

NHS BLOOD AND TRANSPLANT

LIVER ADVISORY GROUP

LIVER SPLITTING ACTIVITY REPORT

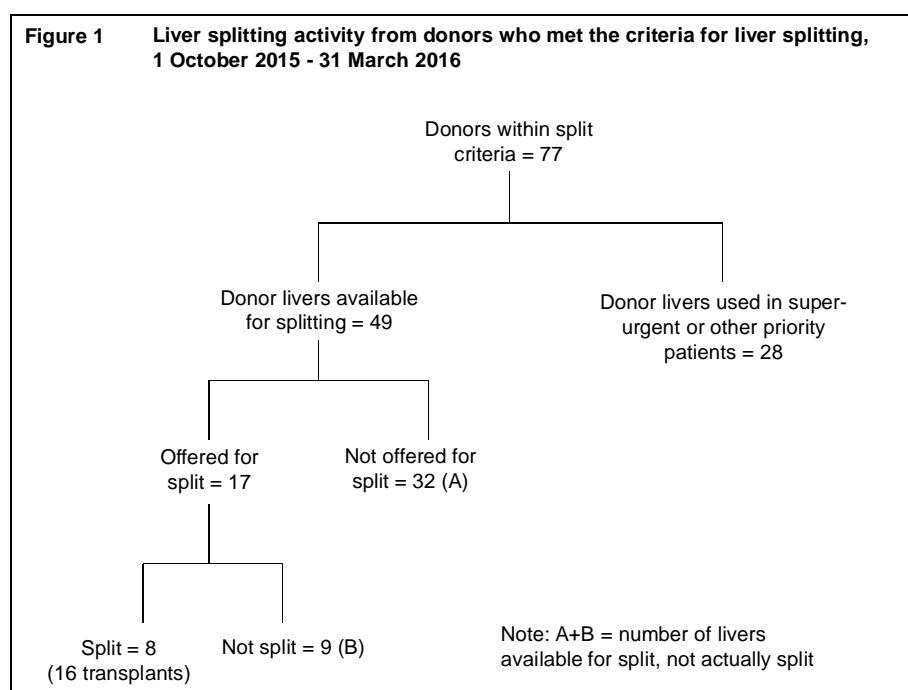
SUMMARY

BACKGROUND

- 1 Donors after brain death (DBD) aged < 40 years, weighing > 50kg and known to have spent < five days in an intensive care unit meet the criteria for liver splitting. If a donated liver is split it can be used to transplant two patients; typically one adult and one paediatric patient. This paper reports on the outcome of livers from DBD donors who donated their liver in a recent time period and who met the criteria for liver splitting. It also reports on survival outcomes of patients who received split liver transplants over the last ten years.

ACTIVITY

- 2 **Figure 1** shows a summary of the liver splitting activity in the 6-month period 1 October 2015 to 31 March 2016.



- 3 The percentage of livers split of those available for splitting increased by about 10% from 23% in 2006/2007 to 33% in 2012/13. In 2012/13, 27 livers were split. Since then there has been a fall to only 16 (16%) livers split in 2014/15, and only 18 (20%) in 2015/16.
- 4 In 2015/16 there were an additional 10 donors outside of the donor splitting criteria that led to 20 split liver transplants.

- 5 In the last ten years CIT was on average 2.7 hours longer for imported liver lobes compared with retained liver lobes for both adult and paediatric recipients.

TRANSPLANT OUTCOMES

- 6 Risk adjusted analysis of transplant outcomes, April 2011-September 2015, showed:
- Evidence of poorer outcomes for split liver recipients compared to whole, $p=0.03$ (HR for split=1.6, 95% CI 1.1-2.5)
 - No significant difference in outcomes for livers split by adult (N=27) and paediatric (N=332) unit surgeons, $p=0.9$ (HR for adult unit=0.9, 95%CI 0.3-3.1)
 - No significant difference in outcomes of retained (N=260) and imported (N=99) split livers, $p=0.3$ (HR for imported=1.4, 95% CI 0.8-2.7).

ACTION

- 7 In 2014/15 only 16% of available livers were split and only 20% in 2015/16, representing the lowest rates and numbers over the last 10 years. Risk adjusted analysis of three year transplant survival shows some evidence that split liver transplants have poorer outcomes than whole livers in the most recent 5 years. Members are asked to consider what action should be taken to optimise use and outcomes of split liver transplantation.

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NHS BLOOD AND TRANSPLANT

LIVER ADVISORY GROUP

LIVER SPLITTING ACTIVITY REPORT

INTRODUCTION

- 1 If a liver from a deceased donor 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. This paper reports on the outcome of livers from donors after brain death (DBD) who donated their liver between 1 October 2015 and 31 March 2016 and who met the criteria for liver splitting. The paper also reports briefly on activity over the last 10 years.
- 2 Liver transplant survival outcomes are analysed for patients who received a DBD donor split liver transplant between 1 April 2006 and 31 March 2016. Comparisons are made between livers retained by the splitting centre and those imported as a split from another centre. A comparative analysis was also performed between split livers that were split by adult vs paediatric unit surgeons. A comparison of the survival of whole versus split livers transplanted into adult patients is also shown. Both univariate and multivariate analyses are reported.

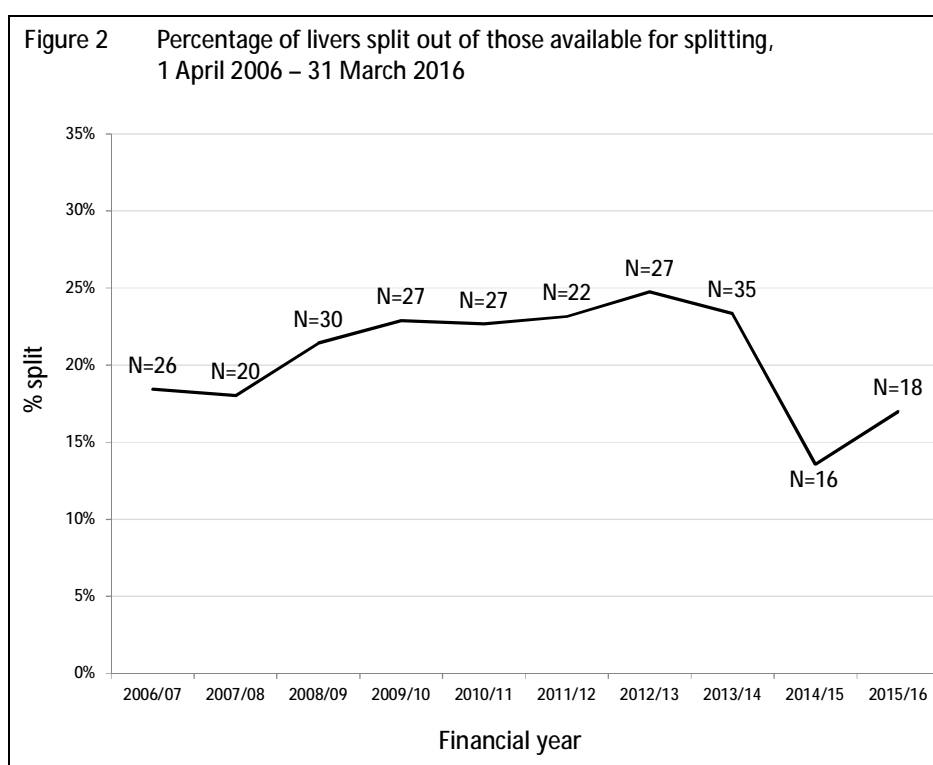
LIVER SPLITTING ACTIVITY

Data and methods

- 3 Donors meeting the criteria for liver splitting are under 40 years of age, weighing more than 50kg and known to have spent less than five days in an intensive care unit (ICU). Time in ICU is calculated as the time between start of ventilation and time of second test for brainstem death.
- 4 Data were obtained from the UK Transplant Registry (UKTR) on the 77 UK DBD donors whose liver was donated in the 6 months between 1 October 2015 and 31 March 2016 and who met the criteria for liver splitting. These livers were transplanted in the UK or the Republic of Ireland. Comparable data were also obtained on the 57 UK DBD liver donors in the previous 6 months (1 April 2015 - 30 September 2015), who met the criteria for liver splitting.
- 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.
- 7 Account is taken of the requirement in place from 6 October 2014 stating that all within-criteria livers offered to Hepatoblastoma patients must be considered for splitting.

Results

- 8 The status of each liver that was transplanted is shown in **Table 2** for October 2015 to March 2016, with April 2015 to September 2015 figures for comparison. For the latest 6 months, 49 (64%) of the 77 DBD donors meeting the splitting criteria were available for splitting. Of these 49 livers, 17 (35%) were offered for splitting. Of the 17 livers offered for splitting, 8 (47%) were actually split. This activity is summarised in **Figure 1**.
- 9 These 77 livers resulted in 92 transplants, of which 16 (17%) were performed in paediatric patients.
- 10 The percentage of livers split out of those available for splitting (N_s / N_A) are plotted in **Figure 2** over the last 10 financial years. This shows a slight rise in the percentage split, followed by a fall in 2014/15. The percentage split is slightly higher in the most recent financial year, but this is based on small numbers. The percentage of livers split of those available for splitting is given in **Table 1**, by donor allocation zone. The number of livers split that were outside splitting criteria are also provided.



Allocation zone	Available for split within criteria N	Split within criteria		Split outside criteria N
		N	%	
Birmingham	93	25	27	23
Cambridge	48	11	23	3
Edinburgh	70	15	21	6
King's College	96	33	34	24
Leeds	76	18	24	13
Newcastle	33	9	27	3
Royal Free	47	8	17	3
TOTAL	463	119	26	75

- 11 A comparison of the number of split liver and living donor liver transplants over the last decade is shown in **Figure 3**. This shows fewer split liver transplants in the last two financial years and an increase in living donor transplants in the last decade. The number of split liver transplants includes those from donors in **Table 3** and also those where the donor did not meet splitting criteria whose livers were split for transplant. In 2015/16, there were 10 donors outside of the donor splitting criteria. These are only included in **Figure 3** in the report, and summarised in **Table 2**.

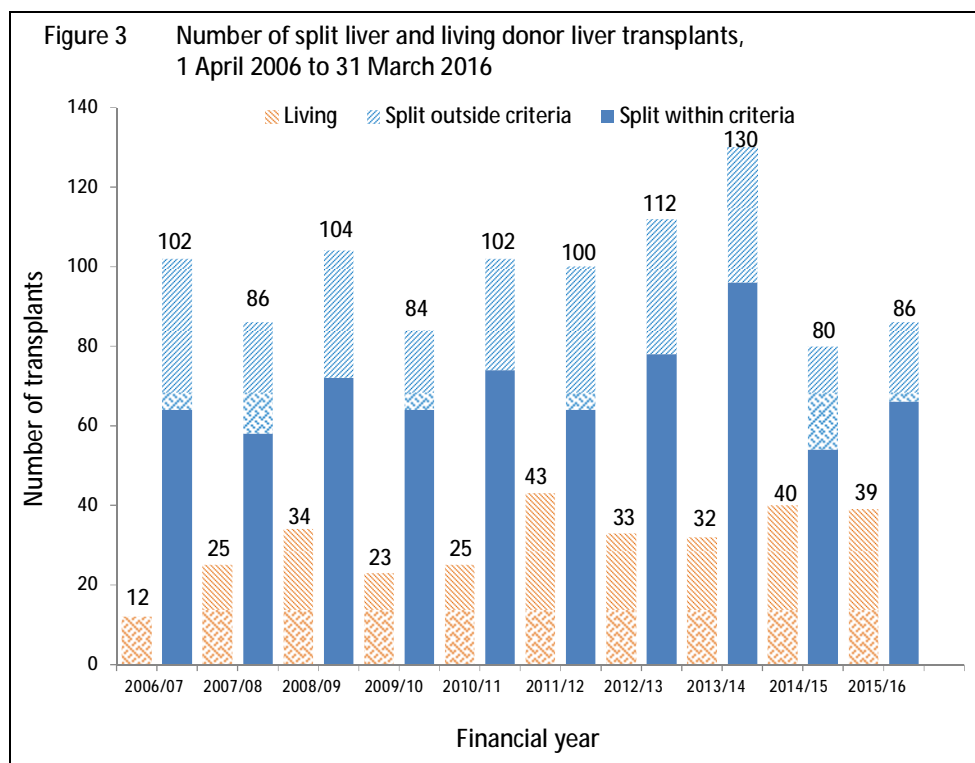


Table 2 Characteristics of liver donors who were outside of splitting criteria but whose livers went on to be split, 1 April 2006 to 31 March 2016

Year	Aged 40 or more		Weighing 50kg or less		Spent 5 days or more in ICU		Total
	N	%	N	%	N	%	
2006/07	10	53	6	32	3	16	19
2007/08	11	79	1	7	2	14	14
2008/09	7	44	7	44	3 ²	19	16
2009/10	7	70	0	0	3 ¹	30	10
2010/11	9	64	2	14	4 ¹	29	14
2011/12	10	56	5	28	5	28	18
2012/13	12	71	4	24	2	12	17
2013/14	11	65	5	29	3	18	17
2014/15	6	46	4	31	3	23	13
2015/16	8	80	2	20	1	10	10

Note: Numbers and % may not add up to total in each row as some donors are outside of more than one criteria

¹ includes one donor with unknown ICU length of stay

² includes two donors with unknown ICU length of stay

Table 3 Donors meeting criteria for liver splitting, by donor allocation zone, 1 October 2015 to 31 March 2016 (1 April 2015 to 30 September 2015)

Donor allocation zone	Total meeting liver splitting criteria and transplanted		Super-urgent liver or intestinal/hepatoblastoma recipients		Elective intestinal/multi-organ recipients		Available for splitting		Offered for splitting				Split				Whole		Reduced	
	N		N _{P1}		N _{P2}		N _A		N _O		% of available		N _S		% of offered		N _w		N _r	
Birmingham	15	(15)	6	(3)	3	(1)	6	(11)	2	(5)	33	(45)	2	(4)	100	(80)	0	(1)	0	(0)
Cambridge	9	(4)	2	(3)	2	(0)	5	(1)	3	(1)	60	(100)	2	(0)	67	(0)	1	(0)	0	(1)
Edinburgh	9	(5)	3	(2)	0	(0)	6	(3)	3	(1)	50	(33)	1	(0)	33	(0)	2	(1)	0	(0)
King's College	17	(18)	3		1	(1)	13	(13)	3	(8)	23	(62)	2	(4)	67	(50)	1	(4)	0	(0)
				(4)																
Leeds	14	(8)	6	(3)	1	(0)	7	(5)	2	(1)	29	(20)	0	(1)	0	(100)	2	(0)	0	(0)
Newcastle	5	(3)	1	(1)	0	(0)	4	(2)	0	(1)	0	(50)	0	(1)	-	(100)	0	(0)	0	(0)
Royal Free	8	(4)	0	(0)	0	(0)	8	(4)	4	(2)	50	(50)	1	(0)	25	(0)	3	(2)	0	(0)
TOTAL	77	(57)	21 ¹	(16 ²)	7 ³	(2 ⁴)	49	(39)	17	(19)	35	(49)	8	(10)	47	(53)	9	(8)	0	(1)

¹ Four of these livers were split and used to transplant one super-urgent/ hepatoblastoma recipient and one elective liver only recipient

² Seven of these livers were split and six were used to transplant one super-urgent/ hepatoblastoma recipient and one elective liver only recipient and one was used to transplant one super-urgent recipient and one hepatoblastoma recipient

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

⁴ One of these livers were 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
 $N = N_{P1} + N_{P2} + N_A$; $N_O = N_S + N_W + N_R$

Reasons for not offering for split transplantation

- 12 **Table 4** details the reasons given by the transplanting centre or noted by the ODT Duty Office for 32 livers not being offered for splitting (78% of the 41 livers available for splitting that were not split). In 11 cases there were concerns over liver function tests. The donor AST level, reported on the Core Donor Data Form, is presented in the table but is not well reported.

Table 4 Reasons given for why 32 livers from donors meeting the liver splitting criteria, between 1 October 2015 and 31 March 2016, were not offered for splitting				
Donor	Donor allocation zone	Transplanting centre	Reason for liver not being offered for splitting	AST (iu/l)
Donor reasons				
1	Birmingham	Birmingham	Size match, downtime and bloods	274
2	Birmingham	Birmingham	Left lobe laceration	
3	Birmingham	Birmingham	Large and fatty	
4	Birmingham	Birmingham	Function	
5	Cambridge	Cambridge	Abnormal live function tests	914
6	Cambridge	Cambridge	Split accepted in Leeds - their paediatric surgeon attended and deemed unsplittable	
7	Edinburgh	King's College	Function - raised bilirubin	
8	King's College	King's College	Fatty liver/anatomy	
9	King's College	King's College	Donor injury	118
10	King's College	King's College	Liver injury from defibrillation of donor burn lesion	
11	King's College	King's College	Abnormal liver size shape anatomy of left lateral segment	
12	King's College	King's College	Did not perfuse well - weight 1.7 kg congested liver	
13	King's College	King's College	Function AST and high sodium (Na)	381
14	King's College	King's College	Function (Liver function tests)	
15	King's College	Royal Free	Raised liver function tests	
16	King's College	Royal Free	Medical history of donor	
17	Leeds	Edinburgh	Abnormal liver function tests (ALT 900) and presumed ischaemic damage. They would not split a liver in this condition.	45
18	Leeds	Leeds	Too fatty	
19	Leeds	Leeds	Unsuitable due to anatomy	
20	Leeds	Leeds	Liver was too large	
21	Leeds	Royal Free	Raised ALT	
22	Newcastle	Cambridge	Grossly abnormal liver function	
23	Newcastle	King's College	Mild to moderately fatty	
24	Newcastle	Leeds	Damaged	
25	Newcastle	Newcastle	Recipient needed whole liver as they had narrow hepatic arteries from previous transplant. Therefore needed to ensure there were long vessels to make transplant successful	

Table 4 Reasons given for why 32 livers from donors meeting the liver splitting criteria, between 1 October 2015 and 31 March 2016, were not offered for splitting

Donor	Donor allocation zone	Transplanting centre	Reason for liver not being offered for splitting	AST (iu/l)
26	Royal Free	Royal Free	Trauma and possible damage	180
27	Royal Free	Royal Free	Function - rising Liver function tests	
28	Royal Free	Royal Free	Abnormal liver function tests	240
29	Royal Free	Royal Free	Abnormal liver function tests	216
Recipient reasons				
30	Edinburgh	Edinburgh	Top band recipient was so unwell that whole liver was required	18
Other reasons				
31	Edinburgh	Leeds	Poor perfusion	20
32	King's College	Royal Free	Liver was accepted for transplant with small bowel. The intended bowel recipient died, so the liver was offered on at a stage which precluded splitting	

Reasons why livers offered for split transplant were not split

13 Nine livers were offered for splitting but were not split. The reasons given for not splitting are detailed in **Table 5**.

Table 5 Reasons given for why 9 livers from donors meeting the split liver criteria, between 1 October 2015 and 31 March 2016, that were offered for splitting were not split

Donor	Donor allocation zone	Transplanting centre	Details of why liver was not split	AST (iu/l)
Donor reasons				
1	Cambridge	Cambridge	Left lateral declined due to anatomy	
2	Leeds	Edinburgh	Left lateral declined by all paediatric centres as fatty	42
3	Leeds	Royal Free	Left lateral declined due to anatomy	
4	Royal Free	Royal Free	Left lateral offered but declined due to donor medical history	71
Recipient reasons				
5	King's College	King's College	Left lateral initially accepted in Leeds. Intended recipient found to be unsuitable at a stage where an alternative could not be found. Liver not split	96
Other reasons				
6	Edinburgh	Edinburgh	Left lateral declined due to medical history and no suitable recipients	90
7	Edinburgh	Edinburgh	Left lateral declined due to fatty liver/transport difficulties/tumour	73
8	Royal Free	Edinburgh	Left lateral declined by all centres - No suitable recipients and Size	42

Table 5 Reasons given for why 9 livers from donors meeting the split liver criteria, between 1 October 2015 and 31 March 2016, that were offered for splitting were not split				
Donor	Donor allocation zone	Transplanting centre	Details of why liver was not split	AST (iu/l)
9	Royal Free	Royal Free	Left lateral offered but not accepted due to function/no suitable recipients	

- 14 There was 1 liver transplant recipient with Hepatoblastoma transplanted from a DBD donor between 1 October 2015 and 31 March 2016. Details of this transplant are in **Table 6**.

Table 6 Details of Hepatoblastoma patients transplanted between 1 October 2015 and 31 March 2016					
Donor	Transplanting centre	Transplant type	Donor age (years)	Recipient age (years)	Reason for not splitting
1	Birmingham	Split	24	1	
Note: On 6 October 2014 it became a requirement to split livers, within criteria for splitting, offered to Hepatoblastoma patients					

TRANSPLANT SURVIVAL

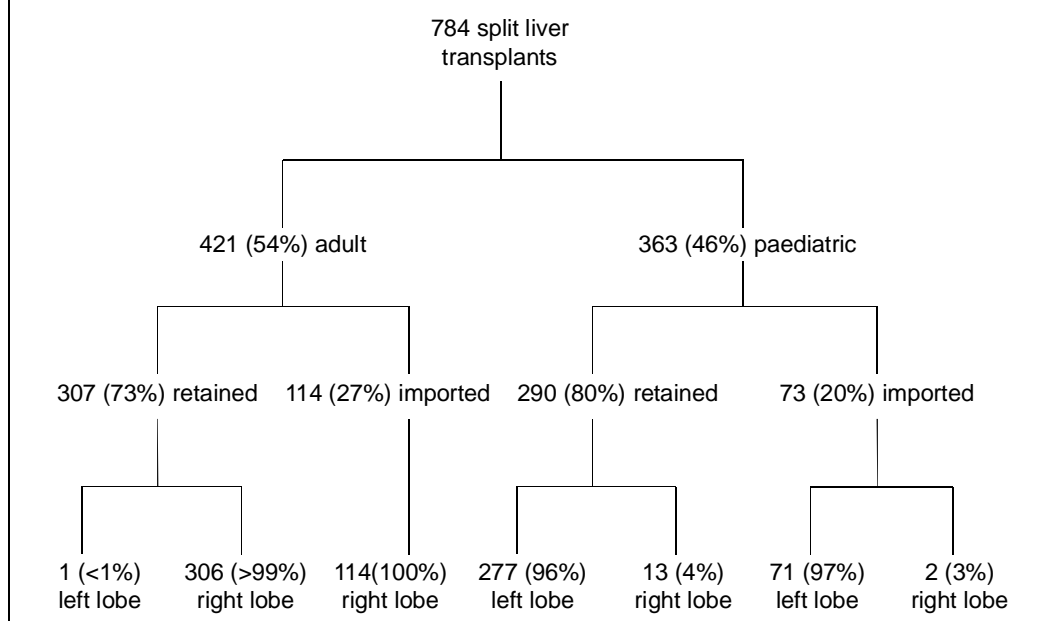
Data and methods

- 15 Data on 784 NHS group 1 first elective split liver only transplants in the UK using livers from DBD donors between 1 April 2006 and 30 September 2015 were analysed. Auxiliary and intestinal transplants were excluded from this cohort as were regrafts. Follow-up data were as recorded on the UKTR on 10 April 2016.
- 16 Each split liver was categorised into “retained”/ “imported” and “split by adult unit surgeon”/ “split by paediatric unit surgeon” (where surgeons from Birmingham, King’s College and Leeds are classed as paediatric unit surgeons). Data returned via the Split Liver Information form was the primary source for categorising split livers into these groups. “Retained”/ “imported” was determined using the centre where the splitting was performed, which was reported in 60% of cases, and “split by adult unit surgeon”/ “split by paediatric unit surgeon” was determined by the centre where the splitting surgeon was appointed, which was reported in 61% of cases. The secondary source for finding out this information was the ODT Duty Office notes. If it was not clear from these notes where the liver was split and who performed the split, a judgement call was made (for instance, if the zonal centre was a paediatric centre who retained the left lobe and exported the right lobe, then we assumed that the paediatric centre performed the split in-house if the primary and secondary sources were insufficient, <1% of cases).
- 17 Survival up to five years post-split liver transplant (where the outcome event is graft failure or patient death) was compared for “retained” and “imported” split livers and for “adult unit surgeon” and “paed unit surgeon” split livers, separately for adult and paediatric patients. These analyses were performed using the Kaplan-Meier estimation method and the log-rank test. Risk-adjusted Cox regression models were also fitted to control for confounding factors. Risk factors included were those found to be significant in the post transplant outcome modelling in the development of the liver transplant benefit allocation scheme. Factors adjusted for were: recipient - age, HCV status, ln(creatinine), ln(INR), albumin, location, whether on renal replacement therapy; donor – age, diabetes; transplant – split or whole, imported/retained, adult/paediatric unit surgeon. Median cold ischaemia time (CIT) was also compared, for retained and imported split livers, using the Mann-Whitney U test.
- 18 A comparison of the survival of whole and split liver transplants up to five years was also made, for adult recipients only. This analysis included 3,842 NHS group 1 first adult elective patients transplanted in the UK between 1 April 2006 and 30 September 2015. A sub-group analysis was performed on just those transplants performed between 1 April 2011 and 30 September 2015 (N=1,983). Again, auxiliary and multi-organ transplants and regrafts were excluded and follow-up data were as recorded on the UKTR on 10 April 2016.

Results

- 19 **Figure 4** shows a breakdown of the 784 split liver transplants by recipient age group (adult (≥ 17 years), paediatric (< 17 years)) and whether the liver was retained or imported.

Figure 4 Breakdown of NHS group 1 elective split liver only transplants in the UK using livers from donors after brain death, 1 April 2006 and 30 September 2015



20 **Table 7** shows a breakdown of the 784 split liver transplants by recipient age group, transplant centres and whether the liver was retained or imported.

Table 7 NHS group 1 first elective split liver only transplants in the UK using livers from donors after brain death, 1 April 2006 – 30 September 2015

Transplant centre	Retained N (%)	Imported N (%)	Total
Paediatric recipients			
Birmingham	114 (86)	19 (14)	133
King's College	128 (76)	41 (24)	169
Leeds	48 (79)	13 (21)	61
Total	290 (80)	73 (20)	363
Adult recipients			
Birmingham	124 (95)	6 (5)	130
Cambridge	13 (43)	17 (57)	30
Edinburgh	22 (34)	43 (66)	65
King's College	95 (92)	8 (8)	103
Leeds	39 (80)	10 (20)	49
Newcastle	4 (27)	11 (73)	15
Royal Free	10 (34)	19 (66)	29
Total	307 (73)	114 (27)	421
TOTAL	597 (76)	187 (24)	784

- 21 **Table 8** shows the median and range of CIT, in hours, of retained and imported split livers transplanted in adult and paediatric patients (left lobes transplanted in adult patients and right lobes transplanted in paediatric patients were excluded (N=16)). On average, CIT was 2.7 hours longer for imported liver lobes compared with retained liver lobes for both adult and paediatric recipients (Mann-Whitney U test: $p < 0.0001$ for both). Data are shown separately for 2006-2011 and 2011-2015 and the more recent cohort shows a CIT that is 1.6 hours longer for imported rather than retained left lobes for paediatric patients, and 3.0 hours longer for imported right lobes for adult patients. In adult recipient transplants CIT are longer in the most recent time period.

Table 8 Cold ischaemic times (CIT) of retained and imported split livers, transplanted in NHS group 1 elective liver only patients in the UK between 1 April 2006 and 30 September 2015				
		N ¹	CIT (hours)	
			Median	Range
Left lobes transplanted in paediatric patients				
1 April 2006 – 31 March 2011	Retained	130	9.0	3.6 – 13.9
	Imported	39	11.8	2.9 – 16.5
1 April 2011 – 30 September 2015	Retained	85	9.1	3.8 – 16.2
	Imported	18	10.7	7.0 – 16.0
Overall	Retained	215	9.0	3.6 – 16.2
	Imported	57	11.7	2.9 – 16.5
Right lobes transplanted in adult patients				
1 April 2006 – 31 March 2011	Retained	164	9.8	4.8 – 17.6
	Imported	42	12.5	6.6 – 16.3
1 April 2011 – 30 September 2015	Retained	122	9.5	2.6 – 18.1
	Imported	65	12.5	6.6 – 15.6
Overall	Retained	286	9.7	2.6 – 18.1
	Imported	107	12.5	6.6 – 16.3

¹ CIT was not reported for a total of 103 split livers

Unadjusted survival analysis

- 22 **Figure 5** shows the Kaplan-Meier estimated survival curves up to five years post-transplant for paediatric and adult patients, by whether the split liver was retained or imported. The log-rank test showed no statistical difference in the overall survival curves in the paediatric analysis ($p=0.3$) or the adult analysis ($p=0.1$), although retained livers appear to do better in the adult patients with a 6% survival benefit at 5 years.
- 23 **Figure 6** shows the Kaplan-Meier estimated survival curves up to five years post-transplant for paediatric and adult patients, by whether the liver was split by an adult unit surgeon or a paediatric unit surgeon. Note that there were only eight events in the “split by adult unit surgeon” group in the paediatric analysis and also the adult analysis, so the

results should be viewed with caution. There was no statistically significant difference found between these groups in the paediatric or adult analyses.

Figure 5 Five year transplant survival of split livers transplanted in NHS group 1 elective patients in the UK, April 2006 – September 2015 – RETAINED vs IMPORTED

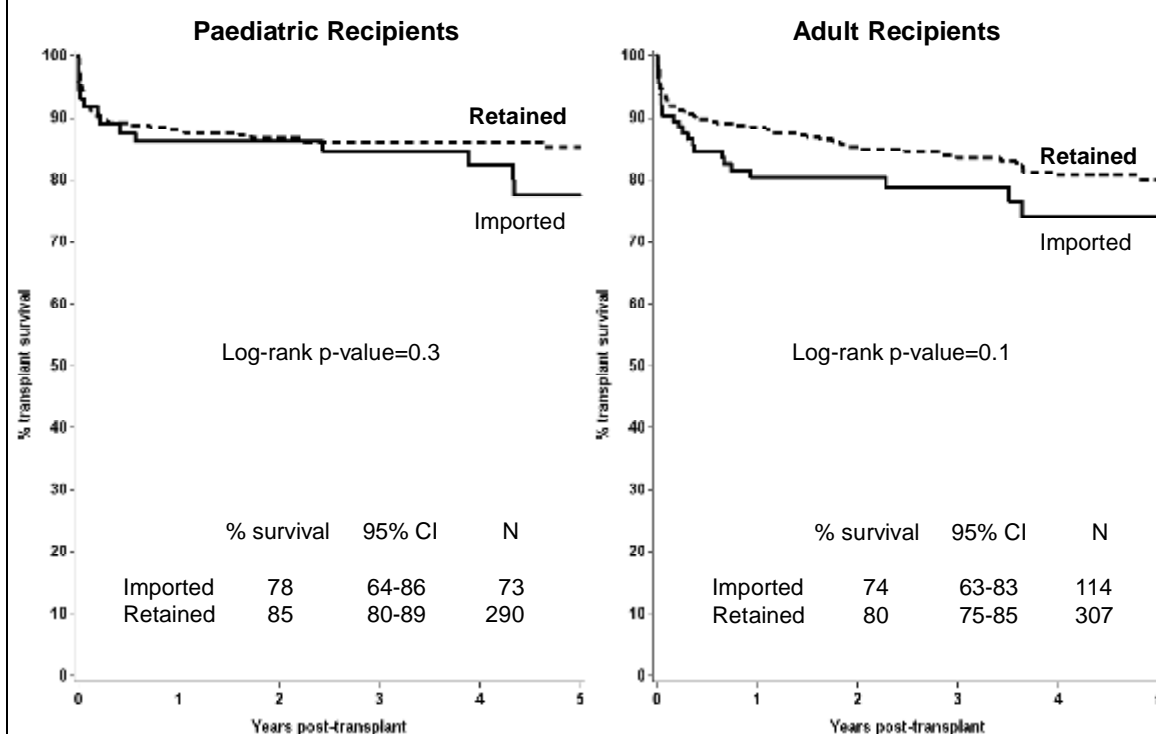
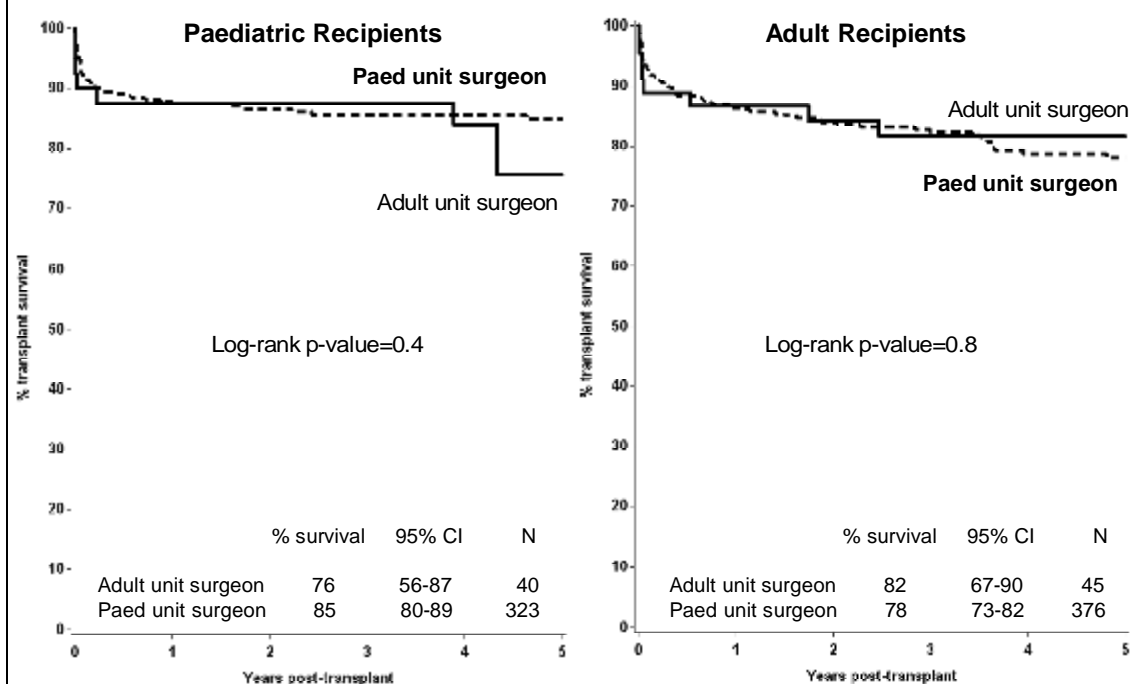
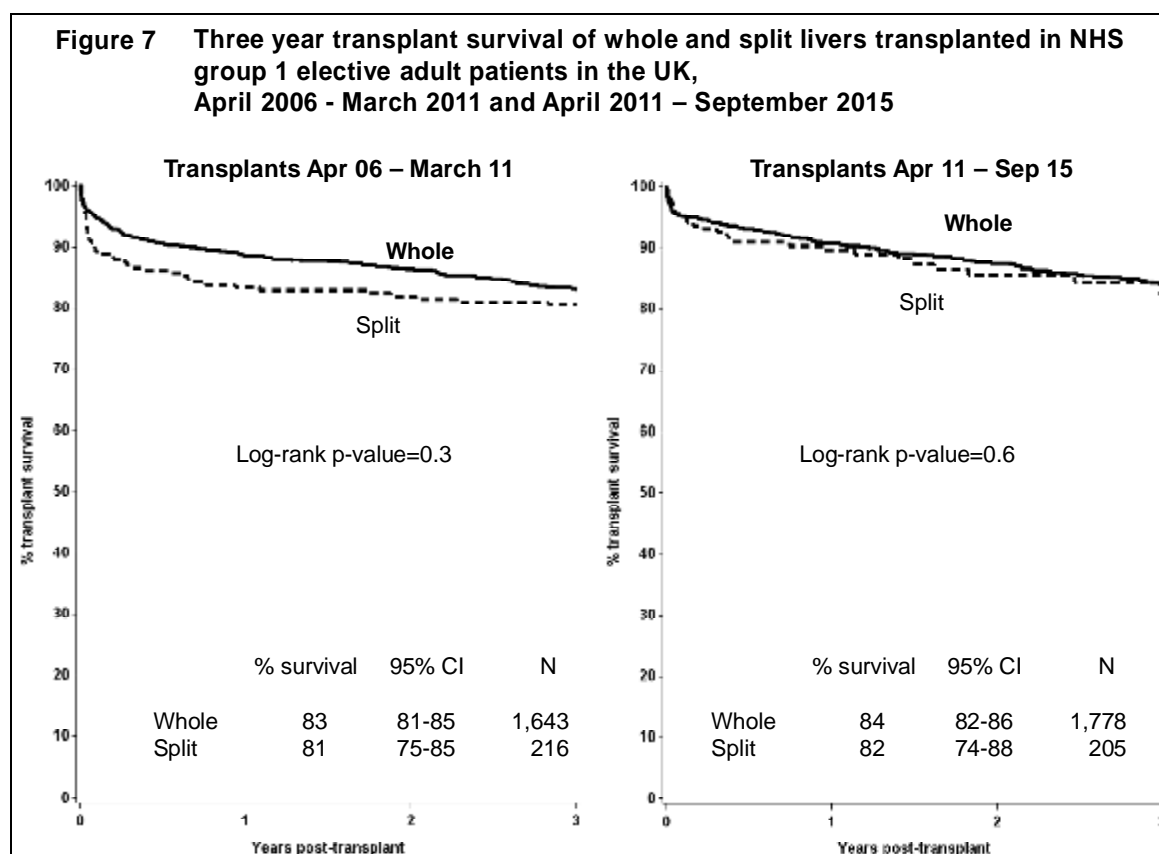


Figure 6 Five year transplant survival of split livers split transplanted in NHS group 1 elective patients in the UK, April 2006 – September 2015 – ADULT vs PAEDIATRIC UNIT SURGEONS



- 24 Causes of graft failure or patient death that were reported to the UKTR for the 130 out of 784 split liver transplant recipients who died or whose graft failed within five years following transplant are presented for reference in **Appendix I** by age group, by whether the split liver was retained/ imported and by whether the liver was split by an adult/ paediatric unit surgeon.
- 25 Unadjusted survival analysis at three years post-transplant for more recent transplants (1 April 2011 - 30 September 2015) can be seen in **Appendix II**. Results support the lack of a significant difference in all comparisons.
- 26 **Figure 7** shows the Kaplan-Meier estimated survival curves comparing transplant survival up to three years for whole and split liver transplants between 1 April 2006 and 31 March 2011 and between 1 April 2011 and 30 September 2015. There is no significant difference between whole and split liver transplants although there is a suggestion that split liver outcomes are improved in the short-term in the later period. There is no significant change in split liver outcomes ($p=0.3$) or whole liver outcomes ($p=0.2$) over this time period.



- 27 Risk-adjusted analyses were carried out using Cox Proportional Hazards regression modelling for three year transplant survival. The results are shown in **Table 9** for transplants April 2006 – March 2011 and in **Table 10** for April 2011 – September 2015. After risk adjustment there is some evidence that split liver transplants have a higher hazard of patient death or graft failure for the most recent time period ($p=0.03$), not seen in the unadjusted results. Note that the median (IQR) donor age for split liver transplants was 29 (21-37), compared to whole liver transplants 54 (43-64) in the recent period. The results showed no difference between retained and imported livers or between paediatric and adult unit surgeons in either time period.

Table 9 Cox regression model for risk of graft failure or patient death within 3 years, 1 April 2006 – 31 March 2011							
Factor	Level	Whole and split liver transplants			N	Split liver transplants	
		N	Hazard ratio (95% CI)	p-value		Hazard ratio (95% CI)	p-value
Transplant							
Liver split	Whole	1581	1.00	-	-	-	-
	Split	382	1.35 (0.94 - 1.92)	0.1	-	-	-
Unit surgeon							
	Paediatric	-	-	-	331	1.00	-
	Adult	-	-	-	51	0.77 (0.34 - 1.72)	0.5
Location							
	Retained	-	-	-	301	1.00	-
	Imported	-	-	-	81	1.13 (0.62 - 2.05)	0.7
Recipient							
Age at transplant	Adult	1769	1.00	-	211	1.00	-
	Paediatric	194	1.32 (0.8 - 2.17)	0.3	171	1.10 (0.57 - 2.11)	0.8
HCV indicator	No	1575	1.00	-	341	1.00	-
	Yes	388	1.21 (0.93 - 1.57)	0.1	41	0.95 (0.41 - 2.18)	0.9
Ln(creatinine)		1963	1.58 (1.18 - 2.13)	0.002	382	1.40 (0.82 - 2.40)	0.2
Ln(INR)		1963	0.53 (0.34 - 0.82)	0.005	382	0.56 (0.22 - 1.41)	0.2
Albumin		1963	0.99 (0.97 - 1.00)	0.1	382	1.01 (0.97 - 1.05)	0.6
Renal replacement therapy	No	1881	1.00	-	367	1.00	-
	Yes	82	1.53 (0.98 - 2.37)	0.06	15	2.16 (0.85 - 5.45)	0.1
Patient location	Outpatient	1645	1.00	-	324	1.00	-
	Inpatient	318	1.34 (1.00 - 1.80)	0.05	58	1.18 (0.59 - 2.37)	0.6
Donor							
Donor age		1963	1.01 (1.00 - 1.02)	0.03	382	1.01 (0.98 - 1.03)	0.7
History of diabetes	No	1860	1.00	-	378	1.00	-
	Yes	103	1.36 (0.89 - 2.07)	0.2	4	0 (0 - 0)	>0.9

Table 10 Cox regression model for risk of graft failure or death within 3 years, 1 April 2011 – 30 September 2015							
Factor	Level	Whole and split liver transplants			Split liver transplants		
		N	Hazard ratio (95% CI)	p-value	N	Hazard ratio (95% CI)	p-value
Transplant							
Liver split	Whole	1734	1.00	-	-	-	-
	Split	359	1.62 (1.05 - 2.49)	0.03	-	-	-
Unit surgeon							
	Paediatric	-	-	-	332	1.00	-
	Adult	-	-	-	27	0.92 (0.28 - 3.09)	0.9
Location							
	Retained	-	-	-	260	1.00	-
	Imported	-	-	-	99	1.44 (0.75 - 2.74)	0.3
Recipient							
Age at transplant	Adult	1911	1.00	-	203	1.00	-
	Paediatric	182	1.08 (0.56 - 2.09)	0.8	156	0.74 (0.27 - 2.00)	0.5
HCV indicator	No	1715	1.00	-	324	1.00	-
	Yes	378	1.25 (0.91 - 1.72)	0.2	35	2.07 (0.88 - 4.88)	0.1
Ln(creatinine)		2093	1.34 (0.98 - 1.85)	0.07	359	0.78 (0.43 - 1.41)	0.4
Ln(INR)		2093	0.98 (0.60 - 1.59)	0.9	359	1.43 (0.54 - 3.82)	0.5
Albumin		2093	1.00 (0.98 - 1.02)	0.8	359	1.01 (0.97 - 1.05)	0.6
Renal replacement therapy	No	1971	1.00	-	340	1.00	-
	Yes	122	0.89 (0.5 - 1.58)	0.7	19	0.83 (0.20 - 3.52)	0.8
Patient location	Outpatient	1760	1.00	-	299	1.00	-
	Inpatient	333	1.22 (0.86 - 1.73)	0.3	60	1.50 (0.69 - 3.27)	0.3
Donor							
Donor age		2093	1.01 (1.00 - 1.02)	0.07	359	1.01 (0.98 - 1.04)	0.6
History of diabetes	No	1940	1.00	-	350	1.00	-
	Yes	153	1.44 (0.94 - 2.21)	0.1	9	1.69 (0.40 - 7.17)	0.5

- 28 Data on 47 NHS group 1 first super urgent split liver only transplants in the UK using livers from DBD donors between 1 April 2006 and 30 September 2015 were also analysed. Auxiliary and intestinal transplants were excluded from this cohort as were regrafts. Follow-up data were as recorded on the UKTR on 10 April 2016. Of these there were 10 (26%) deaths or failed grafts in the 38 paediatric recipients, and 3 (33%) deaths or failed grafts in the 9 adult recipients. Due to these small numbers no survival analysis could be performed.

SUMMARY

ACTIVITY

- 29 There were 77 livers donated between 1 October 2015 and 31 March 2016 from donors who met the criteria for liver splitting (35% more than previous six months). Of these, 49 (64%) were available for splitting for elective recipients, having not been used in super-urgent, hepatoblastoma, intestinal or multi-organ recipients. Of these, 17 (35%) were offered for splitting and 8 (47% of the 17) were actually split (20% fewer than previous six months). In over a third of the 32 cases where the liver was available for splitting but was not offered for splitting, abnormal or raised liver function tests were cited as the reason for not considering splitting. Nine livers were offered for splitting but instead used whole or reduced. Common reasons for not splitting these livers were the fattiness of the organ or a lack of suitable paediatric patients for the left lateral segment.
- 20 The percentage of livers split of those available for splitting increased by about 10% from 23% in 2006/2007 to 33% in 2012/13. In 2012/13, 27 livers were split. Since then there has been a fall to only 16 livers split in 2014/15, and only 18 in 2015/16.

TRANSPLANT OUTCOMES

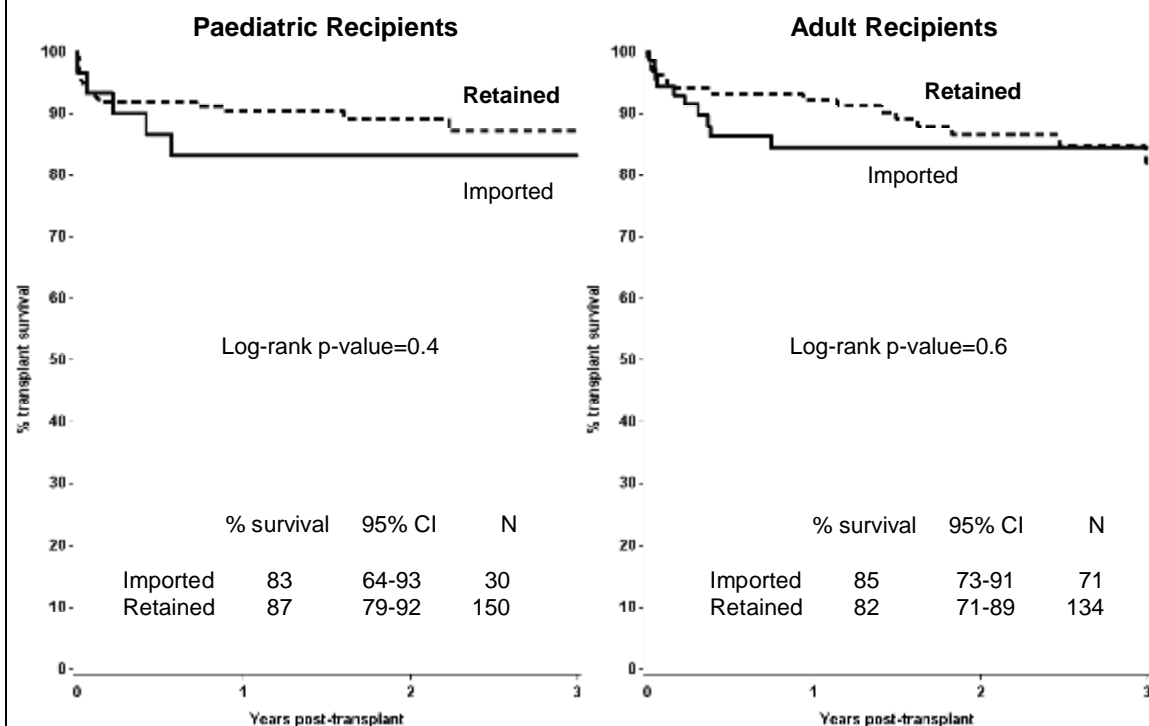
- 31 Unadjusted analysis of transplant outcomes, April 2006 – September 2015, showed:
- No significant difference in 5 year transplant survival when comparing:
 - retained and imported split livers in paediatric recipients ($p=0.3$)
 - retained and imported split livers in adult recipients ($p=0.1$).
 - livers split by an adult or paediatric unit surgeon ($p>0.4$)
 - No significant difference between whole and split liver transplant survival at 3 years for earlier transplants (April 2006-March 2011), $p=0.3$, or more recent transplants (April 2011-September 2015), $p=0.6$.
- 32 Risk adjusted analysis of transplant outcomes, April 2010- September 2015, showed:
- Evidence of poorer outcomes for split liver recipients compared to whole, $p=0.03$ (HR for split=1.6, 95% CI 1.1-2.5)
 - No significant difference in outcomes for livers split by adult ($N=27$) and paediatric ($N=332$) unit surgeons, $p=0.9$ (HR for adult unit=0.9, 95%CI 0.3-3.1)
 - No significant difference in outcomes of retained ($N=260$) and imported ($N=99$) split livers, $p=0.3$ (HR for imported=1.4, 95% CI 0.8-2.7).

Appendix I Causes of graft failure or patient death for NHS group 1 elective split liver only transplant recipients in the UK between 1 April 2006 and 30 September 2015 who died or whose graft failed within five years following transplant, by age group, whether the split liver was retained/ imported and whether the liver was split by an adult/ paediatric unit surgeon

Causes of graft failure or patient death	Retained split liver	Imported split liver	Liver split by paediatric unit surgeon	Liver split by adult unit surgeon	Total
	N	N	N	N	N
PAEDIATRIC PATIENTS					
<i>Cause of graft failure - patient did not die</i>					
Hepatic artery thrombosis	13	3	14	2	16
Primary non-function	3	2	3	2	5
Chronic rejection	1	1	2	0	2
Other	4	1	4	1	5
Not reported	1	0	1	0	1
Total	22	7	24	5	29
<i>Cause of death</i>					
Multi-system failure	5	2	7	0	7
Haemorrhage	1	2	2	1	3
Primary non-function -> multi-system failure	3	0	3	0	3
Septicaemia	1	0	1	0	1
Recurrent disease	1	0	1	0	1
Other	6	0	6	0	6
Not reported	0	3	1	2	3
Total	17	7	21	3	24
TOTAL	39	14	45	8	53
ADULT PATIENTS					
<i>Cause of graft failure - patient did not die</i>					
Hepatic artery thrombosis	12	5	14	3	17
Other	5	3	7	1	8
Total	17	8	21	4	25
<i>Cause of death</i>					
Multi-organ failure	5	5	9	1	10
Hepatic artery thrombosis -> multi-system failure/myocardial infarction/pulmonary infection	4	4	7	1	8
Non-lymphoid malignant disease	6	1	7	0	7
Non-thrombotic infarction -> multi-system failure/septicaemia	4	0	4	0	4
Recurrent disease	2	1	3	0	3
Cerebro-vascular accident	2	0	2	0	2
Renal failure	2	0	2	0	2
Vascular occlusion -> multi-system failure	2	0	2	0	2
Rejection/primary non-function	1	1	1	1	2
Other	5	3	7	1	8
Not reported	3	1	4	0	4
Total	36	16	48	4	52
TOTAL	53	24	69	8	77

Appendix II

Comparison of three year transplant survival of split livers transplanted in NHS group 1 elective patients in the UK between 1 April 2011 and 30 September 2015 – RETAINED vs IMPORTED



Comparison of three year transplant survival of split livers split transplanted in NHS group 1 elective patients in the UK between 1 April 2011 and 30 September 2015 – ADULT vs PAEDIATRIC UNIT SURGEONS

