

INTERIM REPORT ON PANCREAS AND ISLET TRANSPLANTATION

5 YEAR REPORT (1 OCTOBER 2015 – 30 SEPTEMBER 2020)

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Executive Summary

This report presents key figures about pancreas and islet transplantation in the UK. The period reported covers five years of pancreas and islets transplant data, from 1 October 2015. The report presents information on the number of pancreas and islet transplants as well as survival analysis after first simultaneous pancreas and kidney and pancreas only transplantation on a national and centre-specific basis.

Key findings

- On the 30 September 2020, there were 135 patients on the UK active pancreas and islet transplant list, which represents a 47% decrease in the number of patients from one year earlier, due to the ongoing COVID-19 pandemic. The number of patients on the active pancreas list decreased by 41% to 125 in one year, while the active islet transplant list decreased by 77% to 10 patients in the same time period.
- There were 36 pancreas transplants and 3 islet transplants performed in the UK from April to September 2020. Of these 39 transplants, 74% of transplants were from donations after brain death. From 1 October 2019 to 30 September 2020, 26% of pancreas and islet transplants were from donations after circulatory death.
- The median waiting time for patients registered, between 1 October 2014 to 30 September 2018, for a pancreas transplant in the UK was 356 days (95% confidence interval (CI) 331 381 days). The median ranged from 186 to 520 days depending on which centre the patient was registered at. The median waiting time for a routine islet (including simultaneous islet and kidney) transplant for patients registered in the same time frame was 555 days (95% CI 349 761 days).
- The national rates of <u>graft</u> survival one- and five-years after first simultaneous pancreas and kidney transplant from deceased donors are 92% and 80%, respectively. These rates vary between centres, ranging from 85% to 97% at oneyear and 71% to 91% at five-years. All centre rates are <u>risk-adjusted</u>.
- The national rates of <u>patient</u> survival one- and five-years after first simultaneous pancreas and kidney transplant from deceased donors are 99% and 89%, respectively. These rates vary between centres, ranging from 95% to 100% at one-year and 85% to 98% at five-years. All centre rates are <u>risk-adjusted</u>.
- The national rates of <u>graft</u> survival one- and five-years after first pancreas only transplant from deceased donors are 84% and 53%, respectively. The national rates of patient survival one- and five-years are 95% and 90%. Centre specific estimates of these rates must be interpreted with caution due to the small number of transplants upon which they are based.

Introduction

This report presents information on pancreas and islet transplant activity between 1 October 2015 and 30 September 2020, for all eight centres performing pancreas transplantation and all seven centres performing islet transplantation in the UK. Data were obtained from the UK Transplant Registry, at NHS Blood & Transplant, that holds information relating to donors, recipients and outcomes for all pancreas and islet transplants performed in the UK. Throughout this report West London Renal and Transplant Centre is labeled as WLRTC, simultaneous pancreas and kidney transplants and simultaneous islet and kidney transplants are reported as SPK and SIK transplants, respectively.

Data were obtained from the UK Transplant Registry, at NHS Blood & Transplant, that holds information relating to donors, recipients and outcomes for all pancreas and islet transplants performed in the UK. <u>Graft</u> and <u>patient</u> pancreas survival estimates are reported at one-year post-transplant for the period 1 October 2015 to 30 September 2019 and five-year post-transplant for the period 1 October 2011 to 30 September 2015.

The centre specific results for survival estimates after first simultaneous pancreas and kidney transplants are adjusted for differences in <u>risk factors</u> between the centres. The risk models used are described in the Appendix.

Methods used are also described in the Appendix.

Patients requiring <u>multi-organ transplants</u> (except SPK and SIK) are excluded from all analyses apart from in the introduction. All results are described separately for pancreas and islet patients other than those presented in the introduction section. Intestinal transplants that involve a pancreas are excluded from all sections of the report.

The COVID-19 pandemic has led to unprecedented challenges for UK transplantation. Concerns about the ability to care for transplant recipients, lack of access to resource because it is being used for patients in the pandemic, and the risk versus benefit for immunosuppressed transplant recipients, have resulted in a major reduction in the number of organ transplants undertaken.

Waiting list figures at the 31 March and 30 September 2020 do not accurately reflect the need for pancreas and islet transplantation due to the COVID-19 pandemic. Different practices were established across the UK centres with regards to waiting list management.

Figure 2.1 shows the number of patients on the pancreas and islet <u>transplant list</u> at 31 March and 30 September each year from 2016 to 2020. Overall the number of patients actively waiting for a pancreas or islet transplant has decreased this year, from 254 at 30 September 2019 to 135 at 30 September 2020.

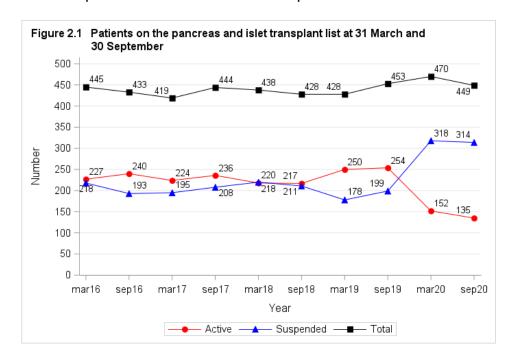


Figure 2.2 shows the number of patients on the pancreas and islet <u>transplant list</u> at 30 September 2020 for each transplant centre. Cambridge, Cardiff, Guy's and WLRTC only perform pancreas transplants while Bristol, King's College and The Royal Free only perform islet transplants. Oxford had the largest <u>transplant list</u> with 55 patients registered for a pancreas or islet transplant. There were no patients registered for an SIK transplant.

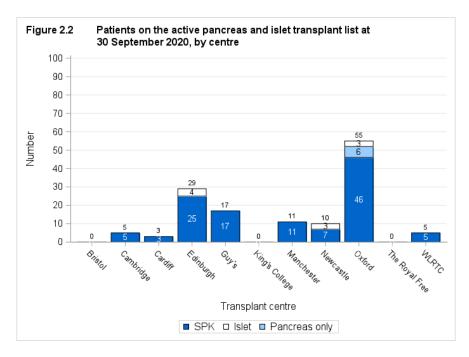


Figure 2.3 shows the total number of pancreas and islet transplants performed in the last five years. There was a decrease of 29% in transplant activity between October 2018 – September 2019 and October 2019 – September 2020, 196 and 140 respectively.

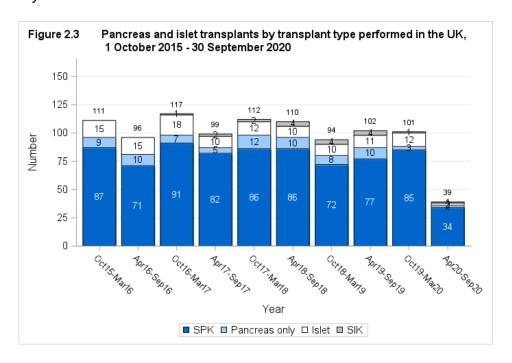


Figure 2.4 shows the total number of pancreas and islet transplants performed from April to September 2020 at each transplant centre. Cambridge performed the most transplants, a total of 16 transplants.

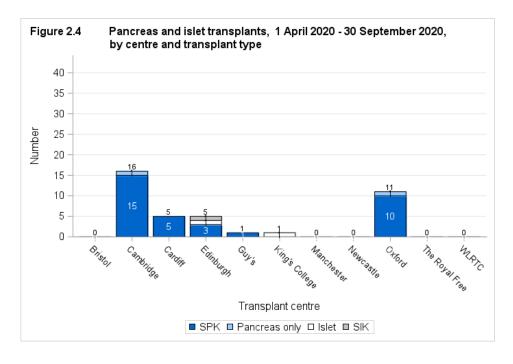


Figure 2.5 details the 39 pancreas and islet transplants performed in the UK between 1 April 2020 and 30 September 2020. 74% of these were from DBD deceased donors. 36 were pancreas transplants and three were islet transplants. 94% of pancreas transplants were SPK's in this time period. For islet transplantation, one was a routine SIK transplant and two were priority top-up grafts.

Pancreas transplants
1 April 2019 – 30 September 2019
39

Deceased donor islet transplants
36

DBD transplants
27

DBD transplants
27

DBD transplants
28

DBD transplants
29

DBD transplants
1

Simultaneous pancreas and kidney
9

Pancreas alone
Pancreas alone
Pancreas alone
Pancreas alone
Pancreas alone
Pancreas alone
Priority
Priority
O
Priority
O

Figure 2.5 Pancreas and islet transplants performed in the UK, 1 April 2020 – 30 September 2020

^{*} Includes 1 simultaneous islet and kidney transplants

Pancreas transplant list

3.1 Patients on the pancreas transplant list as at 31 March and 30 September, 2016 – 2020

Figure 3.1 shows the number of patients on the pancreas <u>transplant list</u> at 31 March and 30 September between 2016 and 2020. Overall the number of patients actively waiting for a pancreas transplant has decreased from 199 in March 2016 to 125 in September 2020, 86 less than in September 2019 primarily due to the COVID-19 pandemic.

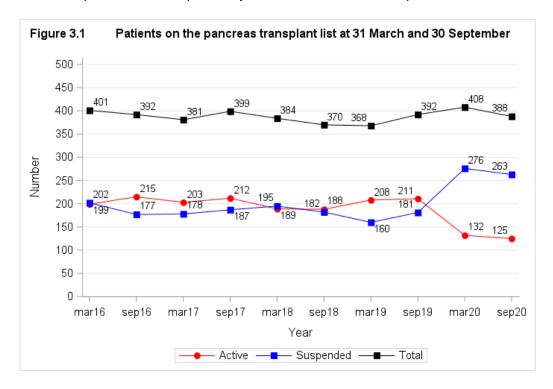
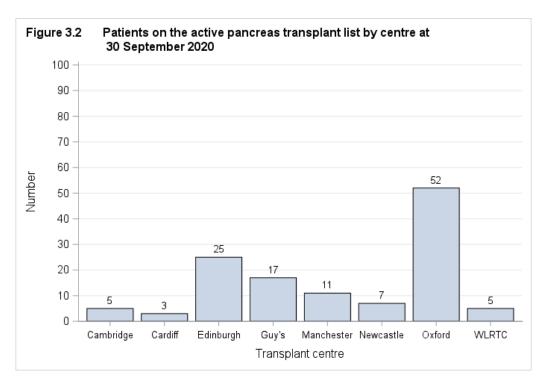


Figure 3.2 shows the number of patients on the active pancreas <u>transplant list</u> at 30 September 2020 by centre. Oxford had the largest proportion on the <u>transplant list</u> (42%) and Cardiff had the smallest proportion (2%).



3.2 Median waiting time to transplant, 1 October 2014 - 30 September 2018

The length of time a patient waits for a pancreas transplant varies across the UK. The <u>median</u> waiting time for deceased donor pancreas transplantation is shown in **Figure 3.3** and **Table 3.1** for patients registered at each individual unit.

The <u>median</u> waiting time to transplant for patients registered on the pancreas <u>transplant</u> <u>list</u> between 1 October 2014 and 30 September 2018 is 356 days, less than a year. This ranged from 186 days at WLRTC to 520 days at Edinburgh.

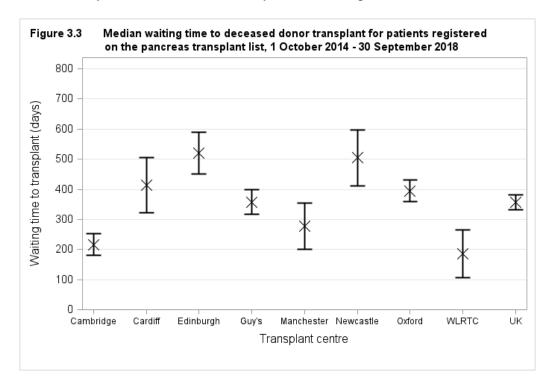


Table 3.1 Median waiting time to pancreas transplant in the UK, for patients registered 1 October 2014 - 30 September 2018											
Transplant centre	Number of patients	Wa	iting time (days)								
	registered	Median	95% Confidence interval								
Cambridge	102	216	180 - 252								
Cardiff	46	414	322 - 506								
Edinburgh	92	520	451 - 589								
Guy's	154	357	316 - 398								
Manchester	150	278	202 - 354								
Newcastle	40	504	412 - 596								
Oxford	285	395	358 - 432								
WLRTC	50	186	106 - 266								
UK	919	356	331 - 381								

Response to pancreas offers

4.1 Offer decline rates, 1 April 2017 – 30 September 2020

Pancreas offers from <u>DBD</u> and <u>DCD</u> donors whose pancreas was retrieved, offered directly on behalf of a named individual patient and resulted in transplantation are included in the analysis. Any offers of pancreases declined for transplantation, pancreases offered for <u>multi-organ</u> or small bowel transplant were excluded, as were offers made through the fast track scheme or the reallocation of the pancreas.

<u>Funnel plots</u> are used to compare centre specific offer decline rates and indicate how consistent the rates of the individual transplant centres are with the national rate. Patient <u>case mix</u> is known to influence the number of offers a centre may receive. In this analysis however only individual offers for named patients were considered which excluded any <u>ABO</u>- and <u>HLA</u>-incompatible patients. For this reason it was decided not to risk adjust for known centre differences in patient <u>case mix</u>.

Figure 4.1 compares individual centre offer <u>DBD</u> decline rates with the national rate over the time period, 1 April 2017 and 30 September 2020. Centres can be identified by the information shown in **Table 4.1**. Cambridge had an offer decline rate significantly lower than the national average, whilst Edinburgh had significantly higher offer decline rates than the national average.

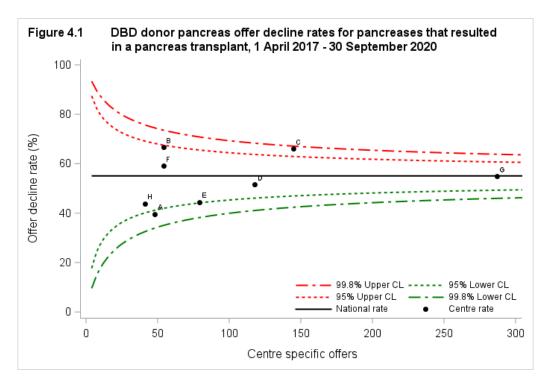


Table 4.1 compares individual centre offer decline rates over time by financial year. The decline rates from April to September 2020 highlight the low number of patient specific offers made during the pandemic. Some centres only reopened in September.

Table 4.1			ancreas offo nd 30 Septo			transpla	ant centre,				
Centre	Code	20)17/18	20	18/19	20	19/20	Apr -	- Sep 20	Overall	
		No.	(%	No.	(%	No.	(%	No.	(%	No.	(%
		offers	declined)	offers	declined)	offers	declined)	offers	declined)	offers	declined)
Cambridge	Α	23	(39)	14	(43)	6	(67)	5	(0)	48	(40)
Cardiff	В	15	(73)	18	(61)	19	(68)	2	(50)	54	(67)
Edinburgh	С	48	(73)	40	(65)	54	(63)	3	(33)	145	(66)
Guy's	D	39	(51)	39	(56)	39	(49)	1	(0)	118	(52)
Manchester	Е	19	(32)	19	(42)	41	(51)	0	-	79	(44)
Newcastle	F	23	(65)	21	(62)	10	(40)	0	-	54	(59)
Oxford	G	97	(56)	82	(51)	98	(62)	10	(10)	287	(55)
WLRTC	Н	14	(43)	14	(50)	13	(38)	0	-	41	(44)
uĸ		278	(56)	247	(55)	280	(58)	21	(14)	826	(55)
	Centr	e has re	ached the u	pper 99.	8% confider	nce limit					
	Centr	e has re	ached the u	pper 95%	% confidenc	e limit					
	Centr	e has re	ached the lo	wer 95%	6 confidence	e limit					
	Centr	e has re	ached the lo	wer 99.8	3% confiden	ce limit					

Figure 4.2 compares individual centre offer <u>DCD</u> decline rates with the national rate over the time period, 1 April 2017 and 30 September 2020. Centres can be identified by the information shown in **Table 4.2**. Cambridge had offer decline rates significantly lower than the national rate, whilst Newcastle had significantly higher rates than the national average.

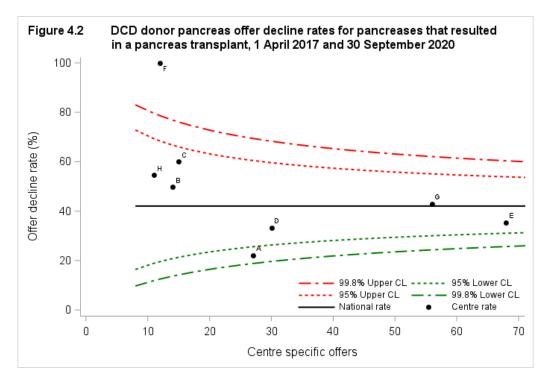


Table 4.2		•	ancreas offe nd 30 Septe			transpla	ant centre,				
Centre	Code	20	17/18	20	18/19	20	19/20	Apr -	- Sep 20	0	verall
		No. offers	(% declined)	No. offers	(% declined)	No. offers	(% declined)	No. offers	(% declined)	No. offers	(% declined)
Cambridge	Α	7	(0)	10	(30)	9	(33)	1	(0)	27	(22)
Cardiff	В	5	(60)	3	(33)	5	(40)	1	(100)	14	(50)
Edinburgh	С	6	(50)	5	(100)	4	(25)	0	-	15	(60)
Guy's	D	7	(29)	12	(33)	11	(36)	0	-	30	(33)
Manchester	Е	25	(16)	28	(43)	15	(53)	0	-	68	(35)
Newcastle	F	3	(100)	5	(100)	4	(100)	0	-	12	(100)
Oxford	G	16	(38)	19	(42)	18	(50)	3	(33)	56	(43)
WLRTC	Н	7	(71)	2	(50)	2	(0)	0	-	11	(55)
UK		76	(34)	84	(46)	68	(46)	5	(40)	233	(42)
	Centr Centr	e has rea	ached the up ached the up ached the lo ached the lo	pper 95% wer 95%	% confidence % confidence	e limit e limit					

Pancreas transplants

5.1 Pancreas transplants, 1 October 2015 – 30 September 2020

Figure 5.1 shows the total number of pancreas transplants performed in the last five years, by type of donor. The figure shows that 33 pancreas transplants were from <u>DCD</u> donors from October 2019 to September 2020; this amounts to 27% of pancreas transplants in that time period. There were 27 <u>DBD</u> pancreas transplants from April to September 2020, a 58% decrease compared to April to September 2019.

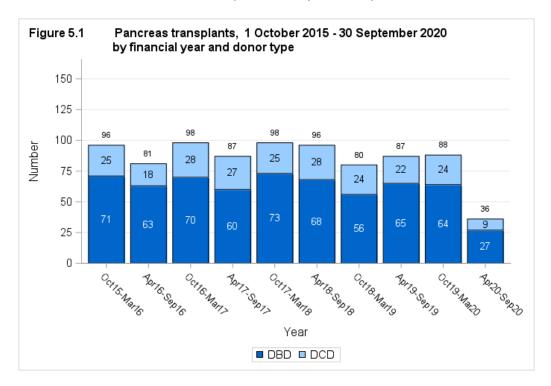
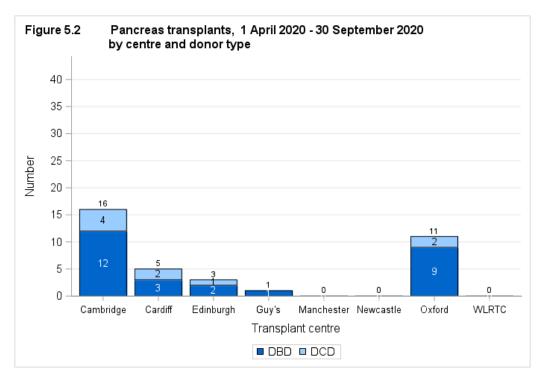
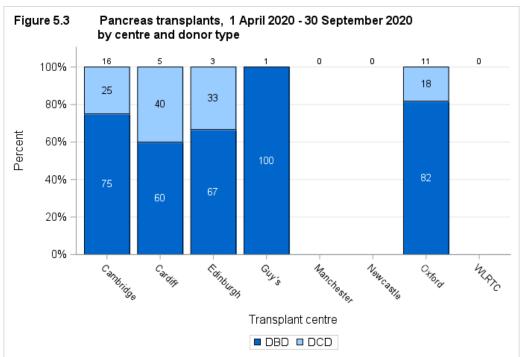


Figure 5.2 shows the total number of pancreas transplants performed from April to September 2020, by centre and type of donor. The same information is presented in **Figure 5.3** but this shows the proportion of <u>DBD</u> and <u>DCD</u> transplants performed at each centre.

Cambridge performed the most <u>DBD</u> and <u>DCD</u> transplants, 16, with 75% being <u>DBD</u> transplants. There were no <u>DCD</u> transplants performed at Guy's, Manchester, Newcastle and WLRTC whilst all other centres had a proportion of 18% or more. Based on small numbers, Cardiff had the largest proportion of <u>DCD</u> transplants at 40%, followed by Edinburgh at 33%.



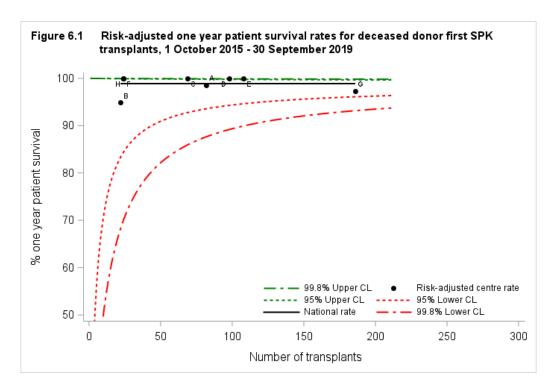


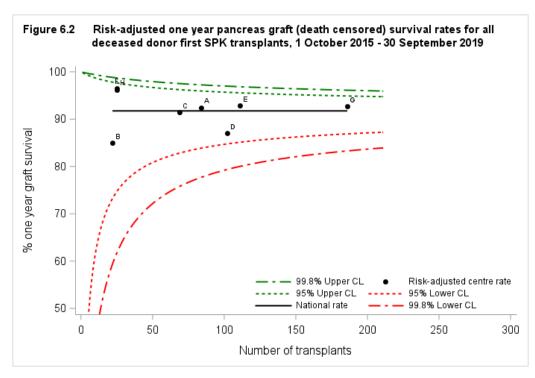
Pancreas outcomes

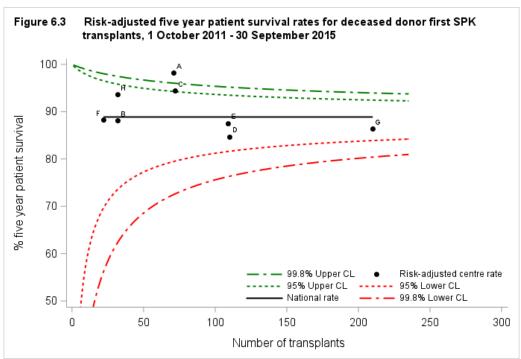
6.1 Deceased donor graft and patient survival for first SPK transplant

<u>Funnel plots</u> are used to compare centre specific <u>risk-adjusted patient</u> and <u>graft</u> survival rates and indicate how consistent these rates are with the national survival rates. Note that some patients return to local renal units for follow-up care after their transplant and although we report survival according to transplant unit, patients may in fact be followed up quite distantly from their transplant centre. It is important to note that adjusting for patient mix through the use of risk-adjustment models may not account for all possible causes of centre differences. There may be other factors that are not taken into account in the risk-adjustment process that may affect the survival rate of a particular centre.

Figures 6.1 and **6.2** compare individual centre survival estimates with the national rates for one-year <u>patient</u> and <u>graft</u> survival for deceased donor first SPK transplants and, for patient survival, first ever transplant. **Figures 6.3** and **6.4** compare five-year survival estimates. The <u>funnel plots</u> show that, for the most part, the centres lie within the <u>confidence limits</u>. Some of the <u>funnel plots</u> show some centres to be above the upper 99.8% <u>confidence limit</u>. This suggests that these centres may have survival rates that are considerably higher than the national rate. None of the <u>funnel plots</u> show centres to be below the lower 95% <u>confidence limit</u>. Centres can be identified by the information shown in **Tables 6.1** and **6.2**.







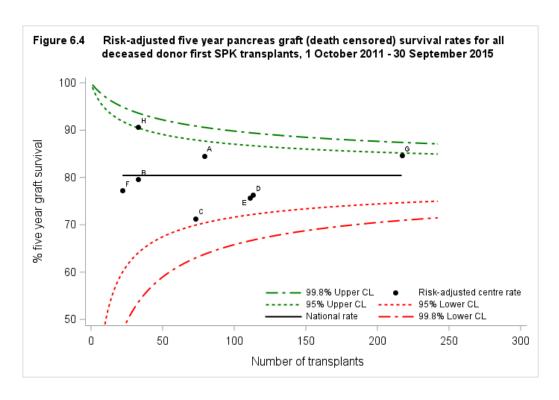


Table 6.1 Risk-adjusted one and five year patient survival for first SPK transplants using pancreases from deceased donors patient survival One-year* Five-year** Centre Code Ν % (95% CI) Ν % (95% CI) (92 - 100)Cambridge Α 82 99 (65 - 98)Cardiff В 22 (72 - 100)32 88 95 Edinburgh С (86 - 98)N/A 72 94 D Guy's 100 N/A 110 85 (73 - 92)Е (78 - 94)Manchester 108 100 N/A 109 88 Newcastle F 22 88 (58 - 99)G Oxford 186 97 (93 - 99)210 86 (80 - 91)WLRTC Н (77 - 99)32 94 UK 613 99 (98 - 99)658 89 (86 - 91)Centre has reached the lower 99.8% confidence limit Centre has reached the lower 95% confidence limit Centre has reached the upper 95% confidence limit Centre has reached the upper 99.8% confidence limit Includes transplants performed between 1 October 2015 - 30 September 2019 Includes transplants performed between 1 October 2011 - 30 September 2015

Table 6.2				ar pancreas gi from decease			irst SPK				
		pancreas <u>graft</u> survival									
			One-y			Five-ye					
Centre	Code	N	%	(95% CI)	N	%	(95% CI)				
Cambridge	Α	84	92	(84 - 97)	79	85	(73 - 92)				
Cardiff	В	22	85	(56 - 97)	33	80	(60 - 91)				
Edinburgh	С	69	91	(80 - 97)	73	71	(54 - 84)				
Guy's	D	102	87	(78 - 93)	113	76	(66 - 84)				
Manchester	E	111	93	(85 - 97)	111	76	(64 - 84)				
Newcastle	F	25	97	(81 - 100)	22	77	(42 - 94)				
Oxford	G	186	93	(88 - 96)	217	85	(78 - 89)				
WLRTC	Н	25	96	(79 - 100)	33	91	(73 - 98)				
UK		624	92	(89 - 94)	681	80	(77 - 83)				
Centre has reached the lower 99.8% confidence limit Centre has reached the lower 95% confidence limit Centre has reached the upper 95% confidence limit Centre has reached the upper 99.8% confidence limit											

6.2 Deceased donor graft and patient survival for first PO transplants

Individual centre survival estimates and national rates for one-year and five-year <u>patient</u> and pancreas <u>graft</u> survival for deceased donor first pancreas only (PO) transplants and, for patient survival, first ever transplant, are shown in **Tables 6.3** and **6.4**, respectively. Centre specific estimates of these rates must be interpreted with caution due to the small number of transplants upon which they are based.

Table 6.3	Unadjusted on transplants us											
		patient survival										
			One-ye			Five-ye	ar**					
Centre	Code	Ν	%	(95% CI)	N	%	(95% CI)					
Cambridge	Α	0	-	-	0	-	-					
Cardiff	В	3	-	-	11	100	-					
Edinburgh	С	0	-	-	0	-	-					
Guy's	D	0	-	-	5	-	-					
Manchester	Е	3	-	-	2	-	-					
Newcastle	F	0	-	-	2	-	-					
Oxford	G	13	92	(57 - 99)	35	87	(69 - 95)					
WLRTC	Н	3	-	-	0	-	-					
UK		22	95	(72 - 99)	55	90	(76 - 96)					
** Includes trans	splants performed be splants performed be ented where less that	etween 1	October	2011 - 30 Septe								

Table 6.4	Unadjusted or transplants us						st PO				
		pancreas graft survival									
			One-ye	ear*		Five-ye	ear**				
Centre	Code	Ν	%	(95% CI)	Ν	%	(95% CI)				
Cambridge	А	0	_	-	3	_	-				
Cardiff	В	4	-	-	17	40	(18 - 62)				
Edinburgh	С	0	-	-	1	-	-				
Guy's	D	0	-	-	7	-	-				
Manchester	Е	11	73	(24 - 93)	4	-	-				
Newcastle	F	3	-	-	5	-	-				
Oxford	G	18	89	(61 - 97)	43	59	(41 - 73)				
WLRTC	Н	4	-	-	8	-	-				
UK		40	84	(67 - 92)	88	53	(42 - 64)				

^{*} Includes transplants performed between 1 October 2015 - 30 September 2019 ** Includes transplants performed between 1 October 2011 - 30 September 2015

Data not presented where less than 10 transplants included

Islet transplant list

7.1 Patients on the islet transplant list as at 31 March and 30 September, 2016 – 2020

Figure 7.1 shows the number of patients on the islet <u>transplant list</u> at 31 March and 30 September each year between 2016 and 2020. The number of patients active on the islet <u>transplant list</u> has decreased by 77%, from 43 in September 2019 to 10 in September 2020, due to patients being suspended from the waiting list and centres being closed during the COVID-19 pandemic.

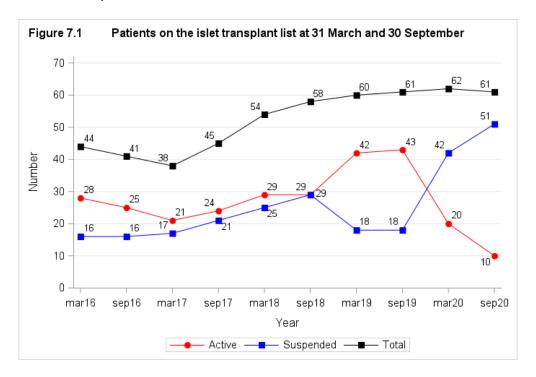
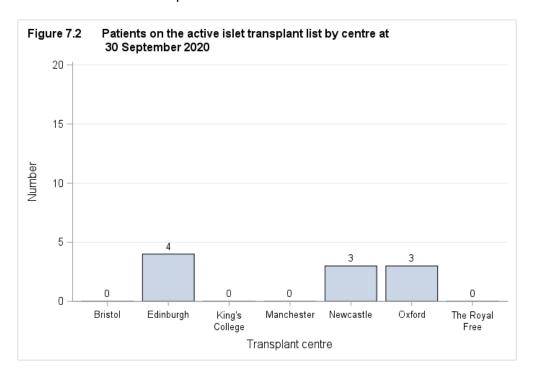


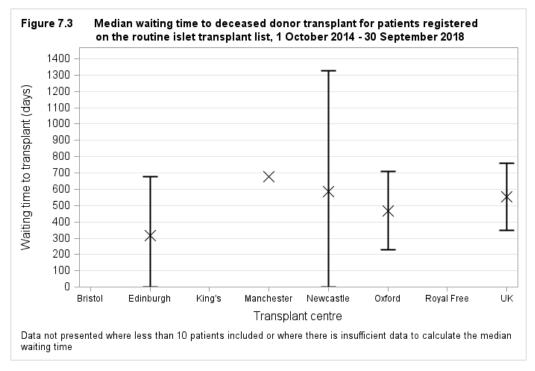
Figure 7.2 shows the number of patients on the active islet <u>transplant list</u> at 30 September 2020 by centre. Four (40%) of the patients on the active <u>transplant list</u> were registered at Edinburgh. Four centres had no patients on the active list due to patients being suspended and centres still closed on 30 September 2020.



7.2 Median waiting time to transplant, 1 October 2014 – 30 September 2018

The length of time a patient waits for a routine islet transplant, including simultaneous islet and kidney transplants, varies across the UK. The <u>median</u> waiting time for deceased donor islet transplantation is shown in **Figure 7.3** and **Table 7.1** for patients registered on the routine list at each individual unit.

The <u>median</u> waiting time to transplant for patients registered on the routine islet <u>transplant</u> <u>list</u> between 1 October 2014 and 30 September 2018 is 555 days, over 18 months, ranging from 318 days at Oxford to 677 days at Manchester.



	dian waiting time to routine patients registered 1 Octob		and the control of th
Transplant centre	Number of patients	Wa	iting time (days)
	registered	Median	95% Confidence interva
Bristol	0	-	-
Edinburgh	39	318	0 - 676
King's	4	-	-
Manchester ¹	24	677	-
Newcastle	13	587	0 - 1326
Oxford	17	469	228 - 710
Royal Free	3	-	-
UK	100	555	349 - 761
Data not proponted :	where less than 10 patients includ	lod	

Response to islet offers

8.1 Offer decline rates, 1 April 2017 – 30 September 2020

Islet offers from <u>DBD</u> donors whose pancreas was retrieved, offered directly on behalf of a named individual patient and resulted in islet transplantation are included in the analysis. Any offers of islets declined for transplantation or <u>DCD</u> offers were excluded, as were offers made through the fast track scheme or the reallocation of the pancreas.

Individual centre offer decline rates over the time period, 1 April 2017 and 30 September 2020 are shown in **Table 8.1**. Note that all rates are based on a small number of offers. King's (0%) and Royal Free (100%) had the lowest and highest overall decline rates, respectively. Of the four centres with over 20 offers in the time period, Edinburgh had the lowest decline rate of 36%.

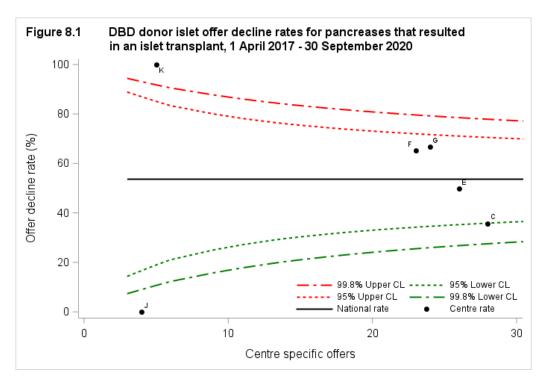
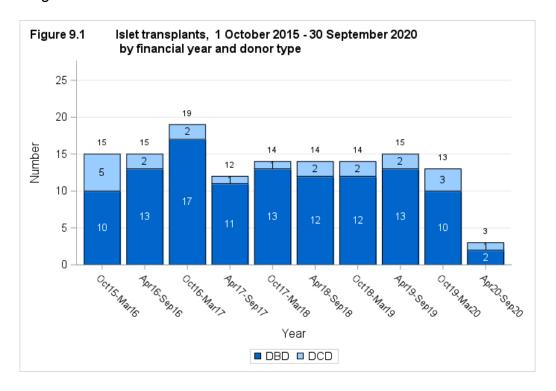


Table 8.1			let offer de nd 30 Sept			plant ce	entre,				
Centre	Code	20)17/18	20	2018/19		19/20	Apr -	Sep 20	Overall	
		No. offers	(% declined)	No. offers	(% declined)	No. offers	(% declined)	No. offers	(% declined)	No. offers	(% declined)
Bristol	I	0	-	0	_	0	-	0	-	0	_
Edinburgh	С	12	(33)	8	(50)	7	(29)	1	(0)	28	(36)
King's	J	1	(0)	2	(0)	1	(0)	0	-	4	(0)
Manchester	E	8	(38)	10	(70)	8	(38)	0	-	26	(50)
Newcastle	F	5	(100)	10	(50)	8	(63)	0	-	23	(65)
Oxford	G	16	(75)	4	(50)	4	(50)	0	-	24	(67)
Royal Free	K	0	-	1	(100)	4	(100)	0	-	5	(100)
UK		42	(57)	35	(54)	32	(50)	1	(100)	110	(54)
	Cent	re has re	ached the u	pper 99.	8% confider	nce limit					
	Centre has reached the upper 95% confidence limit										
	Cent	re has re	ached the lo	wer 95%	6 confidence	e limit					
	Cent	re has re	ached the lo	wer 99.8	3% confiden	ce limit					

Islet transplants

9.1 Islet transplants, 1 October 2015 – 30 September 2020

Figure 9.1 shows the total number of islet transplants performed in the last five years by type of donor. The number of islet transplants has ranged from three to 19 in the six-month periods from October 2015 to September 2020. Of these, <u>DCD</u> islet transplants have ranged from 1 to 5. In the latest six-month period during the COVID-19 pandemic, three islet transplants were performed, two at Edinburgh (one DBD and one DCD) and one at King's College.



Appendix

A1 Glossary of terms

ABO

The most important human blood group system for transplantation is the ABO system. Every human being is of blood group O, A, B, AB, or one of the minor variants of these four groups. ABO blood groups are present on other tissues and, unless special precautions are taken, a blood group A pancreas transplanted to a blood group O patient will be rapidly rejected.

Active transplant list

When a patient is registered for a transplant, they are registered on what is called the 'active' transplant list. This means that when a donor pancreas becomes available, the patient is included among those who are matched against the donor to determine whether or not the pancreas is suitable for them. It may sometimes be necessary to take a patient off the transplant list, either temporarily or permanently. This may be done, for example, if someone becomes too ill to receive a transplant. The patient is told about the decision to suspend them from the list and is informed whether the suspension is temporary or permanent. If a patient is suspended from the list, they are not included in the matching of any donor pancreases that become available.

Calculated Reaction Frequency (cRF)

For a given patient with detectable <u>HLA</u> antibodies, the proportion blood group identical donors from a pool of 10,000 against which the recipient has <u>HLA</u> specific antibodies is calculated. This percentage of donors is termed the 'calculated Reaction Frequency' (cRF), more commonly referred to as the <u>sensitisation</u> level. Patients with no detectable HLA antibodies will have 0 sensitisation (0% cRF).

Case mix

The types of patients treated at a unit for a common condition. This can vary across units depending on the facilities available at the unit as well as the types of people in the catchment area of the unit. The definition of what type of patient a person is depends on the patient characteristics that influence the outcome of the treatment. For example the case mix for patients registered for a pancreas transplant is defined in terms of various factors such as the blood group, tissue type and age of the patient. These factors have an influence on the chance of a patient receiving a transplant.

Cold ischaemia time (CIT)

The length of time that elapses between a pancreas being removed from the donor to its transplantation into the recipient is called the Cold Ischaemia Time (CIT). Generally, the shorter this time, the more likely the pancreas is to work immediately and the better the long-term outcome. The factors which determine CIT include a) transportation of the pancreas from the retrieval hospital to the hospital where the transplant is performed, b) the need to tissue type the donor and cross-match the donor and potential recipients, c) the occasional necessity of moving the pancreas to another hospital if a transplant cannot go ahead, d) contacting and preparing the recipient for the transplant, and e) access to the operating theatre.

Confidence interval (CI)

When an estimate of a quantity such as a survival rate is obtained from data, the value of the estimate depends on the set of patients whose data were used. If, by chance, data from a different set of patients had been used, the value of the estimate may have been different. There is therefore some uncertainty linked with any estimate. A confidence

interval is a range of values whose width gives an indication of the uncertainty or precision of an estimate. The number of transplants or patients analysed influences the width of a confidence interval. Smaller data sets tend to lead to wider confidence intervals compared to larger data sets. Estimates from larger data sets are therefore more precise than those from smaller data sets. Confidence intervals are calculated with a stated probability, usually 95%. We then say that there is a 95% chance that the confidence interval includes the true value of the quantity we wish to estimate.

Confidence limit

The upper and lower bounds of a confidence interval.

Cox Proportional Hazards model

A statistical model that relates the instantaneous risk (hazard) of an event occurring at a given time point to the <u>risk factors</u> that influence the length of time it takes for the event to occur. This model can be used to compare the hazard of an event of interest, such as graft failure or patient death, across different groups of patients.

Cross-match

A cross-match is a test for patient antibodies against donor antigens. A positive cross-match shows that the donor and patient are incompatible. A negative cross-match means there is no reaction between donor and patient and that the transplant may proceed.

Donor after brain death

Donation after Brainstem Death (DBD) means donation which takes place following the diagnosis of death using neurological criteria.

Donor after circulatory death

Donation after Circulatory Death (DCD) means donation which takes place following the diagnosis of death using circulatory criteria.

Funnel plot

A graphical method that shows how consistent the survival rates of the different transplant units are compared to the national rate. The graph shows for each unit, a survival rate plotted against the number of transplants undertaken, with the national rate and confidence limits around this national rate superimposed. In this report, 95% and 99.8% confidence limits were used. Units that lie within the confidence limits have survival rates that are statistically consistent with the national rate. When a unit is close to or outside the limits, this is an indication that the centre may have a rate that is considerably different from the national rate.

Graft survival rate

The percentage of patients whose grafts are still functioning. This is usually specified for a given time period after transplant. For example, a five-year transplant survival rate is the percentage of transplants still functioning five years after transplant. For the purposes of pancreas transplantation, graft failure is defined as a return to permanent insulin dependence while for islet transplantation graft failure is defined as a C-peptide less than 50 pmol/l.

HbA1c

HbA1c refers to glycated haemoglobin which is measured by clinicians to obtain an overall picture of an individual's average blood sugar levels over a particular period. HbA1c is a valuable indicator of diabetes control.

HLA mismatch

Human Leucocyte Antigens (HLA) are carried on many cells in the body and the immune system can distinguish between those that can be recognised as 'self' (belonging to you or identical to your own) and those that can be recognised as 'nonself'. The normal response of the immune system is to attack foreign/non-self material by producing antibodies against the foreign material. This is one of the mechanisms that provide protection against infection. This is unfortunate from the point of view of transplantation as the immune system will see the graft as just another 'infection' to be destroyed, produce antibodies against the graft and rejection of the grafted organ will take place. To help overcome this response, it is recognised that 'matching' the recipient and donor on the basis of HLA (and blood group) reduces the chances of acute rejection and, with the added use of immunosuppressive drugs, very much improves the chances of graft survival. 'Matching' refers to the similarity of the recipient HLA type and donor HLA type. HLA mismatch refers to the number of mismatches between the donor and the recipient at the A, B and DR (HLA) loci. There can only be a total of two mismatches at each locus. For example, an HLA mismatch value of 000, means that the donor and recipient are identical at all three loci, while an HLA mismatch value of 210 means that the donor and recipient differ completely at the A locus, are partly the same at the B locus and are identical at the DR locus.

Hypoglycaemia

Hypoglycaemia occurs when the level of glucose present in the blood falls below a set point and is the most common complication of insulin therapy. Severe hypoglycaemia is defined as having low blood glucose levels that requires third party assistance to treat and is classed as a diabetic emergency.

Inter-quartile range

The values between which the middle 50% of the data fall. The lower boundary is the lower quartile, the upper boundary the upper quartile.

Kaplan-Meier method

A method that allows patients with incomplete follow-up information to be included in estimating survival rates. For example, in a cohort for estimating one year patient survival rates, a patient was followed up for only nine months before they relocated. If we calculated a crude survival estimate using the number of patients who survived for at least a year, this patient would have to be excluded as it is not known whether or not the patient was still alive at one year after transplant. The Kaplan-Meier method allows information about such patients to be used for the length of time that they are followed-up, when this information would otherwise be discarded. Such instances of incomplete follow-up are not uncommon and the Kaplan-Meier method allows the computation of estimates that are more meaningful in these cases.

Median

The midpoint in a series of numbers, so that half the data values are larger than the median, and half are smaller.

Multi-organ transplant

A transplant in which the patient receives more than one organ. For example, a patient may undergo a transplant of a pancreas and liver. Intestinal transplants involving a pancreas are excluded from the whole report.

National Pancreas Offering Scheme

A nationally agreed set of rules for sharing and allocating deceased donor pancreases for pancreas or islet transplant between transplant centres in the UK. The scheme was introduced on 1 December 2010, revised on 11 September 2019 and is administered by NHS Blood and Transplant. Prior to December 2010 deceased donors were allocated on a centre basis.

The Pancreas Offering Scheme, from September 2019, prioritises difficult to match and long-waiting patients in a top tier. The second tier includes all other blood group eligible patients and assigns an individual point score to these patients based on a number of clinically relevant donor, recipient and transplant related factors. The individual points score assigns more points to patients with lower levels of HLA mismatch, longer waiting times, higher levels of patient sensitisation, short travel times between retrieval to transplant centre, longer duration of dialysis and better donor to recipient age matching. In addition, donors with a lower BMI are clinically desirable for pancreas transplantation whereas donors with a higher BMI are preferable for islet transplantation. As a result, where the donor has a low BMI more points are awarded for patients waiting for a pancreas transplant and where the donor has a high BMI more points are awarded to islet patients. Patients listed nationally for either a pancreas or islet transplant are then ranked by their total points score and the pancreas is offered preferentially to the patient with the highest total number of points, no matter where in the UK they receive their treatment or whether they are waiting for a pancreas or islet transplant.

Patient survival rate

The percentage of patients who are still alive (whether the graft is still functioning or not). This is usually specified for a given time period after transplant. For example, a five-year patient survival rate is the percentage of patients who are still alive five years after their first transplant.

p value

In the context of comparing survival rates across centres, the p value is the probability that the differences observed in the rates across centres occurred by chance. As this is a probability, it takes values between 0 and 1. If the p value is small, say less than 0.05, this implies that the differences are unlikely to be due to chance and there may be some identifiable cause for these differences. If the p value is large, say greater than 0.1, then it is quite likely that any differences seen are due to chance.

Risk-adjusted survival rate

Some transplants have a higher chance than others of failing at any given time. The differences in expected survival times arise due to differences in certain factors, the <u>risk factors</u>, among patients. A risk-adjusted survival rate for a centre is the expected survival rate for that centre given the case mix of their patients. Adjusting for case mix in estimating centre-specific survival rates allows valid comparison of these rates across centres and to the national rate.

Risk factors

These are the characteristics of a patient, transplant or donor that influence the length of time that a graft is likely to function or a patient is likely to survive following a transplant. For example, when all else is equal, a transplant from a younger donor is expected to survive longer than that from an older donor and so donor age is a risk factor.

Sensitisation

Potential recipients can develop a number of different <u>HLA</u> antibodies as a result of exposure to the different <u>HLA</u> through blood transfusion, previous transplants and pregnancy. Many patients however, have no detectable <u>HLA</u> antibodies. If a potential recipient has an antibody to an <u>HLA</u> then they cannot receive a transplant from a donor with that <u>HLA</u>, thus restricting the pool of potential donors. Patients who are clinically incompatible with the donor are excluded from the offering sequence by the <u>Pancreas</u> Offering Scheme.

Unadjusted survival rate

Unadjusted survival rates do not take account of <u>risk factors</u> and are based only on the number of transplants at a given centre and the number and timing of those that fail within the post-transplant period of interest. In this case, unlike for risk-adjusted rates, all transplants are assumed to be equally likely to fail at any given time. However, some centres may have lower unadjusted survival rates than others simply because they tend to undertake transplants that have increased risks of failure. Comparison of unadjusted survival rates across centres and to the national rate is therefore inappropriate.

A2 Statistical methodology and risk-adjustment for survival rate estimation

<u>Unadjusted</u> and <u>risk-adjusted</u> estimates of <u>patient</u> and <u>graft</u> survival for pancreas and simultaneous pancreas and kidney (SPK) transplant are given for each centre. <u>Unadjusted</u> rates give an estimate of what the survival rate at a centre is, assuming that all patients at the centre have the same chance of surviving a given length of time after transplant. In reality, patients differ and a <u>risk-adjusted</u> rate that allows for these differences would give a more meaningful estimate of survival.

Computing unadjusted survival rates

<u>Unadjusted</u> survival rates were calculated using the <u>Kaplan-Meier</u> method, which allows patients with incomplete follow-up information to be included in the computation. For example, in a cohort for estimating one-year <u>patient</u> survival rates, a patient was followed up for only nine months before they relocated. If we calculated a crude survival estimate using the number of patients who survived for at least a year, this patient would have to be excluded, as it is not known whether or not the patient was still alive one year after transplant. The <u>Kaplan-Meier</u> method allows information about such patients to be used for the length of time that they are followed-up, when this information would otherwise be discarded. Such instances of incomplete follow-up are not uncommon in the analysis of survival data and the <u>Kaplan-Meier</u> method therefore allows the computation of survival estimates that are more meaningful.

Computing risk-adjusted survival rates

A <u>risk-adjusted</u> survival rate is an estimate of what the survival rate at a centre would have been if they had had the same mix of patients as that seen nationally. The <u>risk-adjusted</u> rate therefore presents estimates in which differences in patient mix across centres have been removed as much as possible. For that reason, it is valid to only compare centres using <u>risk-adjusted</u> rather than <u>unadjusted</u> rates, as differences among the latter can be attributed to differences in patient mix.

Risk-adjusted survival estimates were obtained through indirect standardisation. A Cox Proportional Hazards model was used to determine the probability of survival for each patient based on their individual risk factor values. The sum of these probabilities for all patients at a centre gives the number, E, of patients or grafts expected to survive at least one year or five years after transplant at that centre. The number of patients who actually survive the given time period is given by O. The risk-adjusted estimate is then calculated by multiplying the ratio O/E by the overall unadjusted survival rate across all centres. The risk-adjustment models used were based on results from previous studies that looked at factors affecting the survival rates of interest. The factors included in the models are shown in the table below.

First transplants from deceased donors

Simultaneous pancreas and kidney (SPK) and pancreas only survival

1 and 5 year patient and graft survival Donor age, donor type, donor BMI and waiting time

Funnel plots for comparing risk-adjusted survival rates

The <u>funnel plot</u> is a graphical method to show how consistent the survival rates of the different transplant centres are compared to the national rate. The graph shows for each centre, a survival rate plotted against the number of transplants undertaken, with the national rate and <u>confidence limits</u> around this national rate superimposed. In this report,

95% and 99.8% <u>confidence limits</u> were used. Units that lie within the <u>confidence limits</u> have survival rates that are statistically consistent with the national rate. When a unit is close to or outside the limits, this is an indication that the centre may have a rate that is considerably different from the national rate.

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