

NHS BLOOD AND TRANSPLANT

LIVER ADVISORY GROUP

WAITING TIMES AND DEATHS ON THE LIST BY BLOOD GROUP

SUMMARY

BACKGROUND

- 1 Restrictions in the allocation of livers were introduced in 2006 to reverse the increasingly prolonged waiting time to transplant for blood group O patients. These limited access to blood group O donor livers for elective liver patients of other blood groups. Prior to this, group O livers could be used equally in blood group B patients. This paper reports the median waiting time to elective liver-only transplant and the proportion of patients dying on the transplant list by patient blood group. Some comparisons with super-urgent (SU) patients are also made.

DATA AND METHODS

- 2 Data were obtained from the UK Transplant Registry (UKTR) for all new active Group 1 elective liver only registrations in the UK and Republic of Ireland, 1 April 2012 - 31 March 2015. Multi-organ transplants and registrations ending in living donor liver transplant were excluded. Median waiting time to transplant and post-registration outcomes were compared over patient blood group, financial year of registration and transplant unit. Comparable data for super-urgent patients was also analysed. Earlier registrations were also compared.

RESULTS

- 3 The median waiting time to transplant in 2014/2015, for blood group O adult patients, was double that for blood group B patients (301 and 154 days, respectively), $p=0.001$. No evidence of such a difference was found for adult patients with UKELD score > 62 ($p=0.6$) or for paediatric patients ($p=0.99$). In each of these groups, blood group A and AB patients had much shorter median waiting times (except blood group AB paediatric patients where $N<5$).
- 4 The percentage of blood group O adult patients transplanted within 6-months in 2014/2015 was significantly lower than that of blood group B adult patients (35% and 50%, respectively). By comparison, 59% of group A and 79% of group AB patients were transplanted within 6 months. There was no evidence of any difference in the proportion of adult patients dying on the transplant list within 6 months post registration when comparing blood groups, although by 3 years the death rate was higher for blood group O and B patients than for group A patients.
- 5 Analysis of blood group match between donor and recipient shows that use of O donor livers in elective non-O patients is rare, so little more can be done to limit the waiting times of blood group O patients. The same analysis of super-urgent patients shows that only 62% of O donor livers used for SU patients are used in blood group O patients. In 2014/15, blood group O livers were used in 52 group A patients, 27 group B patients and 3 group AB patients. In 2014/15, 17% of 59 group O SU patients died, compared with 6% of 48 group A SU patients. There were too few B and AB patients for meaningful interpretation.

ACTION

- 6 While death rates on the list at 6 months are comparable across patient blood groups, blood group O elective patients are waiting significantly longer for transplant (10 months) than patients of other blood groups (A: 4 months, B: 5 months, AB: 2½ months) and group O and B patients have a higher death rate on the list than A patients 3 years after listing. Blood group O donor livers are not being used in elective non-O patients, but 9% of all blood group O donor livers transplanted in adult patients are used in non-O SU patients and consideration of priorities in SU allocation is the only means of addressing the poorer access to transplant of elective blood group O patients. LAG are asked to consider whether there is any scope within the SU scheme to limit use of O livers in non-O (or specifically blood group A) patients.

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NHS BLOOD AND TRANSPLANT

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BLOOD GROUP: WAITING TIMES AND DEATHS ON THE TRANSPLANT LIST

INTRODUCTION

1 Restrictions in the allocation of livers were introduced in 2006 as a measure to reverse the increasingly prolonged waiting time to transplant for blood group O patients (see **Appendix 1** for summary of original LAG paper). These restrictions limit access to blood group O donor livers for elective liver patients of other blood groups. Prior to this, blood group O livers could be used equally in blood group B patients.

2 This paper considers the current situation for blood group O patients. It reports the median waiting time to elective liver-only transplant and the proportion of patients dying on the transplant list by patient blood group for the latest three financial years. Some comparisons with super-urgent (SU) patients are also made.

3 The current blood group criteria in the liver allocation policy are as follows:

Blood group O donor livers should be offered in the following priority order:

- 1) Blood group O patients locally*
- 2) Blood group O patients nationally*
- 3) Blood group A, B or AB patients locally
- 4) Blood group A, B or AB patients nationally

** B blood group patients can be considered for liver left lateral segments*

Super-urgent patients take priority in all blood groups

These rules will be waived for fast track liver offers

These rules shall be waived for children under 2 years of age

4 Further, it should be noted that livers offered for SU patients are on the basis of compatible blood groups, with the longest waiting (local then national) patient being prioritised.

DATA AND METHODS

5 Data on all new active Group 1 elective liver only registrations onto the UK liver transplant list between 1 April 2012 and 31 March 2015 were obtained from the UKTR. Registrations for a multi-organ transplant, including intestinal transplants, were excluded from all analyses, as were registrations known to have ended in living donor liver transplant. To gain information about longer term outcomes data were also analysed for registrations for 2009/10, 2010/11, 2011/12.

6 Median waiting times were obtained using Kaplan-Meier methods with transplant as the event and censoring for removal from the list, death or still waiting. Median waiting time to transplant and 6 month post-registration outcomes were compared over patient blood group, financial year of registration and transplant centre for all adult registrations in the results section, for adult registrations for patients with a UKELD score > 62 at time of registration in **Appendix 3**, and finally for paediatric

registrations in **Appendix 4**. The outcome for registrations in each financial year was recorded approximately 6-months after the end of each financial year.

- 7 The donor to recipient ABO match distribution was examined for transplants using livers from DBD and DCD donors, using data on all Group 1 elective liver only transplants in the UK between 1 April 2012 and 31 March 2015, obtained from the UKTR as recorded on 11 October 2015. These data are presented separately for adult transplants, adult transplants for patients with a UKELD score > 62 at time of transplantation (Appendix 3), and for paediatric transplants (Appendix 4).

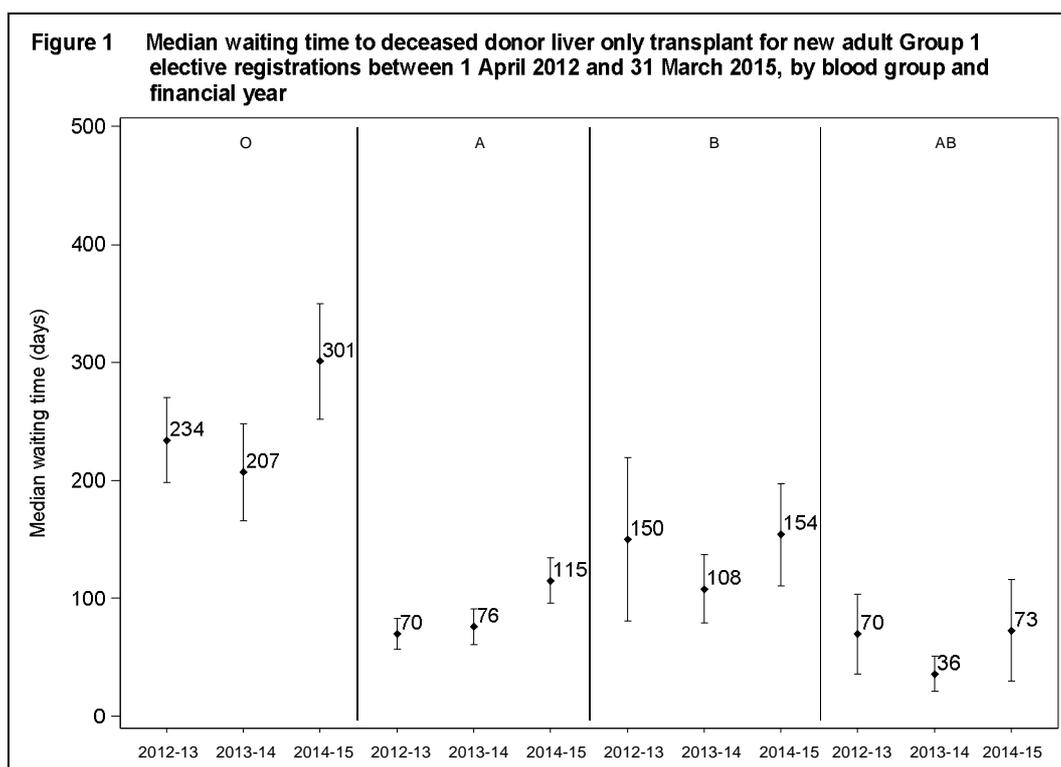
RESULTS

- 8 **Table 1** gives the number of all liver donors, transplant recipients and patients waiting for a liver for the latest financial year, by blood group. At the end of the year, 57% of active patients were blood group O, compared with 48% of donors and 45% of transplant recipients. These figures include SU patients.

Blood group	Donors		Transplant recipients			Active transplant list patients		
	N	(%)	N		(%)	N		(%)
			Elective	SU		Elective	SU	
O	448	(48)	325	50	(45)	347	0	(57)
A	353	(38)	291	46	(40)	179	0	(29)
B	95	(10)	83	9	(11)	79	1	(13)
AB	28	(3)	35	3	(5)	5	0	(1)
TOTAL	924	(100)	734	108	(100)	610	1	(100)

Waiting time to transplant

- 9 The median waiting time to transplant (with 95% confidence intervals) for new adult elective liver only registrations is shown in **Figure 1** by blood group and financial year. This shows that the median waiting time to transplant for all patients, regardless of blood group, has increased in 2014/15 from the previous year. In 2014/2015 the median waiting time to transplant for blood group O patients was twice as long as that for blood group B patients (log-rank test, $p=0.001$), and was significantly longer than waiting times for A and AB patients also.
- 10 **Appendix 2** shows evidence of differences in median waiting times between centres for blood groups O, A, B and AB. Note that due to small numbers in blood group AB the results should be interpreted with caution.



Registration outcome

- 11 Registration outcomes (death, transplant, removal, still waiting) at 6-months post-registration are shown by patient blood group and financial year in **Figure 2**. Removals due to condition deteriorated have been included as deaths in both figures.
- 12 **Comparisons within blood group**
For patients of all blood groups, proportionally fewer registrations resulted in a transplant in 2014/15 relative to earlier years, with some evidence of an increasing proportion dying on the list.
- 13 **Comparisons between blood groups**
 - In 2014/2015, there was a statistically significant difference observed between blood groups in the proportion of patients transplanted within 6 months of registration (chi-squared test, $p < 0.0001$). There was no statistical difference in the proportion of deaths (chi-squared test, $p = 0.3$).
 - Significantly fewer blood group O patients were transplanted within 6 months of listing in 2014/2015 relative to group B patients (chi-squared test $p = 0.002$).
- 14 To gain a longer term understanding of outcomes from registration, Figure 2 was repeated for three year outcomes for earlier years (2009/10, 2010/11, 2011/12). This showed (**Figure 3**) that death rates are higher in blood group O and B patients than in A and AB patients. For patients registered in the most recent year (2011/12), 18% of group O and B patients had died without transplant within three years of being listed. This compares with 13% of group A patients. The proportion removed from the list was also higher in O and B patients.
- 15 Finally, in looking at outcome for SU patients listed in 2014/15, it was noted that 17% of 59 group O SU patients died without transplant, compared with 6% of 48 group A SU patients. There were too few B and AB patients for meaningful interpretation.

Figure 2 6-month registration outcome for new adult Group 1 elective liver only registrations between 1 April 2012 and 31 March 2015, by blood group and financial year

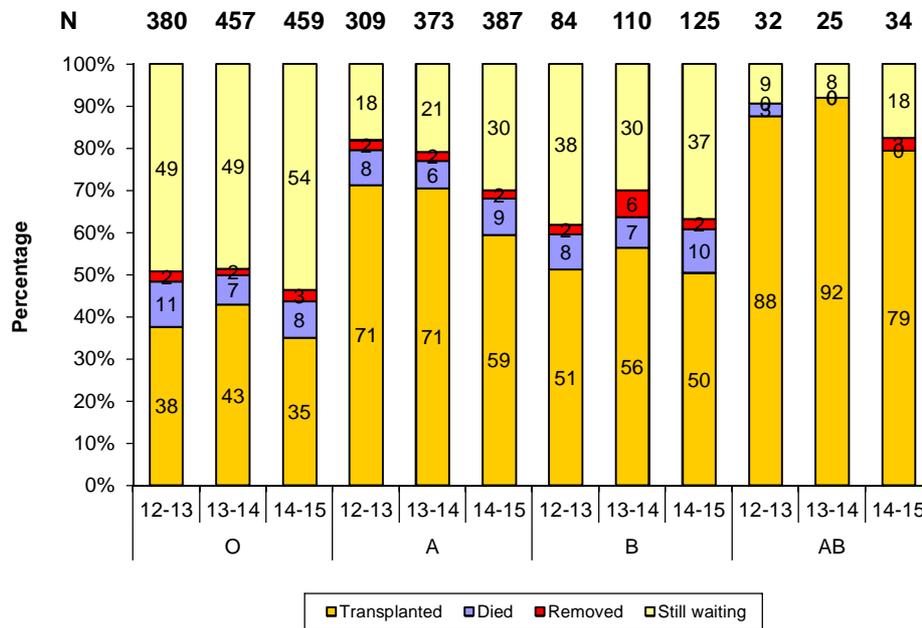
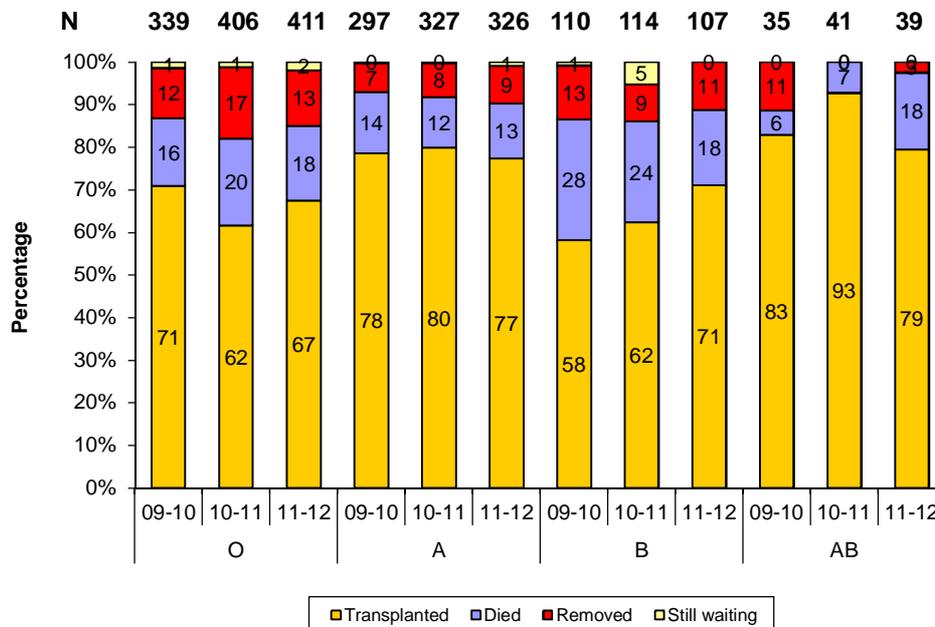


Figure 3 3 year registration outcome for new adult Group 1 elective liver only registrations between 1 April 2009 and 31 March 2012, by blood group and financial year



Donor - recipient blood group match distribution

- 16 **Table 2** shows the donor to recipient ABO blood group match for adult elective liver only transplants using livers from deceased donors split by DBD and DCD donors. This is also shown for super-urgent transplants for comparison in **Table 3**. While use of O donor livers in elective non-O recipients is rare, use is more common in the SU transplant scenario in line with the allocation policy. In total, 9% of all blood group O donor livers transplanted in adult patients are used in non-O SU patients.

Donor type	Donor blood group	Recipient blood group								Total
		O		A		B		AB		
		N	%	N	%	N	%	N	%	
DBD	O	682	99	3	0	3	0	0	0	688
	A	0	0	665	98	0	0	14	2	679
	B	0	0	0	0	198	100	0	0	198
	AB	0	0	2	3	0	0	63	97	65
	Total	682	42	670	41	201	12	77	5	1630
DCD	O	196	98	2	1	1	1	0	0	199
	A	0	0	190	96	0	0	7	4	197
	B	0	0	0	0	48	98	1	2	49
	AB	0	0	0	0	0	0	6	100	6
	Total	196	43	192	43	49	11	14	3	451

Donor type	Donor blood group	Recipient blood group								Total
		O		A		B		AB		
		N	%	N	%	N	%	N	%	
DBD	O	133	62	52	24	27	13	3	1	215
	A	2	3	59	95	0	0	1	2	62
	B	1	6	0	0	15	83	2	11	18
	AB	0	0	0	0	1	50	1	50	2
	Total	136	46	111	37	43	14	7	2	297
DCD	O	1	33	1	33	1	33	0	0	3
	A	0	-	0	-	0	-	0	-	0
	B	0	-	0	-	0	-	0	-	0
	AB	0	-	0	-	0	-	0	-	0
	Total	1	33	1	33	1	33	0	0	3

SUMMARY

- 17 The median waiting time to transplant in 2014/2015, for blood group O adult patients, was double that for blood group B patients (301 and 154 days, respectively), $p=0.001$. No evidence of such a difference was found for adult patients with UKELD score > 62 ($p=0.6$) or for paediatric patients ($p=0.99$). In each of these groups, blood group A and AB patients had much shorter median waiting times (except blood group AB paediatric patients where $N<5$).
- 18 The percentage of blood group O adult patients transplanted within 6-months in 2014/2015 was significantly lower than that of blood group B adult patients (35% and 50%, respectively). By comparison, 59% of group A and 79% of group AB patients were transplanted within 6 months. There was no evidence of any difference in the proportion of adult patients dying on the transplant list within 6 months post registration when comparing blood groups. Death rates at 3 years post listing are higher in blood group O and B patients than group A patients.
- 19 Analysis of blood group match between donor and recipient shows that use of O donor livers in elective non-O patients is rare, so little more can be done to limit the waiting times of blood group O patients. The same analysis of super-urgent patients shows that only 62% of O donor livers used for SU patients are used in blood group O patients. In 2014/15, 17% of 59 group O SU patients died, compared with 6% of 48 group A SU patients. There were too few B and AB patients for meaningful interpretation.

ACTION

- 20 While death rates on the list at 6 months are comparable across patient blood groups, group O elective patients wait significantly longer for transplant (10 months) than other patients (A: 4 months, B: 5 months, AB: 2½ months) and O and B patients have a higher death rate than A patients 3 years after listing. Blood group O donor livers are not being used in elective non-O patients, but 9% of all blood group O donor livers transplanted in adult patients are used in non-O SU patients and consideration of priorities in SU allocation is the only means of addressing access to transplant of elective blood group O patients. LAG are asked to consider whether there is any scope within the SU scheme to limit use of O livers in non-O (or specifically blood group A) patients.

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APPENDIX 1

Summary of results from the LAG paper entitled “Blood group O patients” (Ref: LAG(06)10) presented to the LAG meeting on 26 April 2006

This paper reported on changes in the median waiting time to first adult elective liver only transplant for patients with different blood groups registered between 1 January 2001 and 31 December 2004. The data were analysed in two cohorts; 2001-2002 and 2003-2004.

Unadjusted median waiting time to first transplant for 868 and 991 new active adult Group 1 elective registrations onto the liver transplant list in 2001-2002 and 2003-2004, respectively, were analysed by blood group. Registration outcomes at 12-months post-registration for 1,026 and 1,169 new active adult Group 1 elective registrations in 2001-2002 and 2003-2004, respectively, were analysed to examine the proportion of deaths and transplants on the liver transplant list. To examine the donor to recipient ABO match distribution, data were obtained on 890 and 860 adult deceased donors after brain death transplants performed in the UK in 2001-2002 and 2003-2004, respectively.

In 2003-2004, blood group O patients waited significantly longer to transplant than blood group A, B and AB patients; 132 days (95% Confidence Interval (CI) 108-156 days) compared with 73 days (95% CI 64-82 days), 41 days (95% CI 32-50 days) and 31 days (95% CI 16-46 days), respectively. These differences in median waiting time were not apparent in the earlier time period where blood group O patients waited 80 days (95% CI 70-90 days) compared with 57 days (95% CI 44-70 days), 82 days (95% CI 65-99 days) and 33 days (95% CI 24-42 days) for blood group, A, B and AB patients, respectively.

In 2003-2004, a smaller proportion of blood group O patients were transplanted and a larger proportion had died after one year of registration compared with patients of other blood groups, as shown below. These differences were not evident in the earlier time period.

	Recipient blood group				Chi-squared p-value
	O	A	B	AB	
Number of registrations	530	466	123	50	
% transplanted at 12 months post-registration	70	82	83	88	<0.0001
% died at 12 months post-registration	13	7	7	8	<0.01

For elective transplants, 4% of blood group O donor livers were used for non-O recipients in 2003-2004 compared with 3% in 2001-2002. A slightly smaller proportion of liver donors were blood group O in 2003-2004, 48% compared with 51% in 2001-2002.

APPENDIX 2 – Adult registrations

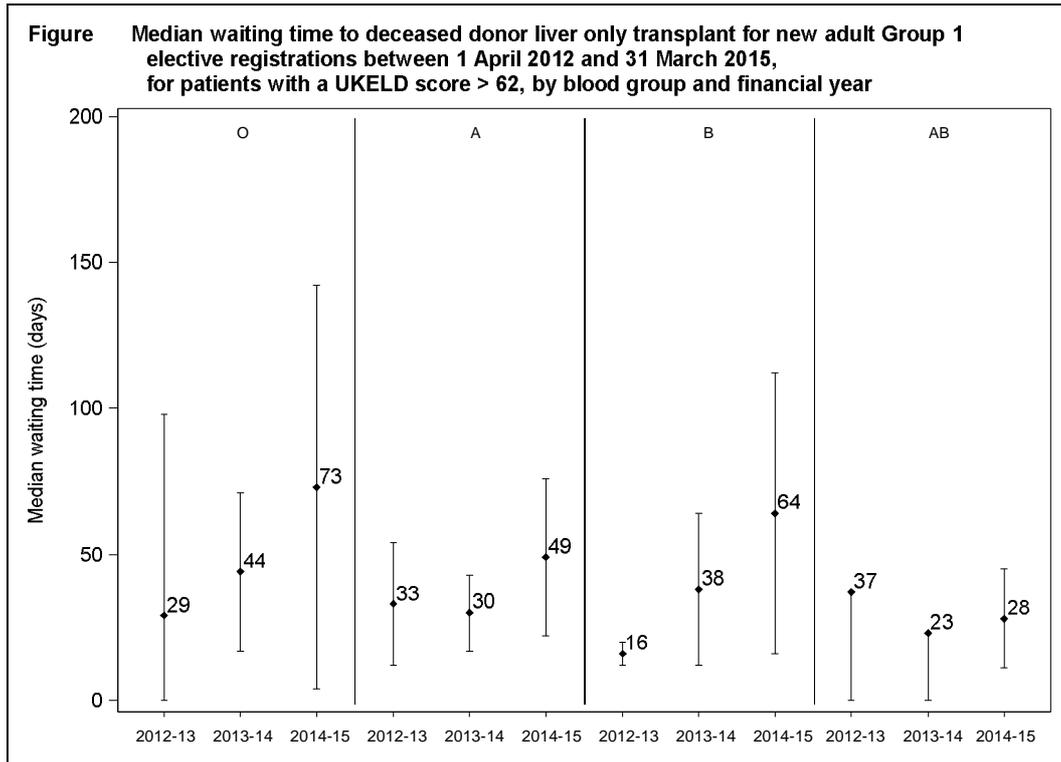
Table Median waiting time to deceased donor liver only transplant for new adult Group 1 elective registrations between 1 April 2012 and 31 March 2015, by blood group and transplant centre					
Blood Group	Transplant centre	No. registrations	Median waiting time (days)	log-rank test p-value	
			95% CI		
O	Birmingham	284	193	(136 - 250)	0.02
	Cambridge	136	230	(134 - 326)	
	Dublin	94	203	(113 - 293)	
	Edinburgh	148	208	(155 - 261)	
	King's College	251	308	(272 - 344)	
	Leeds	179	234	(85 - 383)	
	Newcastle	68	259	(188 - 330)	
	Royal Free	136	219	(128 - 310)	
	OVERALL	1296	243	(219 - 267)	
A	Birmingham	260	69	(51 - 87)	<0.0001
	Cambridge	121	82	(27 - 137)	
	Dublin	56	87	(53 - 121)	
	Edinburgh	96	30	(12 - 48)	
	King's College	221	115	(98 - 132)	
	Leeds	150	67	(44 - 90)	
	Newcastle	46	80	(41 - 119)	
	Royal Free	119	131	(104 - 158)	
	OVERALL	1069	86	(77 - 95)	
B	Birmingham	63	129	(86 - 172)	<0.0001
	Cambridge	28	109	(66 - 152)	
	Dublin	18	190	(75 - 305)	
	Edinburgh	46	57	(38 - 76)	
	King's College	70	192	(128 - 256)	
	Leeds	38	122	(12 - 232)	
	Newcastle	15	133	(77 - 189)	
	Royal Free	41	378	(99 - 657)	
	OVERALL	319	134	(105 - 163)	
AB	Birmingham	27	74	(37 - 111)	0.02
	Cambridge	11	32	(21 - 43)	
	Dublin	6	147	(12 - 282)	
	Edinburgh	8	21	(4 - 38)	
	King's College	13	51	(0 - 107)	
	Leeds	14	64	(3 - 125)	
	Newcastle	4	81	(20 - 142)	
	Royal Free	8	130	(74 - 186)	
	OVERALL	91	56	(26 - 86)	

Outcome as at 11 October 2015

APPENDIX 3 - Adult registrations for patients with a UKELD score > 62

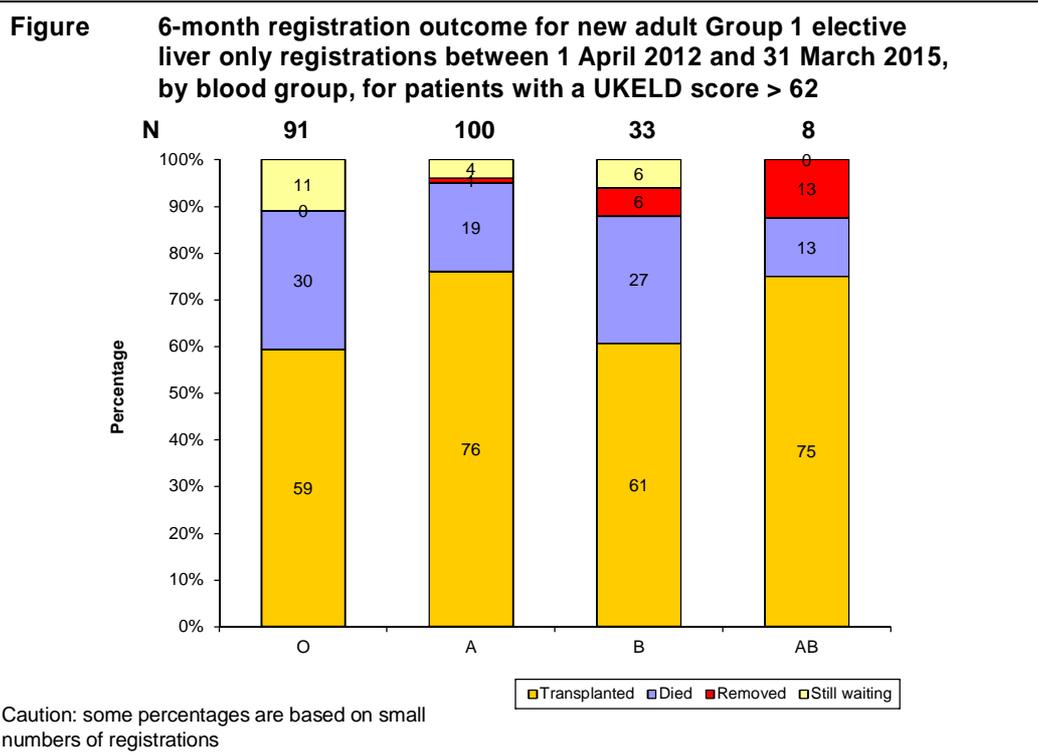
Waiting time to transplant

Note that median waiting times and 95% confidence intervals (CIs) could not be calculated in some cases due to small numbers of registrations in this cohort of patients, in particular for blood group AB patients. The outcome for registrations in each financial year was recorded approximately 6-months after the end of each financial year. In 2014/2015 there was no evidence of differences in median waiting time to transplant for blood group O patients compared with blood group B patients (log-rank test, $p=0.63$).



Registration outcome

Registration outcomes (death, transplant, removal, still waiting) at 6-months post-registration are shown by patient blood group, for patients with a UKELD score > 62 at time of registration. Removals due to condition deteriorated have been included as deaths in both figures. Caution should be taken when interpreting some of the percentages as they are based on small numbers of registrations, in particular for blood group AB.



Donor to recipient ABO match distribution

The **Table** below shows the donor to recipient ABO blood group match for Group 1 adult elective liver only transplants using livers from deceased donors split by DBD donors and DCD donors, for patients with a UKELD score > 62 at time of transplantation.

Table ABO blood group match for Group 1 adult elective liver only transplants using livers from deceased donors, 1 April 2012 - 31 March 2015, by donor type, for patients with a UKELD score > 62¹

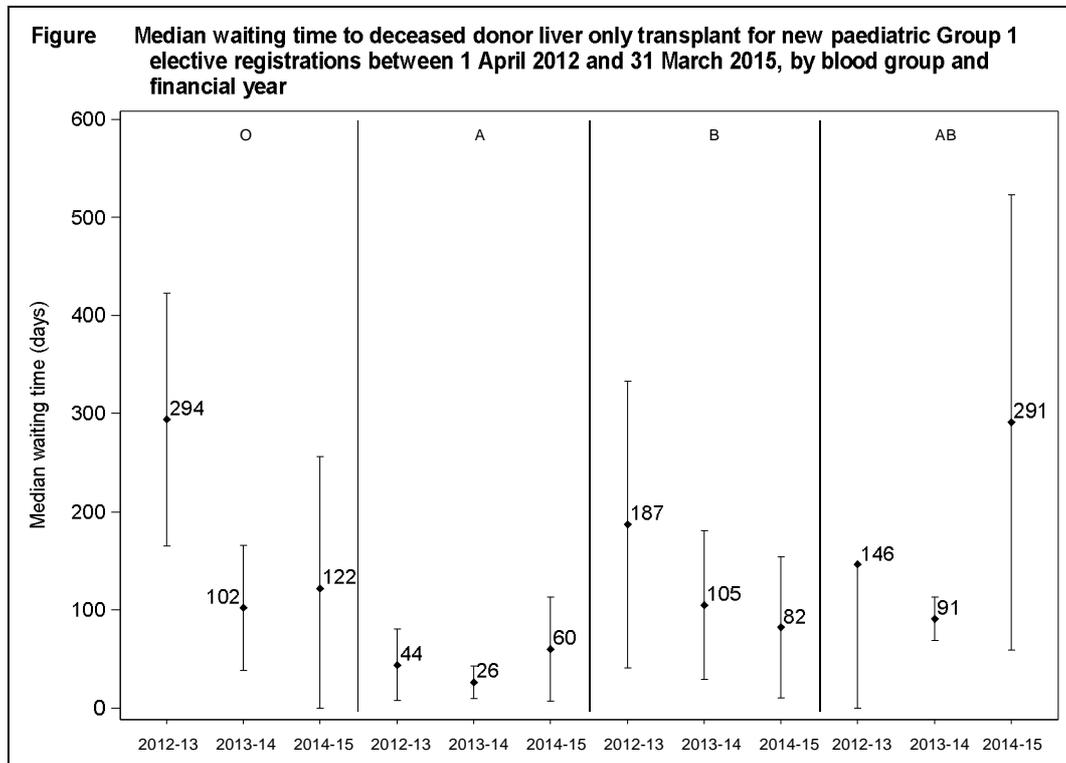
Donor type	Donor blood group	Recipient blood group								Total
		O		A		B		AB		
		N	%	N	%	N	%	N	%	
DBD	O	74	99	1	1	0	0	0	0	75
	A	0	0	74	99	0	0	1	1	75
	B	0	0	0	0	23	100	0	0	23
	AB	0	0	0	0	0	0	6	100	6
	Total	74	41	75	42	23	13	7	4	179
DCD	O	14	93	1	7	0	0	0	0	15
	A	0	0	6	100	0	0	0	0	6
	B	0	0	0	0	2	100	0	0	2
	AB	0	-	0	-	0	-	0	-	0
	Total	14	61	7	30	2	9	0	0	23

¹ UKELD score calculated at time of transplantation

APPENDIX 4 - Paediatric registrations

Waiting time to transplant

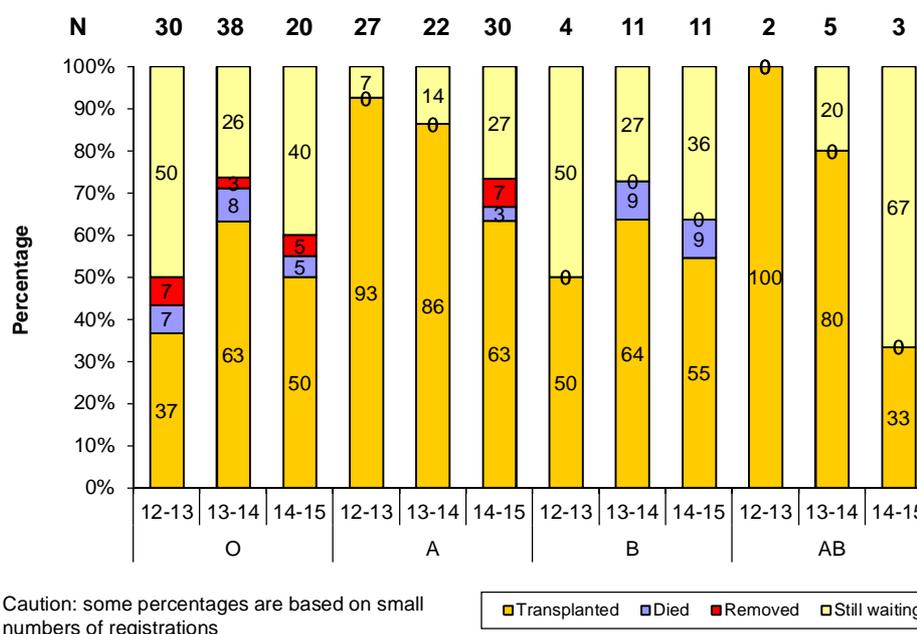
Note that the small numbers of registrations in each blood group means that some caution should be taken when interpreting the median waiting times. In 2014/2015 there was no evidence of differences in median waiting time to transplant for blood group O patients compared with blood B patients (log-rank test, $p=0.99$).



Registration outcome

Registration outcomes (death, transplant, removal, still waiting) at 6-months post-registration are shown by patient blood group and financial year. Removals due to condition deteriorated have been included as deaths in both figures. Caution should be taken when interpreting some of the percentages as they are based on small numbers of registrations, in particular for blood group AB.

Figure 6-month registration outcome for new paediatric Group 1 elective liver only registrations between 1 April 2012 and 31 March 2015, by blood group and financial year



Donor to recipient ABO match distribution

The **Table** below shows the donor to recipient ABO blood group match for Group 1 paediatric elective liver only transplants using livers from deceased donors split by DBD donors and DCD donors.

Table		ABO blood group match for Group 1 paediatric elective liver only transplants using livers from deceased donors, 1 April 2012- 31 March 2015, by donor type								Total
Donor type	Donor blood group	Recipient blood group								
		O		A		B		AB		
		N	%	N	%	N	%	N	%	
DBD	O	64	85	7	9	4	5	0	0	75
	A	3	4	63	90	0	0	4	6	70
	B	0	0	0	0	17	100	0	0	17
	AB	0	0	0	0	0	0	3	100	3
	Total		67	41	70	42	21	13	7	4
DCD	O	4	80	0	0	0	0	1	20	5
	A	0	0	4	100	0	0	0	0	4
	B	0	-	0	-	0	-	0	-	0
	AB	0	-	0	-	0	-	0	-	0
	Total		4	44	4	44	0	0	1	11