

NHS BLOOD AND TRANSPLANT

LIVER ADVISORY GROUP

BLOOD GROUP: WAITING TIMES AND DEATHS ON THE TRANSPLANT LIST

SUMMARY

BACKGROUND

- 1 Restrictions in the allocation of livers were imposed in 2006 as a measure to reverse the prolonged waiting time to transplant in blood group O patients. These restrictions regulate the allocation of livers depending on the blood groups of donor and recipient. This paper reports the median waiting time to elective liver-only transplant and the proportion of patients dying on the transplant list for different blood groups.

DATA AND METHODS

- 2 Data were obtained from the UK Transplant Registry (UKTR) including all new active Group 1 elective liver only registrations between 1 April 2011 and 31 March 2014 and excluding multi-organ transplants and registrations ending in living donor liver transplant. Median waiting time to transplant and post-registration outcomes were compared over patient blood group, financial year of registration and transplant unit.
- 3 This paper now includes details of all patients registered in Dublin as well as the seven UK centres.

RESULTS

- 4 The median waiting time to transplant in 2013/2014 for blood group O adult patients was significantly greater than that for blood group B patients (207 and 108 days, respectively). No evidence of differences was found on this same comparison for adult patients with UKELD score > 62.
- 5 The median waiting times to transplant for adult patients with blood group O, A, B or AB significantly varied between transplant centres (log-rank test, $p=0.002$, $p<0.0001$, $p<0.0001$ and $p=0.002$, respectively).
- 6 The percentage of blood group O adult patients transplanted within 6-months post-registration in 2013/2014 was significantly lower than that of blood group B adult patients (43% and 56%, respectively). This difference was not significant at 12-months post-registration. There was no evidence of differences in the percentage of adult patients that died on the transplant list neither at 6 nor at 12 months post registration when comparing blood groups.

ACTION

- 7 LAG is asked to note that the 2011 and 2012 reports showed no statistically significant differences in median waiting times to transplant, in those years, between blood group O and B. The 2013 and 2014 reports have shown a significantly greater median waiting time to transplant for blood group O than for B.

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INTRODUCTION

- 1 In an attempt to reverse the prolonged waiting time to transplant primarily for blood group O patients, blood group restrictions were imposed on 1 June 2006 (Ref: **LAG(06)10**). These restrictions were that for elective patients, blood group O donor livers could no longer be given to blood group B patients unless first offered to all blood group O patients in the UK. Additionally, blood group B donor livers could no longer be given to blood group AB patients unless first offered to blood group B patients in the UK. A summary of this paper is presented in **Appendix 1**. (There was a subsequent change to this endorsed at the Liver Advisory Group (LAG) meeting on 15 November 2006 which was that blood group B patients could be considered for liver left lateral segments from blood group O donors.)
- 2 Further papers monitoring the impact of this change were presented to the LAG on 17 November 2010 (Ref: **LAG(10)37**), 11 May 2011 (Ref: **LAG(11)16**), 9 November 2011 (Ref: **LAG(11)45**), 14 November 2012 (Ref: **LAG(12)34**) and 13 November 2013 (Ref: **LAG(13)39**). Following the LAG in November 2011, it was requested that this paper be presented annually to continue to monitor waiting times and deaths on the transplant list by blood group.
- 3 This paper therefore reports on changes in the median waiting time to elective liver-only transplant for patients with different blood groups registered between 1 April 2011 and 31 March 2014, and also changes in the proportion of patients with different blood groups dying on the transplant list over the same time period. The data were analysed in three cohorts; 2011/2012, 2012/2013 and 2013/2014.

DATA AND METHODS

- 4 Data on all new active Group 1 elective liver only registrations onto the UK liver transplant list between 1 April 2011 and 31 March 2014 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.
- 5 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 and 12 month post-registration outcomes were compared over patient blood group, financial year of registration and transplant centre for all adult registrations in the first part of the results section, for adult registrations for patients with a UKELD score > 62 at time of registration in the second part of the results section, and finally for paediatric registrations in the third part of the results section.
- 6 The donor to recipient ABO match distribution was examined for transplants using livers from donors after brain death (DBD) and donor after circulatory death (DCD), using data on all Group 1 elective liver only transplants in the UK between 1 April

2011 and 31 March 2014, obtained from the UKTR as recorded on 10 October 2014. These data are presented separately for adult transplants, adult transplants for patients with a UKELD score > 62 at time of transplantation and finally for paediatric transplants.

RESULTS

Adult registrations

Waiting time to transplant

- 7 The median waiting time to transplant for new adult Group 1 elective liver only registrations between 1 April 2011 and 31 March 2014 is presented in **Table 1** by blood group and financial year and in **Table 2** by blood group and transplant centre. In **Table 1** the outcome for registrations in each financial year was recorded approximately 6-months after the end of each financial year. In **Table 2** all outcomes were recorded as at 10 October 2014.
- 8 **Table 1** shows that the median waiting time to transplant for all patients, regardless of blood group, was a lowest in 2013/2014 relative to previous financial years. This decreasing trend was also observed in the median waiting time to transplant for blood group B patients but not for blood group O patients, for which the median waiting time to transplant remained reasonably stable over the years. In fact, in 2013/2014 there was strong evidence of the median waiting time to transplant for blood group O patients being greater than the median waiting time for blood group B patients (log-rank test, $p=0.0008$).
- 9 In **Table 2** it can be seen that the overall median waiting time to transplant for blood group O patients and blood group B patients registered between 1 April 2011 and 31 March 2014 was 218 days and 154 days, respectively. For blood group O patients, the median waiting time was longest at King's College (302 days) and shortest at Cambridge (146 days). For blood group B patients the median waiting time was longest at The Royal Free (363 days) and shortest at Edinburgh (68 days). There is evidence of differences in median waiting times between centres for blood groups O, A, B and AB. However due to small numbers in blood group AB the results should be interpreted with caution.

Table 1 Median waiting time to deceased donor liver only transplant for new adult Group 1 elective registrations between 1 April 2011 and 31 March 2014, by blood group and financial year

Blood group	2011/2012 ¹			2012/2013 ²			2013/2014 ³		
	No. registrations	Median waiting time (days) (95% CI)		No. registrations	Median waiting time (days) (95% CI)		No. registrations	Median waiting time (days) (95% CI)	
O	411	218	(165 - 271)	382	234	(198 - 270)	459	207	(166 - 248)
A	327	106	(84 - 128)	309	70	(57 - 83)	373	76	(61 - 91)
B	107	224	(148 - 300)	84	150	(81 - 219)	110	108	(79 - 137)
AB	39	59	(27 - 91)	32	70	(36 - 104)	25	36	(21 - 51)
Total	884	167	(148 - 186)	807	126	(109 - 143)	967	121	(104 - 138)

¹ Outcome as at 15 October 2012

² Outcome as at 11 October 2013

³ Outcome as at 10 October 2014

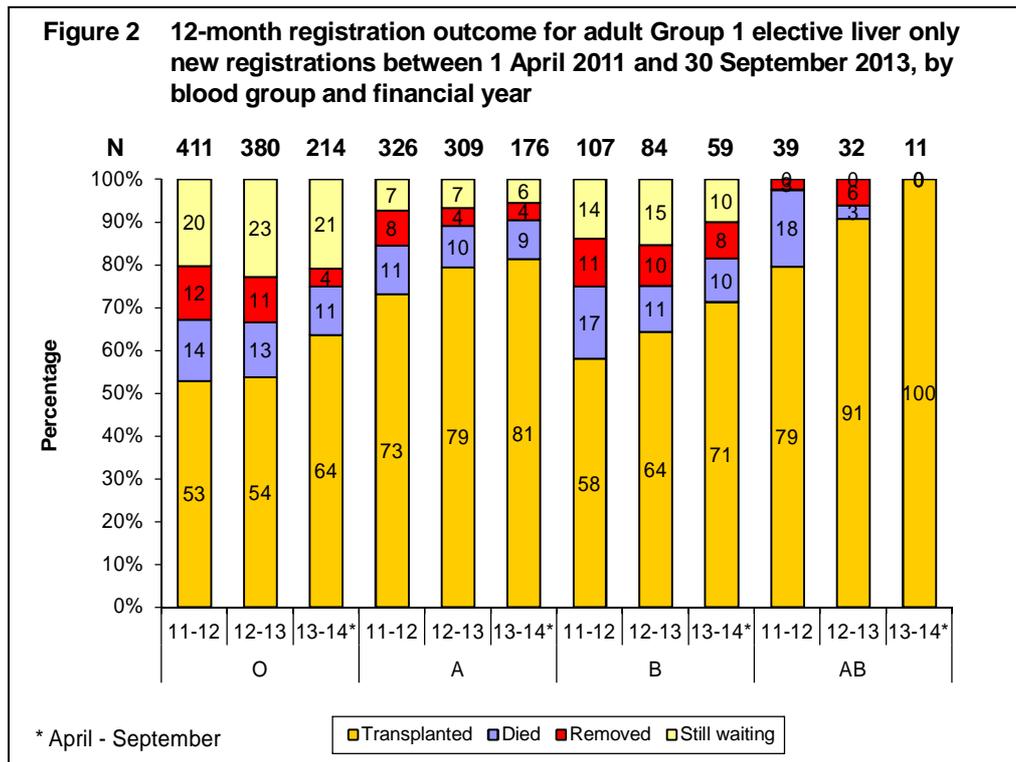
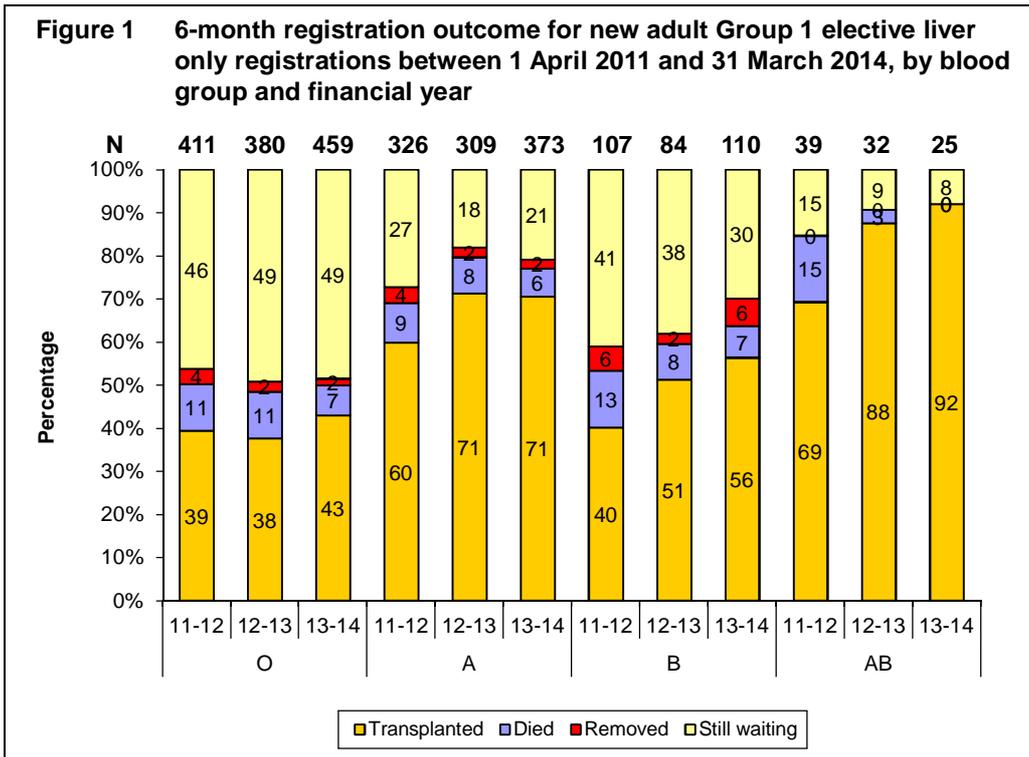
Table 2 Median waiting time to deceased donor liver only transplant for new adult Group 1 elective registrations between 1 April 2011 and 31 March 2014, by blood group and transplant centre

Blood Group	Transplant centre	No. registrations	Median waiting time (days)	95% CI	log-rank test p-value
O	Birmingham	280	201	(160-242)	0.002
	Cambridge	128	146	(85-207)	
	Edinburgh	148	181	(134-228)	
	King's College	224	302	(245-359)	
	Leeds	170	227	(137-317)	
	Newcastle	69	273	(105-441)	
	Royal Free	133	212	(138-286)	
	Dublin	98	164	(134-225)	
	OVERALL	1250	218	(197-239)	
A	Birmingham	247	73	(56-90)	<0.0001
	Cambridge	110	103	(44-162)	
	Edinburgh	108	46	(25-67)	
	King's College	191	97	(76-118)	
	Leeds	143	95	(65-125)	
	Newcastle	52	78	(53-103)	
	Royal Free	106	118	(83-153)	
	Dublin	51	43	(29-57)	
	OVERALL	1008	80	(71-89)	
B	Birmingham	50	113	(49-177)	<0.0001
	Cambridge	20	74	(19-129)	
	Edinburgh	44	68	(44-92)	
	King's College	67	153	(93-213)	
	Leeds	47	270	(180-360)	
	Newcastle	16	115	(90-140)	
	Royal Free	42	363	(282-444)	
	Dublin	14	168	(21-315)	
	OVERALL	301	154	(113-195)	
AB	Birmingham	25	74	(43-105)	0.002
	Cambridge	13	37	(21-53)	
	Edinburgh	7	34	(17-51)	
	King's College	18	58	(35-81)	
	Leeds	17	72	(57-87)	
	Newcastle	3	44	(0-98)	
	Royal Free	8	108	(0-325)	
	Dublin	5	7	(6-8)	
	OVERALL	96	53	(36-70)	

Outcome as at 10 October 2014

Registration outcome

- 10 Registration outcomes (death, transplant, removal, still waiting) at 6-months post-registration are shown by patient blood group and financial year, for new adult Group 1 elective liver only registrations between 1 April 2011 and 31 March 2014, in **Figure 1**. Outcomes at 12-months post-registration are shown in **Figure 2**. Removals due to condition deteriorated have been included as deaths in both figures. Only half of the latest financial year, 2013/2014, has been included in **Figure 2**, in order to allow enough time to obtain 12-month outcomes.
- 11 **Comparisons within blood group.** For blood group O patients registered in the time period, the proportion of registrations that resulted in a transplant or in a death within 6- and 12-months was virtually the same across the three financial years, with the exception of the 12-months follow up for 2013/14 data where there is a slight increase. The proportion of transplanted blood group B patients increased over the course of the three financial years, both within 6- and 12-months of registration. This blood group saw a reduction, in 2013/2014, in the proportion of patients dying on the list within 6- and 12-months post-registration compared with previous years. For blood group A patients the proportion of patients transplanted within 6-months and 12-months of registration remained reasonably stable in the last two time periods, as did the proportion of patients dying on the transplant list. The proportion of registrations resulting in a transplant for blood group AB patients was the highest in 2013/2014 compared with the two previous financial years within 6- and 12-months of registration. Conversely, the proportion of patients dying on the list for this same blood group was at its lowest in 2013/2014 compared with 2011/2012 and 2012/2013.
- 12 **Comparisons between blood groups.** In 2013/2014, there was a statistically significant difference observed between blood groups in the proportion of patients transplanted within 6-months and 12-months of registration (chi-squared test $p < 0.001$ in both cases). However, in that same financial year there was no statistically significant difference observed between blood groups in the proportion of patients that died on the transplant list within both 6-months and 12-months of registration (chi-squared test $p = 0.6$ in both cases). When comparing the proportion of patients transplanted in 2013/2014 for blood group O patients and blood group B patients, there were statistically significant differences observed within 6-months of registration but not within 12-months (chi-squared test $p = 0.01$ and $p = 0.3$, respectively).



Donor to recipient ABO match distribution

- 13 **Table 3** 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 and DCD donors. Five (1%) and three (0%) of blood group O DBD donor livers were transplanted into blood group B and A patients respectively. Three (2%) of blood group O DCD donor livers were transplanted into blood group B patients; the remaining 98% were transplanted into blood group O patients.

Donor type	Donor blood group	O		Recipient blood group				AB		Total
		N	%	N	%	N	%	N	%	
DBD	O	644	99	3	0	5	1	0	0	652
	A	0	0	662	97	0	0	20	3	682
	B	0	0	0	0	188	99	1	1	189
	AB	0	0	2	4	0	0	55	96	57
	Total	644	41	667	42	193	12	76	5	1580
DCD	O	174	98	0	0	3	2	0	0	177
	A	0	0	169	96	0	0	7	4	176
	B	0	0	0	0	48	100	0	0	48
	AB	0	0	0	0	0	0	8	100	8
	Total	174	43	169	41	51	12	15	4	409

Adult registrations for patients with a UKELD score > 62

Waiting time to transplant

- 14 The median waiting time to transplant for new adult Group 1 elective liver only registrations between 1 April 2011 and 31 March 2014 for patients with a UKELD score > 62 at time of registration, by blood group and financial year is presented in **Table 4**. 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. As in **Table 1**, the outcome for registrations in each financial year was recorded approximately 6-months after the end of each financial year. For the overall column, outcomes were recorded as at 10 October 2014. For blood group O patients the median waiting time increased from 29 days for patients registered in 2012/2013 to 44 days for those registered in 2013/2014. In 2013/2014 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=0.94).

Blood group	2011/2012 ²			2012/2013 ³			2013/2014 ⁴			OVERALL ⁴		
	No. registered	Median waiting time (days) (95% CI)		No. registered	Median waiting time (days) (95% CI)		No. registered	Median waiting time (days) (95% CI)		No. registered	Median waiting time (days) (95% CI)	
O	42	56 (37 - 75)		32	29 (0 - 98)		32	44 (17 - 71)		106	54 (34 - 74)	
A	22	31 (15 - 47)		30	33 (12 - 54)		32	30 (17 - 43)		84	31 (22 - 40)	
B	11	28 (7 - 49)		7	16 (12 - 20)		9	38 (12 - 64)		27	28 (7 - 49)	
AB	5	45 (25 - 65)		2	37 -		2	23 -		9	37 (2 - 72)	
Total	80	45 (22 - 68)		71	29 (15 - 43)		75	32 (23 - 41)		226	34 (27 - 41)	

¹ UKELD score calculated at time of registration
² Outcome as at 15 October 2012
³ Outcome as at 11 October 2013
⁴ Outcome as at 10 October 2014

Registration outcome

- 15 Registration outcomes (death, transplant, removal, still waiting) at 6-months post-registration are shown by patient blood group, for new adult Group 1 elective liver only registrations between 1 April 2011 and 31 March 2014 for patients with a UKELD score > 62 at time of registration, in **Figure 3**. Outcomes at 12-months post-registration are shown in **Figure 4**. Removals due to condition deteriorated have been included as deaths in both figures. Only half of the latest financial year, 2013/2014, has been included in **Figure 4**, in order to allow enough time to obtain 12-month outcomes. 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.
- 16 In the cohort of registrations for patients with a UKELD score > 62 and blood group O, A or B, the proportion of registrations resulting in transplant within 6-months and 12-months of registration was highest for blood group A patients. The proportions of deaths on the transplant list were reasonably similar for A and B blood groups within 6- and 12-months post transplant. The cohort of blood group O patients experienced the highest proportion of deaths on the waiting list after 6-months and 12-months of registration compared with blood group A and B patients.

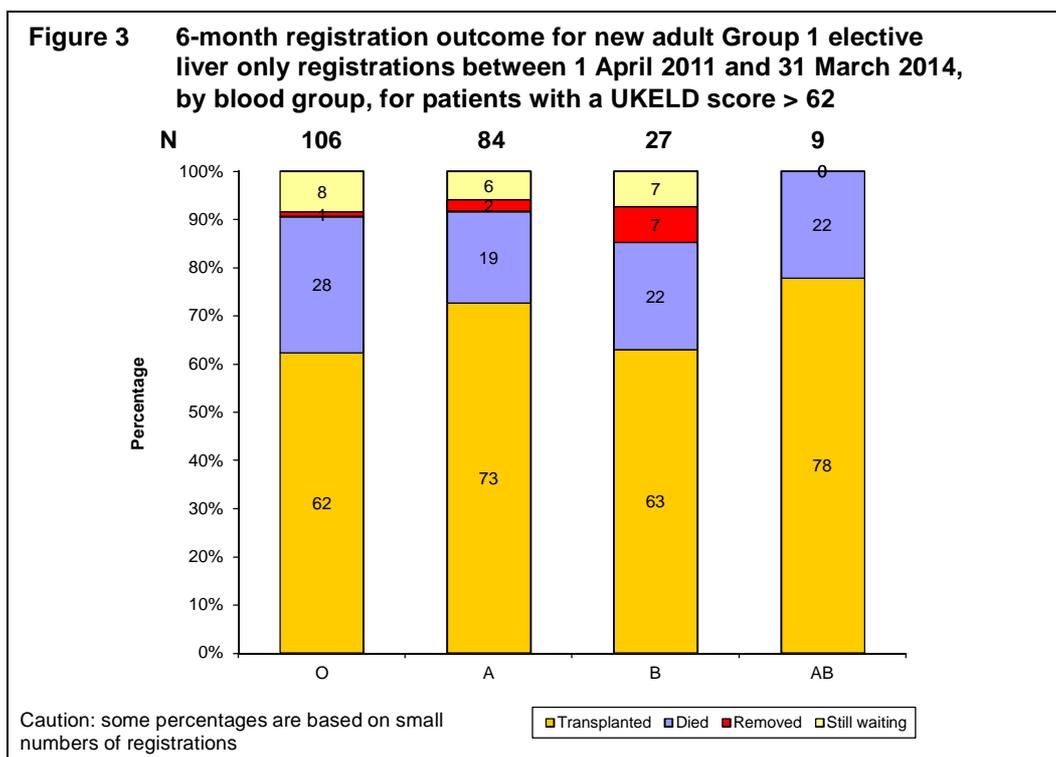
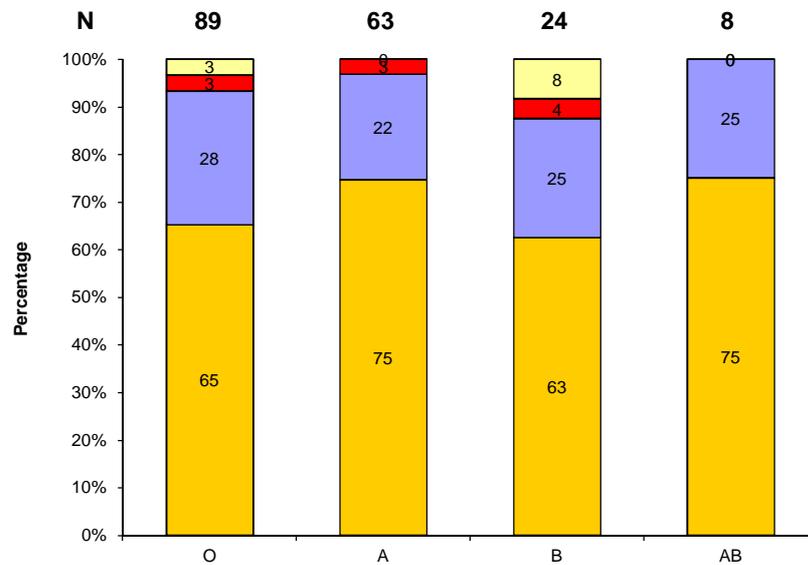


Figure 4 12-month registration outcome for new adult Group 1 elective liver only registrations between 1 April 2011 and 30 September 2013, by blood group, for patients with a UKELD score > 62



Caution: some percentages are based on small numbers of registrations

■ Transplanted ■ Died ■ Removed □ Still waiting

Donor to recipient ABO match distribution

- 17 **Table 5** 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. Two (2%) blood group O DBD donor livers and one (10%) DCD donor liver were transplanted into a blood group B patient with a UKELD score > 62.

Table 5 ABO blood group match for Group 1 adult elective liver only transplants using livers from deceased donors, 1 April 2011 - 31 March 2014, 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	84	98	0	0	2	2	0	0	86
	A	0	0	70	97	0	0	2	3	72
	B	0	0	0	0	19	100	0	0	19
	AB	0	0	0	0	0	0	4	100	4
	Total	84	46	70	39	21	12	6	3	181
DCD	O	9	90	0	0	1	10	0	0	10
	A	0	0	5	100	0	0	0	0	5
	B	0	0	0	0	2	100	0	0	2
	AB	0	-	0	-	0	-	0	-	0
	Total	9	53	5	29	3	18	0	0	17

¹ UKELD score calculated at time of transplantation

Paediatric registrations

Waiting time to transplant

- 18 The median waiting time to transplant for new paediatric Group 1 elective liver only registrations between 1 April 2011 and 31 March 2014, by blood group and financial year is presented in **Table 6**. Note that the small numbers of registrations in each blood group means that some caution should be taken when interpreting the median waiting times. Median waiting times were quite varied for blood group O and blood group B paediatric registrations in the three financial years. There was a decrease in median waiting time between 2012/2013 and 2013/2014 for blood group O and blood group B paediatric registrations. In 2013/2014 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, $p=0.68$).

Table 6 Median waiting time to deceased donor liver only transplant for new paediatric Group 1 elective registrations between 1 April 2011 and 31 March 2014, by blood group and financial year

Blood group	2011/2012 ¹			2012/2013 ²			2013/2014 ³		
	No. registered	Median waiting time (days)	(95% CI)	No. registered	Median waiting time (days)	(95% CI)	No. registered	Median waiting time (days)	(95% CI)
O	28	108	(62 - 154)	31	294	(165 - 423)	38	102	(38 - 166)
A	35	54	(12 - 96)	27	44	(8 - 80)	22	26	(9 - 43)
B	11	76	(1 - 151)	4	187	(41 - 333)	11	105	(29 - 181)
AB	7	13	(12 - 14)	2	146	-	5	91	(69 - 113)
Total	81	76	(36 - 116)	64	75	(0 - 167)	76	80	(57 - 103)

¹ Outcome as at 15 October 2012

² Outcome as at 11 October 2013

³ Outcome as at 10 October 2014

Registration outcome

- 19 Registration outcomes (death, transplant, removal, still waiting) at 6-months post-registration are shown by patient blood group and financial year, for new paediatric Group 1 elective liver only registrations between 1 April 2011 and 31 March 2014, in **Figure 5**. Outcomes at 12-months post-registration are shown in **Figure 6**. Removals due to condition deteriorated have been included as deaths in both figures. Only half of the latest financial year, 2013/2014, has been included in **Figure 6**, in order to allow enough time to obtain 12-month outcomes. 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 5 6-month registration outcome for new paediatric Group 1 elective liver only registrations between 1 April 2011 and 31 March 2014, by blood group and financial year

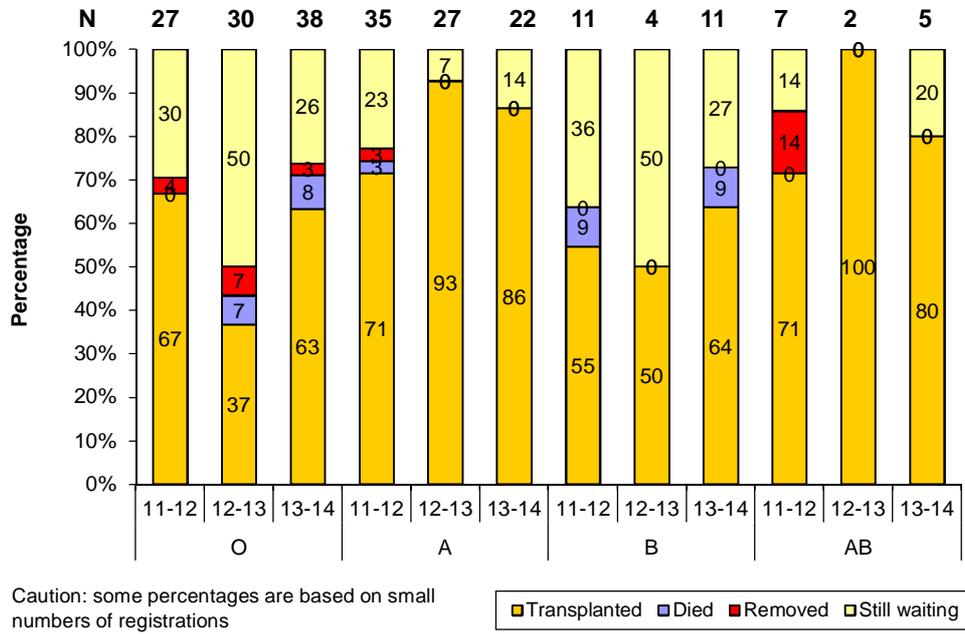
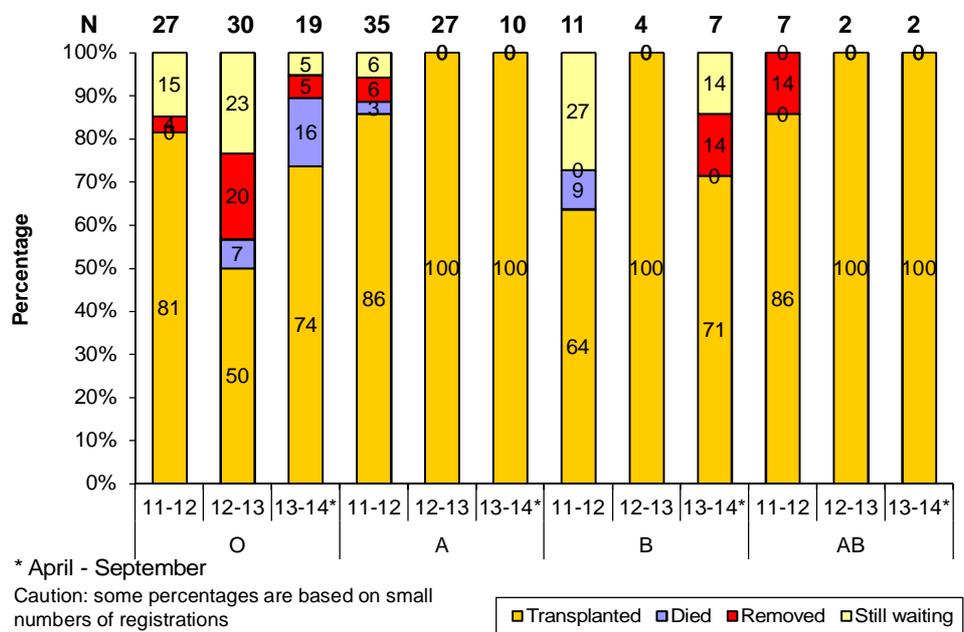


Figure 6 12-month registration outcome for new paediatric Group 1 elective liver only registrations between 1 April 2011 and 30 September 2013, by blood group and financial year



Donor to recipient ABO match distribution

- 20 **Table 7** 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. Five (7%) of blood group O DBD donor livers were transplanted into blood group B paediatric patients, and another five (7%) into blood group A.

Donor type	Donor blood group	Recipient blood group								Total
		O		A		B		AB		
		N	%	N	%	N	%	N	%	
DBD	O	64	86	5	7	5	7	0	0	74
	A	3	4	72	90	0	0	5	6	80
	B	0	0	0	0	20	100	0	0	20
	AB	0	0	0	0	0	0	5	100	5
	Total	67	37	77	43	25	14	10	6	179
DCD	O	4	67	1	17	0	0	1	17	6
	A	0	0	3	100	0	-	0	-	3
	B	0	-	0	-	0	0	0	-	0
	AB	0	-	0	-	0	-	0	0	0
	Total	4	44	4	44	0	0	1	11	9

CONCLUSION

- 21 The median waiting time to transplant for adult patients, regardless of blood group, reached its lowest value in 2013/2014, relative to previous financial years.
- 22 The median waiting time to transplant in 2013/2014 for blood group O adult patients was significantly greater than that for blood group B. No evidence of differences was found when doing the same comparison for adult patients with UKELD score > 62.
- 23 The median waiting times to transplant for adult patients with blood group O, A, B or AB significantly varied between transplant centres.
- 24 The proportion of blood group O adult patients transplanted within 6-months post-registration in 2013/2014 was statistically significantly lower than that of blood group B adult patients. This difference was not significant at 12-months post-registration. In that same year, no statistically significant differences were found in the proportion of adult patients that died on the transplant list neither at 6 nor at 12 months after registration when comparing patients in different blood groups.
- 25 For paediatric registrations, there was a decrease in median waiting time in 2013/2014 for blood groups O and B relative to 2012/2013.

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.