31 March 2022. The median total IEQ per kg transplanted for 15 SIK routine only transplants was 4063 (IQR 2579 5424) and for 12 SIK routine and priority grafts was 8096.5 (IQR 7312 10805.5). This was lower than the median for islet alone transplants in both groups.
- 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 April 2010 and 31 March 2016 and 83%, 95% CI (69-91%) for transplants performed between 1 April 2016 and 31 March 2022, not statistically significantly different (p=0.2568). Five year graft survival is 51%, 95% CI (40-61%) for transplants performed between 1 April 2008 and 31 March 2015 and 63%, 95% CI (48-74%) for transplants performed between 1 March 2015 and 31 March 2022. Although higher for the more recent time period the difference was not statistically significantly different (p=0.2885).
- Figure 5 shows a Kaplan-Meier survival plot of five-year graft survival by type of graft for grafts between 1 April 2008 and 31 March 2022. Estimated five-year graft survival for first routine only grafts is 39%, 95% CI (25-52%) and for first routine grafts followed by a priority graft is 63%, 95% CI (52-72%). This difference was statistically significant, p=0.0002.
- 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 53%, 95% CI (35-68%) and for routine grafts followed by a priority graft is 67%, 95% CI (55-76%). This difference was not statistically significant, p=0.0925.
- Figure 7 shows a Kaplan-Meier survival plot of five-year patient survival after first routine islet alone transplant. Five year patient survival is 92%, 95% CI (85-96%).
- Of the 31 SIK islet transplants in the 1 April 2010 to 31 March 2022 time period, 29 were the first islet transplant for the patient. Of these 29, follow-up information was available for 27 and the estimated one-year graft survival rate is 89%, 95% CI (69-96%).

Figure 3 One-year graft survival following first routine islet alone transplantation performed in the UK between 1 April 2010 and 31 March 2022, by when transplant was performed

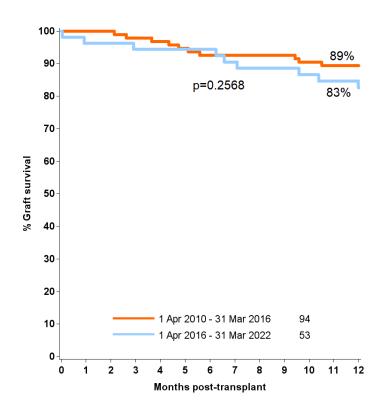


Figure 4 Five-year graft survival following first routine islet alone transplantation performed in the UK between 1 April 2008 and 31 March 2022, by when transplant was performed

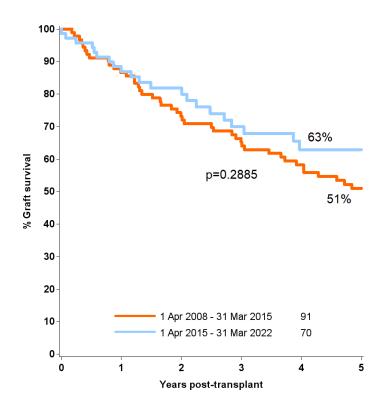


Figure 5 Five-year graft survival following first routine islet alone transplantation performed in the UK between 1 April 2008 and 31 March 2022, by type of graph

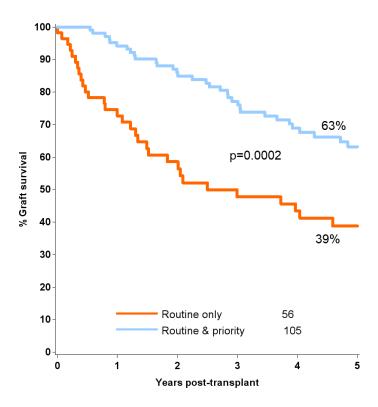


Figure 6 Five-year graft survival following first routine islet alone transplantation where the routine graft was functioning at one year in the UK between 1 April 2008 and 31 March 2022, by type of graph

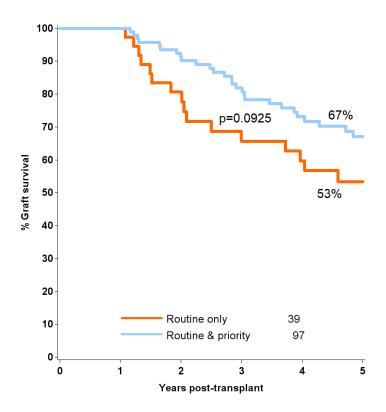
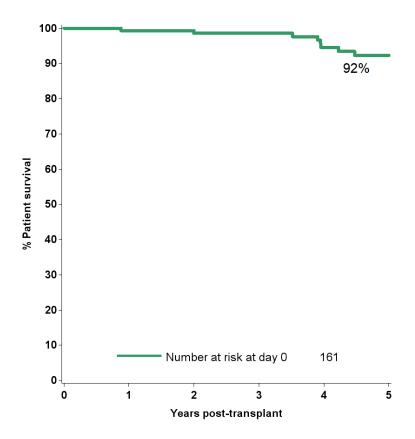


Figure 7 Five-year patient survival following first routine islet alone transplantation performed in the UK between 1 April 2008 and 31 March 2022



- 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 128 cases, 109 (85%) patients experienced no severe hypoglycaemic events during the first year following their routine transplant, whilst 19 (15%) patients experienced between one and five events. Of 123 cases where it could be calculated, 84 (68%) patients had a reduced number of events at one year post-transplant.
- For the 25 SIK transplants where severe hypoglycaemic events were reported at transplant, the median rate was 2 (IQR 0-41) and for the 18 reported at one-year post-transplant, the median rate was 0 (IQR 0-0).
- 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 127 cases at one-year post-transplant and in 105 (83%) patients a reduction in HbA1c was reported. The proportion of patients with HbA1c of less than 53 mmol/mol was 17% of 157 at time of transplant, 56% of 136 patients at one-year post-transplant, 40% of 88 patients at three years and 37% of 49 patients at five years post-transplant.
- For the 26 SIK transplants where HbA1c was reported at transplant, the median was 63 mmol/mol (IQR 56-73) and for the 17 reported at one-year post-transplant, the median was 55 mmol/mol (IQR 45-59).

Figure 8 Median annual rate of severe hypoglycaemic events post-transplant for routine only grafts, 1 April 2010 – 31 March 2022 (excluding SIK transplants)

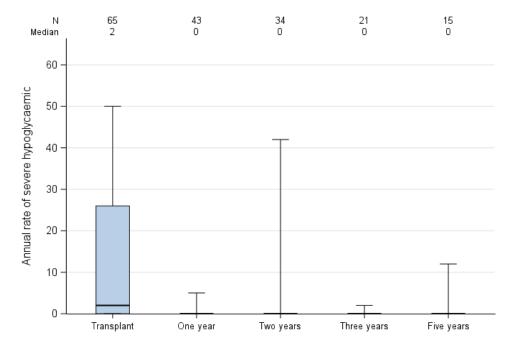


Figure 9 Median annual rate of severe hypoglycaemic events posttransplant for routine and priority grafts, 1 April 2010 – 31 March 2022 (excluding SIK transplants)

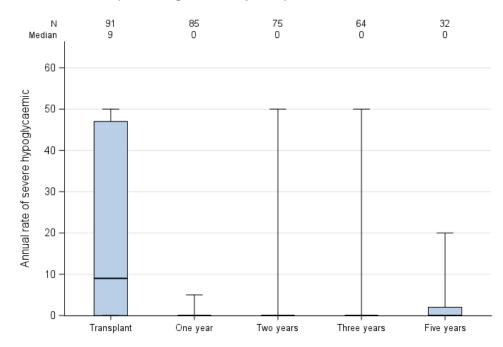


Figure 10 Median HbA1C post-transplant for routine only grafts, 1 April 2010 – 31 March 2022 (excluding SIK transplants)

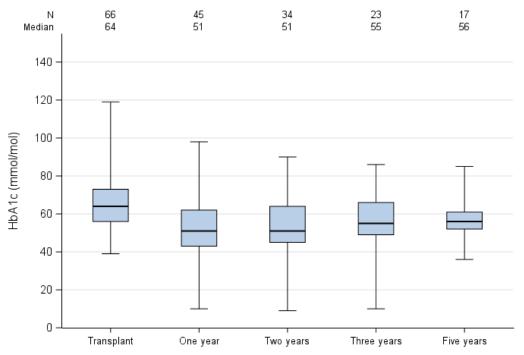


Figure 11 Median HbA1C post-transplant for routine and priority grafts, 1 April 2010 – 31 March 2022 (excluding SIK transplants)

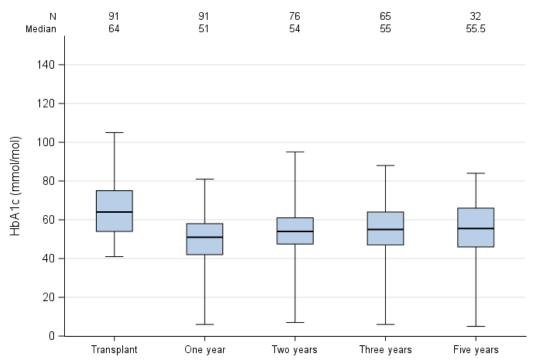


Figure 12 Median insulin dose post-transplant for routine only grafts, 1 April 2010 – 31 March 2022 (excluding SIK transplants)

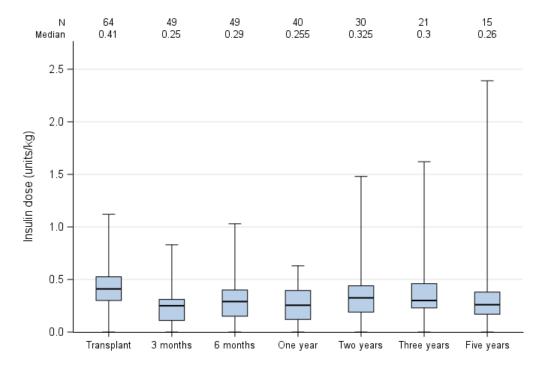
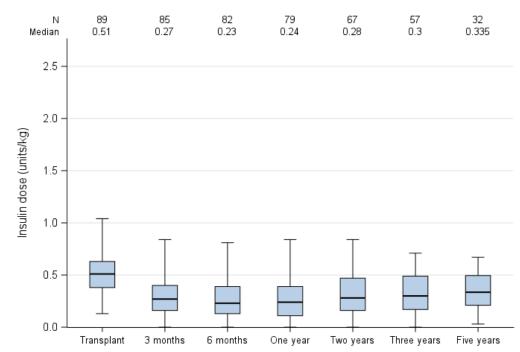


Figure 13 Median insulin dose post-transplant for routine and priority grafts, 1 April 2010 – 31 March 2022 (excluding SIK transplants)



- 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 113 patients where the difference in insulin dose between transplant and one-year post-transplant could be calculated, 101 (89%) reported a reduction. Of the 127 patients with insulin independence status reported for the first-year post-transplant, 44 (35%) achieved insulin independence at some point in the year.
- For the 27 SIK transplants where insulin dose was reported at transplant, the median was 0.48 units/kg (IQR 0.35-0.7) and for the 17 reported at one-year post-transplant, the median was 0.33 units/kg (IQR 0.24-0.47).
- The 28-day islet follow-up form was introduced on 1st January 2022. As at 12th September 2023, 28 follow-up forms had been received. There were 16 routine and 12 priority top-up grafts reported.
- At a meeting on 18th January 2023 with recipient coordinators, statisticians, and Professor James Shaw, it was agreed that centres would report any missing data as '-1' on the form. This has since been implemented to ensure the accuracy and reliability of the data reported.
- A question was raised regarding patients who cannot be followed up at 28 days post-transplant. Members are asked to consider whether a maximum number of days post-transplant should be implemented for data to be reported on the 28-day form.

SUMMARY

- In 2022/23, the number of islet transplants and patients on the waiting list at the end of the financial year have decreased slightly from 2021/22.
- One-year graft survival is 83% for transplants performed between 1 April 2016 and 31 March 2022 and 89% for the earlier cohort between 1 April 2010 and 31 March 2016. Five-year graft survival was 63% overall between 1 April 2015 and 31 March 2022. Those patients receiving a routine and a priority top-up graft had significantly better five-year graft survival than those receiving a routine only, 63% and 39%, respectively, p=0.0002.
- The median annual rate of severe hypoglycaemic events, HbA1c and insulin dose at one-year, two, three and five years post routine transplant were lower than at pre-transplant.

ACTION

Members are asked to consider whether a maximum number of days posttransplant should be implemented, for data to be reported, on the 28-day form.

Lewis Simmonds
Statistics and Clinical Research

September 2023

APPENDIX

Table I	Islet graft fund 31 March 2022		year post	transplant by	transpla	nt centre,	1 April 2010 to
Transplant centre	Routine transplants performed	Priority tra performe routi	ed (% of		nsplant in Graft t (% of l	e year follo the time p failure known ome)	owing routine period Priority grafts with graft failure
Bristol	3	1	(33)	3	0	(0)	0
Edinburgh	74	52	(70)	68	7	(10)	4
King's College	11	7	(64)	10	2	(20)	0
Manchester	26	13	(50)	23	3	(13)	0
Newcastle	37	17	(46)	34	3	(9)	0
Oxford	38	17	(45)	31	9	(29)	2
Royal Free	11	5	(45)	11	1	(9)	0
Total	200¹	112	(56)	180 ²	25 ³	(14)	6

 ¹ Includes 30 SIK transplants: Edinburgh (11), Manchester (17), Newcastle (1), Oxford (2)
 ² Includes 23 SIK transplants: Edinburgh (8), Manchester (14), Newcastle (1)
 ³ Includes 3 SIK transplants: Edinburgh (1), Manchester (2)

Table II	Redu	ıction	in ann	ual rate c	of severe h	ypogl	ycaemic e	events at	one-ye	ar post trar	nsplant, 1	April 2	010 to 31	March 20	22 ¹	
	Rou	tine				Aı	nnual rate	of sever	e hypo	glycaemic	events					
Transplant centre	trans s (c year expe	data		At registra	ation		At transpl			At one-yea			Reduction	n ³	No. with reduced events	Reduction not calculated ⁴
	N	(N)	N	Median	(IQ range)	N	Median	(IQ range)	N	Median	(IQ range)	N	Median	(IQ range)	N	N (%)
Bristol	3	3	3	2	(2 - 3)	3	3	(2 - 50)	3	0	(0 - 0)	3	3	(2 - 50)	3	0 (0)
Edinburgh	63	60	53	45	(10 - 50)	59	29	(8 - 50)	53	0	(0 - 0)	49	32	(8 - 50)	43	11 (18)
King's College	11	9	9	4	(2 - 16)	11	3	(0 - 16)	6	0	(0 - 0)	6	2	(0 - 50)	3	3 (33)
Manchester	9	8	6	5	(1 - 8)	9	3	(1 - 8)	8	0	(0 - 0)	8	4	(1 - 9)	6	0 (0)
Newcastle	36	34	21	10	(2 - 25)	36	18	(2 - 30)	27	0	(0 - 1)	27	8	(1 - 28)	23	7 (21)
Oxford	36	33	7	3	(1 - 4)	28	0	(0 - 1)	22	0	(0 - 0)	21	0	(0 - 0)	5	12 (36)
Royal Free	11	10	3	4	(0 - 8)	10	0	(0 - 0)	9	0	(0 - 0)	9	0	(0 - 0)	1	1 (10)
Total	169	157	102	12	(3 - 50)	156	8	(0 - 34)	128	0	(0 - 0)	123	7	(0 - 37)	84	34 (22)

Excluding SIK transplants
 Follow-up reported or graft not known to have failed
 Between transplant and one-year
 Information missing at either transplant or one-year out of those where expected

Table III	Redu	ction in	HbA1	c at one-	year post t	ranspl	ant, 1 Apr	il 2010 to 3	1 Mar	ch 2022¹			
	Rou	ıtine				н	A1c mm	ol/mol					
Transplant centre	transı (one da	plants -year ata cted ²)		At transp	lant		At one-ye	ear		Reduction	on ³	No. with lower HbA1c	Reduction not calculated ⁴
	N	(N)	N	Median	(IQ	Ν	Median	(IQ	N	Median	(IQ	Ν	N (%)
					range)			range)			range)		
Bristol	3	3	3	68	(53 - 70)	3	56	(33 - 81)	3	0	(0 - 37)	1	0 (0)
Edinburgh	63	60	58	62	(52 - 71)	55	53	(46 - 63)	50	6	(1 - 13)	38	10 (17)
King's College	11	9	11	70	(55 - 86)	6	42	(10 - 45)	6	26	(9 - 87)	6	3 (33)
Manchester	9	8	9	64	(57 - 75)	8	45	(43 - 47)	8	18	(8 - 36)	8	0 (0)
Newcastle	36	34	36	72	(61 - 83)	29	51	(42 - 58)	29	17	(13 - 28)	25	5 (15)
Oxford	36	33	29	62	(55 - 69)	26	49	(41 - 58)	22	17	(10 - 25)	21	11 (33)
Royal Free	11	10	11	61	(56 - 86)	9	51	(43 - 57)	9	4	(0 - 20)	6	1 (10)
Total	169	157	157	64	(55 - 75)	136	51	(43 - 59)	127	12	(3 - 21)	105	30 (19)

Excluding SIK transplants
 Follow-up reported or graft not known to have failed
 Between transplant and one-year
 Information missing at either transplant or one-year out of those where expected

	Rou	ıtine					Insulin do	se/kg					
Transplant centre	transplants (one-year data expected ²)			At trans	plant		At one-y	•		Reduc	tion ³	No. insulin independent	Reduction not calculated ⁴
	N	(N)	Ν	Median	(IQ range)	Ν	Median	(IQ range)	N	Median	(IQ range)	N	N (%)
Bristol	3	3	3	0.42	(0.37 - 0.48)	3	0.20	(0.12 - 0.47)	3	0.22	(0.01 - 0.25)	1	0 (0)
Edinburgh	63	60	58	0.51	(0.36 - 0.61)	51	0.23	(0.10 - 0.39)	46	0.23	(0.14 - 0.36)	24	14 (23)
King's College	11	9	10	0.35	(0.22 - 0.42)	4	0.13	(0.07 - 0.21)	4	0.20	(0.15 - 0.27)	3	5 (56)
Manchester	9	8	9	0.52	(0.45 - 0.55)	7	0.30	(0.23 - 0.38)	7	0.27	(0.25 - 0.35)	3	1 (13)
Newcastle	36	34	36	0.44	(0.33 - 0.56)	25	0.29	(0.12 - 0.40)	25	0.19	(0.04 - 0.28)	5	9 (26)
Oxford	36	33	27	0.45	(0.32 - 0.62)	20	0.26	(0.12 - 0.38)	20	0.26	(0.07 - 0.43)	6	13 (39)
Royal Free	11	10	10	0.56	(0.40 - 0.80)	9	0.42	(0.24 - 0.50)	8	0.14	(0.01 - 0.35)	2	2 (20)
Total	169	157	153	0.47	(0.33 - 0.59)	119	0.25	(0.12 - 0.39)	113	0.23	(0.10 - 0.33)	44	44 (28)

Excluding SIK transplants
 Follow-up reported or graft not known to have failed
 Between transplant and one-year
 Information missing at either transplant or one-year out of those where expected