

# ANNUAL REPORT ON PANCREAS AND ISLET TRANSPLANTATION

REPORT FOR 2017/2018 (1 APRIL 2008 – 31 MARCH 2018)

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PRODUCED IN COLLABORATION WITH NHS ENGLAND

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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 2008. 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 2018, there were 218 patients on the UK active pancreas and islet transplant list, which represents a 3% decrease in number of patients a year earlier. The number of patients on the active pancreas list decreased by 7% to 189 in 2018 while the active islet transplant list increased by 38% to 29 patients in the same time period.
- There were 1966 pancreas transplants performed in the UK in the ten year period and 243 islet transplants performed in the same time period. The number of transplants from donations after brain death has decreased by 4% in the last year to 157. However, the number of transplants from donations after circulatory death has increased by 8% in the last year to 54.
- The national rates of <u>patient</u> survival one- and five-years after first simultaneous pancreas and kidney transplant from deceased donors are 98% and 88%, respectively. These rates vary between centres, ranging from 94% to 100% at oneyear and 73% to 92% 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 89% and 79%, respectively. These rates vary between centres, ranging from 81% to 97% at oneyear and 54% 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 pancreas only transplant from deceased donors are 97% and 78%, respectively. The national rates of <u>graft</u> survival one- and five-years are 88% and 52%. 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 76%. These rates vary between centres, ranging from 72% to 81%. All centre rates are <u>risk-adjusted</u>.
- The national rate of one year <u>graft</u> survival for patients receiving a routine islet transplant is 84%. For patients with a functioning graft at one-year post-transplant, the national rate of five year <u>graft</u> survival was 60% for those patients receiving an additional priority islet graft and 44% for patients who did not.
- Reductions in annual rate of severe <u>hypoglycaemic</u> events and <u>HbA1c</u> 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 2017/18, NHS Blood and Transplant.

### Introduction

This report presents information on pancreas and islet transplant activity between 1 April 2008 and 31 March 2018, 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 2013 to 31 March 2017 and five-year post-transplant for the period 1 April 2009 to 31 March 2013.

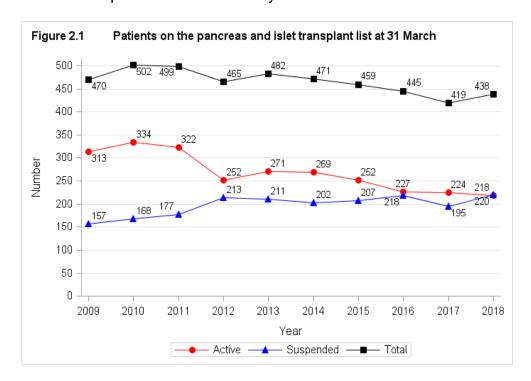
Islet transplant survival is measured by four key variables: graft survival, and a reduction in <a href="HbA1c">HbA1c</a>, insulin requirements and the annual rate of severe <a href="hypoglycaemic">hypoglycaemic</a> events. Islet outcomes are reported at one-year post-transplant for the period 1 April 2013 to 31 March 2017, and <a href="graft">graft</a> survival at five-year post-transplant for the period 1 April 2008 to 31 March 2013, for the national cohort only. Islet outcomes are <a href="mailto:unadjusted">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 (SPK) transplants between 1 January 2006 and 31 December 2017.

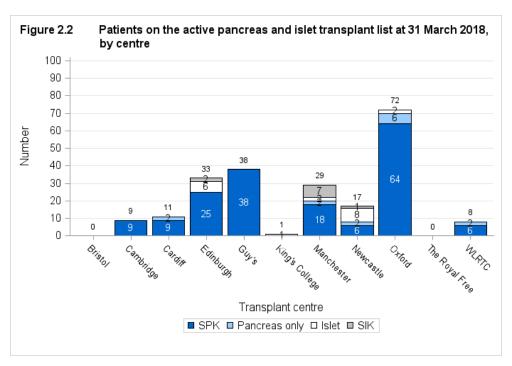
The centre specific results for survival estimates are adjusted for differences in <u>risk</u> <u>factors</u> between the centres. The risk models and methods used are described in the Appendix.

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.

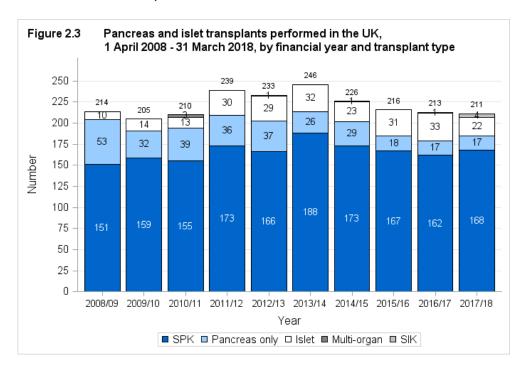
**Figure 2.1** shows the number of patients on the pancreas and islet <u>transplant list</u> at 31 March each year between 2009 and 2018. The number of patients actively waiting for a pancreas or islet transplant has decreased by 30% from 313 in 2009 to 218 in 2018.



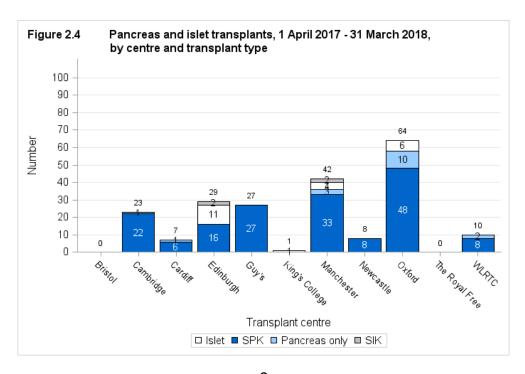
**Figure 2.2** shows the number of patients on the pancreas and islet <u>transplant list</u> at 31 March 2018 for each transplant centre. Oxford has the largest <u>transplant list</u> with 72 patients registered for a pancreas or islet transplant. Of these patients, 64 are registered for a SPK transplant, 6 are registered for a pancreas only transplant and 2 are registered for an islet transplant. Edinburgh, Manchester and Newcastle have patients waiting for an SIK transplant, ten in total. There were no patients on the active islet list at Bristol or the Royal Free at 31 March 2018.



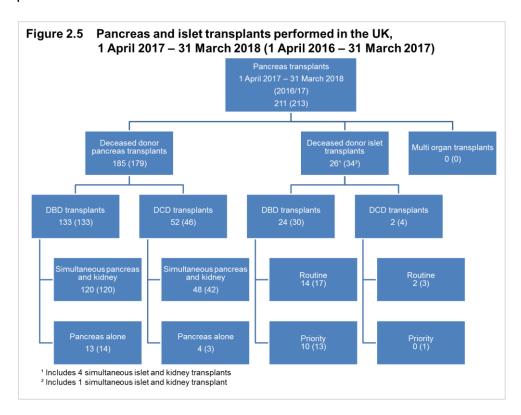
**Figure 2.3** shows the total number of pancreas and islet transplants performed in the last ten financial years. Transplant numbers steadily increased from 214 in 2008/09 to 246 in 2013/14. However, the number of transplants performed in 2014/15 decreased to 226 and further to 211 in 2017/18. In particular the number of pancreas only transplants has decreased from 53 transplants in 2008/09 to 17 in 2017/18.



**Figure 2.4** shows the total number of pancreas and islet transplants performed in 2017/18 at each transplant centre. Oxford performed the most pancreas and islet transplants last year, a total of 64 transplants, whilst Edinburgh performed the most islet and SIK transplants (13). A total of four SIK transplants were performed at Manchester and Edinburgh. The Royal Free and Bristol performed no transplants during this time period.



**Figure 2.5** details the 211 pancreas and islet transplants performed in the UK between 1 April 2017 and 31 March 2018. Data for transplants performed in 2016/17 are also presented. The overall number of whole pancreas transplants performed in 2017/18 has increased compared with 2016/17, 185 and 179 respectively. However, the number of islet transplants has decreased from 34 to 26.



#### Geographical variation in pancreas registration and transplant rates

All NHS group 1 patients who were registered onto the pancreas or islet transplant lists with an active status between 1 April 2017 and 31 March 2018 were extracted from the UK Transplant Registry on 6 June 2018 (numerator). Only patients registered for pancreas only, kidney and pancreas, islet only and islet and kidney were considered. Patients were assigned to Strategic Health Authorities (SHA) in England using their postcode of residence, as reported at registration. The number of registrations per million population (pmp) by SHA was obtained using mid-2016 population estimates based on the Office for National Statistics (ONS) 2011 Census figures (denominator). No SHA age- or sex-specific standardisation of rates was performed.

The registration rates pmp were categorised into four groups – low, low-medium, medium-high and high – based on the quartiles of their distribution and visualised in a map using contrasting colours.

Transplant rates pmp were obtained as the number of pancreas only, pancreas and kidney, islet only and islet and kidney transplants on NHS group 1 recipients from deceased donors between 1 April 2017 and 31 March 2018 (numerator), divided by the mid-2016 population estimates from the ONS (denominator). Transplant rates pmp were categorised and visualised in a map as done for the registration rates.

For <u>systematic component of variation</u> only registrations or transplants in England between 1 April 2017 and 31 March 2018 were included. If a patient was re-registered

during the time period, only the first registration was considered. If a patient underwent more than one pancreas/islet transplant in the time period, only the first transplant was considered.

**Figure 2.6** shows rates of registration to the pancreas transplant list per million population (pmp) between 1 April 2017 and 31 March 2018 compared with pancreas transplant rates pmp for the same time period, by recipient country/Strategic Health Authority (SHA) of residence. **Table 2.1** shows the breakdown of these numbers by recipient country/Strategic Health Authority 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 inevitably be some random variation in rates between areas, the <u>systematic component of variation</u> (SCV) was used to identify if the variation is more (or less) than a random effect for the different SHAs 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. Both registration and transplant rates yielded a low SCV at 0.1 and 0, respectively, and therefore, no evidence of geographical variation beyond what would be expected at random.

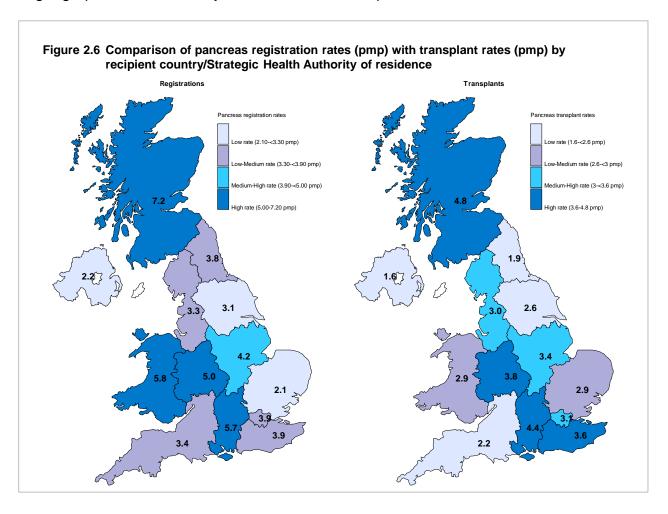


Table 2.1 Pancreas registration and transplant rates per million population (pmp) in the UK, 1 April 2017 - 31 March 2018, by Country/Strategic Health Authority

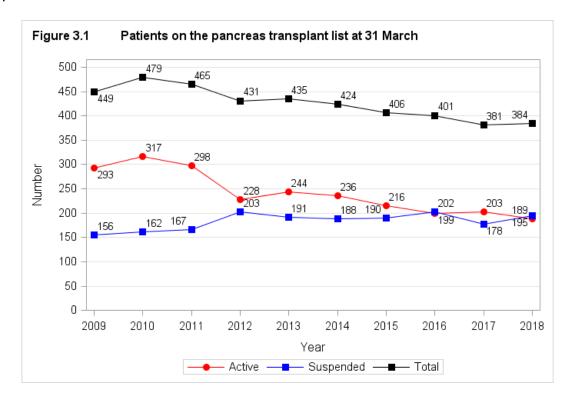
Country/ Strategic Health Authority	Registrations	Transplants (pmp)		
North East North West Yorkshire and The Humber North of England	10 24 17 <b>51</b>	(3.8) (3.3) (3.1) <b>(3.3)</b>	5 22 14 <b>41</b>	(1.9) (3) (2.6) <b>(2.7)</b>
East Midlands West Midlands East of England Midlands and East	20 29 13 <b>62</b>	(4.2) (5) (2.1) (3.7)	16 22 18 <b>56</b>	(3.4) (3.8) (2.9) <b>(3.4)</b>
London	34	(3.9)	27	(3.1)
South East Coast South Central South West South of England	18 25 19 <b>62</b>	(3.9) (5.7) (3.4) <b>(4.3)</b>	17 19 12 <b>48</b>	(3.6) (4.4) (2.2) <b>(3.3)</b>
England Isle of Man Channel Islands	209 0 0	(3.8)	172 0 0	(3.1)
Wales	18	(5.8)	9	(2.9)
Scotland	39	(7.2)	26	(4.8)
Northern Ireland	4	(2.2)	3	(1.6)
TOTAL	271¹	(4.1)	211 <sup>2</sup>	(3.2)

 $<sup>^{1}</sup>$  Includes 1 recipient whose postcode was unknown and excludes 1 recipient who reside in the Republic of Ireland  $^{2}$  Includes 1 recipient whose postcode was unknown

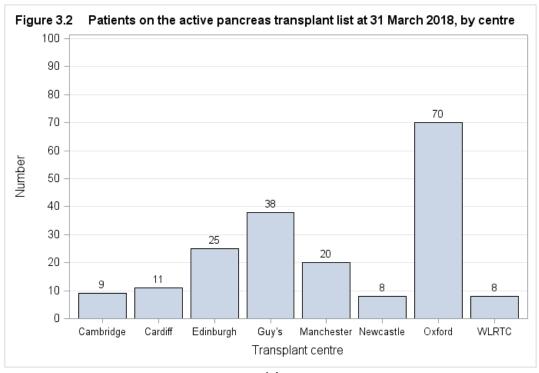
## Pancreas transplant list

#### 3.1 Patients on the pancreas transplant list as at 31 March, 2009 – 2018

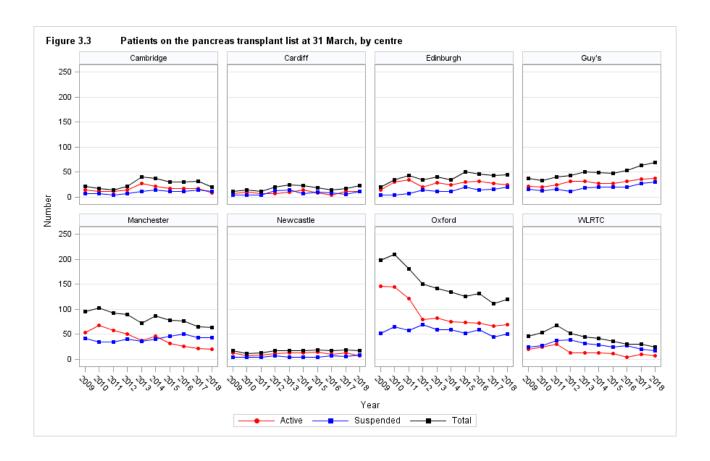
**Figure 3.1** shows the number of patients on the pancreas <u>transplant list</u> at 31 March each year between 2009 and 2018. The number of patients actively waiting for a pancreas transplant was the highest at 317 in 2010 and then fell considerably to 228 in 2012. Since then, numbers have slowly decreased and 189 patients were listed for a pancreas transplant at 31 March 2018.



**Figure 3.2** shows the number of patients on the active pancreas <u>transplant list</u> at 31 March 2018 by centre. Oxford had the largest proportion of the <u>transplant list</u> (37%) and WLRTC and Newcastle had the smallest proportion (4%).

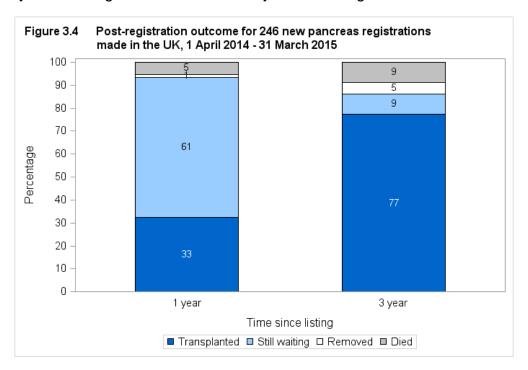


**Figure 3.3** shows the number of patients on the pancreas <u>transplant list</u> at 31 March each year between 2009 and 2018 for each transplant centre. The number of patients actively waiting for a pancreas transplant for most centres has been decreasing slightly of the ten year period, with the most noticeable decrease in Oxford.

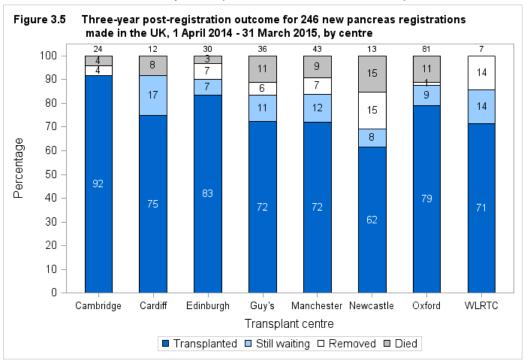


#### 3.2 Post-registration outcomes, 1 April 2014 – 31 March 2015

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 33% of patients registered between 1 April 2014 and 31 March 2015 were transplanted within one year, while three years after listing 77% of patients had received a transplant. There were 5% of patients who had died waiting for a transplant within one year of listing and 9% 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 92% of their patients while Newcastle only transplanted 62% with 15% of patients died on the list.

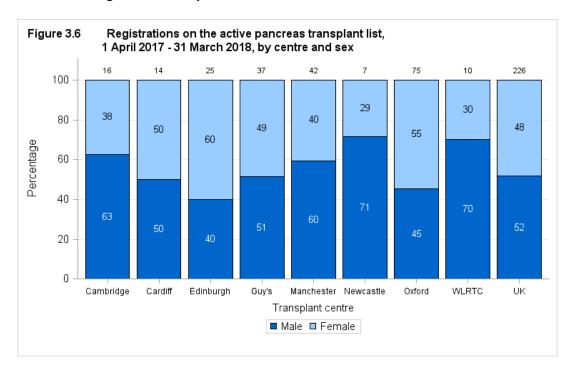


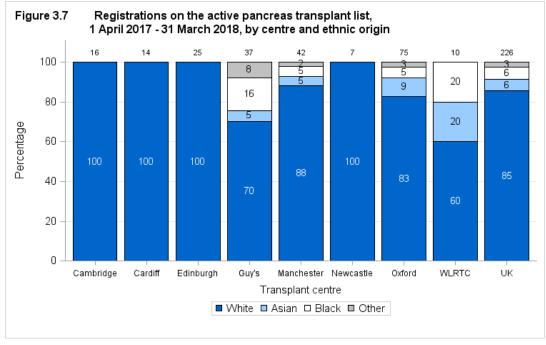
#### 3.3 Demographic characteristics, 1 April 2017 – 31 March 2018

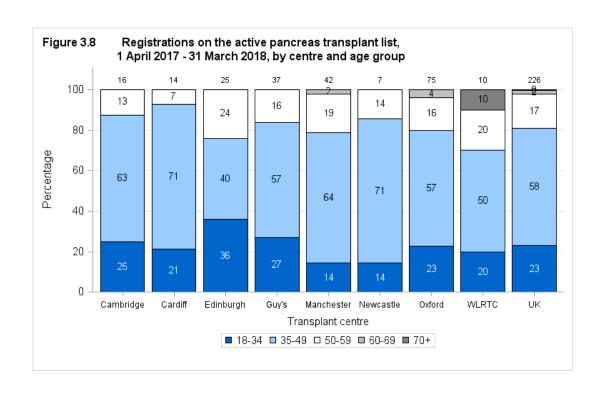
The sex, ethnicity, age group and <u>sensitisiation</u> group (<u>cRF</u>%) of patients registered on the pancreas <u>transplant list</u> in 2017/18 are shown by centre in **Figures 3.6, 3.7, 3.8**, and **3.9** respectively. Note that all percentages quoted are based only on data where relevant information was available.

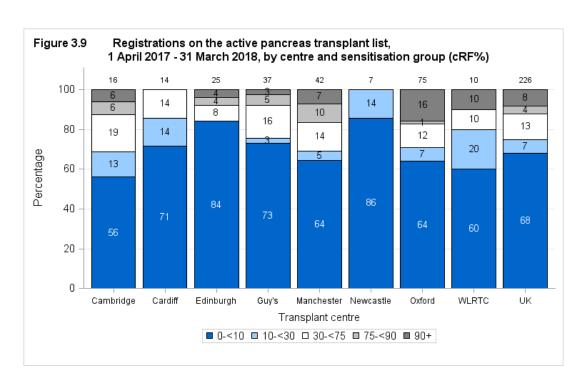
Overall, 226 patients were registered on the pancreas transplant list, 202 (89%) were waiting for a SPK transplant. Of which 51% were male, 84% were white, the median age was 41 years and the median cRF was 0%.

Of the 24 (11%) patients on the pancreas only transplant list, 54% were male, 100% were white, the median age was 46.5 years and the median cRF was 8%.



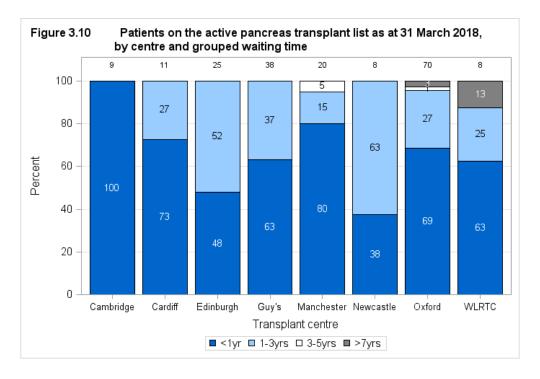






#### 3.4 Patient waiting times for those currently on the list, 31 March 2018

**Figure 3.10** shows the length of time patients have been waiting on the pancreas transplant list at 31 March 2018 by centre. The majority of patients currently listed have been waiting less than one year. However, two patients at Oxford and one patient at WLRTC have been waiting more than 7 years for transplant. The two patients at Oxford (one SPK patient and one pancreas alone patient) are highly sensitised with a <u>cRF</u> of 100% and the one patient at WLRTC is a pancreas alone patient with <u>cRF</u> of 99%.



#### 3.5 Median waiting time to transplant, 1 April 2012 - 31 March 2015

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 calculated using the <u>Kaplan-Meier method</u> and is shown in **Figure 3.11** 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 April 2012 and 31 March 2015 is 342 days, over 11 months. This ranged from 234 days at Cardiff to 521 days at Newcastle.

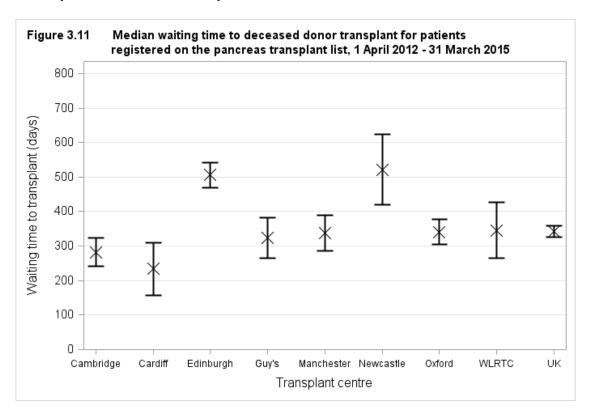


Table 3.1 Median waiting time to pancreas transplant in the UK, for patients registered 1 April 2012 - 31 March 2015										
Transplant centre	Number of patients	Wa	iting time (days)							
	registered	Median	95% Confidence interval							
Cambridge	81	282	241 - 323							
Cardiff	56	234	158 - 310							
Edinburgh	76	506	470 - 542							
Guy's	116	324	265 - 383							
Manchester	124	338	287 - 389							
Newcastle	32	521	419 - 623							
Oxford	241	341	305 - 377							
WLRTC	31	346	265 - 427							
UK	757	342	325 - 359							

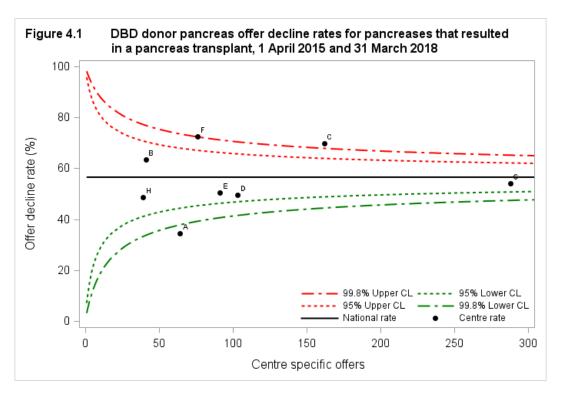
### **Response to pancreas offers**

#### 4.1 Offer decline rates, 1 April 2015 – 31 March 2018

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>.

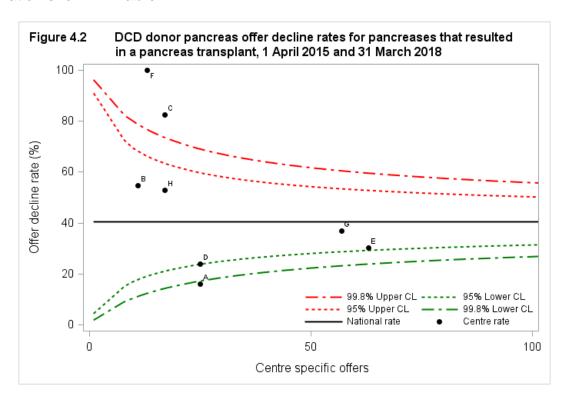
**Figure 4.1** compares individual centre offer <u>DBD</u> decline rates with the national rate over the time period, 1 April 2015 and 31 March 2018. Centres can be identified by the information shown in **Table 4.1**. Cambridge had an offer decline rate significantly better than the national rate, whilst Edinburgh and Newcastle had considerably higher decline rates than the national average.



**Table 4.1** compares individual centre <u>DBD</u> offer decline rates over time by financial year. The offer decline rates have decreased since the last financial year for half of the pancreas centres whilst the other half the decline rates have increased. Cardiff decline rate increased to 73% in 2017/18 from 0% in 2016/17 and WLRTC declined rate decreased to 43% in 2017/18 from 70% in 2016/17.

Table 4.1 DBD donor pancreas offer decline rates by transplant centre, 1 April 2015 and 31 March 2018									
Centre	Code	Code 2015/16		2016/17		2017/18		Overall	
		N	(%)	N	(%)	N	(%)	N	(%)
Cambridge	Α	21	(33)	20	(30)	23	(39)	64	(34)
Cardiff	В	22	(68)	4	(0)	15	(73)	41	(63)
Edinburgh	С	58	(72)	56	(64)	48	(73)	162	(70)
Guy's	D	33	(39)	31	(58)	39	(51)	103	(50)
Manchester	Е	43	(63)	29	(45)	19	(32)	91	(51)
Newcastle	F	24	(79)	29	(72)	23	(65)	76	(72)
Oxford	G	99	(57)	92	(50)	97	(56)	288	(54)
WLRTC	Н	15	(40)	10	(70)	14	(43)	39	(49)
UK		315	(59)	271	(54)	278	(56)	864	(56)
	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 2015 and 31 March 2018. 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. Similarly to <u>DBD</u> decline rates, Cambridge had offer decline rates better than the national rate, whilst Edinburgh and Newcastle had higher decline rates than the national average.

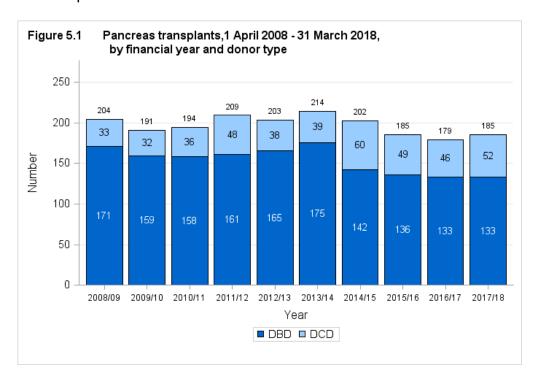
Table 4.2 DCD donor pancreas offer decline rates by transplant centre, 1 April 2015 and 31 March 2018									
Centre	Code	201	5/16	2016	6/17	2017	7/18	Ove	erall
		N	(%)	N	(%)	N	(%)	N	(%)
Cambridge	Α	11	(27)	7	(14)	7	(0)	25	(16)
Cardiff	В	3	(33)	3	(67)	5	(60)	11	(55)
Edinburgh	С	7	(100)	4	(100)	6	(50)	17	(82)
Guy's	D	9	(22)	9	(22)	7	(29)	25	(24)
Manchester	E	21	(43)	17	(35)	25	(16)	63	(30)
Newcastle	F	7	(100)	3	(100)	3	(100)	13	(100)
Oxford	G	19	(32)	22	(41)	16	(38)	57	(37)
WLRTC	Н	5	(40)	5	(40)	7	(71)	17	(53)
UK		82	(45)	70	(41)	76	(34)	228	(40)
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**

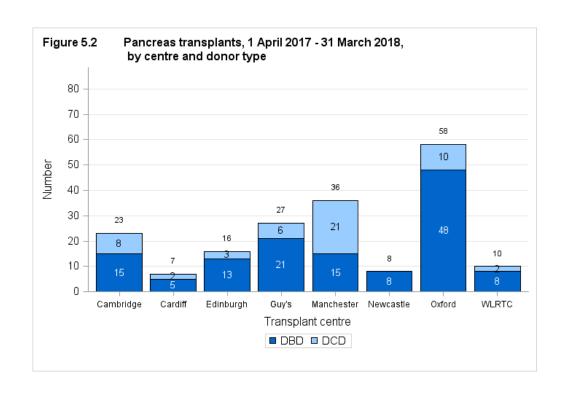
#### 5.1 Pancreas transplants, 1 April 2008 – 31 March 2018

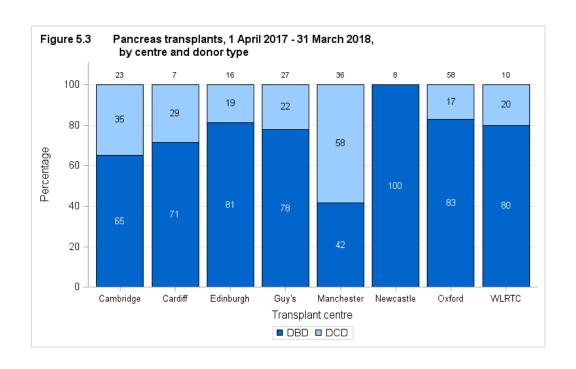
**Figure 5.1** shows the total number of pancreas transplants performed in the last ten financial years, by type of donor. The first <u>DCD</u> pancreas transplant was performed in 2005/06 and by 2008/09 there were 33 <u>DCD</u> transplants (16%). The number of <u>DCD</u> transplants performed reached a peak of 60 in 2014/15, but within the last two financial years, <u>DCD</u> pancreas transplants have dropped to 46 in 2016/17 and 52 in 2017/18 and accounts for around a quarter of pancreas transplants in both years.

After a fall in 2009/10 and 2010/11, <u>DBD</u> numbers steadily increased between 2011/12 and 2013/14. However, the number of <u>DBD</u> transplants has decreased in the last four years to 133 transplants in 2017/18.

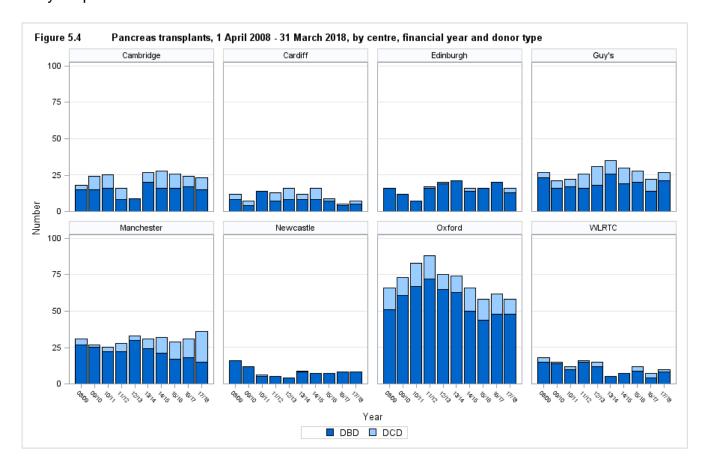


**Figure 5.2** shows the total number of pancreas transplants performed in 2017/18, by centre and type of donor. The same information is presented in **Figure 5.3** but this shows the proportion of <u>DBD</u> and <u>DCD</u> transplants performed at each centre. Oxford performed the most <u>DBD</u> and <u>DCD</u> transplants (58), however Manchester had the largest proportion of <u>DCD</u> transplants (58%). Cardiff had the lowest number of <u>DBD</u> and <u>DCD</u> transplants (7) and there were no <u>DCD</u> transplants performed at Newcastle in the last financial year.





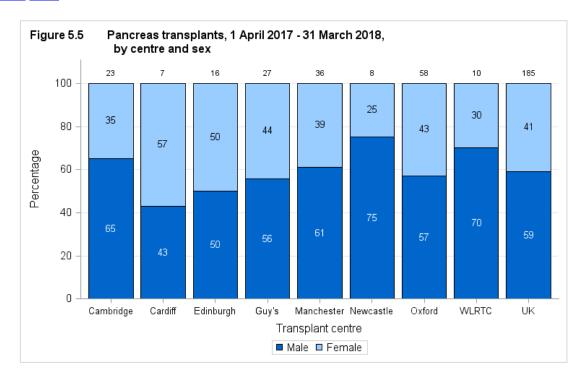
**Figure 5.4** shows the total number of pancreas transplants performed in last ten financial years, by centre and type of donor. Oxford have consistently performed a large number of pancreas transplants since 2008/09 including a number of <u>DCD</u> transplants over the last ten years. However, the number of transplants performed at Oxford has decreased since 2011/12. Edinburgh and Newcastle have not performed many <u>DCD</u> transplants over the ten year period.

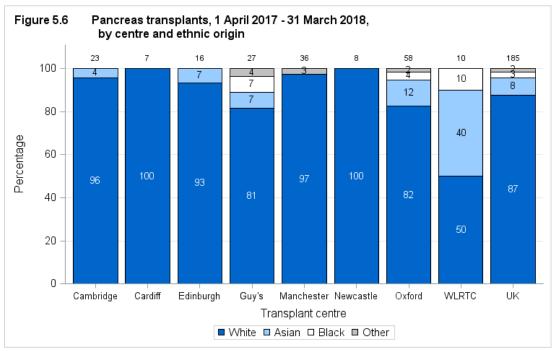


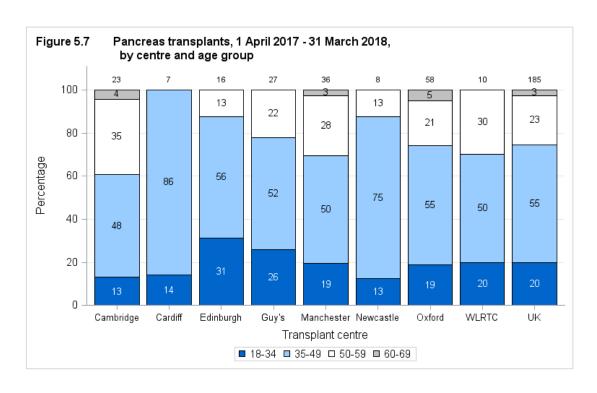
#### 5.2 Demographic characteristics, 1 April 2017 - 31 March 2018

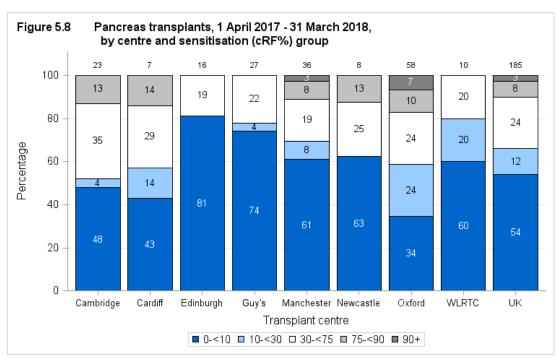
The sex, ethnicity, age group and <u>sensitisation</u> group (<u>cRF</u>%) of patients that received a pancreas transplant in 2017/18 are shown by centre in **Figures 5.5**, **5.6**, **5.7** and **5.8** respectively. Note that all percentages quoted are based only on data where relevant information was available.

Overall, 185 patients were transplanted on the pancreas transplant list, 168 (91%) were SPK transplants. Of which 61% were male, 86% were white, the <u>median</u> age was 42 years and the <u>median cRF</u> was 0%. Of the 17 (9%) patients transplanted as a pancreas only transplant, 41% were male, 100% were white, the <u>median</u> age was 47 years and the <u>median cRF</u> was 36%.





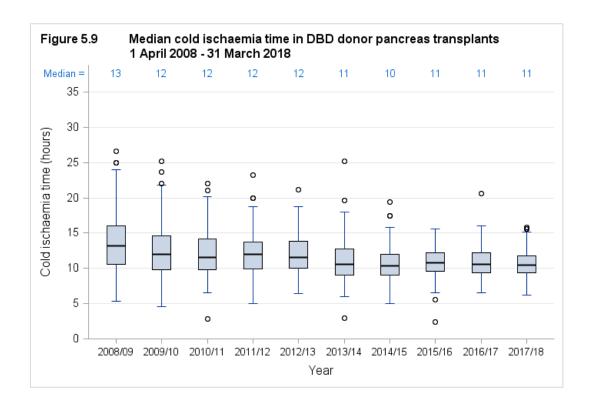




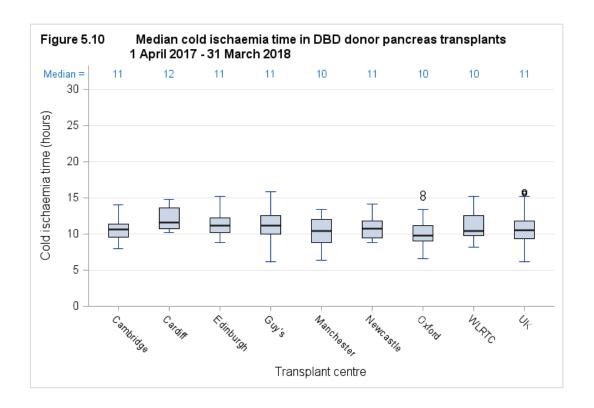
#### 5.3 Cold ischaemia time, 1 April 2008 – 31 March 2018

Median cold ischaemia times (CIT) are shown in addition to inter-quartile ranges in Figures 5.9 to 5.14. 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.

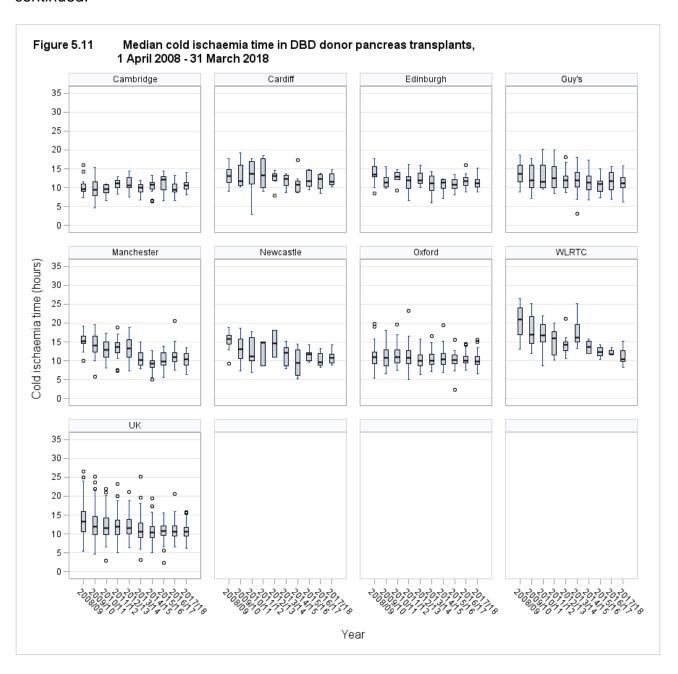
**Figure 5.9** shows the <u>median</u> cold ischaemia time in <u>DBD</u> donor pancreas transplants over the last ten years. During this time period the overall <u>median</u> cold ischaemia time has steadily decreased from 13 hours in 2008/09 to 11 hours in 2017/18.



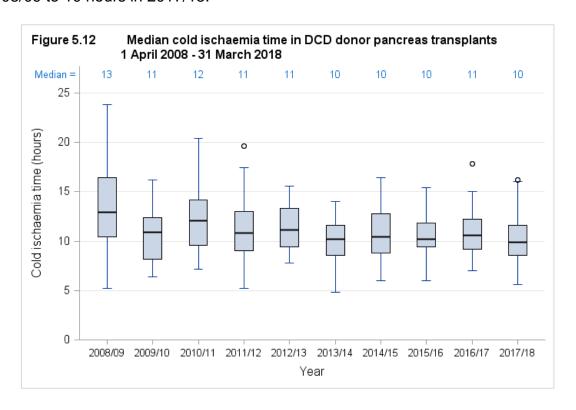
**Figure 5.10** shows the <u>median</u> cold ischaemia time in <u>DBD</u> donor pancreas transplants in 2017/18 for each transplant centre. Cardiff had the longest <u>median</u> cold ischaemia time of 12 hours and Manchester, Oxford and WLRTC had the shortest time of 10 hours.



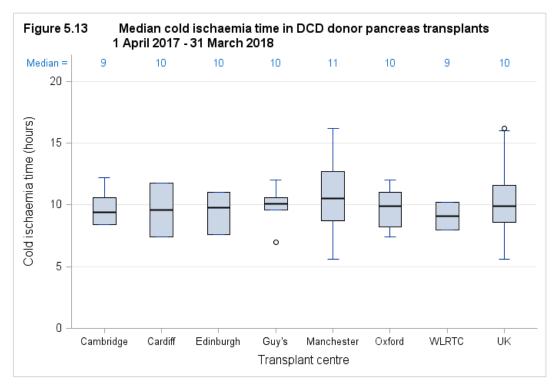
**Figure 5.11** shows the <u>median</u> cold ischaemia time in <u>DBD</u> donor pancreas transplants over the last ten years for each transplant centre. WLRTC <u>median</u> cold ischaemia times has notably decreased over the ten year period. Overall, the <u>median</u> cold ischaemia times have remained constant, however the <u>inter-quartile</u> ranges have reduced as time has continued.



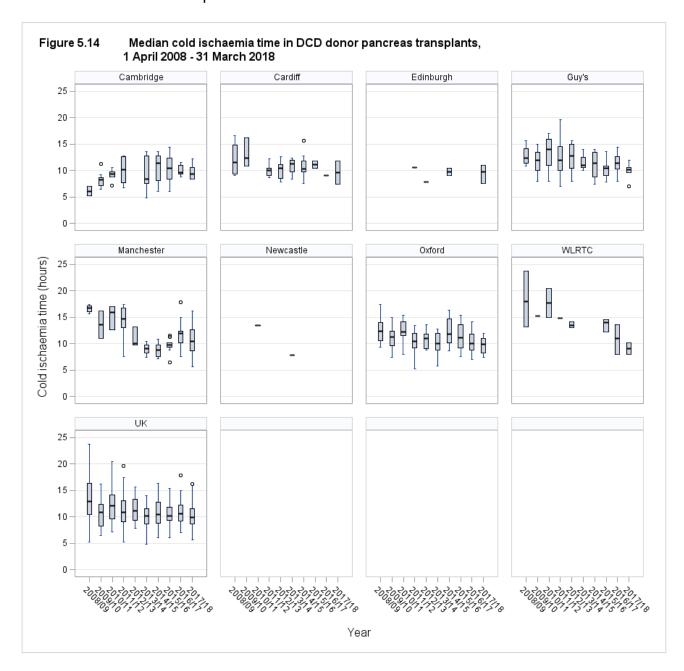
**Figure 5.12** shows the <u>median</u> cold ischaemia time in <u>DCD</u> donor pancreas transplants over the last ten years. Overall <u>median</u> cold ischaemia time has decreased from 13 hours in 2008/09 to 10 hours in 2017/18.



**Figure 5.13** shows the <u>median</u> cold ischaemia time in <u>DCD</u> donor pancreas transplants in 2017/18 for each transplant centre. Cambridge and WLRTC had the shortest <u>median</u> cold ischaemia time of 9 hours, whilst Manchester had the longest <u>median</u> cold ischaemia time of 11 hours. Newcastle is not presented as no <u>DCD</u> transplants were performed in 2017/18.



**Figure 5.14** 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 2008/09 to 2017/18 with some minor fluctuations over the time period.

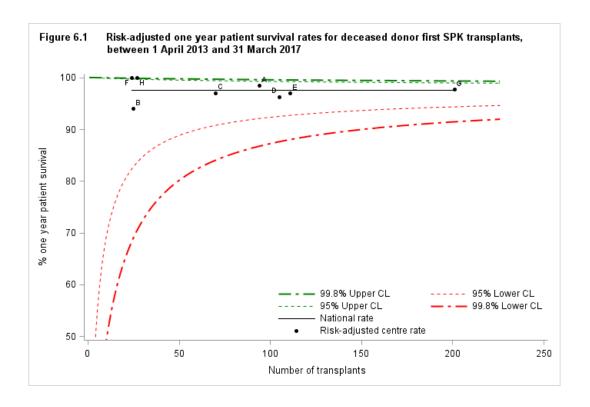


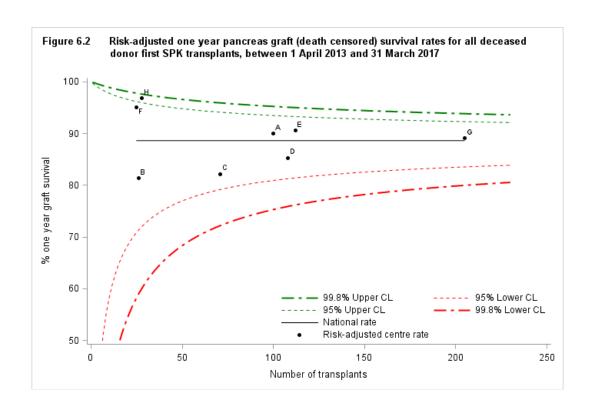
### **Pancreas outcomes**

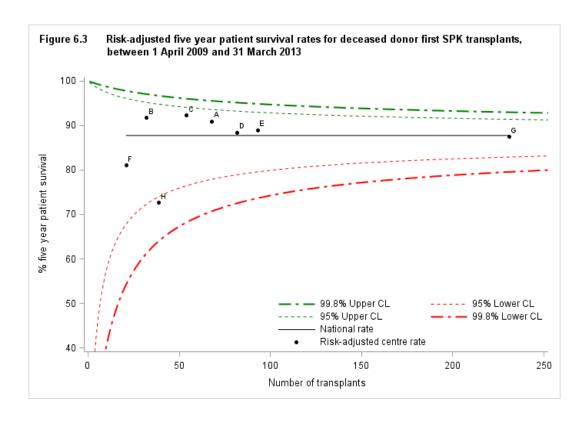
#### 6.1 Deceased donor graft and patient survival for first SPK transplant

<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.

**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. **Figure 6.3** shows one centre outside the lower 95% <u>confidence limit</u>, indicating that this centre may have a significantly lower five-year <u>patient</u> survival rate than the national rate. Similarly, **Figure 6.4** shows that one centre may have a significantly lower five year <u>graft</u> survival rate compared with the national rate. Centres can be identified by the information shown in **Tables 6.1** and **6.2**.







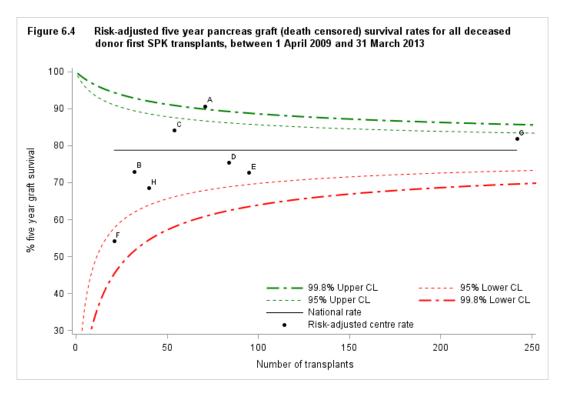


Table 6.1	Risk-adjusted transplants us						<b>⟨</b>			
	transplants us	ning paric	cases	nom decease	eu uonors					
				patient	survival					
			One-ye	ear*		Five-ye	ar**			
Centre	Code	N	%	(95% CI)	N	%	(95% CI)			
Cambridge	Α	94	99	(92 – 100)	68	91	(79 - 97)			
Cardiff	В	25	94	(67 - 100)	32	92	(70 - 99)			
Edinburgh	С	70	97	(89 - 100)	54	92	(80 - 98)			
Guy's	D	105	96	(89 - 99)	82	88	(76 - 95)			
Manchester	E	111	97	(91 - 99)	93	89	(79 - 95)			
Newcastle	F	24	100	N/A	21	81	(45 - 96)			
Oxford	G	201	98	(95 - 99)	231	87	(82 - 92)			
WLRTC	Н	27	100	N/A	39	73	(46 - 88)			
UK		657	98	(96 - 99)	620	88	(85 - 90)			
	Centre	has reach	ed the le	ower 99.8% co	onfidence l	imit				
	Centre	has reach	ed the le	ower 95% con	fidence lin	nit				
	Centre	has reach	ed the u	upper 95% con	fidence lir	nit				
				upper 99.8% c						
* Includes transplants performed between 1 April 2013 - 31 March 2017 ** Includes transplants performed between 1 April 2009 - 31 March 2013										

Table 6.2 Risk-adjusted one and five year pancreas graft survival for first SPK transplants using pancreases from deceased donors pancreas graft survival One-year\* Five-year\*\* Code (95% CI) Ν (95% CI) Centre Ν % Cambridge 100 90 (82 - 95)Α В Cardiff 26 81 (57 - 94)32 73 (49 - 88)С Edinburgh 71 82 (67 - 91)54 84 (69 - 93)(62 - 85) Guy's D 108 85 (76 - 92)84 75 Manchester Ε 95 112 91 (83 - 96)73 (59 - 82)F Newcastle 25 95 (73 - 100)21 54 (16 - 78)G Oxford 205 89 (84 - 93)242 82 (75 - 87)**WLRTC** Н 28 97 (82 - 100)40 69 (44 - 84)UK 675 89 (86 - 91)639 79 (75 - 82)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 2013 - 31 March 2017 \*\* Includes transplants performed between 1 April 2009 - 31 March 2013

#### 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	transplants using pancreases from deceased donors													
				patient s	survival									
	One-year* Five-year**													
Centre	Code	N	%	(95% CI)	N	%	(95% CI)							
Cambridge	Α	0	-	-	0	-	-							
Cardiff	В	6	-	-	9	-	-							
Edinburgh	С	0	-	-	1	-	-							
Guy's	D	2	-	-	4	-	-							
Manchester	Е	3	-	-	5	-	-							
Newcastle	F	2	-	-	2	-	-							
Oxford	G	26	96	(76 - 99)	49	75	(59 - 86)							
WLRTC	Н	0	-	-	0	-	-							
UK		39	97	(83 – 100)	70	78	(64 - 87)							
** Includes tran	splants performed b splants performed b ented where less tha	etween	1 April 20	009 - 31 March 2										

Unadjusted one and five year pancreas graft survival for first PO transplants using pancreases from deceased donors Table 6.4

				pancreas gi	aft surviv	al		
			One-ye			Five-year**		
Centre	Code	Ν	%	(95% CI)	Ν	%	(95% CI)	
Cambridge	Α	2			1			
ū			-	(44 05)	1	-	(00 70)	
Cardiff	В	10	80	(41 - 95)	14	50	(23 - 72)	
Edinburgh	С	1	-	-	1	-	-	
Guy's	D	2	-	-	7	-	-	
Manchester	E	6	-	-	11	27	(7 - 54)	
Newcastle	F	6	-	-	4	-	-	
Oxford	G	36	89	(73 - 96)	59	61	(47 - 72)	
WLRTC	Н	2	-	-	11	73	(37 - 90)	
UK		65	88	(77 - 94)	108	52	(42 - 61)	

<sup>\*</sup> Includes transplants performed between 1 April 2013 - 31 March 2017
\*\* Includes transplants performed between 1 April 2009 - 31 March 2013
- 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 2006 and 31 December 2017. 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. Cambridge has ten year survival rates above the upper 95% <u>confidence limit</u> indicating that their survival rates from listing that are higher than the national rate. The ten year survival rate for Manchester and Oxford were near the lower 95.5% <u>confidence limit</u>. This suggests that ten year survival from listing at Oxford is significantly lower than the national rate. 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.

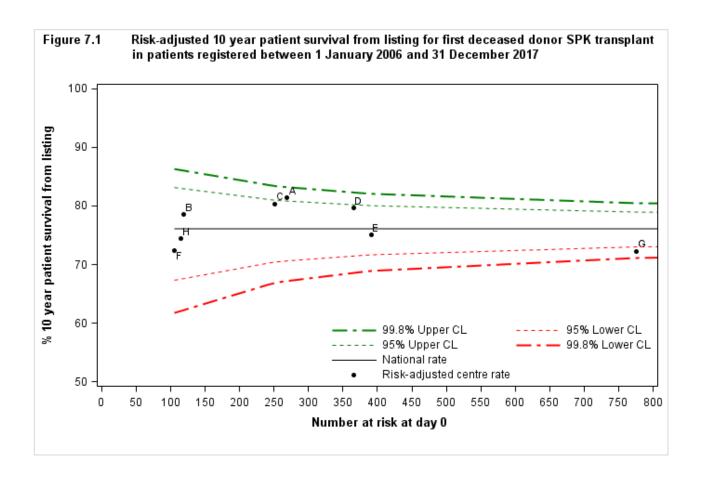
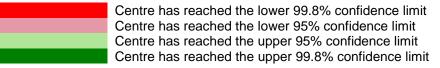


Table 7.1 Risk-adjusted 1, 5 and 10 year patient survival from listing for first deceased donor SPK transplant in patients registered between 1 January 2006 and 31 December 2017

Centre	Code	Number at risk <sup>1</sup> at day 0	Survival rate at 1 year (%)	Number at risk <sup>1</sup> at 1 year	Survival rate at 5 years (%)	Number at risk <sup>1</sup> at 5 years	Survival rate at 10 years (%)	Number at risk <sup>1</sup> at 10 years
Cambridge	Α	269	97	(244)	89	(123)	81	(27)
Cardiff	В	119	97	(103)	87	(58)	79	(15)
Edinburgh	С	251	97	(224)	88	(101)	80	(20)
Guy's	D	365	97	(326)	87	(152)	80	(32)
Manchester	Е	391	97	(343)	85	(169)	75	(35)
Newcastle	F	106	96	(92)	84	(42)	72	(8)
Oxford	G	776	96	(703)	83	(349)	72	(86)
WLRTC	Н	115	97	(118)	87	(66)	75	(12)
UK		2392	97	(2153)	85	(1060)	76	(235)



<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 2017

Form return rates are reported in **Table 8.1** for the pancreas transplant record, three month and 1 year follow up form, along with lifetime follow up (more than 2 years). These include all pancreas transplants performed between 1 January and 31 December 2017 for the transplant record, and all requests for follow up forms issued in this time period. Centres highlighted are transplant centres. Overall, 99% of transplant record forms issued and 83% of lifetime follow-up forms issued have been returned.

Table 8.1 Form return rates following pan 1 January - 31 December 2017	icreas	transplanta	tion,	by centre,				
Centre	Tı	ransplant		3 month		2 month	Lifeti	me follow-
		record	T	ollow-up	T	ollow-up		up
	l	%		%		%		%
	N	returned	N	returned	N	returned	N	returned
Aberdeen, Aberdeen Royal Infirmary					1	0	19	63
Bangor, Ysbyty Gwynedd District General	1				•		3	100
Hospital								100
Basildon, Basildon Hospital							4	100
Belfast, Antrim Hospital							2	100
Belfast, Belfast City Hospital					1	100	4	100
Belfast, The Ulster Hospital					'	100	1	0
Birmingham, Birmingham Heartlands Hospital							14	100
Birmingham, Queen Elizabeth Hospital							35	100
Birmingham								100
Bradford, St Lukes Hospital					2	50	5	100
Brighton, Royal Sussex County Hospital					_		24	100
Bristol, Southmead Hospital							47	100
Cambridge, Addenbrookes Hospital	21	100	25	100	21	100	108	100
Canterbury, Kent And Canterbury Hospital		100	1	100	2	100	31	100
Cardiff, University Of Wales Hospital	9	100	7	100	4	100	77	100
Carlisle, Cumberland Infirmary					1	100	3	100
Carshalton, St Helier Hospital							15	60
Chelmsford, Broomfield Hospital							1	100
Chester, Countess Of Chester Hospital							2	50
County Down, Daisy Hill Hospital							4	100
Coventry, University Hospital (walsgrave)							25	96
Derby, Royal Derby Hospital					1	100	7	100
Doncaster, Doncaster Royal Infirmary					·		3	100
Dorchester, Dorset County Hospital			1	100	2	100	31	100
Douglas, Nobles I-o-m Hospital			·		_		4	100
Dudley, Russells Hall Hospital					1	100	1	100
Dulwich, Kings College							2	100
Dumfries, Dumfries And Galloway Royal							3	100
Infirmary								
Dundee, Ninewells Hospital					3	100	15	100
Edinburgh, Royal Infirmary Of Edinburgh	16	100	14	86	9	33	61	38
Exeter, Royal Devon And Exeter Hospital			2	100	1	100	20	100
(wonford)								
Glasgow, Queen Elizabeth University Hospital							25	96
Gloucester, Gloucestershire Royal Hospital							13	62
Hereford, The County Hospital							2	100
Hull, The Hull Royal Infirmary					2	100	15	73
Inverness, Raigmore Hospital			1	100	2	100	9	100
Ipswich, Ipswich Hospital							7	86

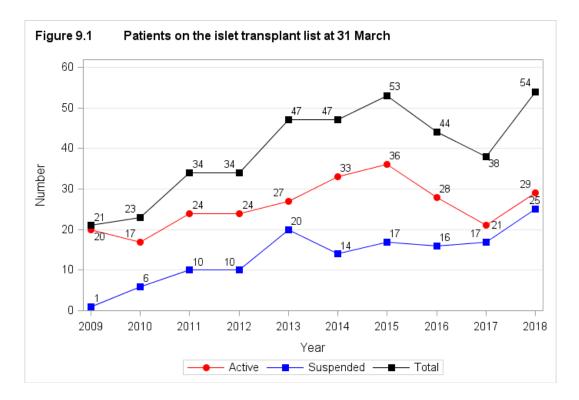
Table 8.1 Form return rates following pancreas transplantation, by centre, 1 January - 31 December 2017

Centre		ansplant record		B month ollow-up		2 month ollow-up	Lifeti	me follow- up
		%		%		%		%
	N	returned	N	returned	N	returned	N	returned
Kilmarnock, Crosshouse Hospital							4	50
Leeds, St Jamess University Hospital			2	100	2	100	13	100
Leicester, Leicester General Hospital					1	100	19	100
Lincoln, Lincoln County Hospital							3	100
Liverpool, Royal Liverpool University Hospital							9	100
Liverpool, University Hospital Aintree							1	0
London, Guys Hospital	24	100	20	100	14	100	121	100
London, Kings College Hospital					1	100		
London, St Georges Hospital							4	0
London, The Royal Free Hospital			1	100	2	100	41	100
London, The Royal London Hospital			1	100	1	100	9	100
(whitechapel)								
Londonderry, Altnagelvin Area Hospital							1	100
Manchester, Manchester Royal Infirmary	36	100	36	100	14	100	83	100
Manchester, Royal Manchester Childrens Hospital (pendlebury)							1	100
Middlesbrough, The James Cook University							16	100
Hospital							'	.00
Newcastle, Freeman Hospital	9	100	8	100	4	100	40	100
Northampton, Northampton General Hospital		100		100		100	7	71
Norwich, Norfolk And Norwich University					1	100	21	100
Hospital						100		100
Nottingham, Nottingham University Hospitals							29	59
City Campus								00
Omagh, Tyrone County Hospital							1	100
Oxford, Churchill Hospital	63	98	48	100	29	97	140	23
Peterborough, Peterborough City Hospital						<u> </u>	1	0
Plymouth, Derriford Hospital			1	0	4	100	18	100
Portsmouth, Queen Alexandra Hospital			2	100	6	100	40	100
Preston, Royal Preston Hospital					2	100	17	100
Reading, Royal Berkshire Hospital					1	100	24	96
Rhyl, Royal Alexandra Hospital						100	2	100
Salford, Salford Royal							18	100
Sheffield, Northern General Hospital					1	100	10	80
Shrewsbury, Royal Shrewsbury Hospital						100	2	50
St Helier, Jersey General Hospital							1	100
Stevenage, Lister Hospital							5	60
Stoke-on-trent, Royal Stoke University Hospital					3	100	9	100
Sunderland, Sunderland Royal Hospital						100	5	40
Swansea, Morriston Hospital	1						11	100
Truro, Royal Cornwall Hospital (treliske)			1	0			22	0
West London Renal Transplant Centre	9	100	10	100	8	100	86	64
West London Renal Hansplant Centre  Westcliff On Sea, Southend Hospital	9	100	10	100	0	100	2	100
Wirral, Arrowe Park Hospital							3	67
					1	100	21	100
Wolverhampton, New Cross Hospital						100	<u>∠ I</u>	100
Wrovbam, Masler General Hospital					2	100	1 0	
Wrexham, Maelor General Hospital			1	400	1	100	8 11	88
York, York District Hospital			1	100	1	100	11	100

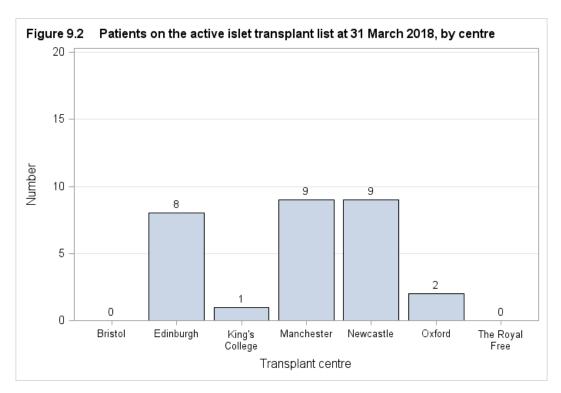
# Islet transplant list

#### 9.1 Patients on the islet transplant list as at 31 March, 2009 – 2018

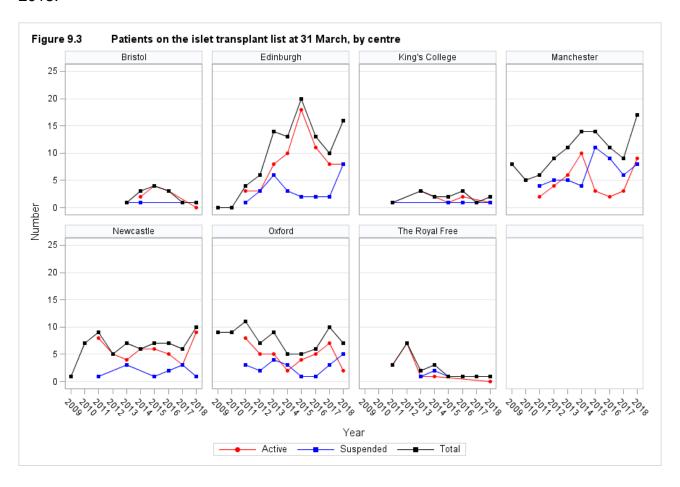
**Figure 9.1** shows the number of patients on the islet <u>transplant list</u> at 31 March each year between 2009 and 2018. The number of patients active on the islet <u>transplant list</u> increased from 20 in 2009 to 36 in 2015, and then decreased for two years to 21 in 2017, but has since risen to 29 in 2018.



**Figure 9.2** shows the number of patients on the active islet <u>transplant list</u> at 31 March 2018 by centre. The majority, 90%, of patients on the active <u>transplant list</u> were registered at one of three centres; Manchester (9), Newcastle (9), Edinburgh (8). There were no patients registered at Bristol and the Royal Free.

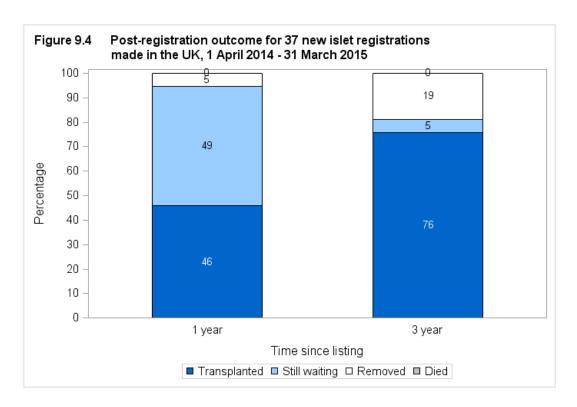


**Figure 9.3** shows the number of patients on the islet <u>transplant list</u> at 31 March each year between 2009 and 2018 for each transplant centre. The number of active and suspended patients by centre is not recorded prior to 2011, hence only the total number are reported in 2009 and 2010. The number of patients actively registered at Edinburgh has decreased from 18 on 31 March 2015 to eight on 31 March 2018. The number of patients on the active list at Manchester has increased from three on 31 March 2015 to nine on 31 March 2018.

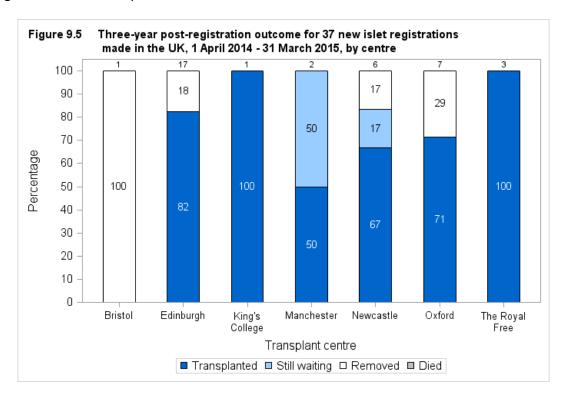


#### 9.2 Post-registration outcomes, 1 April 2014 – 31 March 2015

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>. 46% of patients are transplanted within one year, while three years after listing 76% of patients have received a transplant.



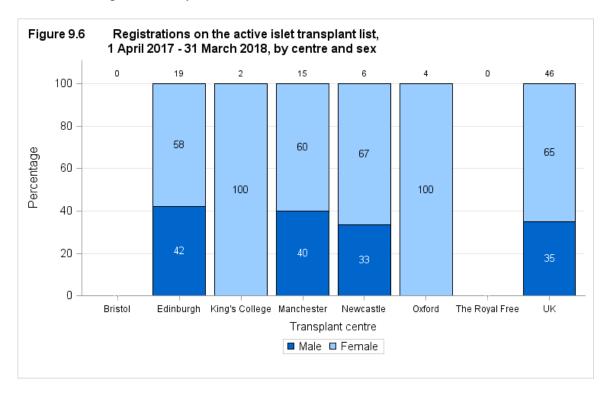
**Figure 9.5** shows the proportion of patients transplanted or still waiting three years after joining the list by centre. Three years after registration, the only patient registered at Bristol was removed and 29% of patients were removed from the list at Oxford, although the number of registrations were also small. Overall the majority of centres transplanted above 50% of their patients registered within three years. There were no patients who died whilst waiting for an islet transplant.

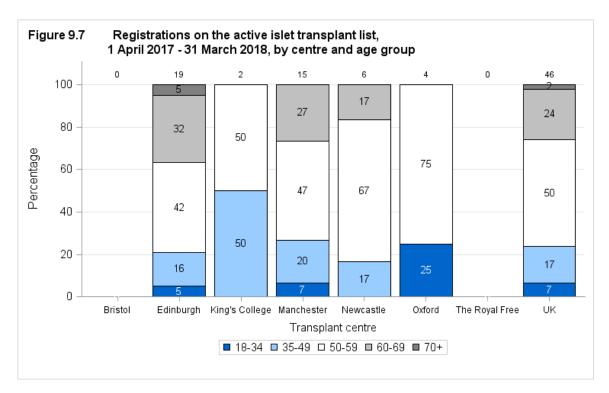


#### 9.3 Demographic characteristics, 1 April 2017 – 31 March 2018

The sex and age group of patients registered on the islet <u>transplant list</u> during 2017/18 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.

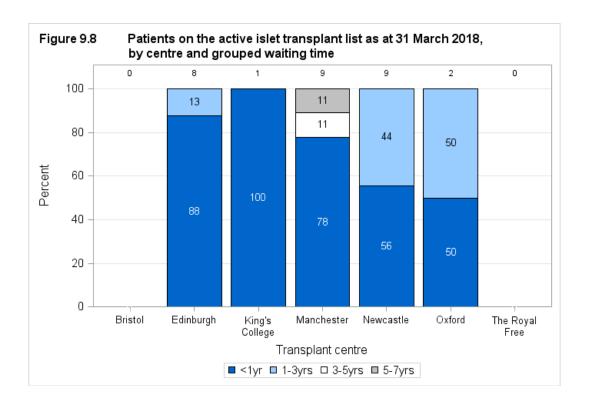
Overall, the majority of patients registered on the islet transplant list were female (65%) and the median age was 53 years.





#### 9.4 Patient waiting times for those currently on the list, 31 March 2018

**Figure 9.8** shows the length of time patients have been waiting on the islet <u>transplant list</u> at 31 March 2018 by centre. One highly sensitised patient (94% <u>cRF</u>) registered at Manchester has been waiting more than five years for transplant.



#### 9.5 Median waiting time to transplant, 1 April 2012 - 31 March 2015

The length of time a patient waits for an islet transplant varies across the UK. The <u>median</u> 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> waiting time to transplant for patients registered on the islet <u>transplant list</u> between 1 April 2012 and 31 March 2015 is 422 days (over 14 months), ranging from 338 days at Newcastle to 1010 days (over 2 and a half years) at Manchester.

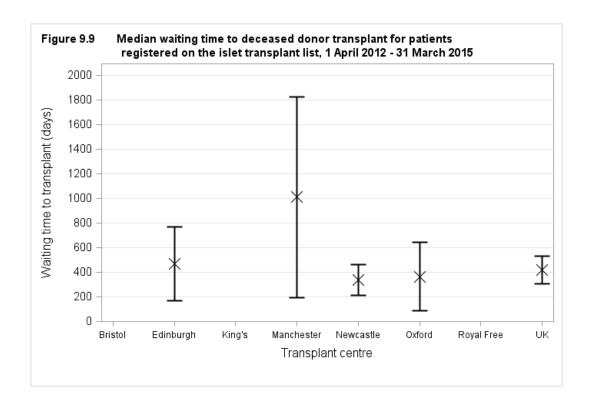


Table 9.1 Median waiting time to islet transplant in the UK, for patients registered 1 April 2012 - 31 March 2015											
Transplant centre	Number of patients	Wa	iting time (days)								
·	registered	Median	95% Confidence interva								
Bristol	5	_	-								
Edinburgh	46	468	170 - 766								
King's	8	-	-								
Manchester	11	1010	194 - 1826								
Newcastle	21	338	215 - 461								
Oxford	24	365	88 - 642								
Royal Free	6	-	-								
UK	121	422	310 - 534								
Data not procenta	d when less than 10 patients	ragiatorad									

## Response to islet offers

#### 10.1 Offer decline rates, 1 April 2015 - 31 March 2018

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 and over the time period, 1 April 2015 and 31 March 2018 are shown in **Table 10.1**. King's College had the lowest overall decline rates (17%) whilst Newcastle had the highest decline rate (72%). Note that all rates are based on a small number of offers.

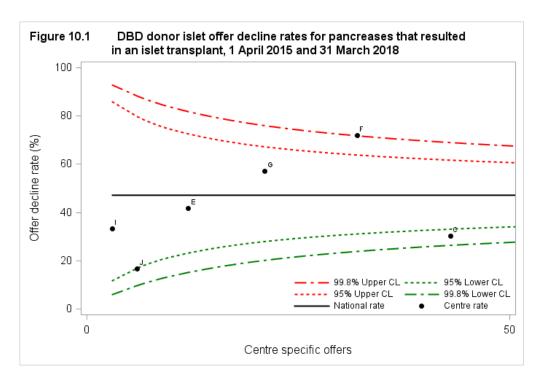
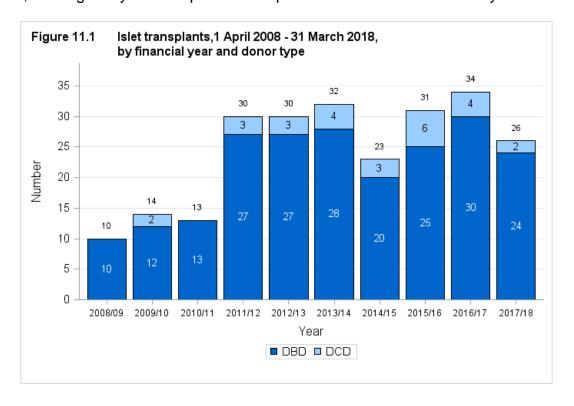


Table 10.1	Table 10.1 DBD donor islet offer decline rates by transplant centre, 1 April 2015 and 31 March 2018														
Centre	Code	2015	5/16	2016	6/17	2017	7/18	Ove	erall						
		N	(%)	N	(%)	N	(%)	N	(%)						
Bristol	I	2	(50)	1	(0)	0	-	3	(33)						
Edinburgh	С	17	(35)	15	(20)	11	(36)	43	(30)						
King's	J	2	(50)	3	(0)	1	(0)	6	(17)						
Manchester	Е	1	(0)	5	(60)	6	(33)	12	(42)						
Newcastle	F	15	(60)	12	(75)	5	(100)	32	(72)						
Oxford	G	2	(0)	6	(50)	13	(69)	21	(57)						
Royal Free	K	0	-	0	-	0	-	0	-						
UK		39	(44)	42	(43)	36	(56)	117	(47)						
	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 Centre has reached the lower 99.8% confidence limit														

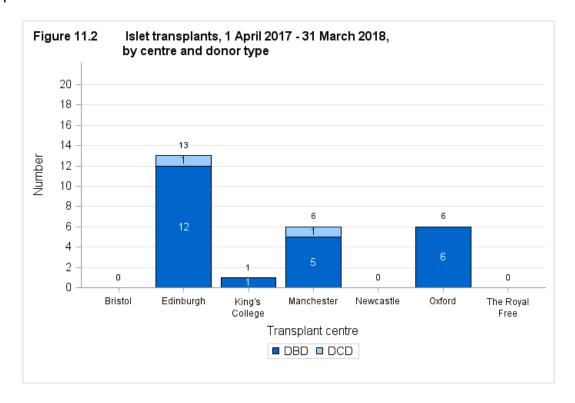
## **Islet transplants**

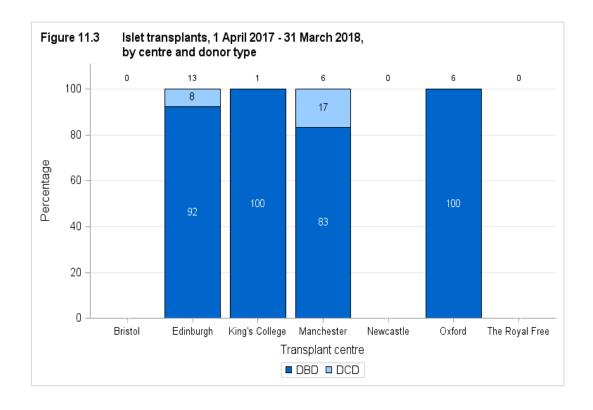
#### 11.1 Islet transplants, 1 April 2009 – 31 March 2018

**Figure 11.1** shows the total number of islet transplants performed in the last ten financial years, by type of donor. There was a significant increase in 2011/12 from 13 to 30 transplants a year, following the introduction of the national <u>Pancreas Allocation Scheme</u> in 2010. This provided islet patients with equal access to donated pancreases for the first time. Since 2011/12, the number of islet transplants increased to 34 transplants in 2016/17, although only 26 transplants were performed in the last financial year.

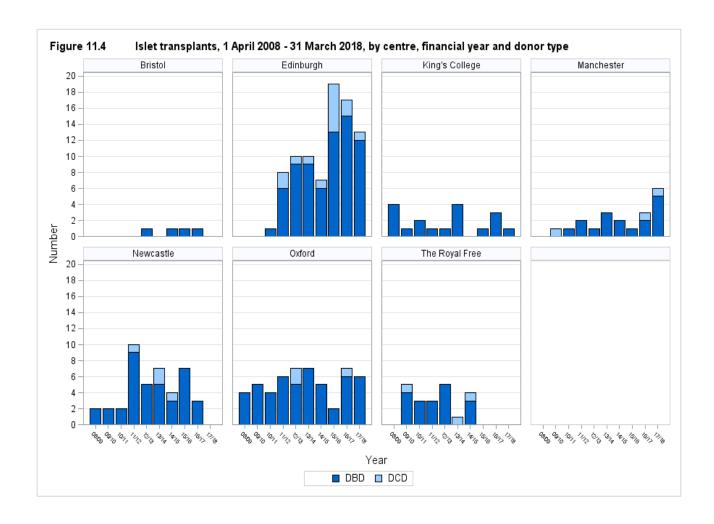


**Figure 11.2** shows the total number of islet transplants performed in 2017/18, by centre and type of donor. The same information is presented in **Figure 11.3** but this shows the proportion of <u>DBD</u> and <u>DCD</u> transplants performed at each centre. Edinburgh performed the most islet transplants in 2017/18 (13), followed by Oxford and Manchester (6). Edinburgh and Manchester were the only centres who performed <u>DCD</u> transplants as well as <u>DBD</u> transplants. Royal Free, Bristol and Newcastle did not perform any islet transplants in 2017/18.



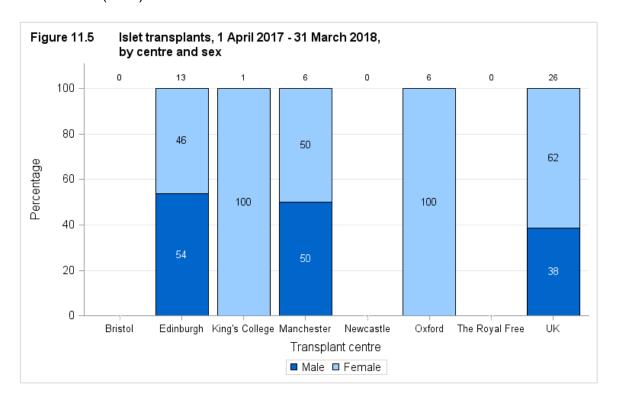


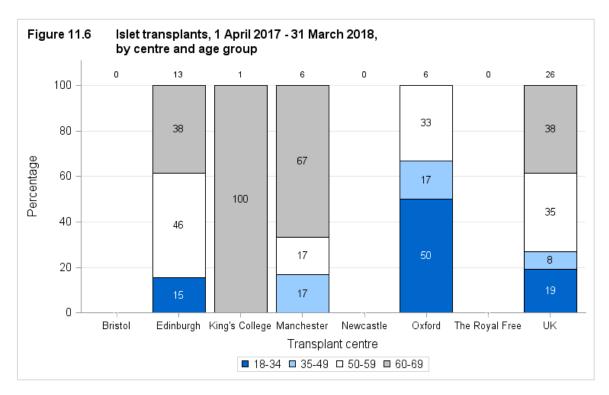
**Figure 11.4** shows the total number of islet transplants performed in last ten years, by centre and type of donor. Oxford and Newcastle have consistently performed a number of islet transplants each year, while Edinburgh has increased their transplant activity in the last four years. Bristol has performed very few transplants over the ten year period.



#### 11.2 Demographic characteristics, 1 April 2017 - 31 March 2018

The sex and age group of patients that received an islet transplant in 2017/18 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, 26 patients were transplanted on the islet transplant list, the <u>median</u> age was 54.5 years and the majority were female 16 (62%).



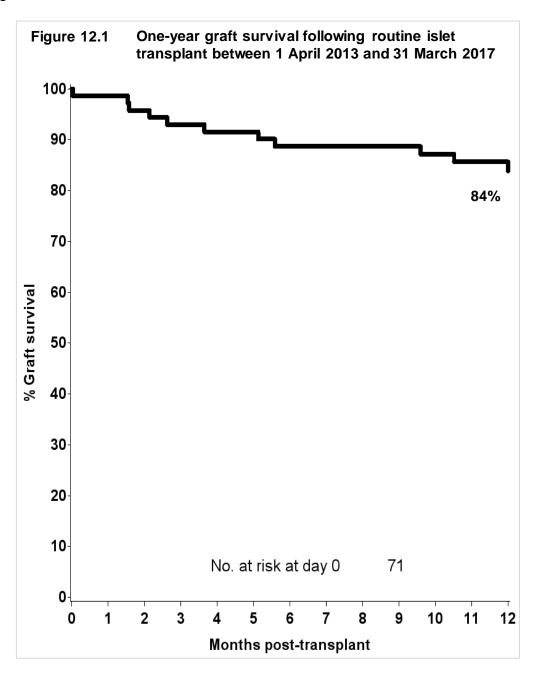


### **Islet outcomes**

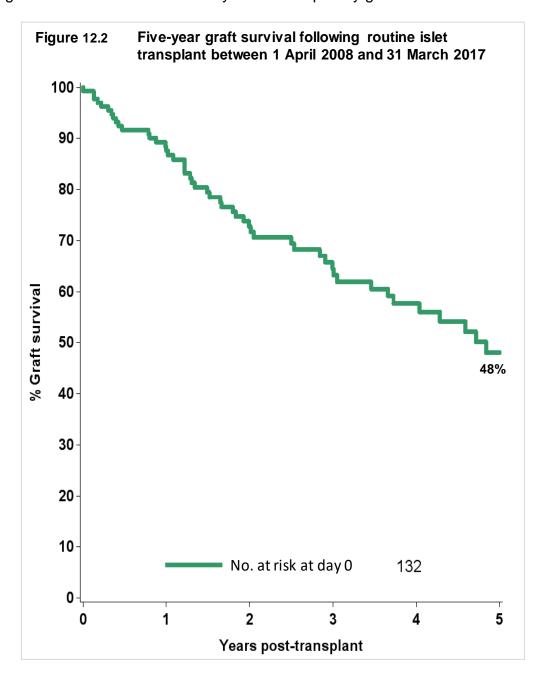
#### 12.1 Outcome measures for routine islet transplants

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 2008 and 31 March 2017.

A one-year Kaplan-Meier graft survival plot for islet transplants between 1 April 2013 – 31 March 2017 is shown in **Figure 12.1**. Estimated one-year graft survival following a routine islet transplant is 84% with 95% confidence interval (CI) (73-91%). This includes 28 patients who received only a routine graft and 43 patients who additionally received a priority graft.

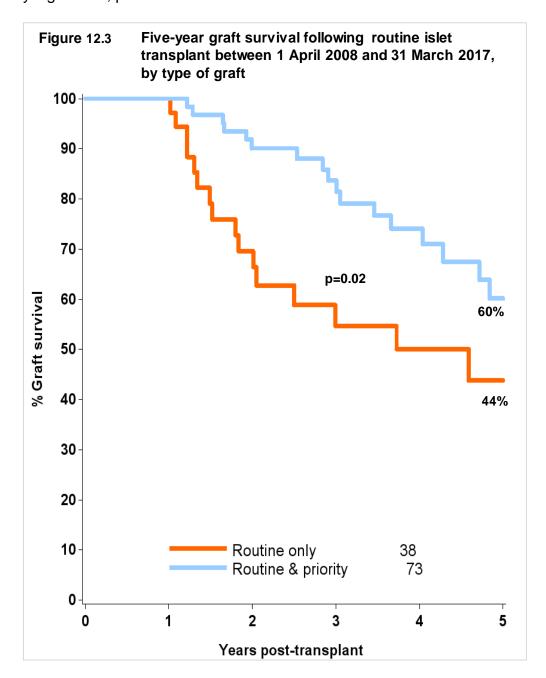


A five-year <u>Kaplan-Meier graft survival</u> plot for islet transplants between 1 April 2008 – 31 March 2017 is shown in **Figure 12.2**. Estimated five-year <u>graft survival</u> following a routine islet transplant is 48% with 95% CI (36-59%). This includes patients who received only a routine graft and those who additionally received a priority graft.



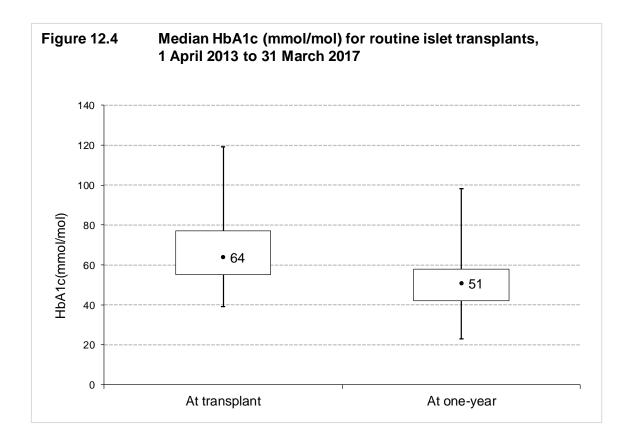
Further, a five-year <u>Kaplan-Meier graft survival</u> plot by type of graft is shown in **Figure 12.3**, for islet transplants between 1 April 2008 – 31 March 2017, where the graft (routine only or routine followed by a priority) was still functioning at one year post-transplant. In order to receive 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.

Estimated five-year <u>graft survival</u> is 44% for routine only grafts, 95% CI (24-62%) and for routine followed by priority grafts is 60%, 95% CI (42-74%). This difference was statistically significant, p=0.02.

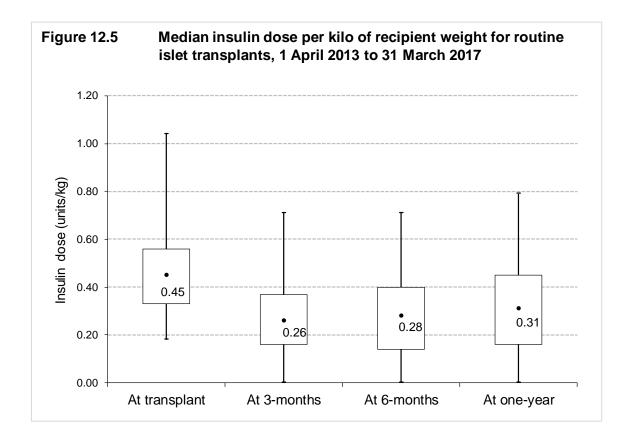


For transplants between 1 April 2013 – 31 March 2017, the <u>median</u> annual rate of severe <u>hypoglycaemic</u> events prior to transplant (reported as number of events between registration and transplant) was 9 events per year (<u>Interquartile range</u> 0-34), and at one-year post-transplant this had been reduced to no events per year. Of the 50 patients where the number of severe hypoglycaemic events at one-year post-transplant was available, 41 (82%) experienced no severe <u>hypoglycaemic</u> events, 4 (8%) experienced one or two events and 5 (10%) experienced three or more events.

**Figure 12.3** shows the reduction in <u>median HbA1c</u> (mmol/mol) for routine islet transplants between 1 April 2013 – 31 March 2017. <u>Median HbA1c</u> dropped from 64mmol/mol prior to transplant to 51mmol/mol at one-year post-transplant. Of those 56 patients with HbA1c reported at one-year, 32 (57%) had an HbA1c less than 53mmol/mol.



**Figure 12.4** 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 transplants between 1 April 2013 – 31 March 2017. Prior to transplant the <u>median</u> insulin dose is 0.45 units/kg, by three-months the <u>median</u> dose has dropped to 0.26 units/kg and then increased at one-year post-transplant with a <u>median</u> dose of 0.31 units/kg. Following islet transplantation of the 56 patients where information was reported, 17 (30%) achieved insulin independence at some point during their first year post-transplant.



### Form return rates

#### 13.1 Islet form return rates, 1 January – 31 December 2017

Form return rates are reported in **Table 13.1** for the islet transplant record, three month and 1 year follow up form, along with lifetime follow up (more than 2 years). These include all islet transplants performed between 1 January and 31 December 2017 for the transplant record, and all requests for follow up forms issued in this time period. Centres highlighted are transplant centres. There were 96% of transplant forms returned, whereas only 89% of 3-month follow up forms and 82% of lifetime forms were returned.

Table 13.1 Form return rates followin 1 January - 31 December 2		transplantat	ion, by	centre,				
Centre		ansplant	3 mo	nth follow-		2 month	Lifet	ime follow-
		record		up	to	llow-up		up
		%		%		%		%
	N	returned	N	returned	N	returned	N	returned
Bristol, Southmead Hospital					1	100	1	100
Edinburgh, Royal Infirmary Of Edinburgh	11	100	7	100	8	100	21	100
Glasgow, Queen Elizabeth University Hospital							1	0
London, Kings College Hospital			1	100	1	100	4	100
London, The Royal Free Hospital			1	100			3	100
Manchester, Manchester Royal Infirmary	2	100	1	100			5	100
Newcastle, Freeman Hospital	1	100	1	100			14	93
Oxford, Churchill Hospital	9	89	7	71	2	50	13	31
Overall	23	96	18	89	12	92	62	82

## **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 of blood group identical donors from a pool of 10,000 and for which they would be <u>HLA</u> compatible 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 <u>HLA</u> antibodies will have 0 <u>sensitisation</u> (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 <a href="cross-match">cross-match</a> 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

A donor whose heart is still beating when their entire brain has stopped working so that they cannot survive without the use of a ventilator. Organs for transplant are removed from the donor while their heart is still beating, but only after extensive tests determine that the brain cannot recover and they have been certified dead.

#### Donor after circulatory death

A donor whose heart stops beating before their brain stops working and who is then certified dead. The organs are then removed.

#### **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 Antigen (HLA) antigens 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.

#### 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 Allocation 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 and is administered by NHS Blood and Transplant. Prior to December 2010 deceased donors were allocated on a centre basis.

The Pancreas Allocation Scheme prioritises all 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 <a href="https://px.ncbi.nlm.nih.goograpse-patient-sensitisation">https://px.ncbi.nlm.nih.goograpse-patient-sensitisation</a>, 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> antigens 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> antigen then they cannot receive a transplant from a donor with that <u>HLA</u> antigen, 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 Allocation 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 English Strategic Health Authority (SHA), 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.

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