

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 2013 - 31 March 2016. 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 In 2015/2016, the median waiting time to transplant for blood group O patients was over a quarter longer than for blood group B patients (208 and 153 days, respectively), $p=0.1$. No evidence of such a difference was found for adult patients with UKELD score > 62 ($p=0.85$). Group B paediatric patients waited longer than group O paediatric patients ($p=0.03$). 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 2015/2016 was significantly lower than that of blood group B adult patients (43% and 52%, respectively). By comparison, 69% of group A and 86% of group AB patients were transplanted within 6 months. The proportion of deaths ranged from 6% to 12% of adult patients on the transplant list within 6 months post registration across the blood groups. Death rates at 3 years post listing are higher in blood group O and B patients than group A and AB 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 57% of O donor livers used for SU patients are used in blood group O patients. 80% of SU adult patients listed in 2015/16 were transplanted, 16% were removed and 3% died.
- 6 While death rates on the list at 6 months are comparable across patient blood groups, group O elective patients wait longer for transplant (median of 7 months) than other patients (A: 2½ months, B: 5 months, AB: 2¾ months) and O and B patients have a higher death rate than A and AB patients 3 years after listing. Blood group O donor livers are very rarely being used in elective non-O patients, but 10% 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. (See LAG(16)9 and LAG(M)(16)1).

ACTION

- 7 This paper is presented for information of LAG members.

Cathy Hopkinson, Statistics and Clinical Studies

November 2016

NHS BLOOD AND TRANSPLANT

LIVER ADVISORY GROUP

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 2013 and 31 March 2016 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 2010/11, 2011/12, 2012/13.
- 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 2013 and 31 March 2016, obtained from the UKTR as recorded on 24 October 2016. 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**).

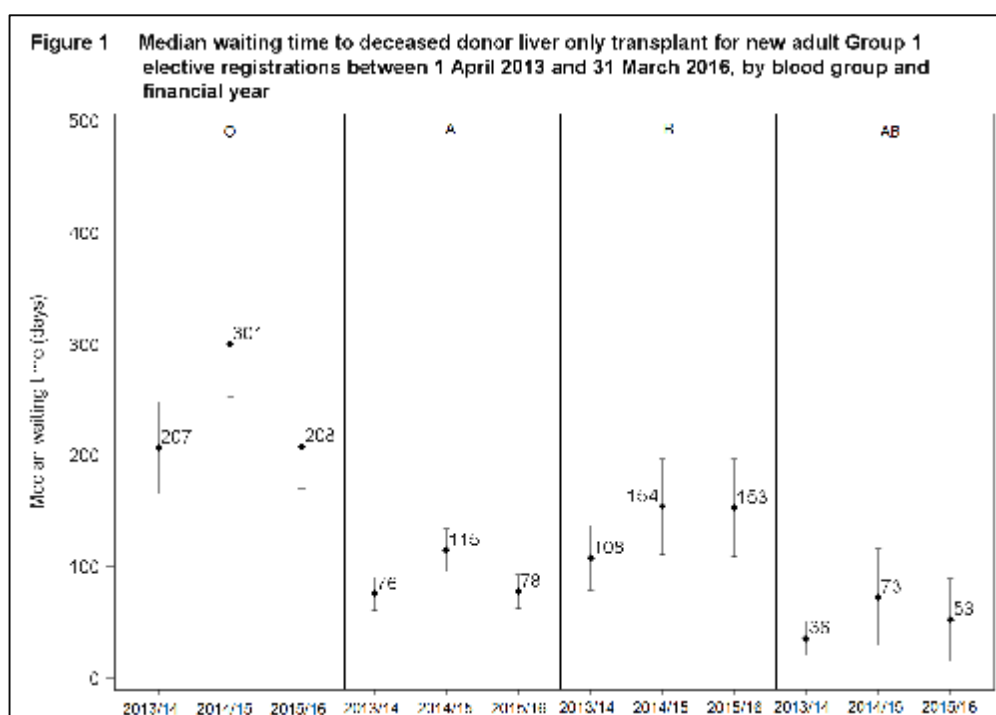
RESULTS

- 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, 64% of active patients were blood group O, compared with 47% of donors and 40% 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	473	(47)	307	48	(40)	375	0	(64)
A	420	(42)	353	40	(45)	126	0	(22)
B	95	(9)	83	15	(11)	80	0	(14)
AB	23	(2)	28	4	(4)	2	1	(1)
TOTAL	1011	(100)	771	107	(100)	583	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 decreased in 2015/16 from the previous year. In 2015/2016, the median waiting time to transplant for blood group O patients was over a quarter longer than for blood group B patients (log-rank test, $p=0.1$), 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 2015/16 relative to earlier years, with some evidence of an increasing proportion dying on the list.
- 13 **Comparisons between blood groups**
- In 2015/2016, 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, $p = 0.3$).
 - Blood group O patients transplanted within 6 months of listing in 2015/2016 relative to group B patients was not significant (chi-squared test $p = 0.1$).
- 14 To gain a longer term understanding of outcomes from registration, **Figure 2** was repeated for three year outcomes for earlier years (2010/11, 2011/12, 2012/13). 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 (2012/13), 14% of group B and 16% of group O had died without transplant within three years of being listed. This compares with 10% 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 2015/16, 4% of 50 group O SU patients died without transplant, compared with 2% of 53 group A SU patients. There were too few B and AB patients for meaningful interpretation. 80% of SU patients listed in 2015/16 were transplanted, 16% were removed and 3% died.

Figure 2 6-month registration outcome for new adult Group 1 elective liver only registrations between 1 April 2013 and 31 March 2016, by blood group and financial year

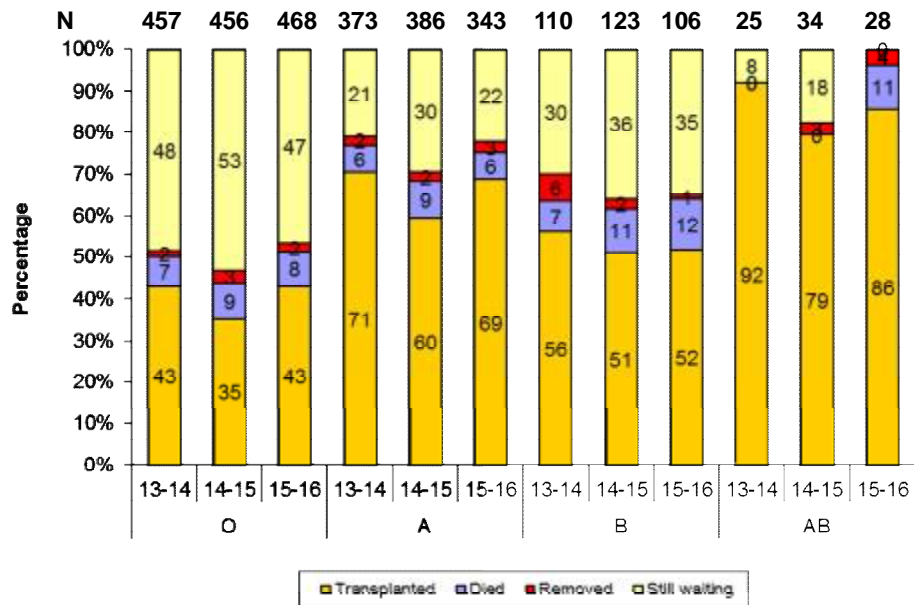
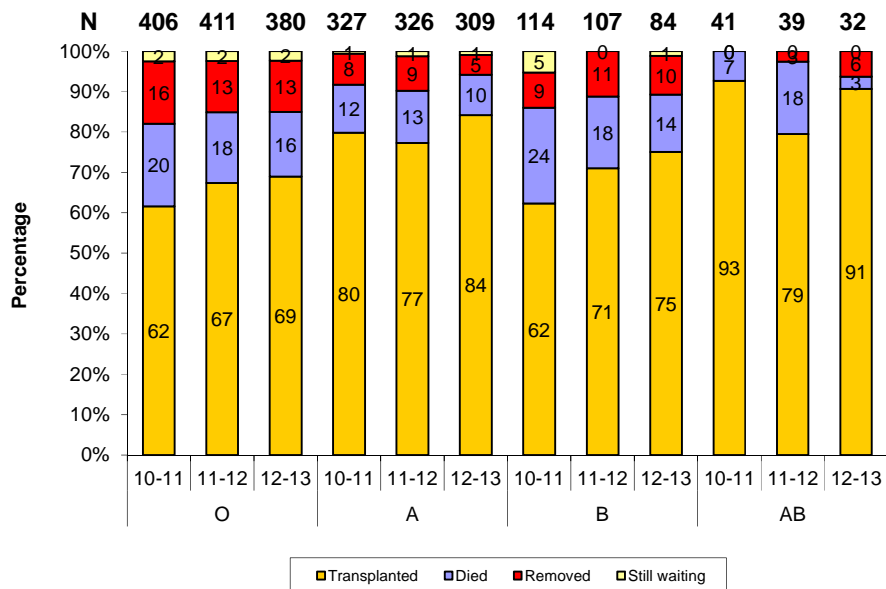


Figure 3 3 year registration outcome for new adult group 1 elective liver only registrations between 1 April 2010 and 31 March 2013, by blood group and financial year



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, 10% 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	695	99	4	1	5	1	0	0	704
	A	0	0	689	98	0	0	16	2	705
	B	0	0	0	0	200	96	1	1	201
	AB	0	0	2	4	0	0	55	96	57
	Total	695	42	695	42	205	12	72	4	1667
DCD	O	234	98	2	1	2	1	0	0	238
	A	1	0	217	98	0	0	3	1	221
	B	0	0	0	0	51	98	1	2	52
	AB	0	0	0	0	0	0	7	100	7
	Total	235	45	219	42	53	10	11	2	518

Donor type	Donor blood group	Recipient blood group								Total
		O		A		B		AB		
		N	%	N	%	N	%	N	%	
DBD	O	127	57	61	28	30	14	3	1	221
	A	2	3	65	96	0	0	1	1	68
	B	1	8	0	0	10	77	2	15	13
	AB	0	0	0	0	0	0	0	0	0
	Total	130	43	126	42	40	13	6	2	302
DCD	O	3	50	0	0	2	33	1	17	6
	A	0	0	0	0	0	0	0	0	0
	B	0	0	0	0	0	0	0	0	0
	AB	0	0	0	0	0	0	0	0	0
	Total	3	50	0	0	2	33	1	17	6

SUMMARY

- 17 The median waiting time to transplant in 2015/2016, for blood group O adult patients, was roughly a quarter longer than that for blood group B patients (208 and 153 days, respectively), $p=0.1$. No evidence of such a difference was found for adult patients with UKELD score > 62 ($p=0.85$) although there was a difference for paediatric patients ($p=0.03$) where group B patients waited longer. 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 2015/2016 was significantly lower than that of blood group B adult patients (43% and 52%, respectively). By comparison, 69% of group A and 86% of group AB patients were transplanted within 6 months. The proportion of deaths ranged from 6% to 12% of adult patients on the transplant list within 6 months post registration across the blood groups. Death rates at 3 years post listing are higher in blood group O and B patients than group A and AB 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 57% of O donor livers used for SU patients are used in blood group O patients. 80% of SU adult patients listed in 2015/16 were transplanted, 16% were removed and 3% died.
- 20 While death rates on the list at 6 months are comparable across patient blood groups, group O elective patients wait longer for transplant (median of 7 months) than other patients (A: 2½ months, B: 5 months, AB: 2¾ months) and O and B patients have a higher death rate than A and AB patients 3 years after listing. Blood group O donor livers are very rarely being used in elective non-O patients, but 10% 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. (See LAG(16)9 and LAG(M)(16)1).

ACTION

- 21 This paper is presented for information of LAG members.

Cathy Hopkinson
Statistics and Clinical Studies

November 2016

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 2013 and 31 March 2016, 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	311	165	(126 - 204)	0.0003
	Cambridge	154	218	(146 - 290)	
	Dublin	100	203	(121 - 285)	
	Edinburgh	154	200	(145 - 255)	
	King's College	271	340	(305 - 375)	
	Leeds	196	261	(121 - 401)	
	Newcastle	68	259	(213 - 305)	
	Royal Free	127	161	(94 - 228)	
	OVERALL	1381	234	(211 - 257)	
A	Birmingham	270	63	(46 - 80)	<0.0001
	Cambridge	129	69	(34 - 104)	
	Dublin	53	85	(58 - 112)	
	Edinburgh	106	33	(21 - 45)	
	King's College	234	137	(122 - 152)	
	Leeds	139	50	(31 - 69)	
	Newcastle	47	80	(41 - 119)	
	Royal Free	124	149	(95 - 203)	
	OVERALL	1102	88	(79 - 97)	
B	Birmingham	73	149	(103 - 195)	<0.0001
	Cambridge	26	199	(29 - 369)	
	Dublin	24	154	(82 - 226)	
	Edinburgh	50	52	(39 - 65)	
	King's College	70	220	(153 - 287)	
	Leeds	34	122	(82 - 162)	
	Newcastle	17	133	(98 - 168)	
	Royal Free	45	172	(108 - 236)	
	OVERALL	339	134	(107 - 161)	
AB	Birmingham	26	60	(31 - 89)	0.04
	Cambridge	9	74	(18 - 130)	
	Dublin	5*	-	-	
	Edinburgh	8	21	(4 - 38)	
	King's College	13	51	(6 - 96)	
	Leeds	16	60	(6 - 114)	
	Newcastle	3*	-	-	
	Royal Free	7*	-	-	
	OVERALL	87	53	(37 - 69)	

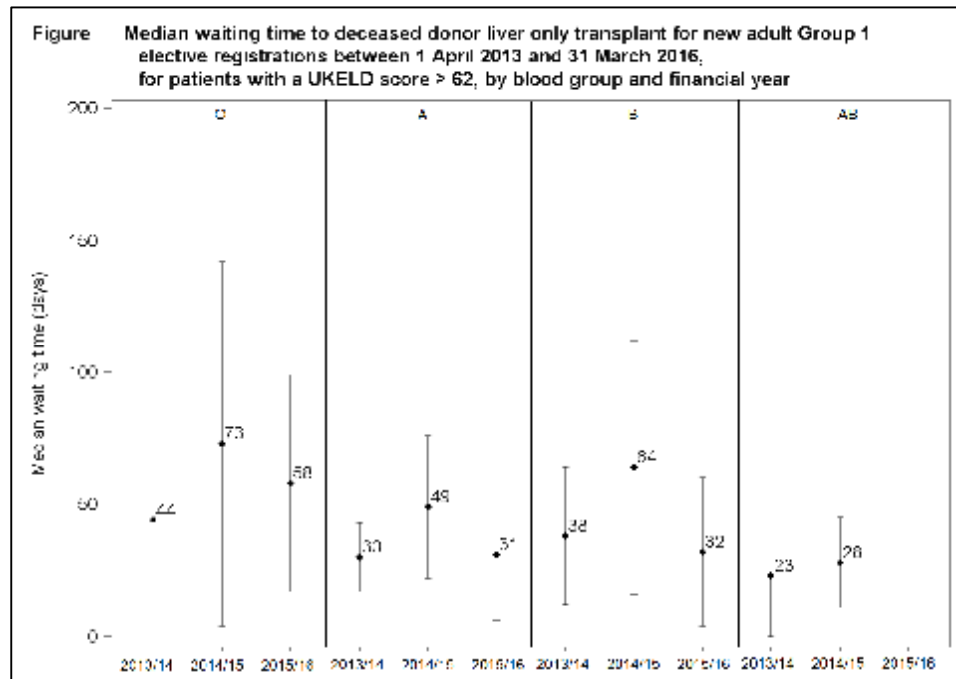
Outcome as at 21 October 2016

* Median and 95% CI are not presented for n < 8

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

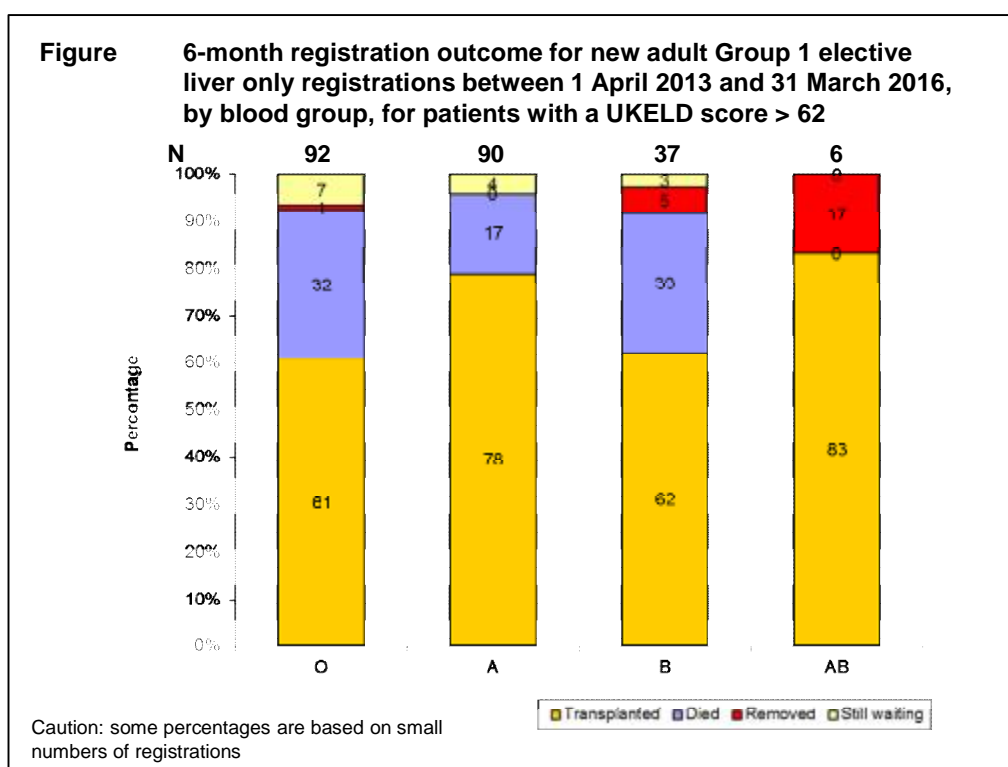
Waiting time to transplant

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 2015/2016 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, $p=0.85$).



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 2013 - 31 March 2016, by donor type, for patients with a UKELD score > 62¹

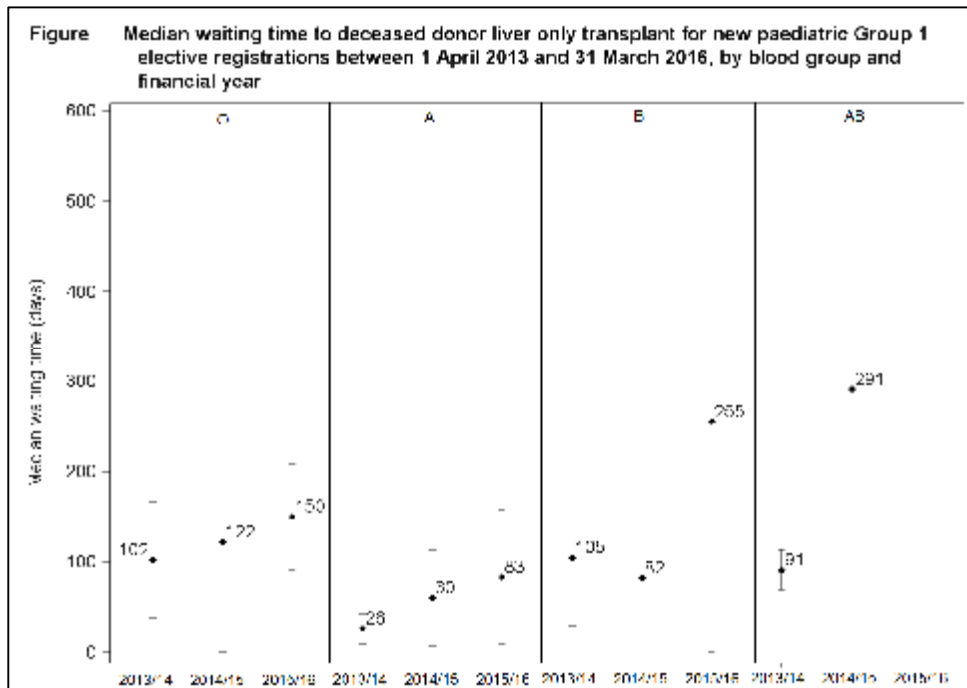
Donor type	Donor blood group	Recipient blood group								Total
		O		A		B		AB		
		N	%	N	%	N	%	N	%	
DBD	O	89	98	1	1	1	1	0	0	91
	A	0	0	68	100	0	0	0	0	68
	B	0	0	0	0	22	100	0	0	22
	AB	0	0	0	0	0	0	5	100	5
	Total		89	48	69	37	23	12	5	3
DCD	O	14	93	1	7	0	0	0	0	15
	A	0	0	7	100	0	0	0	0	7
	B	0	0	0	0	2	100	0	0	2
	AB	0	0	0	0	0	0	0	0	0
	Total		14		8		2		0	0

¹ UKELD score calculated at time of transplantation

APPENDIX 4 - Paediatric registrations

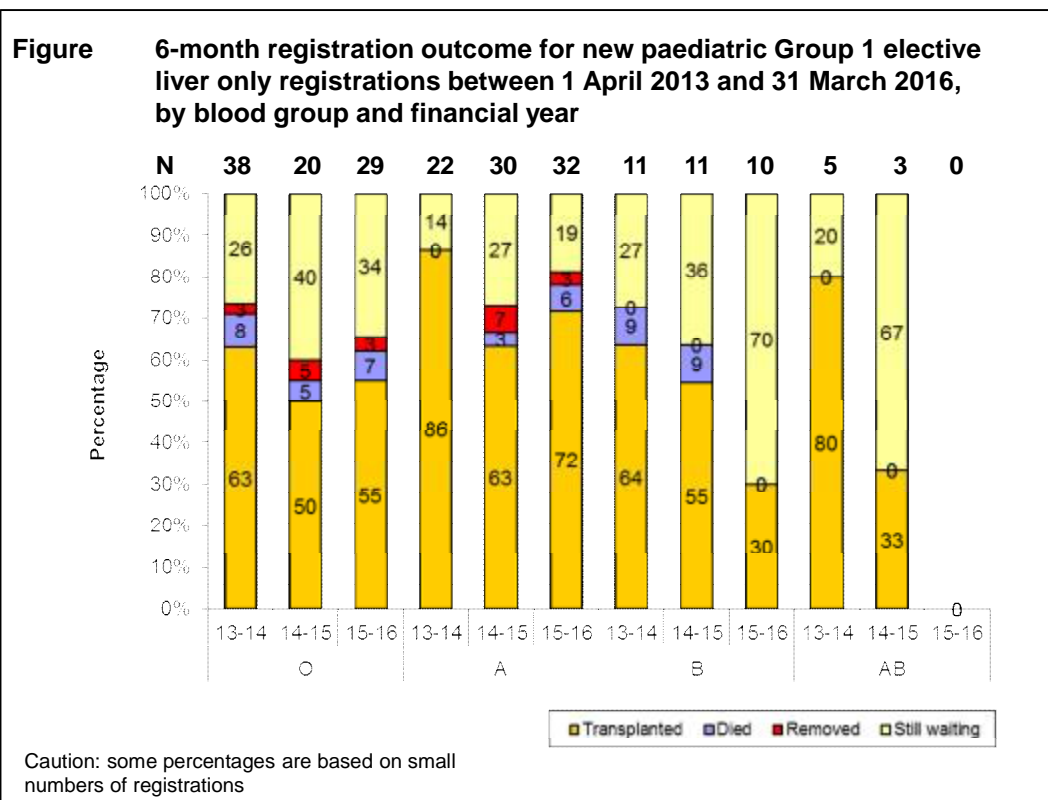
Waiting time to transplant

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 2015/2016 there was evidence of differences in median waiting time to transplant for blood group O patients compared with blood B patients (log-rank test, $p=0.03$).



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.



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 2013- 31 March 2016, by donor type

Donor type	Donor blood group	Recipient blood group								Total
		O		A		B		AB		
		N	%	N	%	N	%	N	%	
DBD	O	60	82	8	11	5	7	0	0	73
	A	3	4	61	88	0	0	5	7	69
	B	0	0	0	0	16	100	0	0	16
	AB	0	0	0	0	0	0	3	100	3
	Total	63	39	69	43	21	13	8	5	161
DCD	O	6	86	0	0	1	14	0	0	7
	A	0	0	3	100	0	0	0	0	3
	B	0	0	0	0	0	0	0	0	0
	AB	0	0	0	0	0	0	0	0	0
	Total	6	60	3	30	1	10	0	0	10