

NHS BLOOD AND TRANSPLANT**LIVER ADVISORY GROUP****LIVER SPLITTING ACTIVITY REPORT****SUMMARY****BACKGROUND**

- 1 Donors after brain death (DBD) under 40 years of age, weighing more than 50kg and known to have spent less than five days in an intensive care unit (ICU) meet the criteria for liver splitting. If a donated liver is split it can be used to transplant two patients; typically an adult patient receives the right liver lobe and a paediatric patient receives the left lobe or the left lateral segment.

DATA ANALYSIS

- 2 Of the 91 livers from DBD donors whose liver was donated between 1 April and 30 September 2013 and who met the criteria for liver splitting, 63 (69%) were available for splitting for elective recipients, having not been used in super-urgent, hepatoblastoma, intestinal or multi-organ recipients. Of these 63 livers, 37 (59%) were offered for splitting and 22 (59% of the 37) were actually split. Donor reasons were reported most frequently (85% of cases) for why 26 livers available for splitting were not offered for splitting, in particular relating to inadequate liver function (27% of all cases). 15 livers were offered for splitting but used whole. In a third of cases this was due to a lack of suitable paediatric patient for the left lateral segment, however a variety of reasons were reported.
- 3 An unadjusted analysis of short-term survival following split liver transplantation, comparing retained and imported split livers transplanted between 1 April 2006 and 31 March 2013, showed no evidence of an impact on transplant survival depending on whether the split liver was retained or imported, for both adult and paediatric patients.
- 4 A comparison of the short-term unadjusted survival rates following whole and split liver transplantation in adult patients, between 1 April 2006 and 31 March 2013, showed that those adults who received split livers had a slightly poorer post-transplant survival rate compared with those adults who received whole livers. However, for just those whole and split liver transplants performed in the most recent years (1 April 2008 to 31 March 2013), unadjusted transplant survival rates were comparable.

ACTION

- 5 Completion of the Split Liver Information form is essential to obtain information on which centre performed the split, and therefore whether the split liver was retained or imported, to be recorded on the UKTR and used in analyses.
- 6 There will be a review within ODT of the process for recording reasons for not splitting livers from donors who meet the liver splitting criteria as the current process is quite convoluted and time consuming.

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November 2013

NHS BLOOD AND TRANSPLANT

LIVER ADVISORY GROUP

LIVER SPLITTING ACTIVITY REPORT

INTRODUCTION

- 1 This paper reports on the outcome of livers from donors after brain death (DBD) who donated their liver between 1 April and 30 September 2013 and who met the criteria for liver splitting.
- 2 The paper also reports on a comparison of the short-term post-transplant survival of patients who received a split liver transplant using livers from DBD donors, between 1 April 2006 and 31 March 2013, at centres that had retained the split liver for transplantation versus those that had imported the split liver for transplantation. A comparison of the unadjusted short-term survival of whole versus split livers transplanted into adult patients is also shown.

LIVER SPLITTING ACTIVITY

Data and methods

- 3 Data were obtained from the UK Transplant Registry (UKTR) on the 91 UK DBD donors whose liver was donated between 1 April and 30 September 2013 and who met the criteria for liver splitting. These were donors under 40 years of age, weighing more than 50kg and were known to have spent less than five days in an intensive care unit (ICU). The time in ICU was calculated as the time lapse between start of ventilation and time of second test for brainstem death. These livers were transplanted in the UK or the Republic of Ireland.
- 4 For comparison, data were also obtained on the 66 UK DBD whose liver was donated between 1 October 2012 and 31 March 2013 and who met the criteria for liver splitting. These livers were also transplanted in the UK or the Republic of Ireland.
- 5 Donated livers were classed as split livers when they were used to transplant two patients and as reduced livers when cut down and used for one patient. Consequently reduced livers were not classed as split livers.
- 6 Livers were classed as offered for splitting if there was a record in the UKTR stating that part of the liver had been offered to a centre (offers that were withdrawn were discounted), as recorded by the ODT Duty Office.

Results

- 7 The status of each liver that was transplanted is shown in **Table 1** for April to September 2013, with October 2012 to March 2013 figures for comparison. Between 1 April and 30 September 2013, of the 91 DBD donors meeting the splitting criteria (66 between 1 October 2012 and 31 March 2013), 63 (69%) livers were available for splitting (48 (73%) between October 2012 and March 2013). Of these 63 livers, 37 (59%) were offered for splitting (22 of the 48 (46%) between October 2012 and March 2013). Of the 37 livers offered for splitting, 22 (59%) were actually split (11 of the 22 (50%) were split between October 2012 and March 2013).

Table 1 Donors meeting criteria for liver splitting, by donor allocation zone, 1 April to 30 September 2013 (1 October 2012 to 31 March 2013)

Donor allocation zone	Total meeting liver splitting criteria and transplanted		Super-urgent liver or intestinal patients/hepatoblastoma recipients		Elective intestinal/multi-organ recipients		Available for splitting		Offered for splitting				Split		Whole		Reduced			
	N		N		N		N		N	% of available			N	% of offered	N		N			
Birmingham	16	(18)	5	(5)	1	(3)	10	(10)	5	(4)	50	(40)	2	(2)	40	(50)	8	(8)	0	(0)
Cambridge	6	(10)	2	(1)	0	(0)	4	(9)	0	(5)	0	(56)	0	(1)	-	(20)	4	(8)	0	(0)
Edinburgh	17	(7)	3	(1)	0	(0)	14	(6)	8	(3)	57	(50)	4	(1)	50	(33)	9	(5)	1	(0)
King's College	19	(12)	7	(1)	1	(0)	11	(11)	9	(4)	82	(36)	7	(4)	78	(100)	4	(7)	0	(0)
Leeds	18	(10)	3	(3)	1	(0)	14	(7)	11	(3)	79	(43)	6	(2)	55	(67)	8	(4)	0	(1)
Newcastle	4	(6)	0	(2)	0	(0)	4	(4)	2	(3)	50	(75)	1	(1)	50	(33)	3	(3)	0	(0)
Royal Free	11	(3)	5	(1)	0	(1)	6	(1)	2	(0)	33	(0)	2	(0)	100	-	4	(1)	0	(0)
TOTAL	91	(66)	25¹	(14²)	3³	(4⁴)	63	(48)	37	(22)	59	(46)	22	(11)	59	(50)	40	(36)	1	(1)

¹ Six of these livers were split: one liver was used to transplant one super-urgent recipient and one hepatoblastoma patient and each of the other five livers were used to transplant one super-urgent/hepatoblastoma recipient and one elective liver only recipient

² Seven of these livers were split: one liver was used to transplant two super-urgent recipients and each of the other six livers were used to transplant one super-urgent/hepatoblastoma recipient and one elective liver only recipient

³ Two livers were split and used to transplant one multi-organ recipient and one elective liver only recipient

⁴ One liver was split and used to transplant one multi-organ recipient and one elective liver only recipient

Note: Due to small numbers the percentages presented must be viewed with caution
Livers were not necessarily transplanted by the centre that resides in the donor allocation zone

- 8 These 91 livers resulted in 121 transplants, of which 31 (26%) were performed in paediatric patients (the 66 livers between October 2012 and March 2013 resulted in 85 transplants, 20 (24%) of which were performed in paediatric patients).
- 9 **Table 2** details the reasons given by the transplanting centre or noted by the ODT Duty Office for 26 livers not being offered for splitting (63% of the 41 livers available for splitting that were not split). Of these 26 livers, 22 (85%) were not offered for splitting for donor related reasons, three were not offered for recipient related reasons and one was not offered due to an other reason.

Table 2 Reasons given for why 26 livers from donors meeting the liver splitting criteria, between 1 April and 30 September 2013, were not offered for splitting

Donor	Donor allocation zone	Transplanting centre	Reason for liver not being offered for splitting
Donor reasons			
1	Birmingham	Birmingham	Donor fragile/acidotic
2	Birmingham	Birmingham	Liver was nodular and the anatomy was not suitable
3	Birmingham	Birmingham	Medication/acidosis
4	Birmingham	Birmingham	Raised liver function tests
5	Birmingham	Newcastle	Donor history/anatomy
6	Cambridge	Cambridge	Abnormal liver function tests
7	Cambridge	Cambridge	Abnormal liver function tests
8	Cambridge	Cambridge	Paediatric donor
9	Cambridge	Newcastle	Hepatitis B donor
10	Edinburgh	Edinburgh	Deranged liver function tests
11	Edinburgh	Edinburgh	Donor history
12	Edinburgh	Edinburgh	Size ratio (female to male) and past history of cancer
13	King's College	King's College	Donor tumour (cause of death = brain tumour)
14	King's College	King's College	Hepatitis C and B core antibody donor
15	Leeds	Edinburgh	Liver fatty and large
16	Leeds	King's College	Abnormal liver function tests
17	Leeds	Leeds	High donor BMI
18	Newcastle	Royal Free	Donor medical history
19	Royal Free	Birmingham	Donor had extensive abdominal trauma
20	Royal Free	Royal Free	Abnormal liver function tests
21	Royal Free	Royal Free	Abnormal liver function tests
22	Royal Free	Royal Free	Donor had 2x stays in ITU and elevated sodium levels
Recipient reasons			
23	Edinburgh	Newcastle	SN-OD reports that Newcastle required whole liver as it was a re-transplant and they needed extra vessels. Newcastle reports that they asked the SN-OD to offer on the left lateral segment but were told that there were no suitable recipients
24	Edinburgh	Edinburgh	Split was offered but withdrawn as Edinburgh recipient became too ill and needed whole liver
25	Newcastle	Newcastle	SN-OD reports that Newcastle required whole liver for NLA transplant and that they were not asked to offer on the left lat segment. Newcastle reports that they required the liver for an NLA recipient and asked the SN-OD to offer on the left lateral segment but were told there were no suitable recipients
Other reasons			
26	Edinburgh	King's College	Offering information states whole liver was offered and declined by all centres (no suitable recipients) except King's College who were not obliged to split as all other centres had declined

- 10 The reasons given for not splitting the remaining 15 livers that were offered for splitting but were not split (37% of the 41 livers available for splitting that were not split) are detailed in **Table 3**. In a third of cases this was due to a lack of suitable paediatric patient for the left lateral segment.

Table 3 Reasons given for why 15 livers from donors meeting the split liver criteria, between 1 April and 30 September 2013, that were offered for splitting were not split

Donor	Donor allocation zone	Transplanting centre	Details of why liver was not split
Donor reasons			
1	Birmingham	Birmingham	Donor medical history
2	Birmingham	Birmingham	Liver thought to be thrombotic, size/blood type/c-reactive protein also given as reasons for declining left lateral segment
3	Edinburgh	Edinburgh	Liver was deemed not splittable as a result of conversation between King's College and Edinburgh
4	Leeds	Edinburgh	Donor anatomy. Whole liver used in NLA recipient
5	Leeds	Edinburgh	Liver was deemed not splittable so Edinburgh used whole for NLA recipient
Recipient reasons			
6	Edinburgh	Edinburgh	No suitable paediatric patients for left lateral segment
7	King's College	King's College	No suitable paediatric patients for left lateral segment
8	King's College	King's College	No suitable paediatric patients for left lateral segment
9	Leeds	Edinburgh	No suitable paediatric patients for left lateral segment
10	Newcastle	Edinburgh	King's College's paediatric recipient was not fit enough to receive left lateral segment but Edinburgh's recipient had already been prepared so Edinburgh were able to transplant the liver whole
Other reasons			
11	Birmingham	Birmingham	Paediatric centres declined left lateral segment as no suitable recipients/lack of theatre time
12	Edinburgh	Leeds	Birmingham declined left lateral segment on logistics (donor in Northern Ireland), King's College due to major theatre problems regarding a liver/kidney transplant and Leeds due to a lack of theatre time. Liver had already been split so Leeds used reduced and King's College used left lateral segment for hepatocyte transplantation
13	Edinburgh	Leeds	Leeds initially accepted liver for splitting but had to offer on left lateral segment as couldn't perform both transplants at the same time. Birmingham declined on size and King's College on cold ischaemic time
14	Leeds	Leeds	Left lateral segment was too big for Leeds' paediatric patient and King's College and Birmingham declined on cold ischaemic time
15	Leeds	Leeds	Poor function and cold ischaemic time

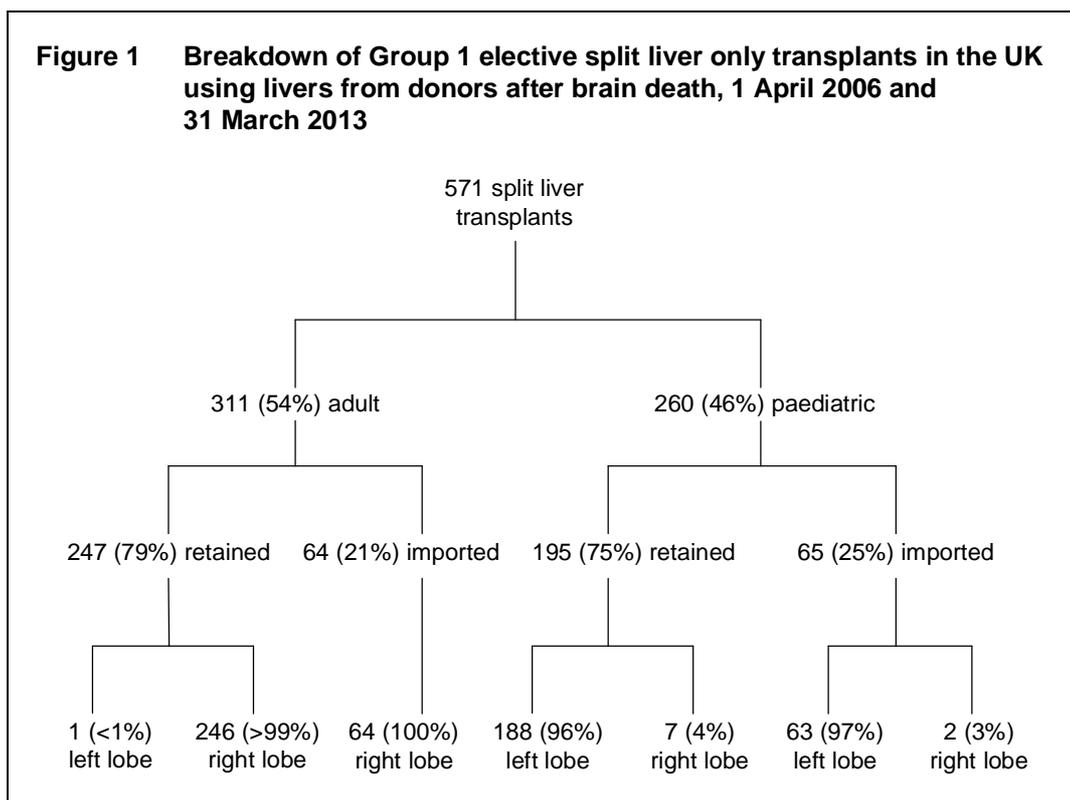
TRANSPLANT SURVIVAL

Data and methods

- 11 Data on 571 Group 1 first elective split liver only transplants in the UK using livers from DBD donors between 1 April 2006 and 31 March 2013 were analysed. Heterotopic, auxiliary and intestinal transplants were excluded from this cohort as were regrafts. Follow-up data were as recorded on the UKTR on 24 October 2013.
- 12 For each donor liver, information from the Split Liver Information form and the Duty Office notes was examined in order to identify the centre that split the liver. For those split livers where there was no information available on the centre that carried out the split and the transplant centre and donor allocation centre were the same for both split transplants, the assumption was that the liver was split at that centre. In a small number of cases where it was not clear where the split was performed and the transplant centres were different for the two parts of the liver a judgement was made, based on the Duty Office notes, as to where the split was performed.
- 13 The information regarding the centre that split the liver was used to categorise the liver transplant according to whether the split liver was 'retained' i.e. the liver was split in the same centre that transplanted that part of the liver, or the split liver was 'imported' i.e. the liver was split at a different centre and that part of the liver was imported and transplanted.
- 14 Short-term unadjusted transplant survival rates were compared for retained and imported split livers transplanted in adult and paediatric patients, using the Kaplan-Meier estimation method and the log-rank test. Cold ischaemic time (CIT) was also compared for retained and imported split livers. The Mann-Whitney U test was used to compare median CIT.
- 15 A comparison of the unadjusted short-term survival rates of whole and split livers transplanted in 2,962 Group 1 first adult elective patients in the UK in the same time period, 1 April 2006 to 31 March 2013, was also undertaken. Heterotopic, auxiliary and multi-organ transplants were excluded, as were regrafts. Follow-up data were as recorded on the UKTR on 24 October 2013.

Results

- 16 **Figure 1** shows a breakdown of the 571 split liver transplants by recipient age group (adult (≥ 17 years), paediatric (< 17 years)) and whether the liver was retained or imported.



17 **Table 4** shows a breakdown of the 571 split liver transplants by recipient age group, transplant centres and whether the liver was retained or imported.

Table 4 Group 1 first elective split liver only transplants in the UK using livers from donors after brain death, 1 April 2006 – 31 March 2013

Transplant centre	Retained N	Imported N	Total
Paediatric recipients			
Birmingham	81	16	97
King's College	83	36	119
Leeds	31	13	44
Total	195	65	260
Adult recipients			
Birmingham	103	2	105
Cambridge	14	8	22
Edinburgh	22	27	49
King's College	69	2	71
Leeds	27	6	33
Newcastle	4	7	11
Royal Free	8	12	20
Total	247	64	311
TOTAL	442	129	571

- 18 **Table 5** shows the median and range of cold ischaemic times (CIT), in hours, of retained and imported split livers transplanted in adult and paediatric patients. Median CIT was significantly longer for imported right liver lobes than retained right liver lobes ($p < 0.0001$), which was also the case for imported left liver lobes compared with retained left liver lobes ($p < 0.0001$).

	N ¹	CIT (hours)	
		Median	Range
Left lobes transplanted in paediatric patients			
Retained	165	9.0	3.6 – 16.2
Imported	56	11.4	1.3 – 16.5
Right lobes transplanted in adult patients			
Retained	234	9.8	3.9 – 17.6
Imported	62	12.5	6.6 – 16.3

¹ CIT was not reported for a total of 44 split livers

Unadjusted survival analysis

- 19 **Figure 2** shows the Kaplan-Meier transplant survival curves up to 90 days and one year post-transplant (where the outcome event is graft failure or patient death) for paediatric patients, by whether the split liver was retained or imported. In both cases, there is no evidence of a difference in early transplant survival for the retained and imported split liver groups. Note that there is a small number of observed events in the imported split liver group, which means that the results should be viewed with caution.
- 20 **Figure 3** gives the same information but for adult patients who received a split liver transplant. Here there is also no evidence of an impact on early post-transplant survival depending on whether the split liver was retained or imported. Again, note that there are only a small number of observed events in the imported split liver group; so the results should be viewed with caution.

Figure 2 Comparison of 90 day and one year transplant survival of retained and imported split livers transplanted in Group 1 elective paediatric patients in the UK between 1 April 2006 and 30 September 2012

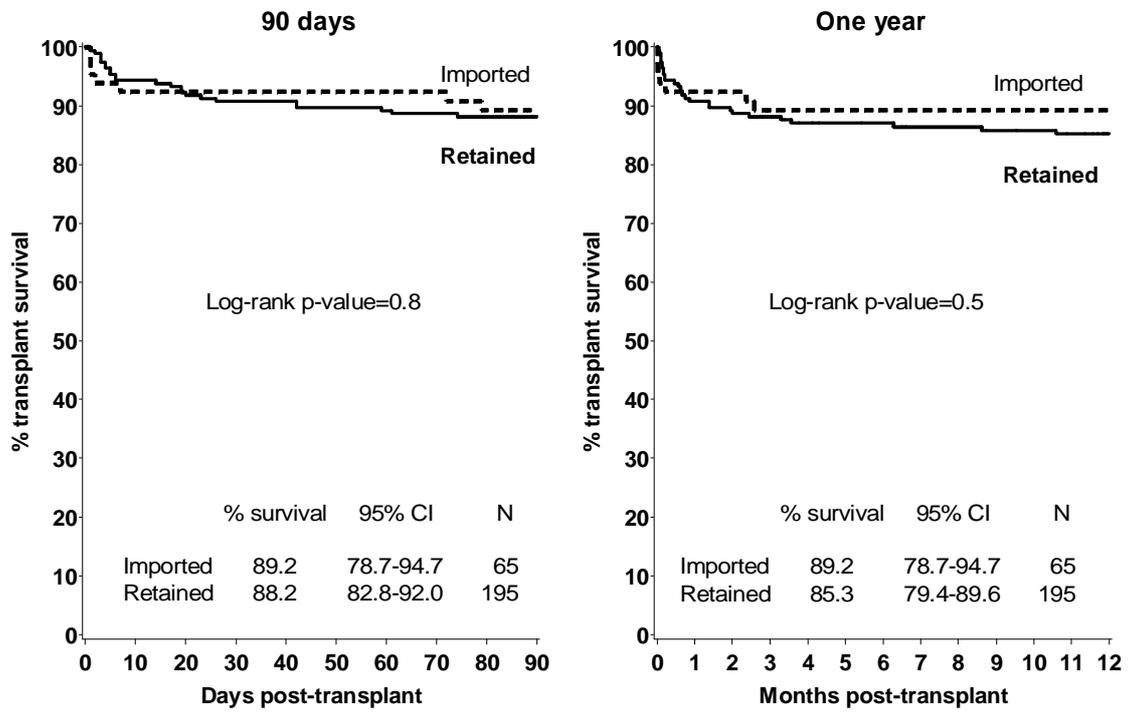
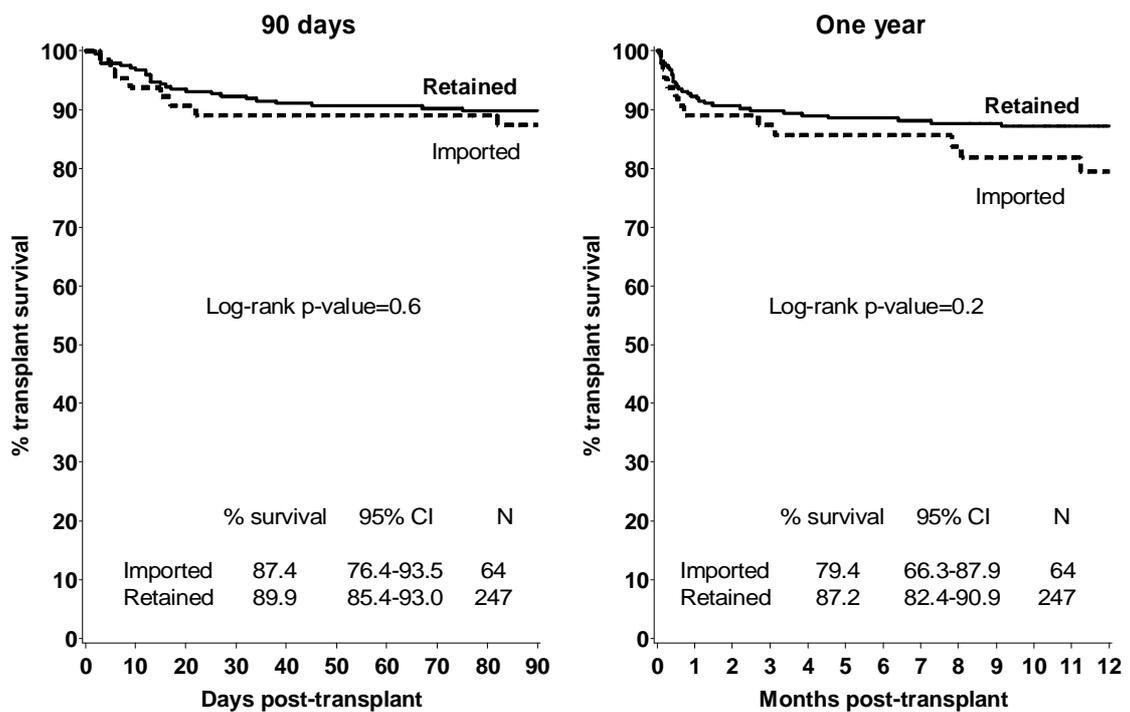
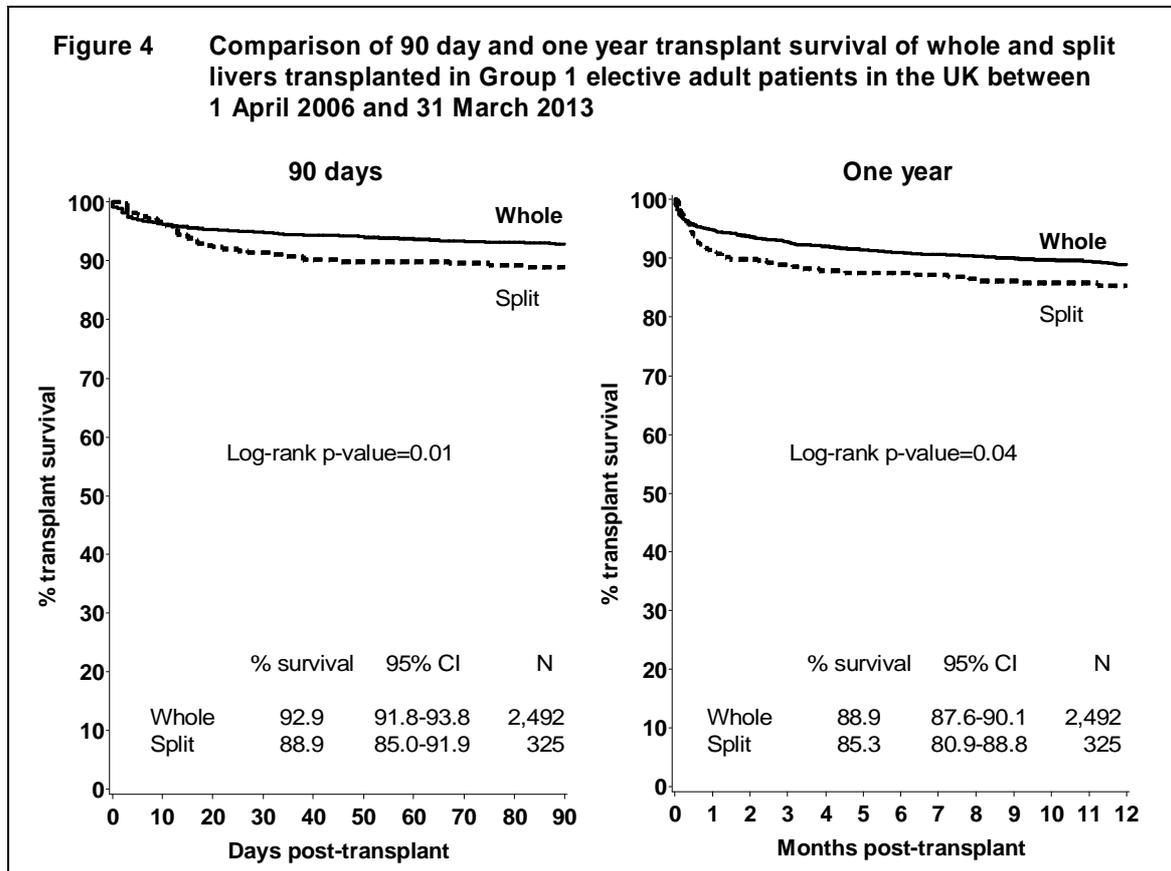


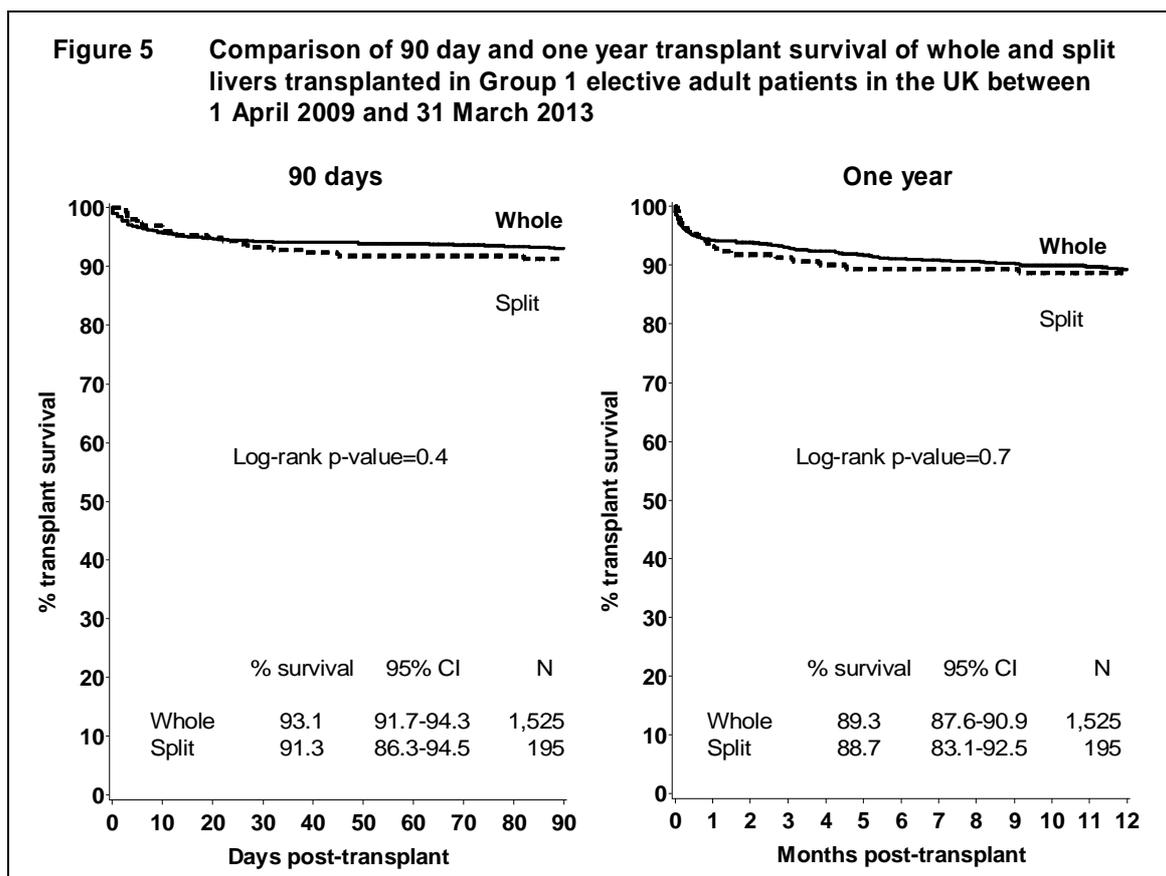
Figure 3 Comparison of 90 day and one year transplant survival of retained and imported split livers transplanted in Group 1 elective adult patients in the UK between 1 April 2006 and 31 March 2013



- 21 **Figure 4** shows the Kaplan-Meier transplant survival curves up to 90 days and one year post-transplant (where the outcome event is graft failure or patient death) for adult patients transplanted between 1 April 2006 and 31 March 2013, by whether the adult received the whole liver or just part of the liver. In both cases there is evidence of inferior survival for recipients of split livers ($p=0.01$ and $p=0.04$ for 90 day and one year, respectively) compared with recipients of whole livers. However, this analysis does not adjust for any differences in the two groups of patients that may affect transplant survival.



- 22 **Figure 5** shows the same information as **Figure 4** but for just those transplants performed in the most recent years (1 April 2009 and 31 March 2013). This unadjusted analysis shows that the survival rates of whole and split liver transplants performed between 1 April 2009 and 31 March 2013 are comparable ($p=0.4$ and $p=0.7$ for 90 days and one year, respectively). Again, this analysis does not account for any confounding factors.



SUMMARY

- 23 Of the 91 livers from DBD donors whose liver was donated between 1 April and 30 September 2013 and who met the criteria for liver splitting, 63 (69%) were available for splitting for elective recipients, having not been used in super-urgent, hepatoblastoma, intestinal or multi-organ recipients. Of these 63 livers, 37 (59%) were offered for splitting and 22 (59% of the 37) were actually split. Donor reasons were reported most frequently (85% of cases) for why 26 livers available for splitting were not offered for splitting, in particular relating to inadequate liver function (27% of cases). 15 livers were offered for splitting but used whole. In a third of cases this was due to a lack of suitable paediatric patients for the left lateral segment.
- 24 An unadjusted analysis of short-term survival following split liver transplantation, comparing retained and imported split livers transplanted between 1 April 2006 and 31 March 2013, showed no evidence of an impact on transplant survival depending on whether the split liver was retained or imported, for both adult and paediatric patients.
- 25 A comparison of the short-term unadjusted survival rates following whole and split liver transplantation in adult patients, between 1 April 2006 and 31 March 2013, showed that those adults who received split livers had a slightly poorer post-transplant survival rate compared with those adults who received whole livers. However, for just those whole and split liver transplants performed in the most recent years (1 April 2008 to 31 March 2013), unadjusted transplant survival rates were comparable.

Action

- 26 The accuracy of the comparison between retained and imported split livers relies on being able to ascertain where the liver splitting took place. Completion of the Split Liver Information form is essential to obtain information on which centre performed the split, and therefore whether the split liver was retained or imported, to be recorded on the UKTR and used in analyses.
- 27 There will be a review within ODT of the process for recording reasons for not splitting livers from donors who meet the liver splitting criteria as the current process is quite convoluted and time consuming.

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November 2013