

NHS BLOOD AND TRANSPLANT

LIVER ADVISORY GROUP

DECLINED LIVER OFFERS FROM DECEASED DONORS

SUMMARY

BACKGROUND

- 1 In the offering sequence, transplanted livers from deceased donors are either accepted by a liver transplant centre on the first offer and transplanted, or declined by one or more centres before being accepted for transplantation.

DATA ANALYSIS

- 2 Of the 1,243 livers from donors after brain death (DBD) transplanted into Group 1 adult elective patients in the UK, 1 April 2013 and 31 March 2016: 884 (71%) were transplanted on the first offer, 176 (14%) were previously declined once and 183 (15%) were previously declined more than once. Of the 514 livers from donors after circulatory death (DCD) transplanted in the same time period, 343 (67%) were transplanted on the first offer, 61 (12%) were previously declined once and 110 (21%) were previously declined more than once.
- 3 The most common reasons for declining liver offers from either DBD or DCD donors whose liver was subsequently transplanted were donor related, followed by logistical issues and the lack of any suitable recipients.
- 4 **Table 1** shows the offer decline rates of each centre. These are further illustrated in funnel plots (**Figure 5** and **Figure 6** of Appendix). Note that these results are somewhat reflective of the size of the centre and the size of their transplant list.

Donor type	Centre offer decline rate						
	Birmingham	Cambridge	Edinburgh	King's College	Leeds	Newcastle	Royal Free
DBD	22%	51%	44%	22%	48%	74%	36%
DCD	23%	37%	56%	19%	49%	80%	44%

- 5 A comparison of both unadjusted and risk adjusted survival of patients who received a donor liver that had previously been declined by another centre for donor related reasons before being transplanted, with all other patients who received a liver transplant, was also undertaken for transplants between 1 April 2010 and 31 March 2016. Patient and transplant survival up to five years after transplantation were not significantly different depending on whether the liver had previously been declined for a donor related reason. This was the case in the separate unadjusted and risk adjusted analyses of DBD and DCD donor liver transplants. Similarly a comparison was undertaken for patient and transplant survival where the liver was accepted on first offer and where the liver was declined at least once and subsequently transplanted. There was no significant difference in the separate unadjusted and risk adjusted analyses for DBD or DCD donor transplants.

ACTIONS

- 6 Members are asked to note these results and agree any actions required.

Agne Zarankaite, Kate Martin and Rachel Johnson
Statistics and Clinical Studies

April 2016

NHS BLOOD AND TRANSPLANT

LIVER ADVISORY GROUP

DECLINED LIVER OFFERS FROM DECEASED DONORS

INTRODUCTION

- 1 This paper reports on declined liver offers from donors after brain death (DBD) and donors after circulatory death (DCD) during the three year period from 1 April 2013 to 31 March 2016. It also reports on a comparison of post-transplant survival of patients who received a donor liver that had previously been declined by another centre for donor related reasons before being transplanted, with all other patients who received a liver transplant, separately for DBD and DCD donor livers. Survival of patients is also compared for those who received a liver accepted on first offer and livers that were declined at least once then subsequently transplanted.

DATA

- 2 Data on 1,757 first Group 1 adult elective whole liver only transplants performed in the UK between 1 April 2013 and 31 March 2016 were included in the analysis, where 1,243 used livers from DBD donors and 514 used livers from DCD donors. The offering data for these transplanted livers were analysed, where fast track liver offers and offers made to super-urgent, Group 2, paediatric, multi-organ or intestinal transplant patients were excluded.

METHODS

- 3 The donor livers analysed in this paper were either accepted by a liver transplant centre on the first offer and transplanted, or declined at least once by one or more centres before being accepted for transplantation. A liver offer can be accepted and then declined after retrieval and for the purposes of this paper these cases are treated the same as liver offers that are declined at time of offer.
- 4 Reasons for decline are recorded from information provided by the centres for each declined offer. These reasons have been summarised by centre, for DBD donor livers in **Table 2** and DCD donor livers in **Table 4**.
- 5 Summary statistics on the cold ischaemia time (CIT) of the DBD and DCD donor livers are presented in **Table 3** and **Table 5** respectively, by the number of times the liver was declined before being accepted and transplanted.
- 6 For donor livers that were declined at least once, the category most commonly stated for decline has been taken (based on groupings in **Table 2** and **Table 4**), in order to classify a donor liver as having been declined for a donor related reason or another reason. Unadjusted post-transplant survival rates and risk adjusted hazard ratios of patient death and transplant failure were then compared for patients who received a liver previously declined for 'donor' reasons and all other patients who received a liver that was either transplanted on the first offer or previously declined by centres for reasons other than donor related.
- 7 Unadjusted post-transplant survival rates and risk adjusted hazard ratios of patient death and transplant failure were also compared for patients who received a liver that

was accepted on the first offer and all patients who received a liver that was declined at least once then subsequently transplanted.

- 8 The survival rates were obtained using the Kaplan-Meier estimation method performed on a reduced cohort of transplants carried out between 1 April 2010 and 31 March 2016. Follow-up data were as recorded on the UK Transplant Registry on 15 April 2016. This analysis is presented separately for transplants using DBD donor livers (N=2,222) and transplants using DCD donor livers (N= 813). Patient survival and transplant survival (where outcome event is graft failure or patient death) rates by decline reason groups, for DBD and DCD donors, are presented in **Figure 1** and **Figure 3**, respectively. Patient survival and transplant survival rates by outcome of first offer, for DBD and DCD donors, are presented in **Figure 2** and **Figure 4**, respectively.
- 9 To account for any differences in patients that may affect their outcomes, risk adjusted analyses were carried out using Cox Proportional Hazards regression modelling for five year survival. A further reduced cohort of transplants carried out between 1 April 2010 and 31 March 2016 was considered. The analysis is presented separately for transplants using DBD donor livers (N= 2,129) and transplants using DCD donor livers (N= 791). Risk adjusted hazard ratios of patient death and of transplant failure (where outcome event is graft failure or patient death) by decline reason group and by outcome of first offer, for DBD donors, are presented in **Table 6**. Corresponding hazard ratios for DCD donors are presented in **Table 7**.

RESULTS

Offering data

Donors after brain death

- 10 Of the 1,243 DBD donor livers that were transplanted in the UK between 1 April 2013 and 31 March 2016, 884 (71%) were transplanted on the first offer, 176 (14%) were declined once before being accepted for transplantation and 183 (15%) were declined more than once before being accepted for transplantation. The total number of offers associated with the 1,243 DBD donor livers was 2,113. These offers are summarised by the centre the offer was made to and the reason for decline in **Table 2**.
- 11 Newcastle declined the highest proportion of DBD donor liver offers (74%). Birmingham and King's College declined the smallest proportion of liver offers (22%, respectively). The other centres declined between 36% and 51% of their offers.
- 12 **Table 2** shows the detailed reasons for decline. The most common cause to decline a DBD donor liver offer was donor reasons (27%), of which donor past history was the most common. The decline rates for liver offers from DBD donors are presented in a funnel plot in **Figure 5** of the Appendix.

Table 2 Number of liver offers declined from donors after brain death in the UK, where livers were subsequently transplanted, by reason of decline and transplant centre, 1 April 2013 to 31 March 2016

	Liver transplant centre															
	Birmingham		Cambridge		Edinburgh		King's College		Leeds		Newcastle		Royal Free		TOTAL	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
DECLINED	79	22	123	51	197	44	75	22	161	48	204	74	91	36	870	41
Donor reasons	53	15	86	35	65	21	60	18	97	29	134	49	73	29	565	27
ABO type	0	0	5	2	5	2	2	1	1	0	3	1	4	2	20	1
Anatomical	0	0	2	1	0	0	2	1	0	0	2	1	0	0	6	0
Ischaemic time too long	1	0	2	0	1	0	0	0	1	0	2	0	1	0	8	0
Donor unsuitable - age	13	4	11	5	4	1	7	2	16	5	7	3	6	2	64	3
Donor unsuitable - cause of death	0	0	1	0	1	0	0	0	1	0	1	0	0	0	4	0
Donor unsuitable - past history	19	5	36	15	28	9	25	7	36	11	64	23	24	9	232	11
Donor unsuitable - size	13	4	1	0	2	1	8	2	12	4	12	4	7	3	55	3
Donor unsuitable - virology	1	0	4	2	4	1	3	1	3	1	7	3	2	1	24	1
Donor unsuitable - other	0	0	2	1	1	0	1	0	3	1	3	1	2	1	12	1
Fatty organ	3	1	3	1	1	0	1	0	5	1	5	2	6	2	24	1
Poor function	3	1	16	7	18	6	11	3	19	6	27	10	20	8	114	5
Tumour	0	0	0	0	0	0	0	0	0	0	1	0	1	0	2	0
Recipient reasons	2	1	2	1	3	1	1	0	6	2	0	0	0	0	14	1
Recipient refused/did not need transplant	1	0	0	0	1	0	1	0	4	1	0	0	0	0	7	0
Recipient unfit	1	0	2	1	2	1	0	0	2	1	0	0	0	0	7	0
NLA PAYBACK	0	0	0	0	29	9	0	0	12	4	12	4	0	0	53	3
No suitable recipients	1	0	19	8	15	5	7	2	16	5	29	11	11	4	98	5
Organ damaged/unsuitable	0	0	1	0	0	0	0	0	4	1	2	0	3	1	10	0
Logistical reasons	23	6	18	8	25	8	7	2	26	8	27	10	4	2	130	6
Centre already retrieving/transplanting	8	2	13	5	17	5	0	0	7	2	15	5	2	1	62	3
No beds/staff/theatre	2	1	0	0	0	0	0	0	12	4	0	0	0	0	14	1
Other	13	4	4	2	7	2	7	2	7	2	12	4	2	1	52	3
Distance (Euro)	0	0	1	0	1	0	0	0	0	0	0	0	0	0	2	0
ACCEPTED	278	78	117	49	177	56	263	78	174	52	70	26	164	64	1243	59
TOTAL NUMBER OF OFFERS	357	100	240	100	314	100	338	100	335	100	274	100	255	100	2113	100
Number of patients on transplant list¹	150		59		47		164		92		27		71		610	100
Number of offers per patient	2		4		7		2		4		10		4		3	

¹ Active adult elective only liver transplant list as at 31/03/2016

- 13 **Table 3** shows the median and range of cold ischaemic times (CIT), in hours, of the 1,243 DBD donor livers by the number of times the liver was declined before being accepted and transplanted. The median CIT was reasonably similar regardless of the number of times the liver was declined.

Number of times the liver was declined before being accepted and transplanted	N ¹	CIT (hours)	
		Median	Range
0	758	8.0	0.8 – 22.6
1	159	9.4	1.7 – 19.0
> 1	170	8.9	1.6 – 15.7
Total	1,087	8.4	0.8 – 22.6

¹ CIT was not reported for a total of 156 livers

Donors after circulatory death

- 14 Of the 514 DCD donor livers that were transplanted in the UK between 1 April 2013 and 31 March 2016, 343 (67%) were transplanted on the first offer, 61 (12%) were declined once before being accepted for transplantation and 110 (21%) were declined more than once before being accepted for transplantation. The total number of offers associated with the 514 DCD donor livers was 855. These offers are summarised by the centre the offer was made to and the reason for decline in **Table 4**.
- 15 Newcastle declined the highest proportion of DCD donor liver offers (80%). King's College and Birmingham declined the smallest proportion of their offers (19% and 23%, respectively). The other centres declined between 37% and 56% of their offers.
- 16 **Table 4** shows the detailed reasons for decline. The most common cause to decline a DCD liver offer was donor reasons (23%), of which donor past history and size were the most common. The decline rates for liver offers from DCD donors are presented in a funnel plot in **Figure 6** of the Appendix.

Table 4 Number of liver offers declined from donors after circulatory death in the UK, where livers were subsequently transplanted, by reason of decline and transplant centre, 1 April 2013 to 31 March 2016

	Liver transplant centre														TOTAL	
	Birmingham		Cambridge		Edinburgh		King's College		Leeds		Newcastle		Royal Free			
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
DECLINED	46	23	47	37	60	56	25	19	63	49	35	80	35	44	341	40
Donor reasons	19	10	24	19	36	34	13	10	36	28	43	53	27	34	198	23
Centre criteria not achieved	0	0	0	0	3	3	0	0	2	2	2	2	0	0	7	1
Fatty organ	0	0	0	0	0	0	1	0	0	0	0	0	1	1	2	0
Donor unsuitable – age	4	2	7	6	13	12	1	1	18	14	12	15	9	11	64	7
Donor unsuitable – past history	7	4	11	9	15	14	6	4	7	5	21	26	9	11	76	9
Donor unsuitable – size	1	1	4	3	0	0	1	1	1	1	1	1	0	0	8	1
Donor unsuitable – virology	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0
Infection	1	1	1	1	0	0	0	0	0	0	1	1	0	0	3	0
Poor function	5	3	1	1	5	5	1	1	6	5	6	7	4	5	28	3
Warm ischaemic time too long	0	0	0	0	0	0	3	2	1	1	0	0	2	3	6	1
Donor unsuitable - other	1	0	0	0	0	0	0	0	1	1	0	0	1	1	2	3
Recipient reasons	1	1	1	1	0	0	1	1	0	0	0	0	1	1	4	0
Recipient refused	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	0
Recipient unfit	1	1	1	1	0	0	0	0	0	0	0	0	1	1	3	0
No suitable recipients	8	4	7	6	9	8	4	3	13	10	13	16	5	6	59	7
Logistical reasons	18	9	15	12	15	14	7	5	14	11	9	11	2	3	80	9
Centre already retrieving/ transplanting	12	6	10	8	8	7	3	2	4	3	5	6	0	0	42	5
No beds/staff/theatre	1	1	2	2	0	0	0	0	2	2	2	2	0	0	7	1
No time	1	1	0	0	1	1	0	0	0	0	0	0	0	0	2	0
Transport difficulties	0	0	0	0	0	0	0	0	1	1	0	0	0	0	1	0
Other	4	2	3	2	6	6	4	3	7	5	2	2	2	3	28	3
ACCEPTED	151	77	79	63	47	44	110	81	66	51	16	20	45	56	514	60
TOTAL NUMBER OF OFFERS	197	100	126	100	107	100	135	100	129	100	81	100	80	100	855	
Number of patients on transplant list¹	150		59		47		164		92		27		71		610	100
Number of offers per patient	1		2		2		<1		1		3		1		1	

¹ Active adult elective only liver transplant list as at 31/03/2016

- 17 **Table 5** shows the median and range of cold ischaemic times (CIT), in hours, of the 514 DCD donor livers by the number of times the liver was declined before being accepted and transplanted. Again, the median CIT was reasonably similar regardless of the number of times the liver was declined.

Number of times the liver was declined before being accepted and transplanted	N ¹	CIT (hours)	
		Median	Range
0	302	7.2	1.4 – 21.7
1	55	7.6	2.0 – 17.3
> 1	98	7.9	1.1 – 22.2
Total	455	7.4	1.1 – 22.2

¹ CIT was not reported for a total of 59 livers

Unadjusted survival analysis

Donors after brain death

- 18 **Figure 1** shows the Kaplan-Meier survival curves for patient and transplant survival up to five years, according to whether the liver had been previously declined for a donor related reason ('donor') against all other transplanted livers ('other/not previously declined'). There was no evidence of a difference between the patient survival rates (p-value=0.9) or the transplant survival rates (p-value=0.4), up to five years, between the 'donor' and 'other' group. *Note that there are only a small number of observed events in the 'donor' group, particularly in the patient survival curve, and hence a small change in the number of events could affect the p-value considerably so the results should be viewed with caution.*
- 19 **Figure 2** shows the Kaplan-Meier survival curves for patient and transplant survival up to five years, by first offer outcome. There was no evidence of a difference between the patient survival rates (p-value=0.9) or the transplant survival rates (p-value=0.8), up to five years, between the 'accepted on first offer' and 'not accepted on first offer' group. *Again, note that there are only a small number of observed events in the 'not accepted on first offer' group and so the results should be viewed with caution.*

Donors after circulatory death

- 20 **Figure 3** shows the Kaplan-Meier survival curves for patient and transplant survival up to five years, according to whether the liver had been previously declined for a donor related reason ('donor') against all other transplanted livers ('other/not previously declined'). There was no evidence of a difference between the patient survival rates (p-value=0.7) or the transplant survival rates (p-value=0.6), up to five years, between the 'donor' and 'other/not previously declined' group. *Note that there are only a small number of observed events in the 'donor' group and hence the results should be treated with caution.*
- 21 **Figure 4** shows the Kaplan-Meier survival curves for patient and transplant survival up to five years, by first offer outcome. There was no evidence of a difference between the patient survival rates (p-value=0.4) or the transplant survival rates (p-value=0.5), up to five years, between the 'accepted on first offer' and 'not accepted on first offer' group. *Again, note that there are only a small number of observed events in the 'not accepted on first offer' group and so the results should be viewed with caution.*

Figure 1 Unadjusted five year patient and transplant survival for first Group 1 adult elective liver only DBD donor transplants in the UK, 1 April 2010 to 31 March 2016, BY DECLINE GROUP REASON

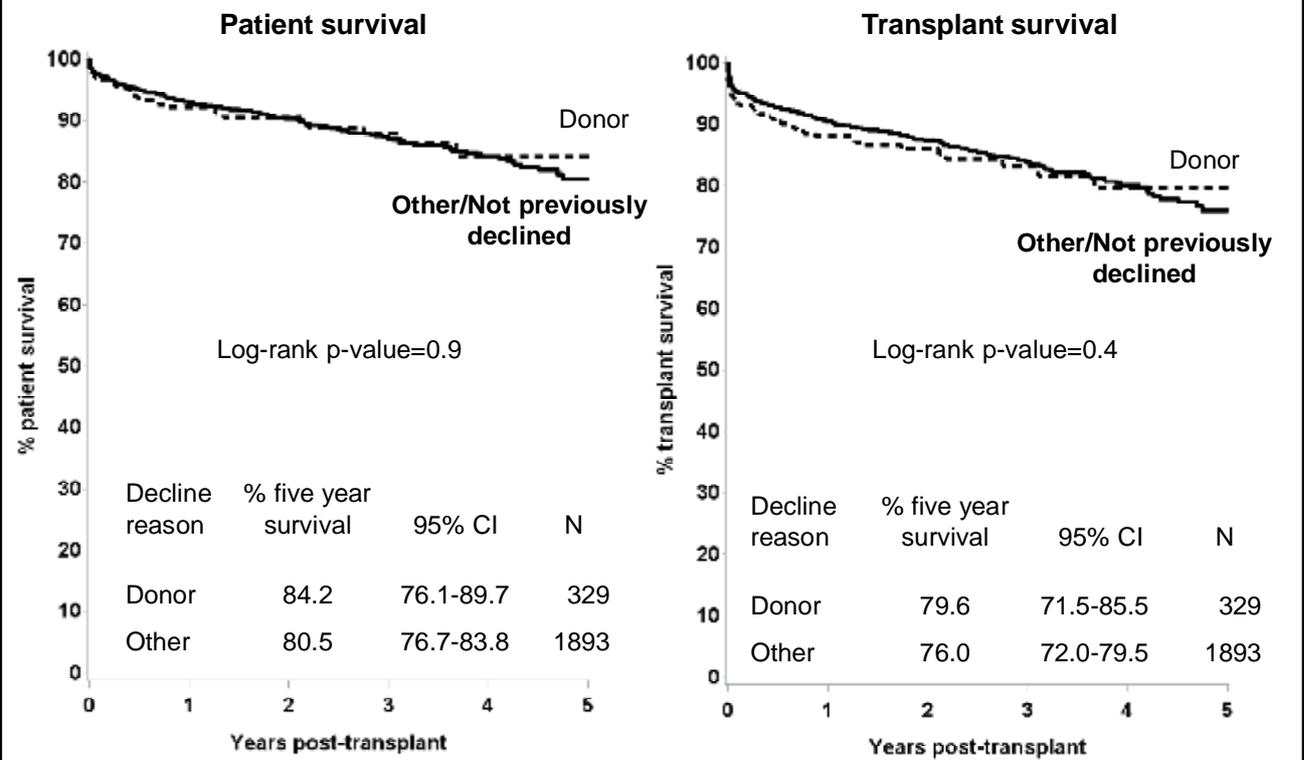


Figure 2 Unadjusted five year patient and transplant survival for first Group 1 adult elective liver only DBD donor transplants in the UK, 1 April 2010 to 31 March 2016, BY FIRST OFFER OUTCOME

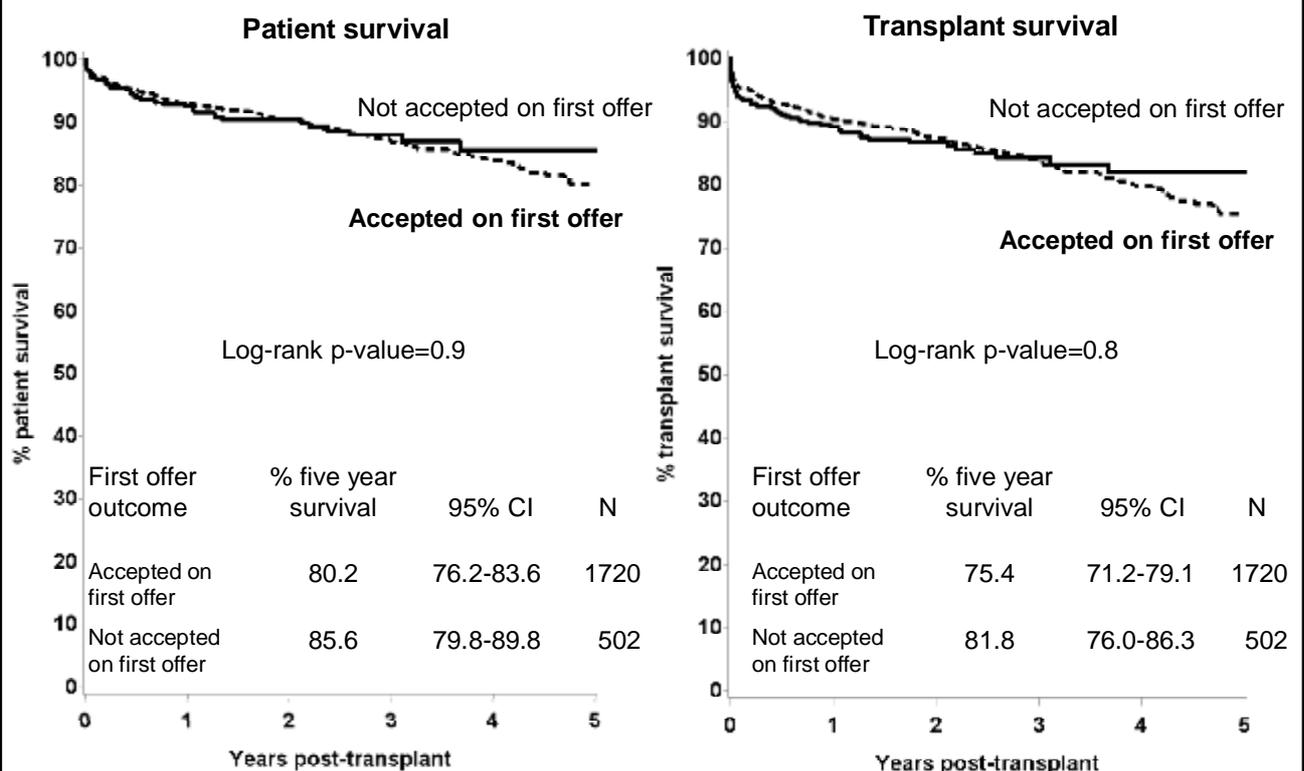


Figure 3 Unadjusted five year patient and transplant survival for first Group 1 adult elective liver only DCD donor transplants in the UK, 1 April 2010 to 31 March 2016, BY DECLINE GROUP REASON

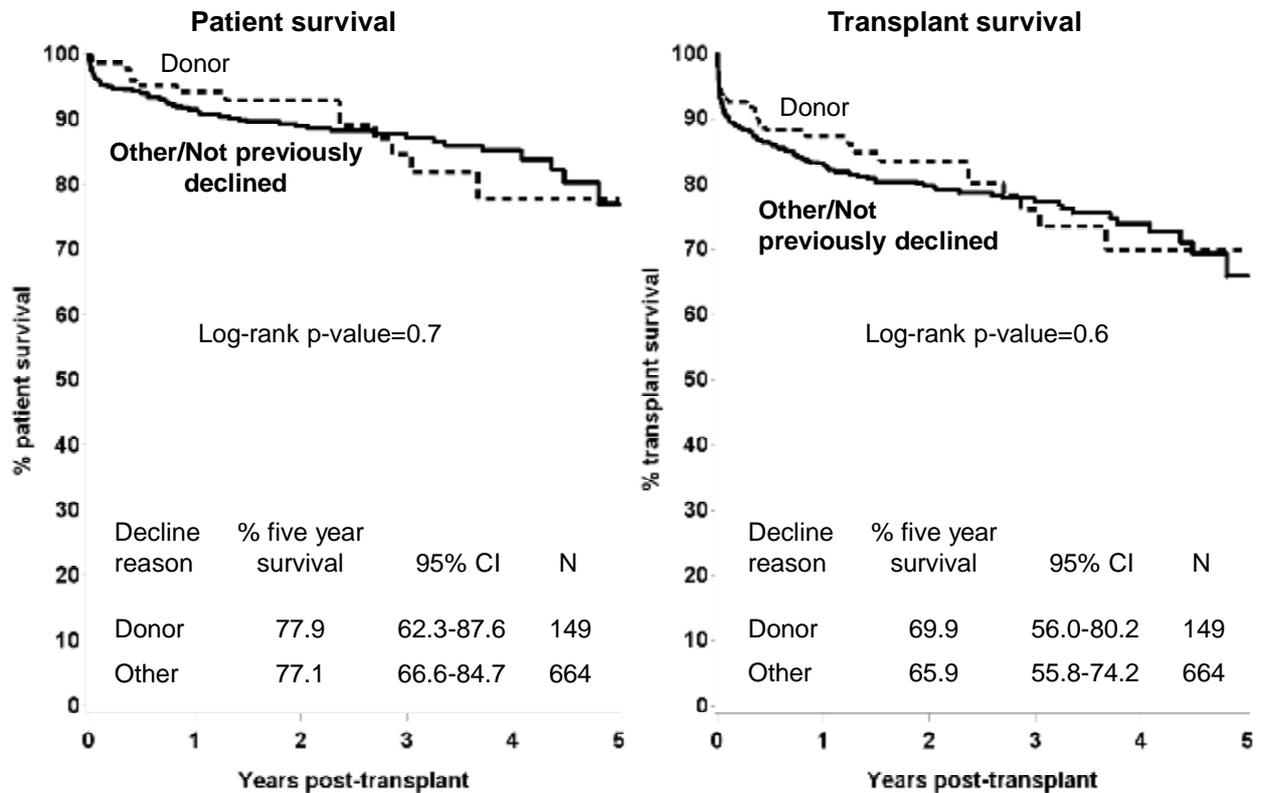
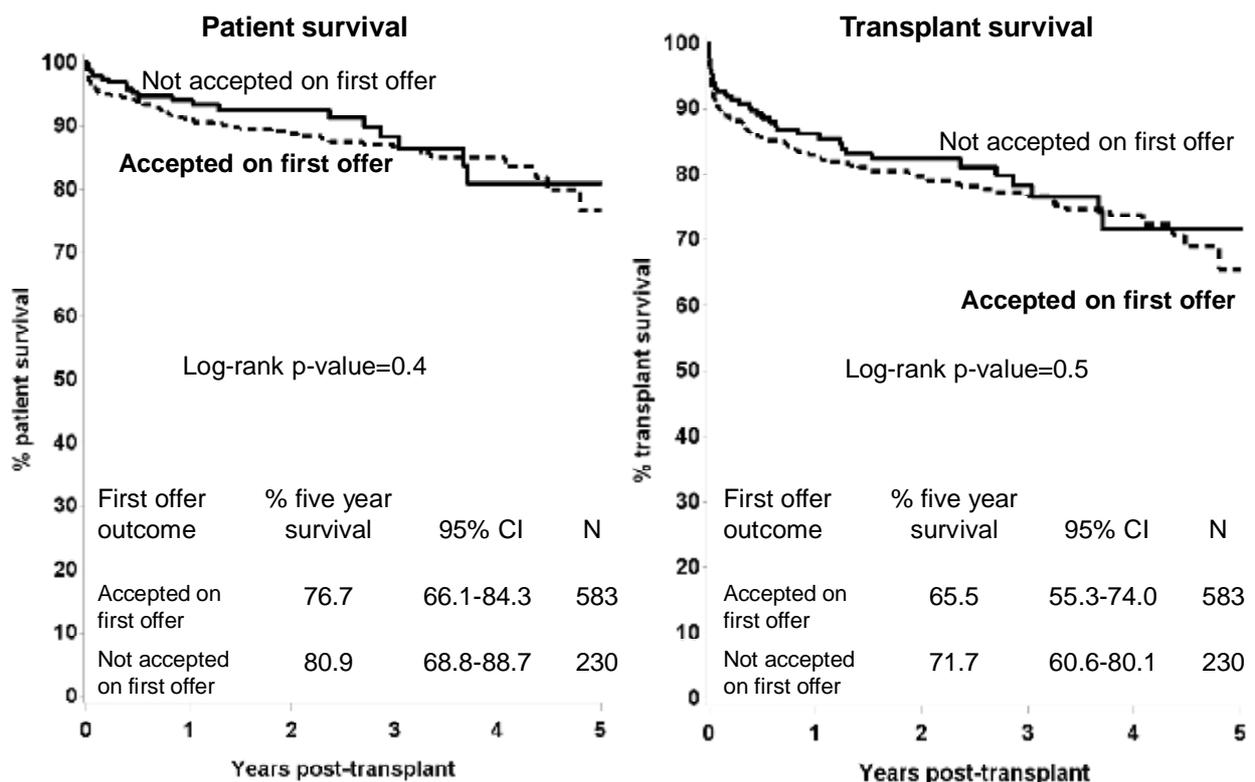


Figure 4 Unadjusted five year patient and transplant survival for first Group 1 adult elective liver only DCD donor transplants in the UK, 1 April 2010 to 31 March 2016, BY FIRST OFFER OUTCOME



Adjusted survival analysis

Donors after brain death

22 **Table 6** shows risk adjusted hazard ratios of patient death and transplant failure by decline reason group and by outcome of first offer, for DBD donors. There is no difference in patient or transplant outcome between 'donor' and 'other/not previously declined' group (p-value= 0.7 and p-value=0.2, respectively). There is also no difference in patient or transplant outcome between 'accepted on first offer' and 'not accepted on first offer' group (p-value= 0.8 and p-value=0.5, respectively).

Factor and its levels	Patient death		Transplant failure	
	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value
DECLINE GROUP				
Donor	1	-	1	-
Other/Not previously declined	0.92 (0.62 - 1.35)	0.7	0.82 (0.59 - 1.13)	0.2
FIRST OFFER OUTCOME				
Accepted on first offer	1	-	1	-
Not accepted on first offer	1.03 (0.74 - 1.45)	0.8	1.11 (0.84 - 1.48)	0.5

¹ Adjusted for the following recipient factors: age at transplant, HCV status, ln(creatinine), ln(INR), albumin, renal replacement therapy and patient location, and the following donor factors: age and history of diabetes

Donors after circulatory death

23 **Table 7** shows risk adjusted hazard ratios of patient death and transplant failure by decline reason group and by outcome of first offer, for DCD donors. There is no difference in patient or transplant outcome between 'donor' and 'other/not previously declined' group (p-value= 0.7 and p-value=0.5, respectively). There is also no difference in patient or transplant outcome between 'accepted on first offer' and 'not accepted on first offer' group (p-value= 0.3 and p-value=0.3, respectively).

Factor and its levels	Patient death		Transplant failure	
	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value
DECLINE GROUP				
Donor	1	-	1	-
Other/Not previously declined	1.12 (0.62 - 2.01)	0.7	1.16 (0.76 - 1.79)	0.5
FIRST OFFER OUTCOME				
Accepted on first offer	1	-	1	-
Not accepted on first offer	0.75 (0.45 - 1.27)	0.3	0.84 (0.58 - 1.21)	0.3

¹ Adjusted for the following recipient factors: age at transplant, HCV status, ln(creatinine), ln(INR), albumin, renal replacement therapy and patient location, and the following donor factors: age and history of diabetes

SUMMARY

- 24 Of the reasons given by centres for the decline of liver offers from DBD donors whose liver was subsequently transplanted, the most common were donor related. This was similar for declined liver offers from DCD donors.
- 25 **Table 8** shows the offer decline rates of each centre. These are further illustrated in funnel plots (**Figure 5** and **Figure 6** of Appendix). Note that these results are somewhat reflective of the size of the centre and the size of their transplant list.

Donor type	Centre offer decline rate						
	Birmingham	Cambridge	Edinburgh	King's College	Leeds	Newcastle	Royal Free
DBD	22%	51%	44%	22%	48%	74%	36%
DCD	23%	37%	56%	19%	49%	80%	44%

- 26 Both unadjusted and risk adjusted survival analyses provided no evidence of a difference in patient or transplant survival up to five years for patients receiving DBD donor livers that were previously declined for donor reasons and patients receiving DBD donor livers that were transplanted on the first offer or previously declined for reasons other than donor related. The results based on DCD donor livers also provided no evidence of a difference. *However, these results should be viewed with some caution as only a small number of patients that received livers that were previously declined for donor reasons experienced an event.*
- 27 Similarly, both unadjusted and risk adjusted analyses provided no evidence of a difference in patient survival up to five years for patients receiving DBD donor livers that were accepted on first offer and patients receiving DBD donor livers that were declined at least once then subsequently transplanted. The results based on DCD donor livers also provided no evidence of a difference. *However, these results should be viewed with some caution as only a small number of patients that received livers that were initially declined experienced an event.*

ACTIONS/SUMMARY

- 28 Members are asked to note that five year survival is now provided, instead of one or two year, as in previous reports.
- 29 Members are also asked to note that both unadjusted and risk adjusted survival analyses are now carried out, instead of only unadjusted survival analysis, as in previous reports.
- 30 Statistics and Clinical Studies is now regularly producing two types of reports that present offer decline data; centre-specific reports on organ offers and the annual report on liver transplantation. The current paper could be regarded as a summary of the centre-specific reports with the added section on survival analysis as LAG requested.

APPENDIX

