

# ANNUAL REPORT ON PANCREAS AND ISLET TRANSPLANTATION

REPORT FOR 2020/2021 (1 APRIL 2011 – 31 MARCH 2021)

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### **Executive Summary**

This report presents key figures about pancreas and islet transplantation in the UK. The period reported covers ten years of pancreas and islet transplant data, from 1 April 2011. The report presents information on the number of transplants and survival analysis after first simultaneous pancreas and kidney and pancreas only transplantation on a national and centre-specific basis. Also reported on a national basis is survival analysis after islet transplantation and additional outcome measures.

#### **Key findings**

- On the 31 March 2021, there were 172 patients on the UK active pancreas and islet transplant list, which represents a 27% decrease in number of patients a year earlier. The number of patients on the active pancreas list decreased by 27% to 153 in 2021 and the active islet transplant list decreased by 32% to 19 patients in the same time period.
- There were 1814 pancreas transplants performed in the UK in the ten year period and 277 islet transplants performed in the same time period. The number of transplants from donations after brain death has decreased by 49% in the last year to 77. The number of transplants from donations after circulatory death has decreased by 53% in the last year to 24.
- 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 97% to 100% at one-year and 82% to 97% 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 simultaneous pancreas and kidney transplant from deceased donors are 93% and 80%, respectively. These rates vary between centres, ranging from 86% to 97% at one-year and 68% to 94% 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 pancreas only transplant from deceased donors are 100% and 84%, respectively. The national rates of <u>graft</u> survival at one- and five-years are 88% and 56%. Centre specific estimates of these rates must be interpreted with caution due to the small number of transplants upon which they are based.
- The national rate of ten year <u>patient</u> survival from listing for deceased donor simultaneous pancreas and kidney transplant is 77%. These rates vary between centres, ranging from 76% to 80%. All centre rates are <u>risk-adjusted</u>.
- The national rates of one- and five-years <u>graft</u> survival for patients receiving a first routine islet transplant are 81% and 55%. For patients with a functioning graft at one-year post-transplant, the national rate of five year <u>graft</u> survival was 69% for patients receiving an additional priority islet graft and 48% for patients who did not.
- Reductions in annual rate of severe <u>hypoglycaemic</u> events, median <u>HbA1c</u> and median insulin requirements have been reported at one-year post routine islet transplant.

Use of the contents of this report should be acknowledged as follows:

Annual Report on Pancreas and Islet Transplantation 2020/21, NHS Blood and Transplant.

### Introduction

This report presents information on pancreas and islet transplant activity between 1 April 2011 and 31 March 2021, for all eight centres performing pancreas transplantation and seven centres performing islet transplantation in the UK. Cambridge, Cardiff, Guy's and WLRTC only perform pancreas transplants while Bristol, King's College and the Royal Free only perform islet transplants. 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 April 2016 to 31 March 2020 and five-year post-transplant for the period 1 April 2012 to 31 March 2016.

Islet transplant survival is measured by four key variables: graft survival, and a reduction in <a href="HbA1c"><u>HbA1c</u></a>, insulin requirements and the annual rate of severe <a href="hypoglycaemic">hypoglycaemic</a> events. Islet outcomes are reported at one-year post-transplant for the period 1 April 2016 to 31 March 2020, and <a href="graft">graft</a> survival at five-year post-transplant for the period 1 April 2011 to 31 March 2020, for the national cohort only. Islet outcomes are <a href="maintainted">unadjusted</a> for risk and islet outcome data from the UK Transplant Registry is supplemented by data collected from the UK Islet Transplant Consortium.

Pancreas <u>patient</u> survival from listing is reported at one, five and ten years post registration for a deceased donor simultaneous pancreas and kidney transplants between 1 January 2008 and 31 December 2020.

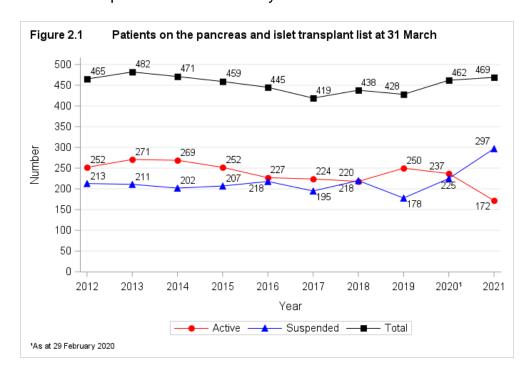
The centre specific results for survival estimates are adjusted for differences in <u>risk</u> <u>factors</u> between the centres. The risk models and methods used are described in the Appendix.

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

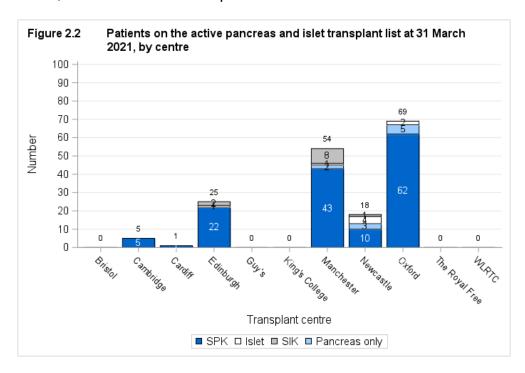
The COVID-19 pandemic has led to unprecedented challenges for UK transplantation. Concerns about the ability to care for transplant recipients, lack of access to resource because it is being used for patients in the pandemic, and the risk versus benefit for immunosuppressed transplant recipients, have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

Waiting list figures at the 31 March 2020 and 2021 do not accurately reflect the need for pancreas and islet transplantation due to the COVID-19 pandemic. In 2020, different practices were established across the UK with regards to waiting list management. Due to this, a snapshot of the waiting list at 29 February 2020 has been used to better reflect activity for the 2019-2020 financial year in figures which use these data.

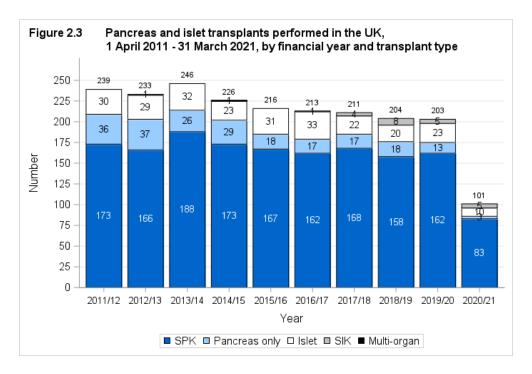
**Figure 2.1** shows the number of patients on the pancreas and islet <u>transplant list</u> at 31 March each year between 2012 and 2021. The number of patients actively waiting for a pancreas or islet transplant has decreased by 32% from 252 in 2012 to 172 in 2021.



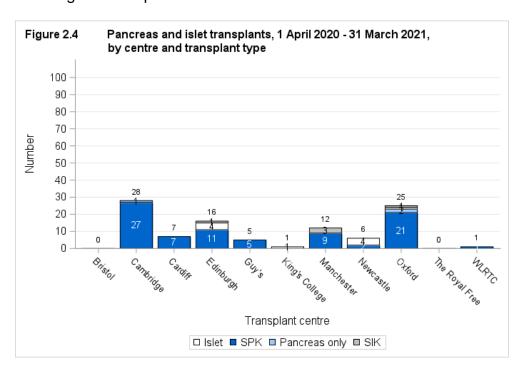
**Figure 2.2** shows the number of patients on the pancreas and islet <u>transplant list</u> at 31 March 2021 for each transplant centre. Oxford has the largest <u>transplant list</u> with 69 patients registered for a pancreas or islet transplant. Of these patients, 62 are registered for a SPK, five for a pancreas only and two for an islet only transplant. Edinburgh, Manchester and Newcastle have patients waiting for an SIK transplant, 11 in total. There were no patients on the active islet list at Bristol, King's College or The Royal Free at 31 March 2021. There were no patients on the active pancreas list at Guy's or WLRTC at 31 March 2021, due to the COVID-19 pandemic.



**Figure 2.3** shows the total number of pancreas and islet transplants performed in the last ten financial years. Transplant numbers increased from 239 in 2011/12 to 246 in 2013/14 but decreased over the last few years to 101 in 2020/21. In particular, the number of pancreas only transplants decreased from 36 transplants in 2011/12 to three in 2020/21.



**Figure 2.4** shows the total number of pancreas and islet transplants performed in 2020/21 at each transplant centre. Cambridge performed the most pancreas and islet transplants last year, a total of 28 transplants, whilst Edinburgh performed the most islet and SIK transplants (five). A total of six SIK transplants were performed at King's, Manchester, Edinburgh and Oxford. The Royal Free and Bristol performed no transplants during this time period.



**Figure 2.5** details the 101 pancreas and islet transplants performed in the UK between 1 April 2020 and 31 March 2021. Data for transplants performed in 2019/20 are also presented. The overall number of whole pancreas transplants performed in 2020/21 has decreased by 89 compared with 2019/20 to 86. The number of islet transplants has decreased by 13 compared with 2019/20 to 15.

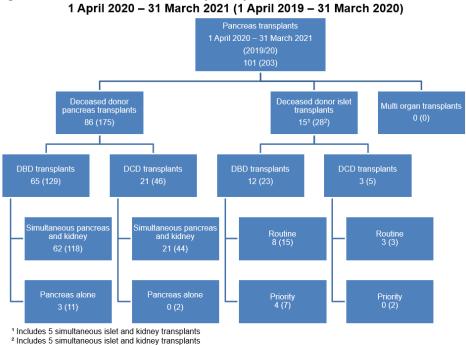


Figure 2.5 Pancreas and islet transplants performed in the UK, 1 April 2020 – 31 March 2021 (1 April 2019 – 31 March 2020)

#### Geographical variation in registration and transplant rates

**Figure 2.6** shows rates of registration to the pancreas transplant list per million population (pmp) between 1 April 2020 and 31 March 2021 compared with pancreas transplant rates pmp for the same time period, by recipient country/NHS region of residence. **Table 2.2** shows the breakdown of these numbers by recipient country/NHS region of residence. No adjustments have been made for potential demographic differences in populations. If a patient has had more than one registration/transplant in the period, each registration/transplant is considered. Note that this analysis only considered NHS Group 1 patients.

Since there will inevitable be some random variation in rates between areas, the systematic component of variation (SCV) was used to identify if the variation is more (or less) than a random effect for the different NHS regions in England only. Only first registrations and transplants in this period were considered. The larger the SCV the greater the evidence of a high level of systematic variation between areas. Registration and transplant rates yielded an SCV of 0.0569 (p-value = 0.025) and 0.2191 (p-value = 0.002), respectively. The p-value shows the probability that an SCV of this size (or higher) would be observed by chance if only random variation existed and therefore moderate evidence of geographical variation beyond what would be expected at random for registrations, and strong evidence for transplants. No adjustment has been made for area-specific demographic characteristics that may impact the rates of registration to the transplant list and transplantation such as age and sex. Therefore, these results should be interpreted with caution.

Figure 2.6 Comparison of pancreas registration rates (pmp) with transplant rates (pmp) by recipient country/NHS region of residence

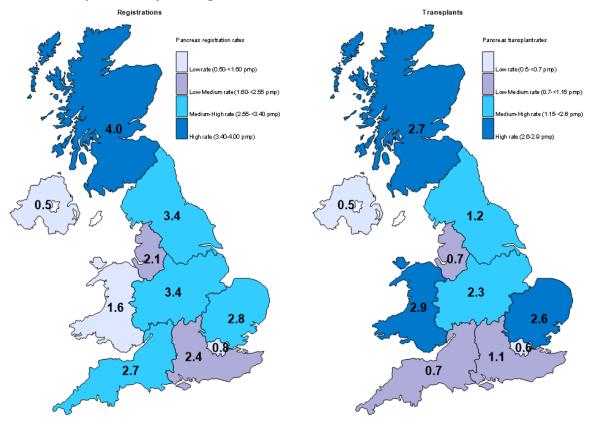


Table 2.1 Pancreas registration and transplant rates per million population (pmp) in the UK, 1 April 2020 - 31 March 2021, by Country/NHS region

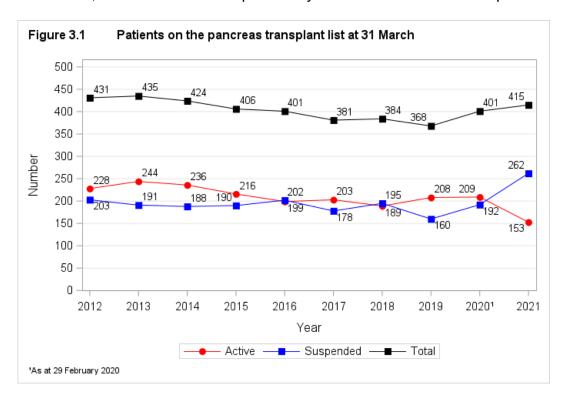
Country/NHS region	Registrations (pmp)		Transplants (pmp)	
North East and Yorkshire	29	(3.4)	10	(1.2)
North West	15	(2.1)	5	(0.7)
Midlands	36	(3.4)	24	(2.3)
East of England	18	(2.8)	17	(2.6)
London	7	(8.0)	5	(0.6)
South East	21	(2.4)	10	(1.1)
South West	15	(2.7)	4	(0.7)
England	141	(2.5)	75	(1.3)
Isle of Man	0	(0.0)	0	(0.0)
Channel Islands	0	(0.0)	0	(0.0)
Wales	5	(1.6)	9	(2.9)
Scotland	22	(4.0)	15	(2.7)
Northern Ireland	1	(0.5)	1	(0.5)
TOTAL	169	(2.5)	101 <sup>1</sup>	(1.5)

<sup>1</sup> Registrations include 1 recipient whose postcode was unknown

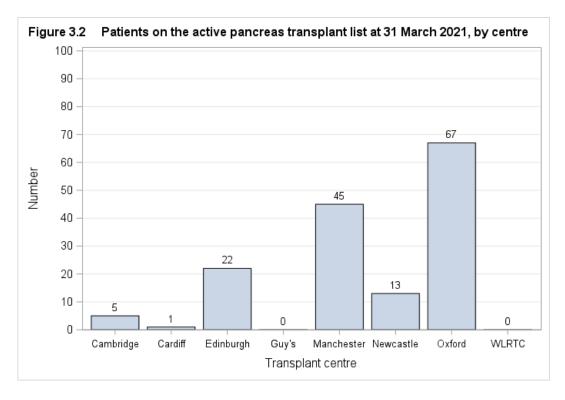
## Pancreas transplant list

#### 3.1 Patients on the pancreas transplant list as at 31 March, 2012 – 2021

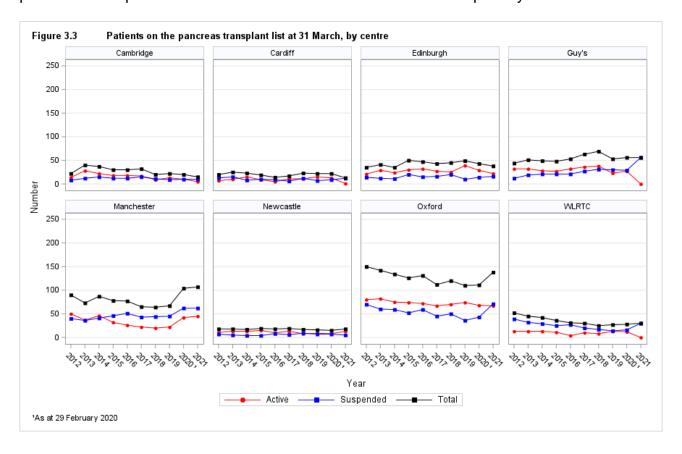
**Figure 3.1** shows the number of patients on the pancreas <u>transplant list</u> at 31 March each year from 2012. The number of patients actively waiting for a pancreas transplant was the highest at 244 in 2013 and then fell to 195 in 2018. On 31 March 2021, there were 153 patients on the list, 27% lower than the previous year due to the COVID-19 pandemic.



**Figure 3.2** shows the number of patients on the active pancreas <u>transplant list</u> at 31 March 2021 by centre. Oxford had the largest proportion of the <u>transplant list</u> (44%) and Guy's and WLRTC had no patients on the active list.

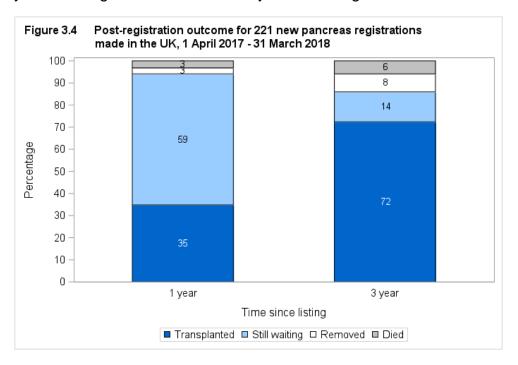


**Figure 3.3** shows the number of patients on the pancreas <u>transplant list</u> at 31 March each year from 2012 by transplant centre. The number of patients actively waiting for a pancreas transplant at Manchester has increased in the last couple of years.

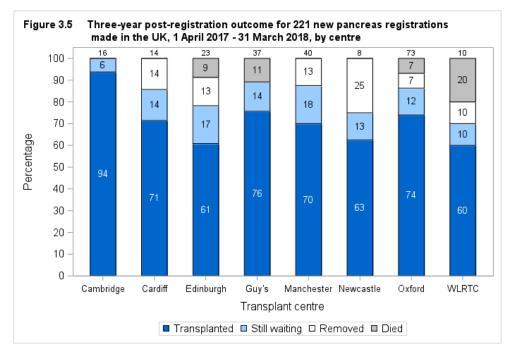


#### 3.2 Post-registration outcomes, 1 April 2017 – 31 March 2018

An indication of outcomes for patients listed for a pancreas transplant is summarised in **Figure 3.4**. This shows the proportion of patients transplanted or still waiting one and three years after joining the list. It also shows the proportion removed from the <u>transplant list</u> (typically because they become too unwell for transplant) and who died while on the <u>transplant list</u>. Only 35% of patients registered between 1 April 2017 and 31 March 2018 were transplanted within one year, while three years after listing 72% of patients had received a transplant. There were 3% of patients who had died waiting for a transplant within one year of listing and 6% within three years of listing.



**Figure 3.5** shows the proportion of patients transplanted or still waiting three years after joining the list by centre. Three years after listing, Cambridge had transplanted 94% of their patients while WLRTC had transplanted 60% and 20% had died waiting.

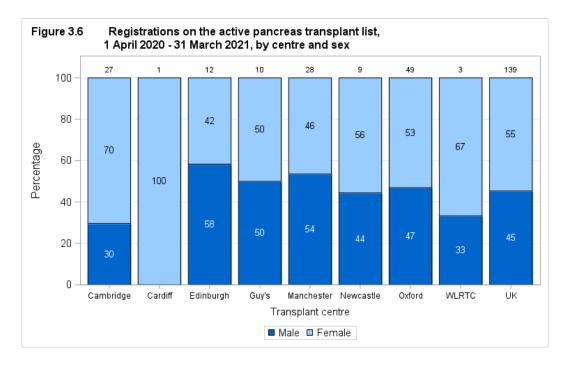


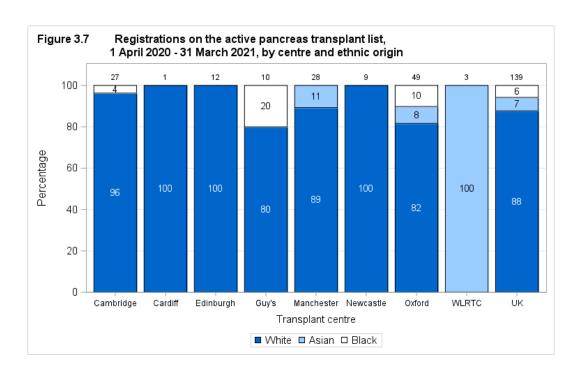
#### 3.3 Demographic characteristics, 1 April 2020 – 31 March 2021

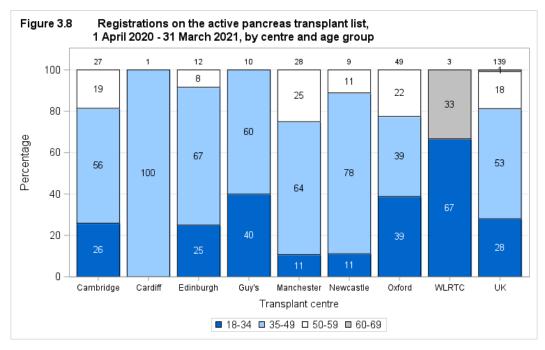
The sex, ethnicity, age group, <u>sensitisation</u> group (<u>cRF</u>%) and <u>matchability points score</u> group of patients registered on the pancreas <u>transplant list</u> in 2020/21 are shown by centre and overall for the UK in **Figures 3.6, 3.7, 3.8, 3.9** and **3.10** respectively. Note that all percentages quoted are based only on data where relevant information was available.

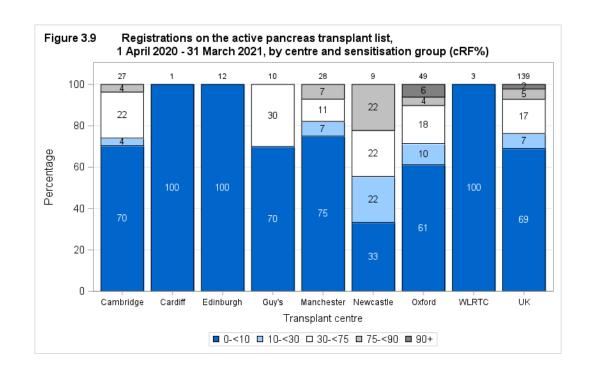
Overall, 139 patients were registered on the pancreas transplant list, 136 (98%) were waiting for a SPK transplant. Of these 136, 46% were male, 87% were white, the median age was 40 years and the median cRF was 0%.

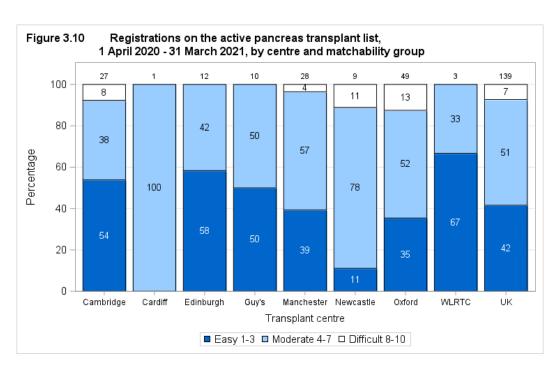
Of the 3 (2%) patients on the pancreas only transplant list, none were male, all were white, the median age was 42 years and the median cRF was 47%.





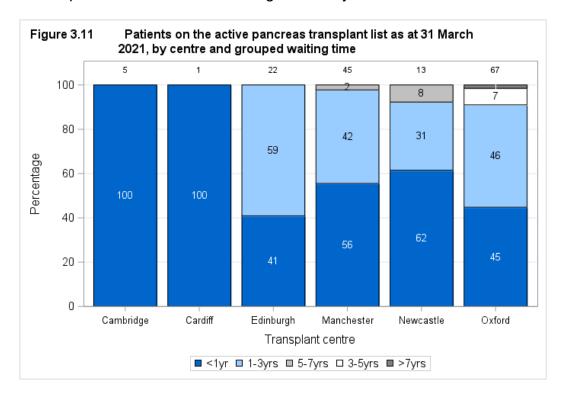






#### 3.4 Patient waiting times for those currently on the list, 31 March 2021

**Figure 3.11** shows the length of time active patients have been waiting on the pancreas transplant list at 31 March 2021 by centre. The majority of patients currently listed have been waiting less than one year. However, one highly sensitised (cRF 100%) patient waiting for a pancreas alone transplant at Oxford has been waiting more than 7 years. There were no patients on the active waiting list at Guy's or WLRTC on 31 March 2021.



#### 3.5 Median active waiting time to transplant, 1 April 2015 - 31 March 2019

The length of time a patient waits for a pancreas transplant varies across the UK. The <u>median</u> active waiting time for deceased donor pancreas transplantation is calculated using the <u>Kaplan-Meier method</u> and is shown in **Figure 3.12** and **Table 3.1** for patients registered at each individual centre.

The <u>median</u> active waiting time to transplant for patients registered on the pancreas <u>transplant list</u> between 1 April 2015 and 31 March 2019 is 363 days. This ranged from 217 days at WLRTC to 546 days at Edinburgh.

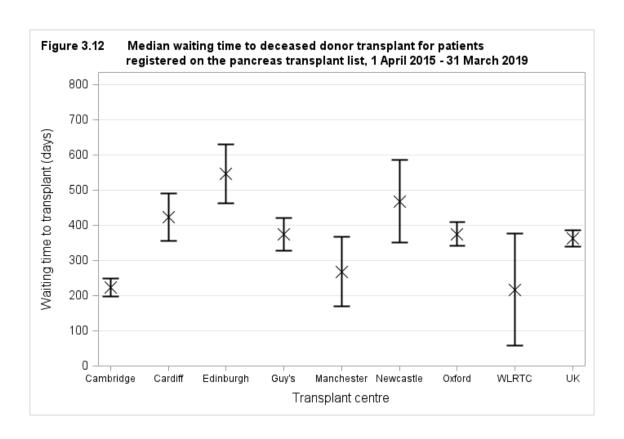


Table 3.1 Median active waiting time to pancreas transplant in the UK, for patients registered 1 April 2015 - 31 March 2019										
Transplant centre	Number of patients	Wa	iting time (days)							
·	registered	Median	95% Confidence interval							
Cambridge	102	223	198 - 248							
Cardiff	42	423	355 - 491							
Edinburgh	90	546	462 - 630							
Guy's	138	375	328 - 422							
Manchester	138	268	169 - 367							
Newcastle	39	468	351 - 585							
Oxford	283	375	341 - 409							
WLRTC	57	217	58 - 376							
UK	889	363	340 - 386							

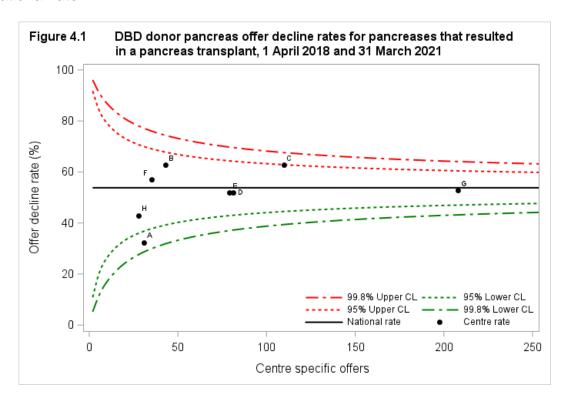
### Response to pancreas offers

#### 4.1 Offer decline rates, 1 April 2018 – 31 March 2021

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 were analysed separately. 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>.

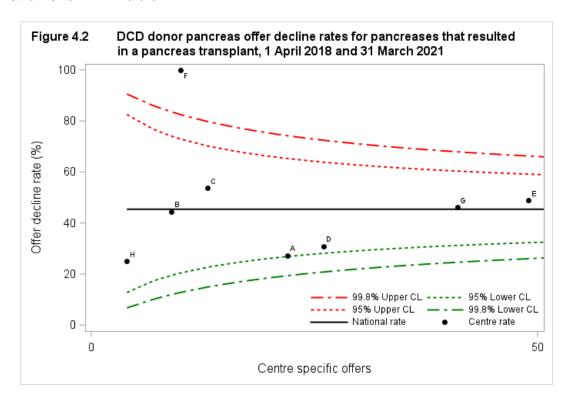
**Figure 4.1** compares individual centre offer <u>DBD</u> decline rates with the national rate over the time period, 1 April 2018 and 31 March 2021. Centres can be identified by the information shown in **Table 4.1**. Cambridge had offer decline rates significantly better than the national rate.



**Table 4.1** compares individual centre <u>DBD</u> offer decline rates over time by financial year. The overall offer decline rate decreased from 58% in 2019/20 to 40% in 2020/21. Newcastle decline rate increased to 75% in 2020/21 from 40% in 2019/20 and Cambridge declined rate decreased to 0% in 2020/21 from 67% in 2019/20.

Table 4.1 DBD donor pancreas offer decline rates by transplant centre, 1 April 2018 and 31 March 2021									
Centre	Code	2018/19		2019/20		2020/21		Overall	
		N	(%)	N	(%)	N	(%)	N	(%)
Cambridge	Α	14	(43)	6	(67)	11	(0)	31	(32)
Cardiff	В	18	(61)	19	(68)	6	(50)	43	(63)
Edinburgh	С	40	(65)	54	(63)	16	(56)	110	(63)
Guy's	D	39	(56)	39	(49)	3	(33)	81	(52)
Manchester	E	19	(42)	41	(51)	19	(63)	79	(52)
Newcastle	F	21	(62)	10	(40)	4	(75)	35	(57)
Oxford	G	82	(51)	98	(62)	28	(25)	208	(53)
WLRTC	Н	14	(50)	13	(38)	1	(0)	28	(43)
UK		247	(55)	280	(58)	88	(40)	615	(54)
	Centre has reached the upper 99.8% confidence limit Centre has reached the upper 95% confidence limit Centre has reached the lower 95% confidence limit Centre has reached the lower 99.8% confidence limit								

**Figure 4.2** compares individual centre offer <u>DCD</u> decline rates with the national rate over the time period, 1 April 2018 and 31 March 2021. Centres can be identified by the information shown in **Table 4.2**.



**Table 4.2** compares individual <u>DCD</u> centre offer decline rates over time by financial year. In 2020/21, Cambridge and Guy's had an offer decline rate better than the national rate, whilst Cardiff and Newcastle had a much higher decline rate than the national average. The number of offers in 2020/21 was 68% lower than the previous year.

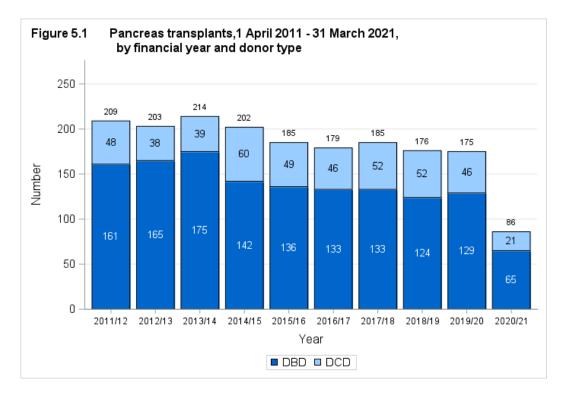
Table 4.2 DCD donor pancreas offer decline rates by transplant centre, 1 April 2018 and 31 March 2021									
Centre	Code	2018/19		2019/20		2020/21		Overall	
		N	(%)	N	(%)	N	(%)	N	(%)
Cambridge	Α	10	(30)	9	(33)	3	(0)	22	(27)
Cardiff	В	3	(33)	5	(40)	1	(100)	9	(44)
Edinburgh	С	5	(100)	4	(25)	4	(25)	13	(54)
Guy's	D	12	(33)	11	(36)	3	(0)	26	(31)
Manchester	E _	28	(43)	15	(53)	6	(67)	49	(49)
Newcastle	F	5	(100)	4	(100)	1	(100)	10	(100)
Oxford	G	19	(42)	18	(50)	4	(50)	41	(46)
WLRTC	Н	2	(50)	2	(0)	0	-	4	(25)
UK		84	(46)	68	(46)	22	(41)	174	(45)
	Centre has reached the upper 99.8% confidence limit Centre has reached the upper 95% confidence limit Centre has reached the lower 95% confidence limit Centre has reached the lower 99.8% confidence limit								

### **Pancreas transplants**

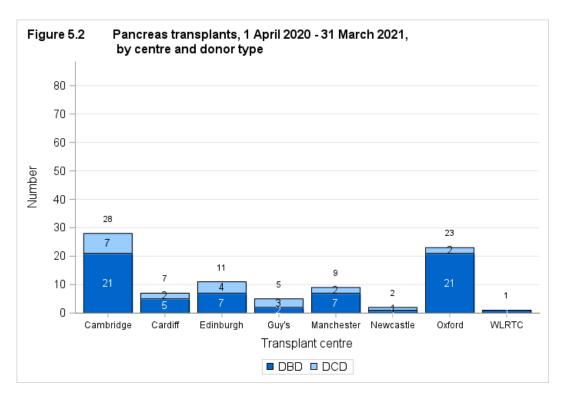
#### 5.1 Pancreas transplants, 1 April 2011 – 31 March 2021

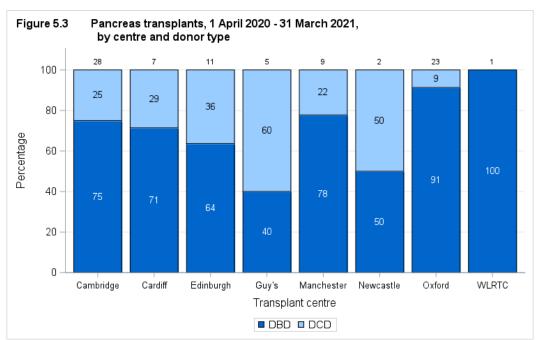
**Figure 5.1** shows the total number of pancreas transplants performed in the last ten financial years, by type of donor. The first <u>DCD</u> pancreas transplant was performed in 2005/06 and by 2011/12 there were 48 <u>DCD</u> transplants (23%). The number of <u>DCD</u> transplants performed reached a peak of 60 in 2014/15 but, within the last two financial years, has dropped to 46 in 2019/20 and 21 in 2020/21 although this still accounts for around a quarter of all pancreas transplants.

In 2013/14 the number of <u>DBD</u> transplants peaked at 175 (82%), however, this has decreased in the last seven years to 65 <u>DBD</u> transplants in 2020/21 due to the COVID-19 pandemic.

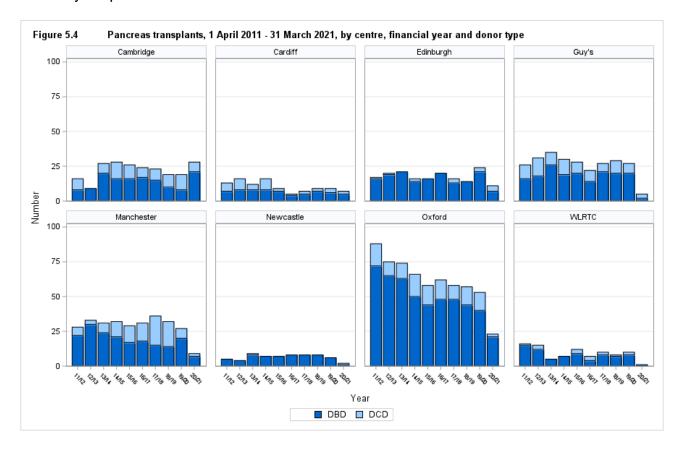


**Figure 5.2** shows the total number of pancreas transplants performed in 2020/21, by centre and type of donor. The same information is presented in **Figure 5.3** but this shows the proportion of <u>DBD</u> and <u>DCD</u> transplants performed at each centre. Cambridge performed the most <u>DBD</u> and <u>DCD</u> transplants (28), however Guy's had the largest proportion of <u>DCD</u> transplants (60%). WLRTC performed the lowest number of transplants (one), and no <u>DCD</u> transplants, in the last financial year.





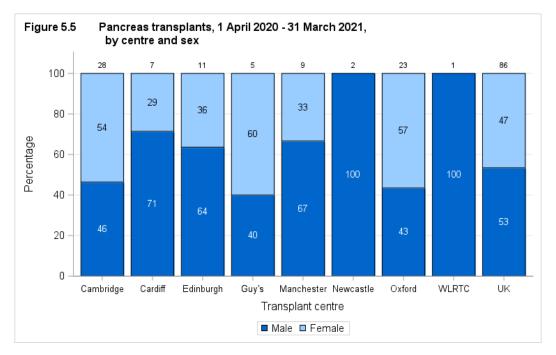
**Figure 5.4** shows the total number of pancreas transplants performed in last ten financial years, by centre and type of donor. Oxford have consistently performed a large number of pancreas transplants including a number of <u>DCD</u> transplants over the last ten years. However, the number of transplants performed at Oxford has been steadily decreasing since 2011/12. Edinburgh and Newcastle have not performed many <u>DCD</u> transplants over the ten year period.

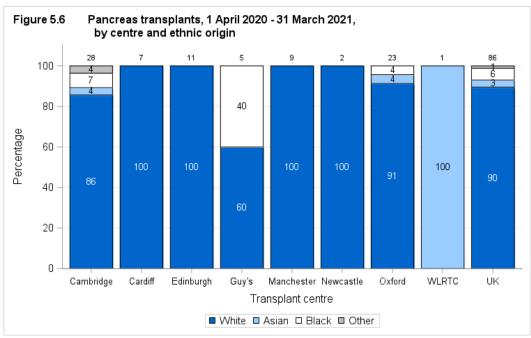


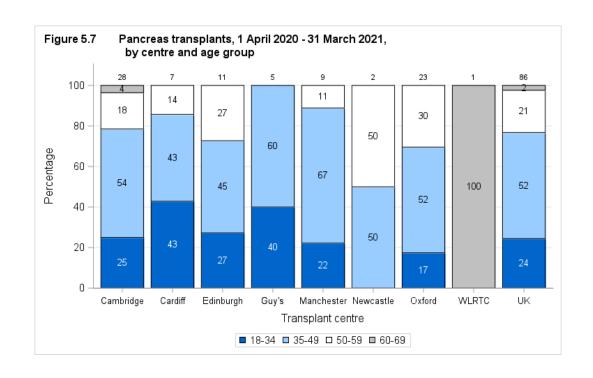
#### 5.2 Demographic characteristics, 1 April 2020 - 31 March 2021

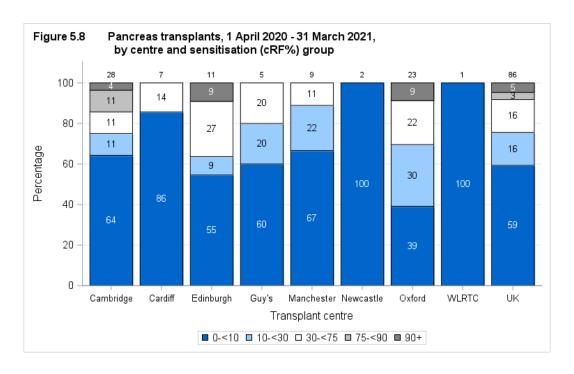
The sex, ethnicity, age group, <u>sensitisation</u> group (<u>cRF</u>%) and <u>matchability points score</u> group of patients that received a pancreas transplant in 2020/21 are shown by centre in **Figures 5.5, 5.6, 5.7** and **5.8** respectively. Note that all percentages quoted are based only on data where relevant information was available.

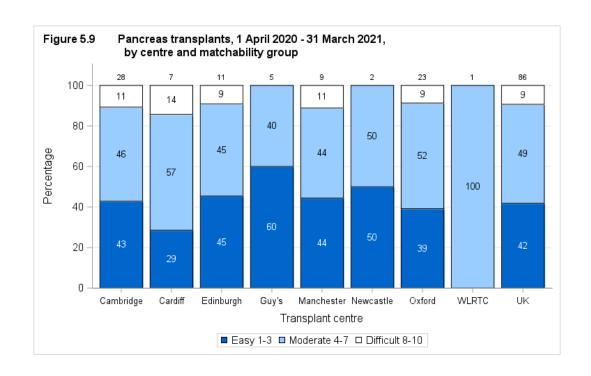
Overall, 86 patients were transplanted on the pancreas transplant list, 83 (97%) were SPK transplants. Of which 54% were male, 89% were white, the <u>median</u> age was 43 years, the <u>median cRF</u> was 0% and 8% were in the difficult match group. Of the 3 (3%) patients transplanted as a pancreas only transplant, 33% were male, 100% were white, the <u>median</u> age was 40 years, the <u>median cRF</u> was 66% and 33% were in the difficult match group.









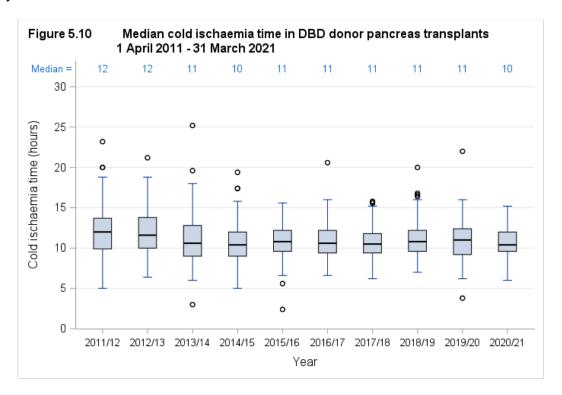


#### 5.3 Cold ischaemia time, 1 April 2011 – 31 March 2021

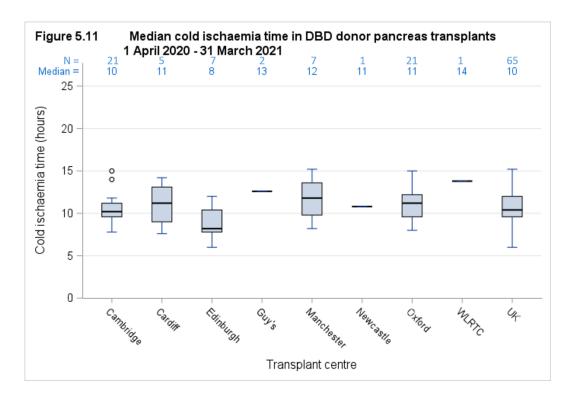
Median cold ischaemia times (CIT) are shown in addition to inter-quartile ranges in Figures 5.10 to 5.15. Fifty percent of the transplants have a CIT within the inter-quartile range (indicated by a box). Where there is only one observation to report, the single data point is represented by a circle and the median for multiple observations is represented by a line. There is some variation in average (median) CIT between different transplant centres although all centres continually try to reduce this time.

The cold ischaemia times used for all donors, is as reported on the pancreas transplant record form and may include periods of machine perfusion; no adjustment has been made for this.

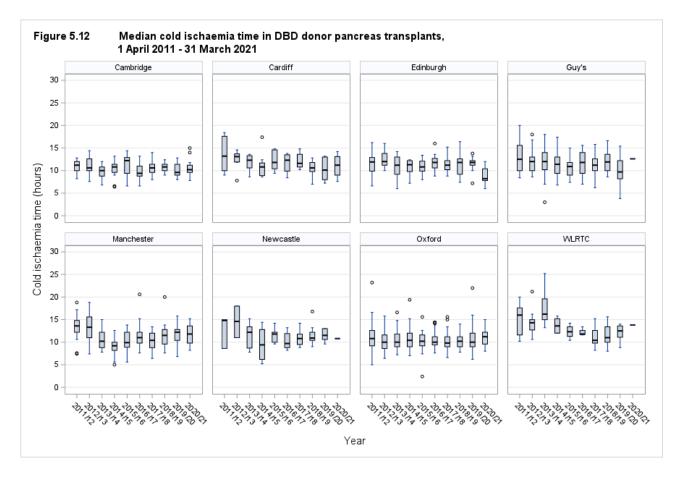
**Figure 5.10** shows the <u>median</u> cold ischaemia time in <u>DBD</u> donor pancreas transplants over the last ten years. During this time period the overall <u>median</u> cold ischaemia time has steadily decreased from 12 hours in 2011/12 to 10 hours in 2020/21.



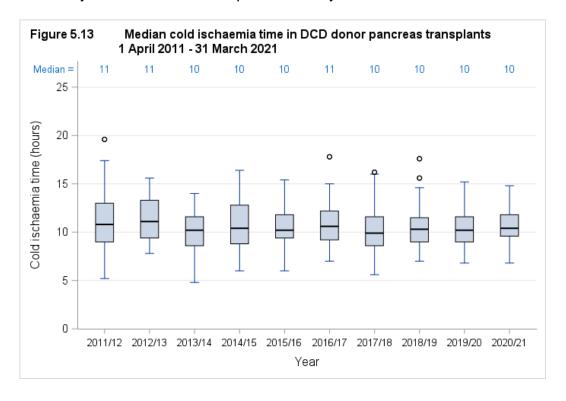
**Figure 5.11** shows the <u>median</u> cold ischaemia time in <u>DBD</u> donor pancreas transplants in 2020/21 for each transplant centre. Please note the small numbers used in the calculations for each centre and interpret with caution.



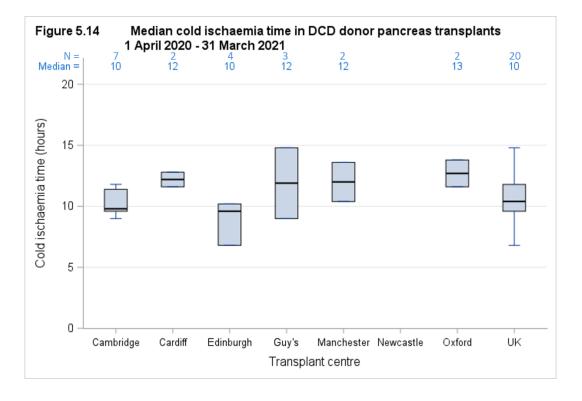
**Figure 5.12** shows the <u>median</u> cold ischaemia time in <u>DBD</u> donor pancreas transplants over the last ten years for each transplant centre. WLRTC <u>median</u> cold ischaemia times had steadily decreased but in the last couple of years has started to rise. Overall, the <u>median</u> cold ischaemia times have remained constant, however the <u>inter-quartile</u> ranges have reduced as time has continued.



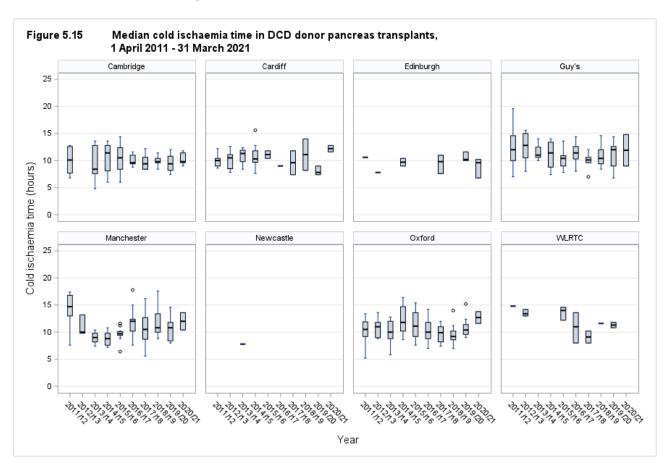
**Figure 5.13** shows the <u>median</u> cold ischaemia time in <u>DCD</u> donor pancreas transplants over the last ten years and overall has predominately been 10 hours.



**Figure 5.14** shows the <u>median</u> cold ischaemia time in <u>DCD</u> donor pancreas transplants in 2020/21 for each transplant centre. Please note the small numbers used in the calculations for each centre and interpret with caution.



**Figure 5.15** shows the <u>median</u> cold ischaemia time in <u>DCD</u> donor pancreas transplants for each transplant centre over the last ten years. It can be more clearly seen that overall the <u>median</u> cold ischaemia time has decreased from 2011/12 to 2020/21 with some minor fluctuations over the time period.



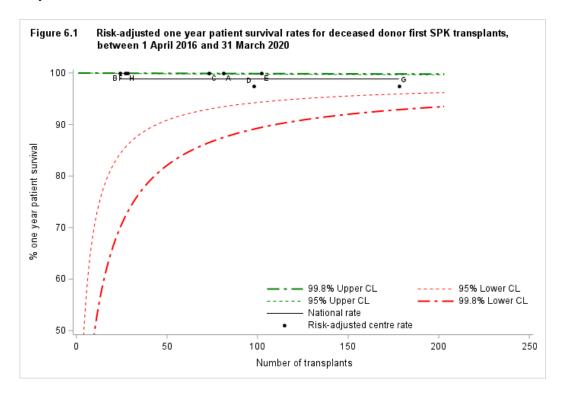
## **Pancreas outcomes**

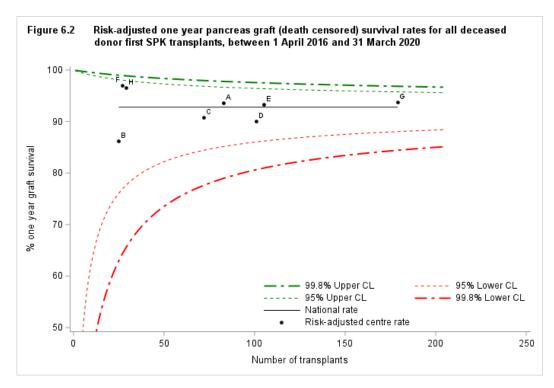
## 6.1 Deceased donor graft and patient survival for first SPK transplant

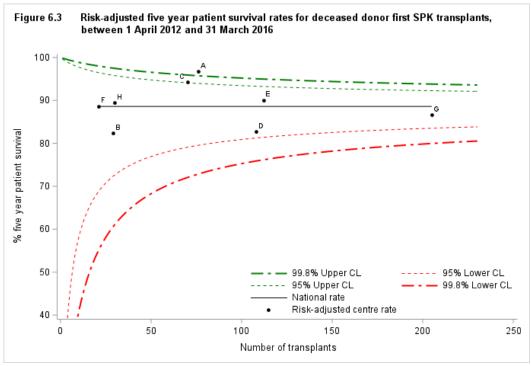
<u>Funnel plots</u> are used to compare centre specific <u>risk-adjusted patient</u> and <u>graft</u> survival rates and indicate how consistent these rates are with the national survival rates. Note that some patients return to local renal units for follow-up care after their transplant and although survival is reported 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.

The survival data used for these analyses is reported to NHSBT via follow-up forms. It should be noted that one centre has a large number of follow-up forms outstanding which will affect the validity of some of the survival rates, especially the 5-year survival rate. Follow-up form return rates by centre, for forms issued during the 2020 calendar year, are presented in Section 8.

**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. **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 95% <u>confidence limit</u>. This suggests that these centres may have survival rates that are considerably higher than the national rate. Centres can be identified by the information shown in **Tables 6.1** and **6.2** for patient and graft survival, respectively.







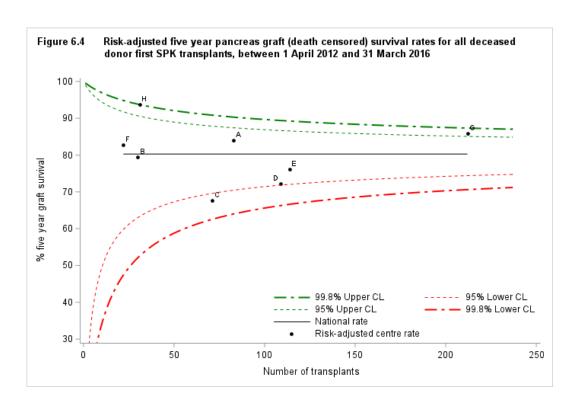


Table 6.1 Risk-adjusted one and five year patient survival for first SPK transplants using pancreases from deceased donors patient survival One-year\* Five-year\*\* (95% CI) Centre Code Ν % (95% CI) Ν % Cambridge Α Cardiff В 29 82 (55 - 95)Edinburgh С 70 94 (85 - 98)D 108 Guy's 98 97 (91 - 100 83 (71 - 91)Manchester Е 112 90 (82 - 95)F Newcastle 21 89 (59 - 99)Oxford G (80 - 91)178 98 (94 - 99)205 87 **WLRTC** Η 30 89 (69 - 98)UK 611 99 (97 - 99)651 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 April 2016 - 31 March 2020 \*\* Includes transplants performed between 1 April 2012 - 31 March 2016

Table 6.2 Risk-adjusted one and five year pancreas graft survival for first SPK transplants using pancreases from deceased donors										
			_	pancreas g	<u>raft</u> surviv		**			
Centre	Code	N	One-ye	ear* (95% CI)	N	Five-ye %	ar** (95% CI)			
Cambridge Cardiff Edinburgh	A B C	83 25 72	94 86 91	(85 - 98) (60 - 97) (80 - 97)	83 30 71	84 79 68	(73 - 91) (58 - 92) (48 - 81)			
Guy's Manchester Newcastle Oxford	D E F G	101 105 27 179	90 93 97 94	(82 - 95) (85 - 98) (83 - 100 (89 - 97)	109 114 22 212	72 76 83 86	(60 - 81) (64 - 85) (49 - 96) (80 - 91)			
WLRTC	Н	29	97	(81 - 100	31	94	(78 - 99)			
UK		621	93	(90 - 95)	672	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										
* Includes transplants performed between 1 April 2016 - 31 March 2020 ** Includes transplants performed between 1 April 2012 - 31 March 2016										

## 6.2 Deceased donor graft and patient survival for first PO transplants

Individual centre unadjusted 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 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 one and five year patient survival for first PO transplants using pancreases from deceased donors Patient survival One-year\* Five-year\*\* Centre Code % (95% CI) Ν % (95% CI) Ν Cambridge Α 0 0 Cardiff В 3 7 Edinburgh С 0 0 D Guy's 0 4 Manchester Е 2 3 Newcastle F 0 2 G 10 Oxford 100 32 83 (64 - 93)**WLRTC** Η 3 0 UK 18 100 48 84 (68 - 93)

<sup>-</sup> Data not presented where less than 10 transplants included

Table 6.4 Unadjusted one and five year pancreas graft survival for first PO transplants using pancreases from deceased donors											
	Pancreas graft survival										
			One-ye			Five-ye	ar**				
Centre	Code	Ν	%	(95% CI)	Ν	%	(95% CI)				
Cambridge	Α	0	_	-	3	_	-				
Cardiff	В	4	-	-	13	37	(13 - 62)				
Edinburgh	С	0	-	-	1	-	- ′				
Guy's	D	0	-	-	9	-	-				
Manchester	E	9	-	-	7	-	-				
Newcastle	F	3	-	-	5	-	-				
Oxford	G	15	92	(57 - 99)	40	60	(43 - 74)				
WLRTC	Н	4	-	-	6	-	-				
UK		35	88	(70 - 95)	81	56	(44 - 66)				

<sup>\*</sup> Includes transplants performed between 1 April 2016 - 31 March 2020

<sup>\*</sup> Includes transplants performed between 1 April 2016 - 31 March 2020

<sup>\*\*</sup> Includes transplants performed between 1 April 2012 - 31 March 2016

<sup>\*\*</sup> Includes transplants performed between 1 April 2012 - 31 March 2016

<sup>-</sup> Data not presented where less than 10 transplants included

## **Survival from listing**

## 7.1 Patient survival from listing for SPK transplant

Survival from listing was analysed for all adult (≥ 18 years) patients registered for the first time for SPK between 1 January 2009 and 31 December 2020. Patients registered for a pancreas only or islet transplant have been excluded from this analysis. Survival time was defined as the time from joining the <u>transplant list</u> to death, regardless of the length of time on the <u>transplant list</u>, whether or not the patient was transplanted and any factors associated with such a transplant e.g. donor type. Survival time was censored at either the date of removal from the list, or at the last known follow up date post-transplant when no death date was recorded, or at the time of analysis if the patient was still active on the <u>transplant list</u>.

The <u>funnel plot</u> shown in **Figure 7.1**, compares centre specific ten-year <u>risk-adjusted</u> <u>patient</u> survival rates from the point SPK transplant listing and indicates how consistent the rates of the individual transplant centres are with the national rate. All centres survival rates were very similar to the national rate of 77%. Centres can be identified by the information shown in **Table 7.1**, which also shows one and five-year <u>risk-adjusted</u> survival rates from the point of transplant listing. Note that all rates (at one, five and ten years) were calculated from the same cohort of patients, and the number of patients remaining at risk of death after each time horizon (i.e. not already censored or deceased) is included in **Table 7.1** for reference.

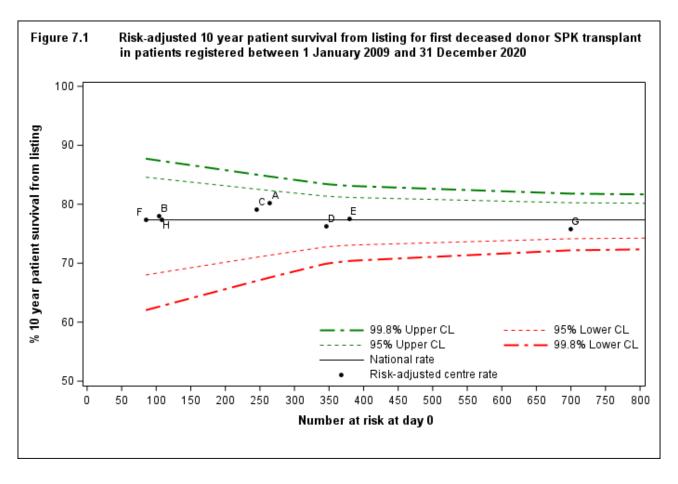
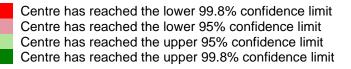


Table 7.1 Risk-adjusted 1, 5 and 10 year patient survival from listing for first deceased donor SPK transplant in patients registered between 1 January 2009 and 31 December 2020

			One year		Five yea	ar	Ten year	
		Number						
Centre	Code	at risk at	Survival rate	Number	Survival rate	Number	Survival rate	Number
		day 0	(%) (95% CI)	at risk1	(%) (95% CI)	at risk1	(%) (95% CI)	at risk1
Cambridge	Α	264	97 (95-98)	239	87 (82-91)	127	80 (72-86)	25
Cardiff	В	104	97 (95-98)	97	86 (84-89)	47	78 (72-83)	10
Edinburgh	С	245	97 (95-98)	229	87 (83-90)	110	79 (73-84)	20
Guy's	D	346	97 (95-98)	324	86 (84-88)	151	76 (71-81)	20
Manchester	Е	379	97 (95-98)	353	86 (84-89)	166	78 (73-81)	38
Newcastle	F	85	97 (95-98)	79	86 (84-89)	35	78 (71-82)	4
Oxford	G	699	96 (94-98)	634	86 (82-89)	289	76 (71-80)	53
WLRTC	Н	107	97 (95-98)	111	86 (84-89)	57	77 (71-82)	16
UK		2229	97 (96-97)	2066	86 (85-88)	982	77 (74-80)	186



<sup>&</sup>lt;sup>1</sup> Number of patients with reported follow-up beyond this time point

## Form return rates

## 8.1 Pancreas form return rates, 1 January – 31 December 2020

Form return rates are reported in **Table 8.1** for the pancreas transplant record, three month and one year follow up form, along with lifetime follow up (more than two years). These include all pancreas transplants performed between 1 January and 31 December 2020 for the transplant record, and all requests for follow up forms issued in this time period. Centres highlighted are transplant centres. Overall, 90% of transplant record forms issued and 78% of lifetime follow-up forms issued have been returned. Of the transplant centres, Oxford and WLRTC have the lowest lifetime follow-up form return rates, 41% and 5%, respectively. Data as on the database at 29<sup>th</sup> July 2021.

Table 8.1 Form return rates following pa 1 January - 31 December 2020		transplan	tation	, by centre	,			
1 January - 31 December 2020	Transplant record			month Ilow-up	12 month follow-up		Lifetime follow-up %	
Centre			10	%				
	N	returned	N	returned	N	returned	N	returned
Aberdeen, Aberdeen Royal Infirmary					1	100	21	100
Airdrie, Monklands District General Hospital					· ·		6	0
Bangor, Ysbyty Gwynedd District General Hospital					1	0	7	57
Basildon, Basildon Hospital							5	0
Belfast, Antrim Hospital							3	0
Belfast, Belfast City Hospital							6	100
Belfast, The Ulster Hospital							2	0
Birmingham, Birmingham Heartlands Hospital							13	23
Birmingham, Queen Elizabeth Hospital Birmingham	•		1	100	3	33	48	90
Bradford, St Luke's Hospital					1	0	9	78
Brighton, Royal Sussex County Hospital			1	100	2	100	27	100
Bristol, Southmead Hospital							36	100
Cambridge, Addenbrookes Hospital	22	95	24	96	16	100	124	95
Canterbury, Kent And Canterbury Hospital Cardiff, University Of Wales Hospital	7	86	12	100	11	100 100	39 69	100
Carlisle, Cumberland Infirmary	/	00	12	100	- 11	100	4	100
Carshalton, St Helier Hospital	•	•	•		<u>·</u> 1	100	16	56
Chelmsford, Broomfield Hospital					<u> </u>	100	1	0
Chester, Countess Of Chester Hospital							2	0
Closed - Glasgow, Glasgow Western Infirmary							5	20
County Down, Daisy Hill Hospital							7	86
Coventry, University Hospital (Walsgrave)			1	100	1	100	31	100
Derby, Royal Derby Hospital					2	100	12	100
Doncaster, Doncaster Royal Infirmary							6	100
Dorchester, Dorset County Hospital					2	100	34	97
Douglas, Nobles I-o-m Hospital							4	50
Dudley, Russells Hall Hospital							4	25
Dulwich, Kings College							2	50
Dumfries, Dumfries And Galloway Royal Infirmary	•		•	.	•		3	67
Dundee, Ninewells Hospital							23	96
Edinburgh, Royal Infirmary Of Edinburgh	13	100	17	94	18	100	46	93
Exeter, Royal Devon And Exeter Hospital (Wonford)					1	100	26	62
Glasgow, Queen Elizabeth University Hospital							24	8
Gloucester, Gloucestershire Royal Hospital			1	0			14	57
Hereford, The County Hospital							3	67

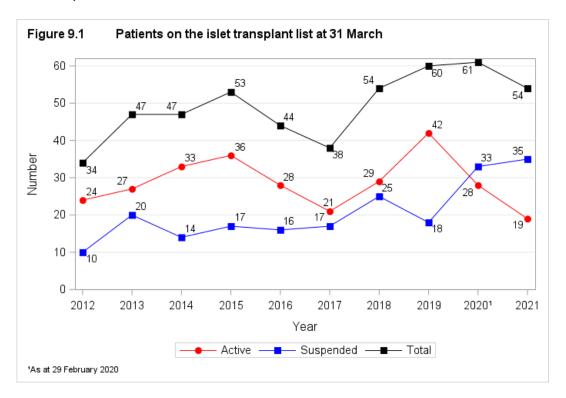
Table 8.1 Form return rates following pancreas transplantation, by centre, 1 January - 31 December 2020

Centre  Hull, The Hull Royal Infirmary Inverness, Raigmore Hospital	N	ecord % returned	N N	llow-up %	fOI	low-up %	foll	ow-up
Hull, The Hull Royal Infirmary	N		N	%		0/_		
	N	returned	N					%
	<u>.</u>		IN	returned	<u>N</u>	returned	N	returned
Inverness, Raigmore Hospital					2	50	17	76
							15	100
Ipswich, Ipswich Hospital							6	100
Kilmarnock, Crosshouse Hospital		-		-			9	56
Kirkcaldy, Victoria Hospital							2	50
Larbert, Forth Valley Royal Hospital							5	0
Leeds, St James's University Hospital					1	0	19	100
Leicester, Leicester General Hospital			1	100	2	0	24	67
Lincoln, Lincoln County Hospital						•	4	75
Liverpool, Royal Liverpool University Hospital							6	67
Liverpool, University Hospital Aintree							2	50
London, Guy's Hospital	12	67	7	100	21	81	143	62
London, St Georges Hospital							5	0
London, The Royal Free Hospital					4	75	47	98
London, The Royal London Hospital			3	33			13	77
(Whitechapel)								
Manchester, Manchester Royal Infirmary	10	100	8	88	18	67	98	69
Middlesbrough, The James Cook University							12	92
Hospital	-	•		-	-	-		0_
Newcastle, Freeman Hospital	2	50	1	100	8	100	56	98
Northampton, Northampton General Hospital				100		100	23	70
Norwich, Norfolk And Norwich University	•				<u>.</u> 1	100	29	100
Hospital	•	•	•	•	•	100	20	100
Nottingham, Nottingham University Hospitals					2	0	34	3
City Campus	•	•		•	_	o	0.	Ü
Omagh, Tyrone County Hospital							1	0
Oxford, Churchill Hospital	33	91	32	94	32	47	161	57
Peterborough, Peterborough City Hospital	00			J-1	02	71	5	0
Plymouth, Derriford Hospital	•	•	•	•	<u>.</u> 1	100	24	88
Portsmouth, Queen Alexandra Hospital		•	•	•	- '	100	58	100
Portsmouth, St Marys Hospital	•		1	0	•	•	1	100
Preston, Royal Preston Hospital	•			0	2	0	26	4
Reading, Royal Berkshire Hospital	•			-		U	29	59
Rhyl, Royal Alexandra Hospital	•		•		•	•	29	
	•				•		17	100
Salford, Salford Royal	•				•			24
Sheffield, Northern General Hospital					•		10	100
Shrewsbury, Royal Shrewsbury Hospital		-		-	<u>.</u>		5	40
St Helier, Jersey General Hospital					1	100	1	0
Stevenage, Lister Hospital							8	88
Stoke-on-Trent, Royal Stoke University Hospital							13	15
Swansea, Morriston Hospital					2	100	13	100
Truro, Royal Cornwall Hospital (Treliske)			1	0			23	0
West London Renal Transplant Centre	3	100	4	50	9	89	95	38
Westcliff On Sea, Southend Hospital					1	0	2	0
Wirral, Arrowe Park Hospital					•		4	0
Wolverhampton, New Cross Hospital			1	0			31	100
Wolverhampton, West Park Hospital							1	100
Wrexham, Maelor General Hospital							13	92
York, York District Hospital							14	93
Occasil	400	00	440	20	400	75	4040	7.0
Overall	102	90	118	89	169	75	1813	72

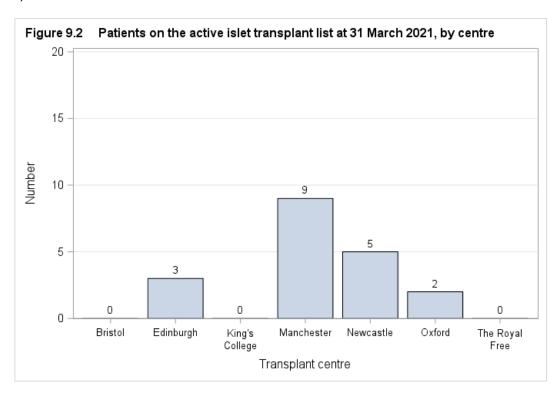
# Islet transplant list

## 9.1 Patients on the islet transplant list as at 31 March, 2012 – 2021

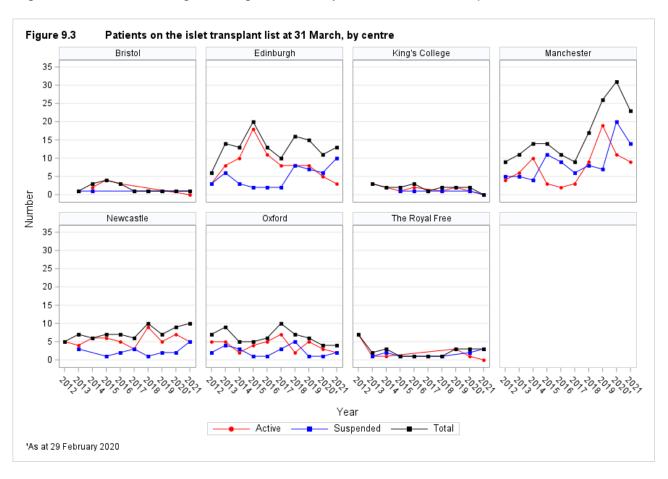
**Figure 9.1** shows the number of patients on the islet <u>transplant list</u> at 31 March each year. The number of patients active on the islet <u>transplant list</u> has decreased by 32% from 28 on 29 February 2020 to 19 on 31 March 2021. Of the 19, 58% (11) patients were registered for an SIK transplant.



**Figure 9.2** shows the number of patients on the active islet <u>transplant list</u> at 31 March 2021 by centre. Of the 19 patients on the active <u>transplant list</u> 47% were registered at Manchester, of which eight were SIK, 26% at Newcastle (one SIK) and 16% at Edinburgh (two SIK).

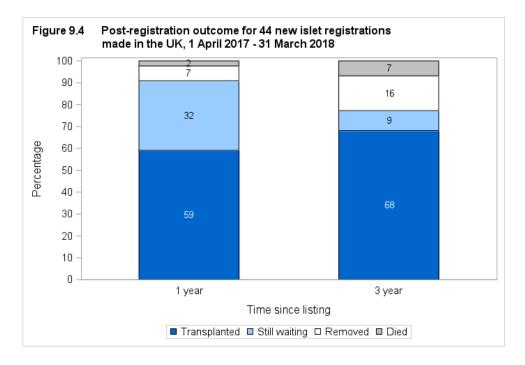


**Figure 9.3** shows the number of patients on the islet <u>transplant list</u> at 31 March each year between 2012 and 2021 for each transplant centre. There have been very few patients registered at Bristol, King's College or the Royal Free, in the time period.

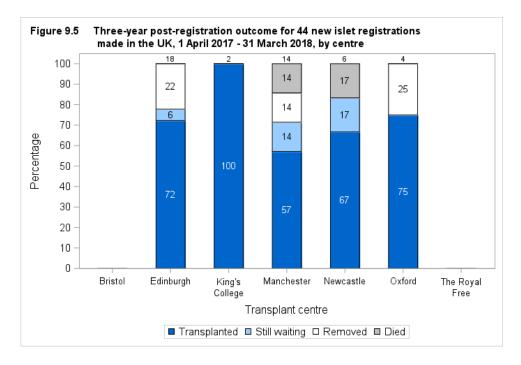


## 9.2 Post-registration outcomes, 1 April 2017 – 31 March 2018

An indication of outcomes for patients listed for an islet transplant is summarised in **Figure 9.4**. This shows the proportion of patients transplanted or still waiting one and three years after joining the list. It also shows the proportion removed from the <u>transplant list</u> (typically because they become too unwell for transplant) and those who died while on the <u>transplant list</u>. 59% of patients were transplanted within one year, while three years after listing 68% of patients had received a transplant and 16% were removed from the list.



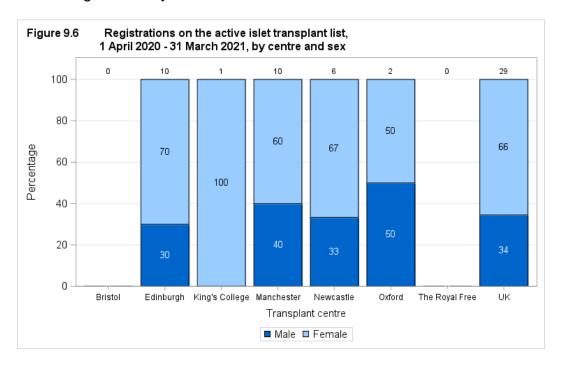
**Figure 9.5** shows the proportion of patients transplanted or still waiting three years after joining the list by centre. Three years after registration, 25%, 22% and 14% of patients were removed from the list at Oxford, Edinburgh and Manchester, respectively. Of those centres with patients registered in this time period, all transplanted 50% or more of their patients within three years. 17% and 14% of patients died whilst waiting for an islet transplant at Newcastle and Manchester, respectively.

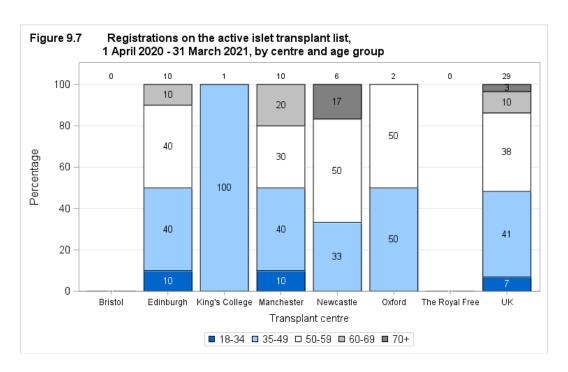


## 9.3 Demographic characteristics, 1 April 2020 – 31 March 2021

The sex and age group of patients registered on the islet <u>transplant list</u> during 2020/21 are shown by centre in **Figures 9.6** and **9.7**. Note that all percentages quoted are based only on data where relevant information was available.

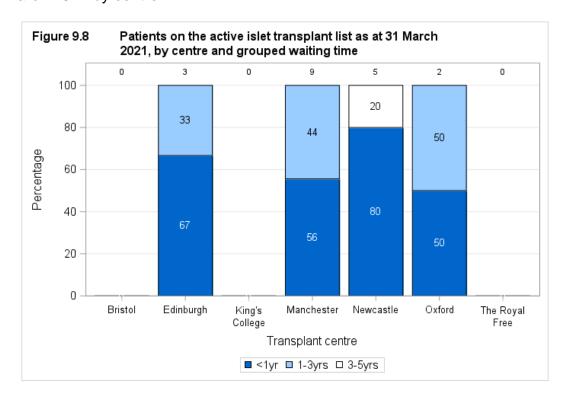
Overall, the majority of patients registered on the islet transplant list were female (66%) and the median age was 50 years.





## 9.4 Patient waiting times for those currently on the list, 31 March 2021

**Figure 9.8** shows the length of time patients have been waiting on the islet <u>transplant list</u> at 31 March 2021 by centre.



## 9.5 Median active waiting time to transplant, 1 April 2015 - 31 March 2019

The length of time a patient waits for any islet transplant varies across the UK. The <u>median</u> active waiting time for deceased donor islet transplantation is calculated using the <u>Kaplan-Meier method</u> and is shown in **Figure 9.9** and **Table 9.1** for patients registered at each individual unit.

The <u>median</u> active waiting time to transplant for patients registered on the islet <u>transplant</u> <u>list</u> between 1 April 2015 and 31 March 2019 is 564 days (around 18 months). The median active waiting time is not shown where less than 10 patients are registered.

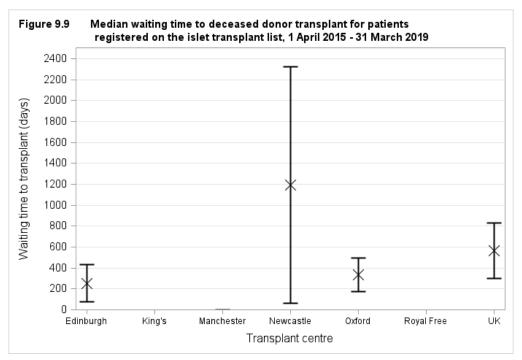


Table 9.1 Median active waiting time to islet transplant in the UK, for patients registered 1 April 2015 - 31 March 2019									
Transplant ce	ntre 1	Number of patients	Waiti	ng time (days)					
·		registered	Median	95% Confidence interval					
Bristol		2	-	-					
Edinburgh		39	253	74 - 432					
King's		5	-	-					
Manchester <sup>1</sup>		31	-	-					
Newcastle		13	1192	64 - 2320					
Oxford		15	336	173 - 499					
Royal Free		3	-	-					
UK		106	564	301 - 827					
<ul> <li><sup>1</sup> Insufficient data to calculate median waiting time to transplant.</li> <li>- Data not presented when less than 10 patients registered</li> </ul>									

# Response to islet offers

## 10.1 Offer decline rates, 1 April 2018 – 31 March 2021

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 by financial year, 1 April 2018 and 31 March 2021 are shown in **Table 10.1**. King's College had the lowest overall decline rate (0%) whilst Royal Free had the highest decline rate (100%). Bristol had no patients registered and received no offers in this time period. Note that all rates are based on a small number of offers.

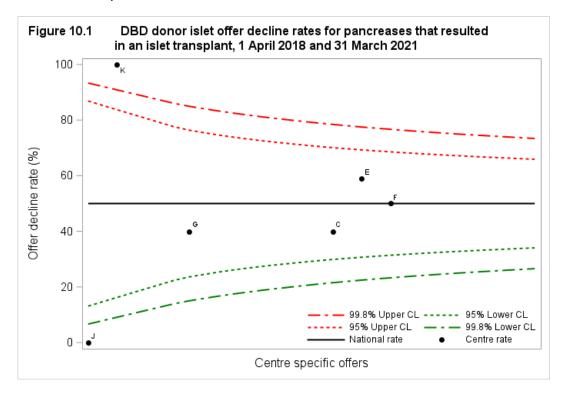
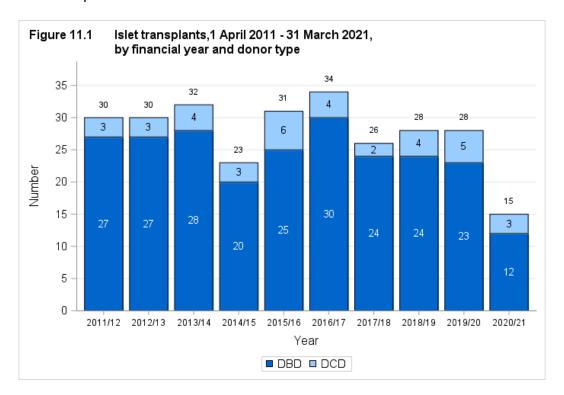


Table 10.1	DBD donor islet offer decline rates by transplant centre, 1 April 2018 and 31 March 2021										
Centre	Code	2018	8/19	2019	9/20	2020	0/21	Ove	erall		
		N	(%)	N	(%)	N	(%)	N	(%)		
Edinburgh	С	8	(50)	7	(29)	5	(40)	20	(40)		
King's	J	2	(0)	1	(0)	0	-	3	(0)		
Manchester	E	10	(70)	8	(38)	4	(75)	22	(59)		
Newcastle	F	10	(50)	8	(63)	6	(33)	24	(50)		
Oxford	G	4	(50)	4	(50)	2	(0)	10	(40)		
Royal Free	K	1	(100)	4	(100)	0	`-	5	(100)		
UK		35	(54)	32	(50)	17	(41)	84	(50)		
Centre has reached the upper 99.8% confidence limit Centre has reached the upper 95% confidence limit Centre has reached the lower 95% confidence limit Centre has reached the lower 99.8% confidence limit											

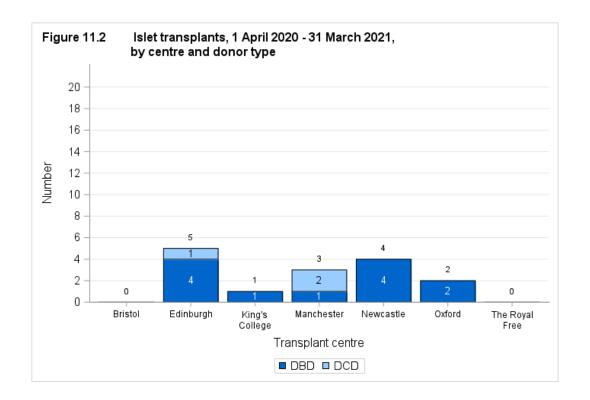
# **Islet transplants**

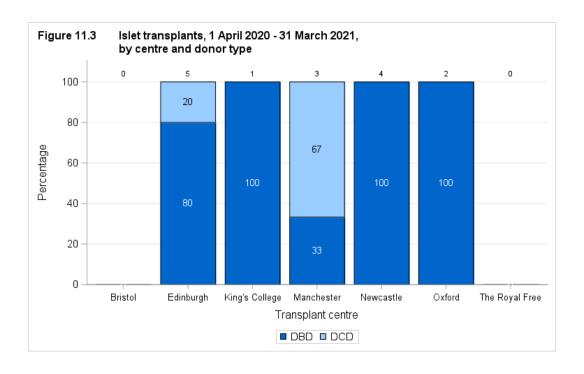
## 11.1 Islet transplants, 1 April 2011 – 31 March 2021

**Figure 11.1** shows the total number of islet transplants performed in the last ten financial years, by type of donor. Since 2011/12, the number of islet transplants has fluctuated around 30 each year. Only 15 were performed in the last financial year due to the impact of the COVID-19 pandemic.

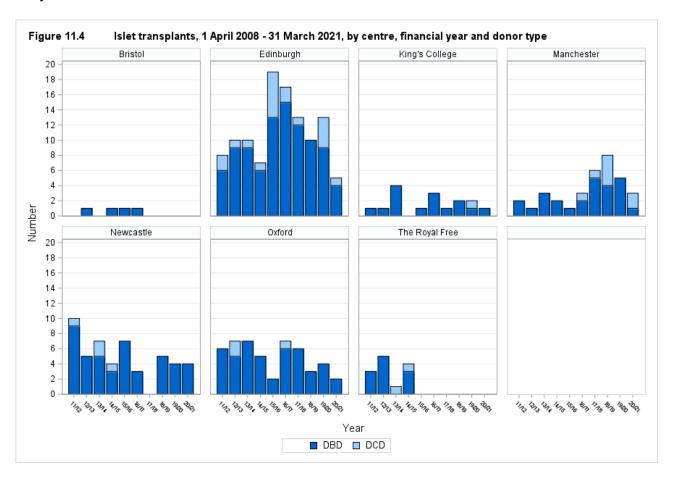


**Figure 11.2** shows the total number of islet transplants performed in 2020/21, by centre and type of donor. The same information is presented in **Figure 11.3** but this shows the proportion of <u>DBD</u> and <u>DCD</u> transplants performed at each centre. Edinburgh performed the most islet transplants in 2020/21 (five), followed by Newcastle (four). Edinburgh and Manchester were the only centres to perform <u>DCD</u> as well as <u>DBD</u> transplants. Royal Free and Bristol did not perform any islet transplants in 2020/21.



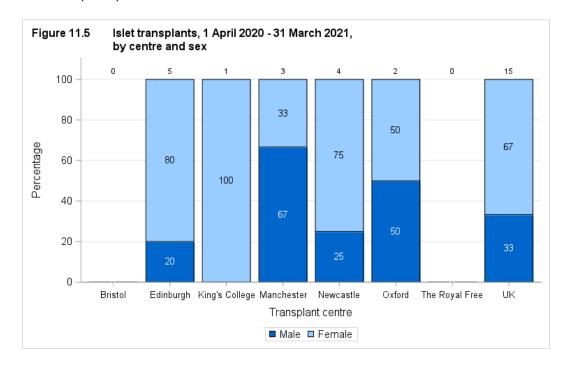


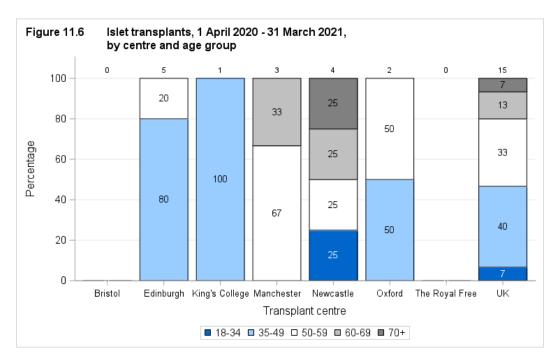
**Figure 11.4** shows the total number of islet transplants performed in last ten years, by centre and type of donor. Oxford and Manchester have consistently performed a number of islet transplants each year, with Manchester increasing their transplant activity in the last two years. Edinburgh have consistency performed the most transplants each year in the last eight years. Bristol has performed very few transplants over the ten year period and none in the last four years. Royal Free have performed no islet transplant in the last six years.



## 11.2 Demographic characteristics, 1 April 2020 - 31 March 2021

The sex and age group of patients that received an islet transplant in 2020/21 are shown by centre in **Figures 11.5** and **11.6** respectively. Note that all percentages quoted are based only on data where relevant information was available. Overall, 15 patients were transplanted on the islet transplant list, the <u>median</u> age was 53 years and the majority were female 10 (67%).





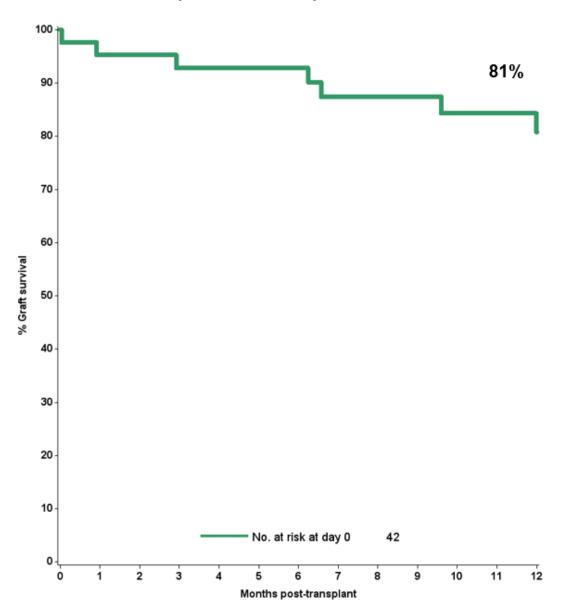
## **Islet outcomes**

## 12.1 Outcome measures for routine islet transplants

Key measures of islet outcome include <u>graft survival</u>, annual rate of severe <u>hypoglycaemic</u> events, <u>HbA1c</u> and insulin requirements. This section includes outcomes reported to NHS Blood and Transplant for islet transplants between 1 April 2011 and 31 March 2020.

A one-year <u>Kaplan-Meier graft survival</u> plot for islet transplants between 1 April 2016 – 31 March 2020 is shown in **Figure 12.1**. Estimated one-year <u>graft survival</u> following a routine islet transplant is 81% with 95% confidence interval (CI) (64-91%). This includes patients who received only a routine graft and those patients who additionally received a priority graft.

Figure 12.1 One-year graft survival following first routine islet transplant between 1 April 2016 and 31 March 2020



A five-year <u>Kaplan-Meier graft survival</u> plot for islet transplants between 1 April 2011 – 31 March 2020 is shown in **Figure 12.2**. Estimated five-year <u>graft survival</u> following a routine islet transplant is 55% with 95% CI (44-64%). This includes patients who received only a routine graft and those who additionally received a priority graft.

Figure 12.2 Five-year graft survival following first routine islet transplant between 1 April 2011 and 31 March 2020

Further, five-year Kaplan-Meier graft survival plots by type of graft are shown in **Figure 12.3** and **12.4**, for islet transplants between 1 April 2011 – 31 March 2021. **Figure 12.4** only includes routine grafts (routine only or routine followed by a priority) that still were functioning at one year post-transplant. In order to receive a priority (top-up) graft the patient's routine graft must still be functioning and the priority graft should be given within the first 12 months post routine transplant. Therefore, to accurately compare the two groups, i.e. those receiving a routine graft alone and those receiving a routine and subsequent priority graft, the survival estimate is conditional on one-year graft survival in both groups.

2

No. at risk at day 0

Years post-transplant

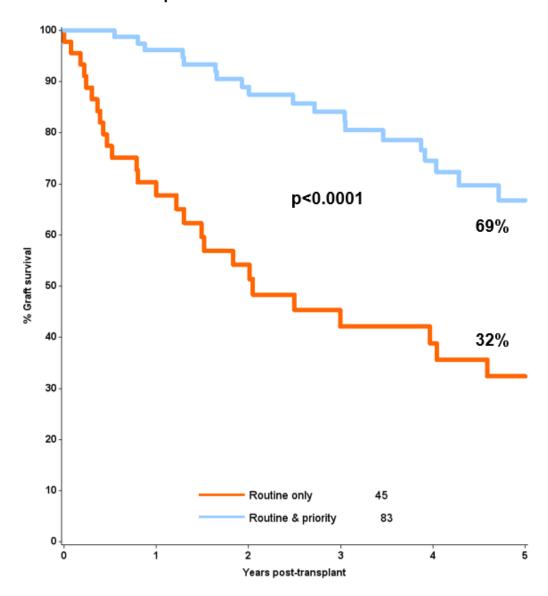
128

4

10

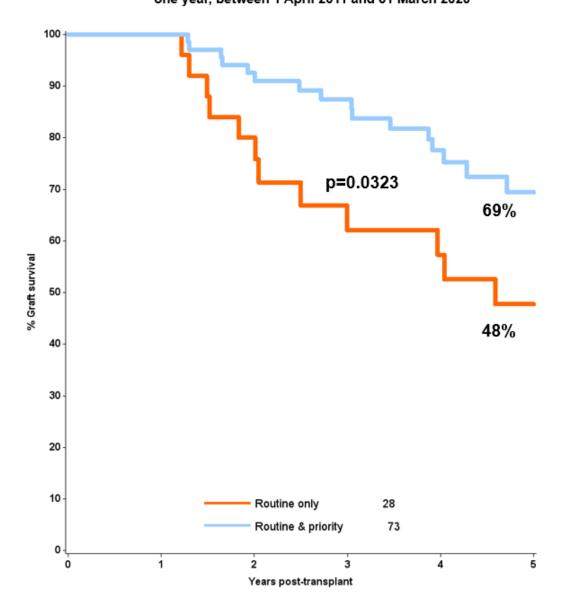
Estimated five-year graft survival (for all islet transplants) is 32% for routine only grafts, 95% CI (18-48%) and for routine followed by priority grafts is 69%, 95% CI (52-78%). This difference was statistically significant, p<0.0001.

Figure 12.3 Five-year graft survival following routine islet transplantation, by type of graft, between 1 April 2011 and 31 March 2020



Estimated five-year graft survival (for islet transplant, where the routine graft was functioning at one year) is 48% for routine only grafts, 95% CI (26-66%) and for routine followed by priority grafts is 69%, 95% CI (54-81%). This difference was statistically significant, p=0.0323.

Figure 12.4 Five-year graft survival following routine islet transplantation, where the routine graft was functioning at one year, between 1 April 2011 and 31 March 2020



**Figure 12.5** shows, for routine islet only transplants between 1 April 2016 – 31 March 2020, the <u>median</u> annual rate of severe <u>hypoglycaemic</u> events, at registration, prior to transplant (reported as number of events between registration and transplant) and at one-year post-transplant. Of the 22 patients where the number of severe hypoglycaemic events at one-year post-transplant was available, 21 (95%) experienced no severe <u>hypoglycaemic</u> events, one (5%) experienced one event.

N 45 49 22

50

40

30

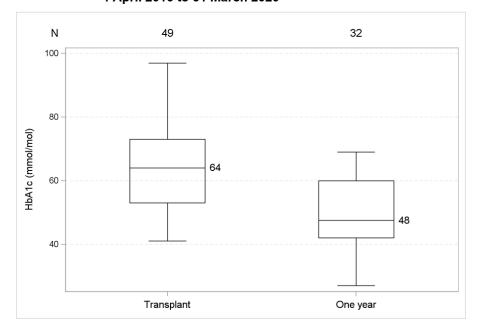
20

Registration Transplant One year

Figure 12.5 Median annual rate of severe hypoglycaemic events for routine islet only transplants, 1 April 2016 to 31 March 2020

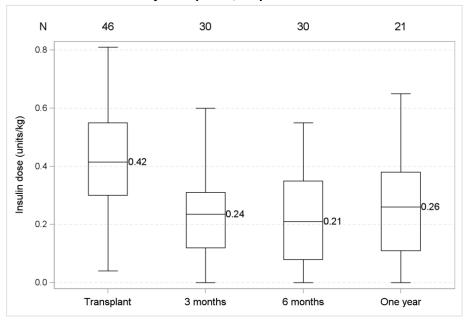
**Figure 12.6** shows the reduction in <u>median HbA1c</u> (mmol/mol) for routine islet only transplants between 1 April 2016 – 31 March 2020. <u>Median HbA1c</u> dropped from 64mmol/mol prior to transplant to 48mmol/mol at one-year post-transplant. Of those 32 patients with HbA1c reported at one-year, 21 (66%) had an <u>HbA1c</u> less than 53mmol/mol.

Figure 12.6 Median HbA1c (mmol/mol) for routine islet only transplants, 1 April 2016 to 31 March 2020



**Figure 12.7** shows the <u>median</u> reduction in insulin dose per kilo recipient body weight at three-months, six-months and one-year post-transplant, for routine islet only transplants between 1 April 2016 – 31 March 2020. Prior to transplant the <u>median</u> insulin dose is 0.42 units/kg, by six-months the <u>median</u> dose has dropped to 0.21 units/kg and then increased slightly at one-year post-transplant with a <u>median</u> dose of 0.26 units/kg. Following islet transplantation, of the 29 patients where information was reported, 15 (52%) achieved insulin independence at some point during their first year post-transplant.

Figure 12.7 Median insulin dose per kilo of recipient weight for routine islet only transplants, 1 April 2016 to 31 March 2020



Form return rates

## 13.1 Islet form return rates, 1 January – 31 December 2020

Form return rates are reported in **Table 13.1** for the islet transplant record, three month and one year follow-up form, along with lifetime follow-up (more than two years). These include all islet transplants performed between 1 January and 31 December 2020 for the transplant record, and all requests for follow-up forms issued in this time period. Centres highlighted are transplant centres. There were 64% of transplant record and 44% of lifetime follow-up forms returned. Only 38% of 3-month and 29% of 12-month follow-up forms were returned. Oxford have the lowest lifetime follow-up return rate of 5%.

Table 13.1 Form return rates following islet transplantation, by centre, 1 January - 31 December 2020										
Contro	Transplant record		3 mo	onth follow- up	_	2 month ollow-up	Lifetime follow- up			
Centre	%		%		%			%		
	N	returned	N	returned	N	returned	N	returned		
Bristol, Southmead Hospital							2	50		
Edinburgh, Royal Infirmary of Edinburgh	5	80	4	25	8	25	32	31		
Glasgow, Queen Elizabeth University Hospital							1	0		
London, Kings College Hospital	1	0	1	0	2	0	4	75		
London, The Royal Free Hospital					•		5	100		
Manchester, Manchester Royal Infirmary	2	50	1	100	3	100	10	100		
Newcastle, Freeman Hospital	4	100	2	100	2	50	13	100		
Oxford, Churchill Hospital	2	0			2	50	20	5		
Overall	14	64	8	50	17	41	87	49		

# **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

Hypoclycaemia 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.

#### Matchability points score

Matchability points score is a score between 1 and 10 reflecting the difficulty with which a well-matched HLA compatible organ can be found and takes into account sensitisation and rareness of HLA type. Scores are updated annually such that 10% of waiting list patients who are easiest to match have score=1 and 10% who are most difficult to match have a score=10.

#### 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 (100%) sensitisation or matchability points score=10) 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 all 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 Offering Scheme</u>.

#### 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 Methods

#### 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.

A fundamentally similar method was used to conduct the survival from listing analysis. The risk factors used are detailed in the table below.

#### First registrations for simultaneous pancreas and kidney (SPK) transplant

1, 5 and 10 year <u>patient</u> Age, gender, grouped registration year, ethnicity, blood group, <u>cRF</u>>85% survival from listing

#### **Systematic Component of Variation**

For a given individual who is a resident in a given NHS region registration to the transplant list is modelled as a Bernoulli trial. At the whole area level, this becomes a Binomial process which can be approximated by a Poisson distribution when rare events are modelled. Transplant counts follow similar assumptions.

To allow for the possibility that, even after allowing for area-specific Poisson rates, area differences remain, introduce an additional multiplicative rate factor which varies from area to area. Postulate a non-parametric distribution for the multiplicative factor, with variance  $\sigma^2$ . If the factor is one for all areas, then area differences are fully explained by the area-specific Poisson rate. If the factor varies with a nonzero variance,  $\sigma^2$ , then we conclude that there are unexplained area differences.

The systematic component of variation (SCV; McPherson et al., N Engl J Med 1982, 307: 1310-4) is the moment estimator of  $\sigma^2$ . Under the null hypothesis of homogeneity across areas, the SCV would be zero. The SCV, therefore, allows us to detect variability across areas beyond that expected by chance; the larger the SCV, the greater the evidence of systematic variation across areas.

A one-sided p-value for the hypothesis that the SCV is greater than zero versus the null hypothesis that the SCV is equal to zero was derived using a parametric bootstrap where data were simulated from the Poisson distribution that would be consistent with the null hypothesis (multiplicative rate factor is equal to one in all areas and  $\sigma^2$  equal to zero). The observed SCV was then compared against this simulated data to calculate the probability that an SCV of at least this size would be observed due to chance if the null hypothesis were true.

10,000 bootstrap samples of size 7 (number of areas) were simulated, where the registration/transplant count in each area was drawn from a Poisson distribution with its expected value being the area-specific expected count (the rate of transplants/registrations in the total population multiplied by the population of the area). The SCV was then calculated in each of the 10,000 samples and a bootstrap p-value for the SCV in the observed data was estimated as:

$$P_{boot} = \frac{1 + \#\{SCV_{sim} \geq SCV_{obs}\}}{10000 + 1}$$

where  $\#\{SCV_{sim} \geq SCV_{obs}\}\$  is the number of SCV values in the simulated datasets which are greater than or equal to the SCV in the observed data. This follows the simulation method given in Ibanez et al., BMC Health Services Research, 2009, 9:60. No adjustment was made for area-specific demographic characteristics that may impact the rates of registration to the transplant list and transplantation such as age and sex.

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