

# NHS BLOOD AND TRANSPLANT

## LIVER ADVISORY GROUP

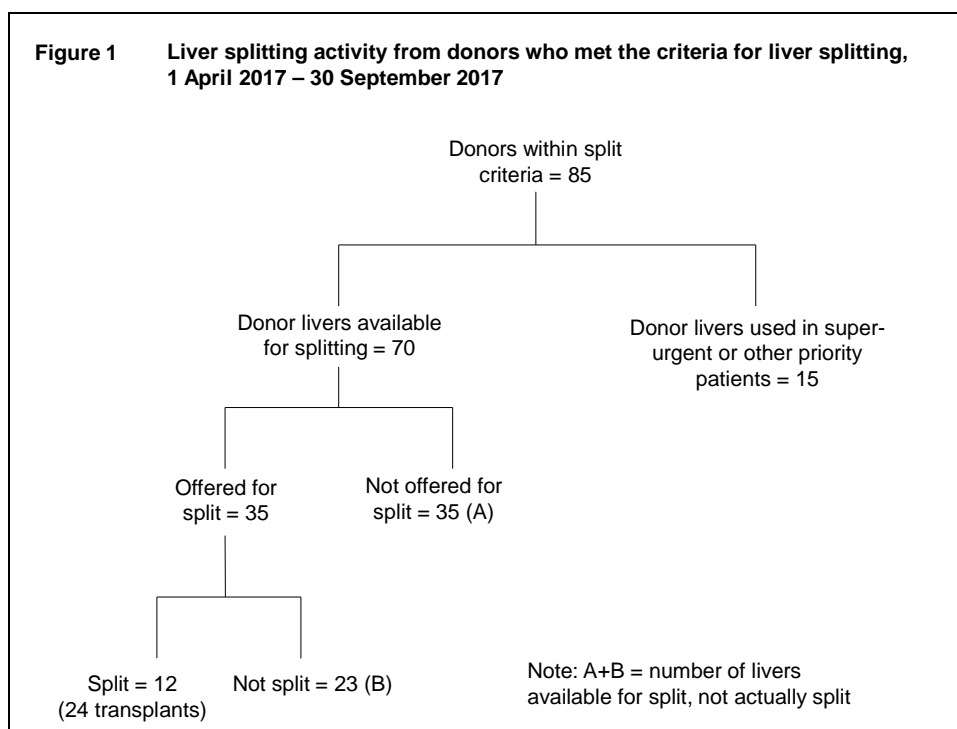
### LIVER SPLITTING ACTIVITY REPORT

#### SUMMARY

- 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 transplant activity of livers from DBD donors who donated their liver in a recent time period and who met the criteria for liver splitting.

#### ACTIVITY

- 2 **Figure 1** shows a summary of the liver splitting activity in the 6-month period 1 April 2017 to 30 September 2017.



- 3 The percentage of livers split of those available for splitting increased from only 16 (16%) in 2014/15 to 18 (20%) in 2015/16, and finally to 44 (35%) in 2016/17, with the highest number of reported split livers. There were 12 (17%) livers split in the first half of 2017/18.
- 4 Between 1 April 2017 and 30 September 2017, there were additional five donors outside of the donor splitting criteria that led to ten split liver transplants.

## TRANSPLANT OUTCOMES

- 5 Transplants performed at Leeds were excluded from unadjusted and risk-adjusted survival analyses due to a lack of follow-up beyond 12 months. Note, however, that there is a plan of action in place to obtain outstanding follow-up data from Leeds.
- 6 Unadjusted analysis of transplant outcomes, 1 April 2007 – 31 March 2017, showed:
  - For adult recipients, a significant difference in the overall survival curves up to five years post-transplant when comparing retained and imported livers ( $p=0.03$ ); with a 9% superiority in survival at 5 years for retained livers compared to imported livers.
  - For paediatric recipients, survival at 5 years post-transplant was superior for retained livers compared to imported livers, but this difference was not statistically significant ( $p=0.08$ ).
  - No significant difference in the overall survival curves up to five years post-transplant when comparing livers split by an adult or paediatric unit surgeon for both paediatric and adult recipients ( $p>0.3$ )
  - No significant difference between whole and split liver transplant survival at 3 years for earlier transplants (1 April 2007 - 31 March 2012),  $p=0.7$ , or more recent transplants (1 April 2012 - 31 March 2017),  $p=0.2$ .
- 7 Risk-adjusted analysis of transplant outcomes within 3 years post-transplant, 1 April 2012- 31 March 2017, showed a significant difference in outcomes for split liver recipients compared to whole,  $p<0.01$  (HR for split=1.85, 95% CI 1.19-2.88).
- 8 Due to low numbers after exclusion of transplants at Leeds, no risk-adjusted analysis was performed to compare split liver transplant outcomes within 3 years post-transplant between retained and imported livers or between livers split by an adult or paediatric unit surgeon.

## ACTION

- 9 Members are asked to note the reduction in the percentage of livers split in the first half of 2017/18, relative to percentages achieved in previous periods.
- 10 Members are asked to note the incompleteness of data reported to NHSBT in Split Liver Information form (see paragraph 18).

## 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 April 2017 and 30 September 2017 and who met the criteria for liver splitting. The paper also reports briefly on activity over the last 10 financial years.
- 2 Liver transplant unadjusted survival outcomes are analysed for patients who received a DBD donor split liver transplant between 1 April 2007 and 31 March 2017. Comparisons are made between livers retained by the splitting centre and those imported as a split from another centre. Comparisons are also made between livers split at an adult or paediatric centre and, more generally, between patients receiving a whole or a split graft.

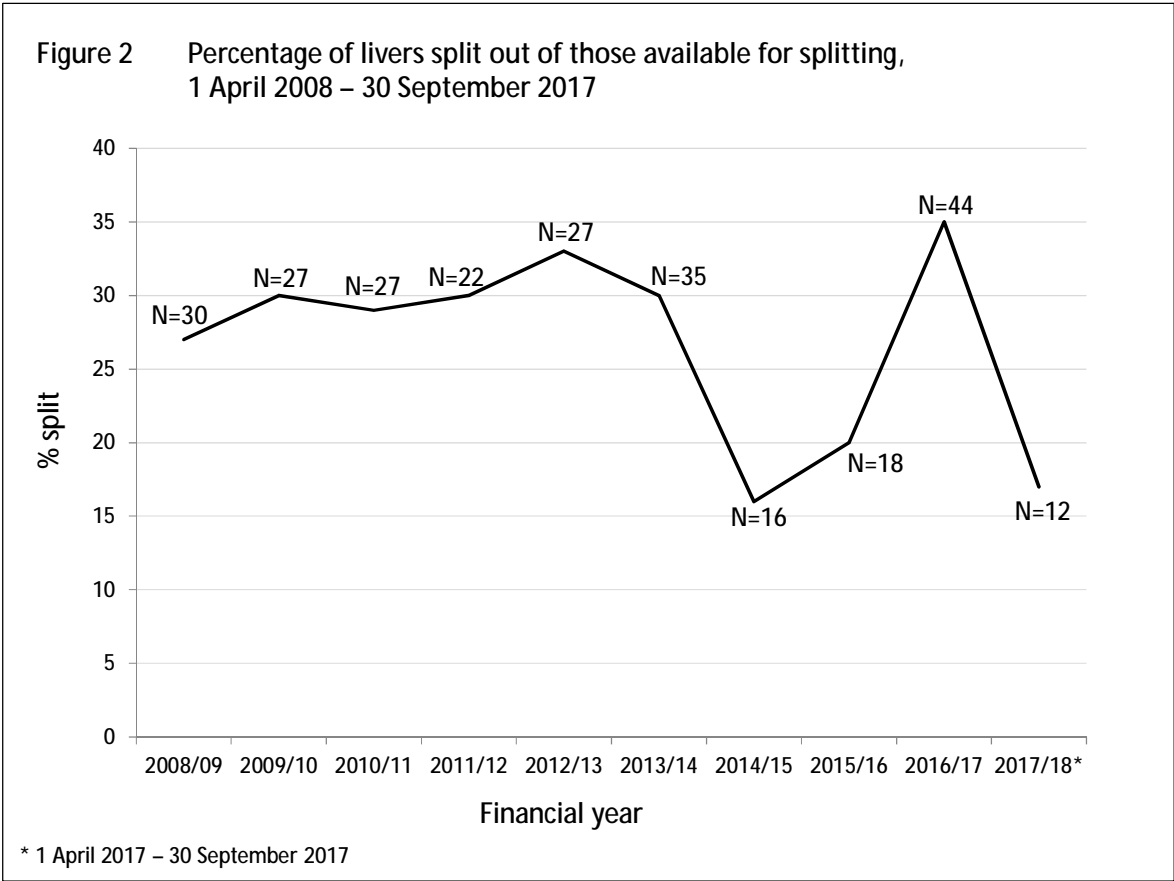
##### LIVER SPLITTING ACTIVITY

###### Data and methods

- 3 Donors meeting the criteria for liver splitting are under 40 years of age, weigh more than 50kg and are 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 85 UK DBD donors whose liver was donated in the 6 months between 1 April 2017 and 30 September 2017 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 86 UK DBD liver donors in the previous 6 months (1 October 2016 - 31 March 2017), 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 Hub Operations, formerly 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 donors meeting criteria for liver splitting and transplanted is shown in **Table 1** for 1 April 2017 to 30 September 2017, with 1 October 2016 to 31 March 2017 figures for comparison. For the latest 6 months, 70 (82%) of the 85 DBD donors meeting the splitting criteria were available for splitting. Of these 70 livers, 35 (50%) were offered for splitting. Of the 35 livers offered for splitting, 12 (34%) were actually split. This activity is summarised in **Figure 1**.
- 9 These 85 livers resulted in 101 transplants, of which 23 (23%) were performed in paediatric patients. In comparison, the 86 livers in the previous six months resulted in 112 transplants, of which 29 (26%) 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 and in the first half of 2017/18. The percentage split is much higher in 2016/17.



**Table 1 Donors meeting criteria for liver splitting, by donor allocation zone, 1 April 2017 to 30 September 2017 (1 October 2016 to 31 March 2017)**

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 <sub>P1</sub>		N <sub>P2</sub>		N <sub>A</sub>		N <sub>O</sub>		% of available		N <sub>S</sub>		% of offered		N <sub>W</sub>		N <sub>R</sub>	
Birmingham	16	(14)	2	(2)	0	(1)	14	(11)	7	(4)	50	(36)	3	(4)	43	(100)	4	(0)	0	(0)
Cambridge	7	(9)	1	(0)	0	(1)	6	(8)	4	(6)	67	(75)	2	(6)	50	(100)	2	(0)	0	(0)
Edinburgh	11	(12)	2	(0)	0	(0)	9	(12)	5	(5)	56	(42)	1	(3)	20	(60)	3	(2)	1	(0)
King's College	17	(12)	4	(3)	1	(1)	12	(8)	5	(1)	42	(13)	3	(1)	60	(100)	2	(0)	0	(0)
Leeds	14	(20)	1	(3)	0	(1)	13	(16)	4	(6)	31	(38)	1	(3)	25	(50)	3	(3)	0	(0)
Newcastle	6	(8)	1	(1)	0	(0)	5	(7)	4	(2)	80	(29)	0	(1)	0	(50)	4	(1)	0	(0)
Royal Free	14	(11)	3	(2)	0	(0)	11	(9)	6	(6)	55	(67)	2	(5)	33	(83)	3	(1)	1	(0)
<b>TOTAL</b>	<b>85</b>	<b>(86)</b>	<b>14<sup>1</sup></b>	<b>(11<sup>2</sup>)</b>	<b>1<sup>3</sup></b>	<b>(4<sup>4</sup>)</b>	<b>70</b>	<b>(71)</b>	<b>35</b>	<b>(30)</b>	50	<b>(42)</b>	12	<b>(23)</b>	34	<b>(77)</b>	21	<b>(7)</b>	2	<b>(0)</b>

<sup>1</sup> There were three instances where a liver was split and used to transplant one super-urgent recipient and one elective liver only recipient

<sup>2</sup> There was one instance where a liver was split and used to transplant one super-urgent recipient and one elective liver only recipient

<sup>3</sup> There was one instance where a liver was split and used to transplant one multi-organ recipient and one elective liver only recipient

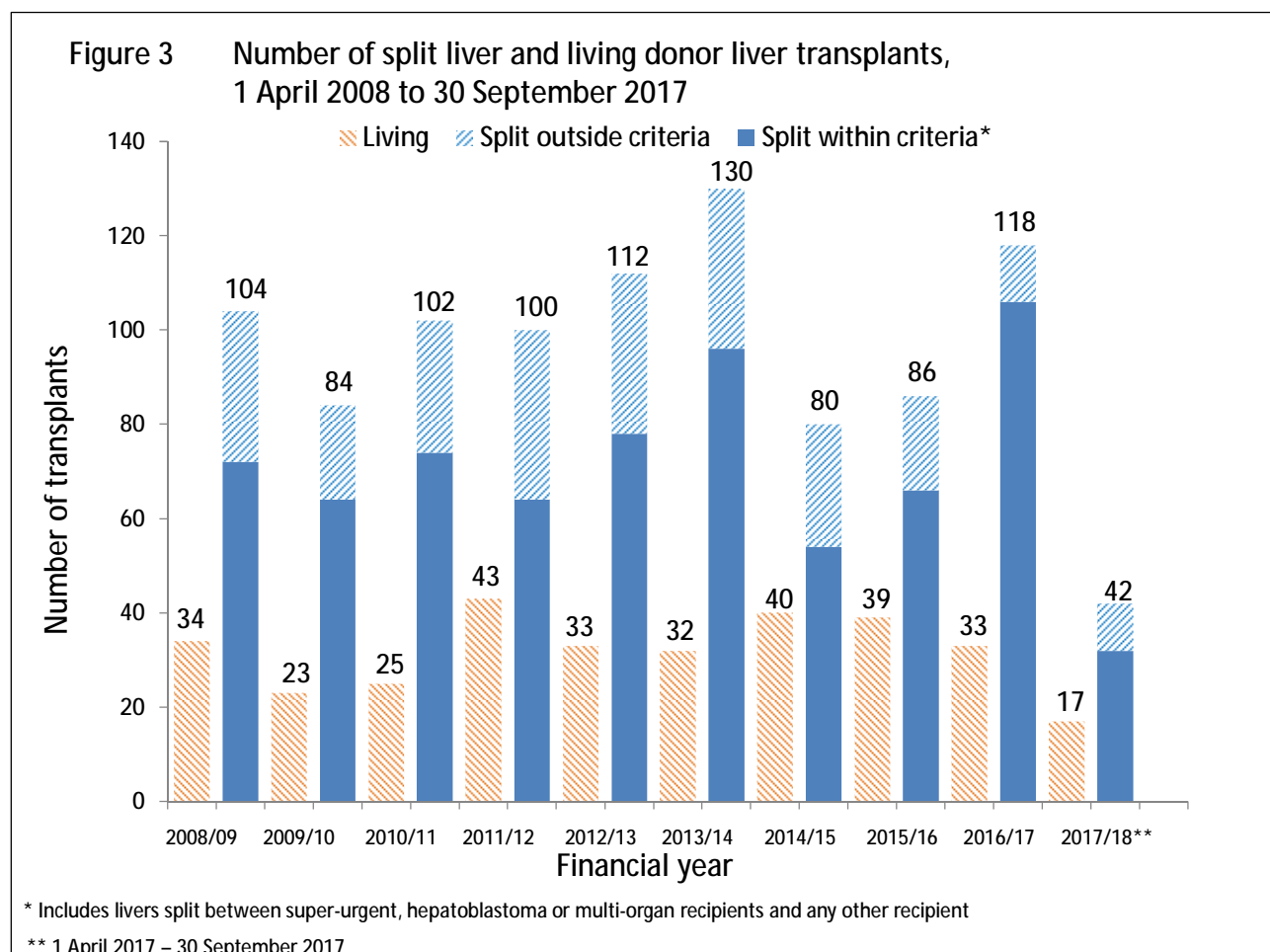
<sup>4</sup> There were two instances where a liver was split and used to transplant one multi-organ recipient and one elective liver only recipient

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  
 $N = N_{P1} + N_{P2} + N_A$ ;  $N_O = N_S + N_W + N_R$

- 11 The percentage of livers split of those available for splitting for the period 1 April 2013 to 30 September 2017 is given in **Table 2**, by donor allocation zone. The number of livers split that were outside splitting criteria is also provided.

Allocation zone	Available for split within criteria	Split within criteria		Split outside criteria
	N	N	%	N
Birmingham	97	22	23	20
Cambridge	44	14	32	2
Edinburgh	74	18	24	3
King's College	95	28	29	17
Leeds	91	20	22	7
Newcastle	38	7	18	2
Royal Free	61	15	25	2
<b>TOTAL</b>	<b>500</b>	<b>124</b>	<b>25</b>	<b>53</b>

- 12 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 2014/15 and 2015/16, with an increase in 2016/2017. The number of split liver transplants includes those from donors in **Table 1** and also those where the donor did not meet splitting criteria whose livers were split for transplant. Between 1 April 2017 and 30 September 2017, there were five donors outside of the donor splitting criteria. These are only included in **Figure 3**, and summarised in **Table 3**.



**Table 3 Characteristics of liver donors who were outside of splitting criteria but whose livers went on to be split, 1 April 2008 to 30 September 2017**

Year	Aged 40 or more		Weighing 50kg or less		Spent 5 days or more in ICU <sup>1</sup>		Total
	N	%	N	%	N	%	
2008/09	7	44	7	44	3	19	<b>16</b>
2009/10	7	70	0	0	3	30	<b>10</b>
2010/11	9	64	2	14	4	29	<b>14</b>
2011/12	10	56	5	28	5	28	<b>18</b>
2012/13	12	71	4	24	2	12	<b>17</b>
2013/14	11	65	5	29	3	18	<b>17</b>
2014/15	6	46	4	31	3	23	<b>13</b>
2015/16	8	80	2	20	1	10	<b>10</b>
2016/17	3	50	2	33	1	17	<b>6</b>
2017/18 <sup>2</sup>	2	40	0	0	3	60	<b>5</b>

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

<sup>1</sup> The length of ICU stay was unknown for 22 donors. The length of ICU stay was calculated as time from ventilation start date to the time of second brainstem death test.

<sup>2</sup> 1 April 2017 - 30 September 2017

### Reasons for not offering for split transplantation

- 13 **Table 4** details the reasons given by the transplanting centre or noted by the ODT Hub Operations for the 35 livers not being offered for splitting (60% of the 58 livers available for splitting that were not split). The donor AST level, reported on the Core Donor Data Form, is presented in the table but is not well reported. Prior to 6 January 2016, the point in time where the liver function tests were performed was not recorded on the Core Donor Data form leading to only one value of AST recorded per donor. On the 6 January 2016, the Core Donor Data form was changed to record liver function tests at four points during the donation process: on admission, on referral to SNOD, on retrieval and as an additional result. In **Table 4** and **Table 5**, the maximum value of AST since admission is reported.

**Table 4 Reasons given for why 35 livers from donors meeting the liver splitting criteria , between 1 April 2017 and 30 September 2017, were not offered for splitting**

Donor	Donor allocation zone	Transplanting centre	Reason for liver not being offered for splitting	AST (iu/l)
<b>Donor reasons</b>				
1	Birmingham	Birmingham	Liver anatomy	
2	Birmingham	Birmingham	Deemed unsplitable on visualisation	
3	Birmingham	Birmingham	High donor body mass index (37kg/m <sup>2</sup> ) and weight (120.5kg)	
4	Birmingham	Birmingham	Function	
5	Birmingham	Birmingham	Deemed unsplitable due to donor history	
6	Birmingham	Birmingham	Not split due to donor alcohol history and raised GGT; also recipient was very sick and required whole graft	44
7	Birmingham	Birmingham	Liver not split due to abnormal liver function tests and also due to liver being small	
8	Cambridge	Cambridge	Abnormal liver function tests	
9	Edinburgh	Birmingham	Donor history	208
10	Edinburgh	King's College	Donor history	172
11	Edinburgh	Leeds	Donor past medical history	623
12	King's College	King's College	Donor history and size	
13	King's College	King's College	Unstable donor- DCD to DBD	67
14	King's College	King's College	Function	269
15	King's College	King's College	History	20
16	King's College	King's College	Function	
17	King's College	King's College	Size match	68
18	Leeds	Birmingham	Function	
19	Leeds	Leeds	Donor size	
20	Leeds	Leeds	Not suitable to split - moderately fatty	
21	Leeds	Leeds	Abnormal liver function tests	
22	Leeds	Leeds	Donor deemed borderline	
23	Leeds	Leeds	Trauma	103
24	Leeds	Leeds	High donor body mass index (>35kg/m <sup>2</sup> )	44
25	Leeds	Royal Free	Abnormal liver function tests	128
26	Newcastle	Newcastle	Due to donor cardiac arrest and abnormal liver function tests	
27	Royal Free	King's College	Liver has already been declined by all other centres on HLA/ABO type	
28	Royal Free	Royal Free	Donor history	
29	Royal Free	Royal Free	Function	140



<b>Table 4 Reasons given for why 35 livers from donors meeting the liver splitting criteria , between 1 April 2017 and 30 September 2017, were not offered for splitting</b>				
<b>Donor</b>	<b>Donor allocation zone</b>	<b>Transplanting centre</b>	<b>Reason for liver not being offered for splitting</b>	<b>AST (iu/l)</b>
30	Royal Free	Royal Free	Marginal donor and abnormal liver function tests	286
<b>Recipient reasons</b>				
31	Leeds	Papworth	A super-urgent lung recipient requiring a lung and liver transplant	16
<b>Other reasons</b>				
32	King's College	King's College	Left lobe was damaged - not splittable	
33	Cambridge	Edinburgh	No time, late acceptance	
34	Edinburgh	Edinburgh	Oversight by centre – centre was not reminded by ODT Hub Operations or Snod.	
35	Royal Free	Royal Free	ODT Hub Operations advised liver centre that liver did not fulfil the splitting criteria incorrectly.	131

### Reasons why livers offered for split transplant were not split

14 23 livers were offered for splitting but were not split. The reasons given for not splitting are detailed in **Table 5**.

<b>Table 5 Reasons given for why 23 livers from donors meeting the split liver criteria, between 1 April 2017 and 30 September 2017, that were offered for splitting were not split</b>				
<b>Donor</b>	<b>Donor allocation zone</b>	<b>Transplanting centre</b>	<b>Details of why liver was not split</b>	<b>AST (iu/l)</b>
<b>Donor reasons</b>				
1	Birmingham	Birmingham	Liver being steatotic with round edges	
2	Cambridge	Cambridge	Deemed unsplittable on visualisation	
3	Edinburgh	Edinburgh	Deemed unsplittable on visualisation	126
4	Edinburgh	Edinburgh	Split was offered but not accepted due to donor history and poor function	61
5	King's College	Cambridge	Due to biopsy report result	224
6	Leeds	Edinburgh	Unsuitable for splitting due to anatomy	
7	Newcastle	Leeds	Unsuitable for splitting due to anatomy (problem with artery/artery)	
8	Royal Free	Royal Free	Poor function	54
9	Royal Free	Royal Free	Donor history and size	
10	Royal Free	Royal Free	Due to donor becoming unstable and marginal and history	93
<b>Other reasons</b>				
11	Birmingham	Birmingham	Split was offered but not accepted due to size/abo and logistics	
12	Birmingham	Edinburgh	Split was offered but not accepted due to no suitable recipients and donor history	
13	Birmingham	Newcastle	Split offered not placed	
14	Cambridge	Cambridge	Large liver, split not suitable for intended recipient and too late to offer on	
15	Edinburgh	Edinburgh	Offered but declined due to cold ischaemia time	69
16	Edinburgh	King's College	Right lobe used for hepatocytes, left lateral transplanted into a paed	15
17	King's College	Cambridge	Left lateral segment declined due to history and no suitable recipients	
18	Leeds	Leeds	Damage	102
19	Leeds	Leeds	Split was offered but not accepted due to no suitable recipients and size	
20	Newcastle	Cambridge	Size and potential cold ischaemia time	
21	Newcastle	Cambridge	Split offered but not accepted due to function and no suitable recipients	
22	Newcastle	Edinburgh	Split offered but not accepted due to poor perfusion	
23	Royal Free	Birmingham	Right lobe disposed of due to recipient being unfit	

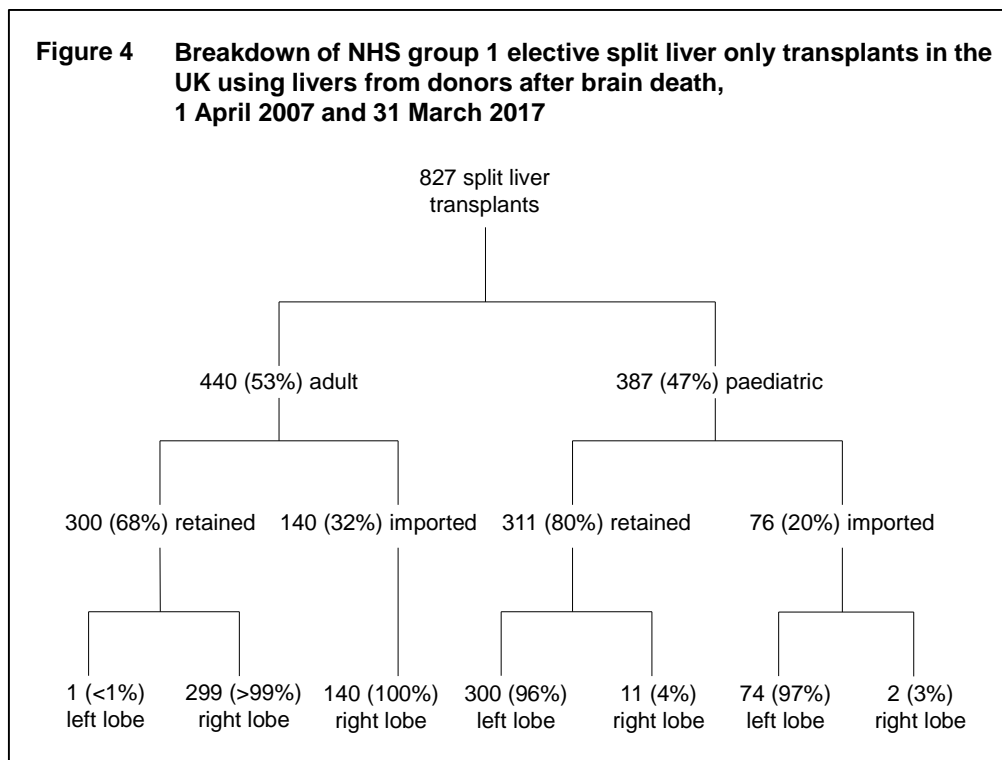
15 There were no liver transplant recipients with hepatoblastoma transplanted between 1 April 2017 and 30 September 2017.

## TRANSPLANT SURVIVAL

- 16 Data on 827 NHS group 1 first elective split liver only transplants in the UK using livers from DBD donors between 1 April 2007 and 31 March 2017 were analysed. Auxiliary and intestinal transplants were excluded from this cohort as were re-grafts. Follow-up data were as recorded on the UKTR on 28 October 2017.
- 17 Transplants performed at Leeds (N=114) were excluded from unadjusted and risk-adjusted survival analyses due to a lack of follow-up beyond 12 months. Leeds have a particularly low lifetime follow-up forms return rate because they do not have the capacity to send paper/electronic lifetime follow up forms; Leeds Data Collector contract ended at the beginning of 2016. Note, however, that this issue is in the process of being resolved.
- 18 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 69% 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 69% of cases. The secondary source for finding out this information was the ODT Hub Operations 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).
- 19 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.
- 20 A comparison of the survival of whole and split liver transplants up to three years was also made, for adult recipients only. This analysis included 3,603 NHS group 1 first adult elective patients transplanted in the UK between 1 April 2007 and 31 March 2017. A sub-group analysis was performed on just those transplants performed between 1 April 2012 and 31 March 2017 (N=1,971). Auxiliary and multi-organ transplants and re-grafts were excluded. Again, transplants performed at Leeds (N=600) were also excluded. Follow-up data were as recorded on the UKTR on 28 October 2017.

## Results

- 21 **Figure 4** shows a breakdown of the 827 split liver transplants by recipient age group (adult ( $\geq 17$  years), paediatric ( $< 17$  years)) and whether the liver was retained or imported.



- 22 **Table 7** shows a breakdown of the 827 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 2007 – 31 March 2017**

Transplant centre	Retained N (%)	Imported N (%)	Total N
<b>Paediatric recipients</b>			
Birmingham	119 (85)	21 (15)	140
King's College	141 (77)	41 (23)	182
Leeds	51 (78)	14 (22)	65
<b>Total</b>	<b>311 (80)</b>	<b>76 (20)</b>	<b>387</b>
<b>Adult recipients</b>			
Birmingham	122 (93)	9 (7)	131
Cambridge	13 (33)	26 (67)	39
Edinburgh	21 (33)	42 (67)	63
King's College	91 (91)	9 (9)	100
Leeds	38 (78)	11 (22)	49
Newcastle	3 (21)	11 (79)	14
Royal Free	12 (27)	32 (73)	44
<b>Total</b>	<b>300 (68)</b>	<b>140 (32)</b>	<b>440</b>
<b>TOTAL</b>	<b>611 (74)</b>	<b>216 (26)</b>	<b>827</b>

- 23 **Table 8** shows the median and range of CIT (min - max), 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=14)). On average, CIT was 2.6 hours and 2.5 hours longer for imported liver lobes compared with retained liver lobes for adult and paediatric recipients, respectively (Mann-Whitney U test:  $p < 0.0001$  for both). Data are shown separately for 2007-2012 and 2012-2017 and the more recent cohort shows a CIT that is 2.9 hours longer for imported right lobes for adult patients and 2.1 hours longer for imported rather than retained left lobes for paediatric patients.

		N <sup>1</sup>	CIT (hours)	
			Median	Range
<b>Left lobes transplanted in paediatric patients</b>				
<b>1 April 2007 – 31 March 2012</b>	Retained	97	9.0	3.6-13.9
	Imported	36	11.7	2.9-16.5
<b>1 April 2012 – 31 March 2017</b>	Retained	120	9.0	3.0-16.2
	Imported	24	11.1	7.0-16.0
<b>Overall</b>	<b>Retained</b>	<b>217</b>	<b>9.0</b>	<b>3.0-16.2</b>
	<b>Imported</b>	<b>60</b>	<b>11.5</b>	<b>2.9-16.5</b>
<b>Right lobes transplanted in adult patients</b>				
<b>1 April 2007 – 31 March 2012</b>	Retained	163	9.7	4.3-17.6
	Imported	42	12.1	6.6-16.3
<b>1 April 2012 – 31 March 2017</b>	Retained	108	9.5	2.5-18.1
	Imported	91	12.4	6.9-16.6
<b>Overall</b>	<b>Retained</b>	<b>271</b>	<b>9.6</b>	<b>2.5-18.1</b>
	<b>Imported</b>	<b>133</b>	<b>12.2</b>	<b>6.6-16.6</b>

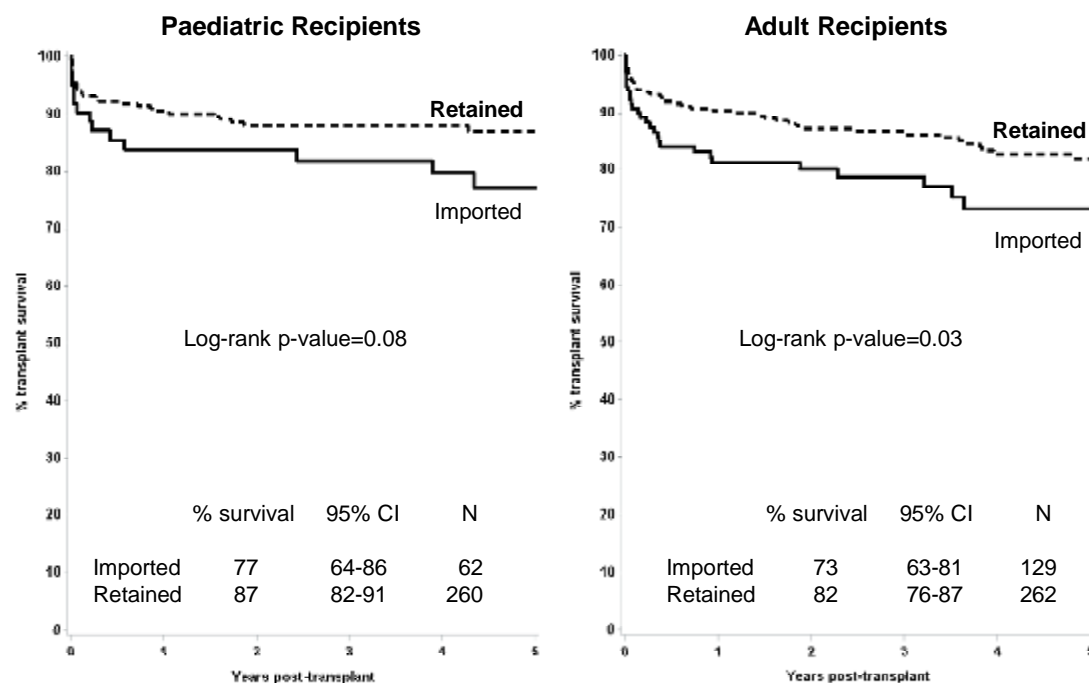
<sup>1</sup> CIT was not reported for a total of 132 split livers

### Unadjusted survival analysis

- 24 **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. There is evidence of a statistical difference in the overall survival curves for adult recipients ( $p=0.03$ ), with a 9% superiority in survival at 5 years for retained livers compared to imported livers. For paediatric patients survival at 5 years post-transplant was superior for retained livers compared to imported livers, but this difference was not statistically significant ( $p=0.08$ ).
- 25 **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 six events in the “split by adult unit surgeon” group in both the paediatric and adult analyses, so the results should

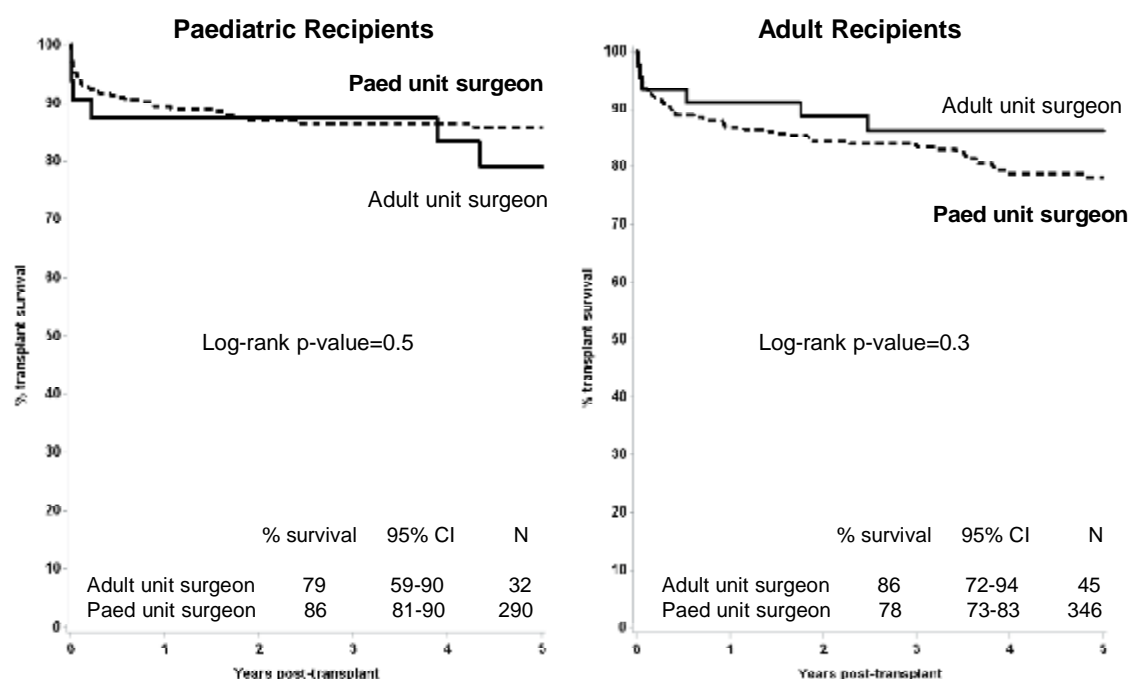
be viewed with caution. There was no statistically significant difference found between these groups in the paediatric or adult analyses.

**Figure 5** Five year transplant survival of split livers transplanted in NHS group 1 elective patients in the UK\*, 1 April 2007 – 31 March 2017 – RETAINED vs IMPORTED



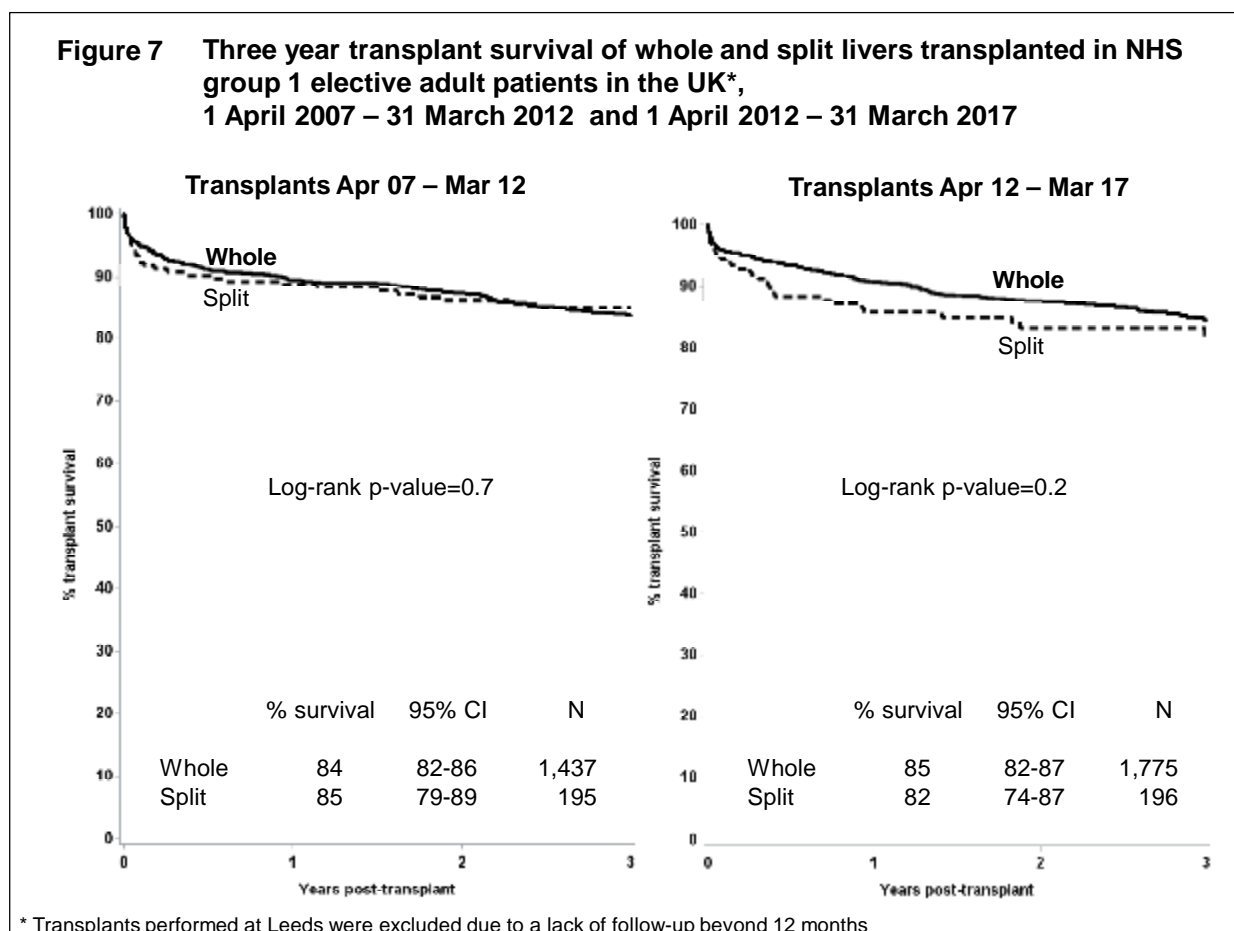
\* Transplants performed at Leeds were excluded due to a lack of follow-up beyond 12 months

**Figure 6** Five year transplant survival of split livers split transplanted in NHS group 1 elective patients in the UK\*, 1 April 2007 – 31 March 2017 – ADULT vs PAEDIATRIC UNIT SURGEONS



\* Transplants performed at Leeds were excluded due to a lack of follow-up beyond 12 months

- 26 Causes of graft failure or patient death that were reported to the UKTR for the 112 out of 713 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. Note that the number of graft failures and patient deaths for transplants performed at Leeds (N=114) was not included due to a lack of follow-up beyond 12 months.
- 27 Unadjusted survival analysis at three years post-transplant for more recent transplants (1 April 2012 - 31 March 2017) can be seen in **Appendix II**. There is evidence of a statistical difference in the overall survival curves for retained vs imported livers for adult recipients ( $p=0.04$ ), with a 9% superiority in survival at 3 years for retained livers compared to imported livers. There is no evidence of a difference in the overall survival curves for retained vs imported livers for paediatric recipients ( $p=0.1$ ). Note that there were only four events in the “imported livers” group in the paediatric analysis, so the results should be viewed with caution. Due to a low number of events, the unadjusted survival analysis comparing livers split by an adult or paediatric unit surgeon was not performed.
- 28 **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 2007 and 31 March 2012 and between 1 April 2012 and 31 March 2017. There is no significant difference between whole and split liver transplants.



### Risk-adjusted survival analysis

29 Risk-adjusted analyses were carried out using Cox Proportional Hazards regression modelling for three year transplant survival for whole and split liver transplants; the results are presented in **Table 9**. Transplants performed at Leeds were excluded (N=659) from the analyses due to a lack of follow-up beyond 12 months. After risk adjustment there is evidence that split liver transplants have a higher hazard of patient death or graft failure for the most recent time period ( $p < 0.01$ ), not seen in the unadjusted results. Note that the median (IQR) donor age for split liver transplants was 28 (21-36), compared to whole liver transplants 54 (43-65) in the recent period. Due to low numbers, the risk-adjusted survival analysis for split liver transplants was not performed to compare transplant outcomes between retained and imported livers and between livers split by an adult or paediatric unit surgeon.

Factor	Level	1 April 2007 - 31 March 2012			1 April 2012 - 31 March 2017		
		N	Hazard ratio (95% CI)	p-value	N	Hazard ratio (95% CI)	p-value
<b>Transplant</b>							
Liver split	Whole	1395	1.00		1709	1.00	
	Split	326	1.06 (0.70 - 1.58)	0.8	336	1.85 (1.19 - 2.88)	<0.01
<b>Recipient</b>							
Age at transplant	Adult	1570	1.00		1877	1.00	
	Paediatric	151	1.23 (0.68 - 2.21)	0.5	168	0.74 (0.35 - 1.56)	0.4
HCV indicator	No	1375	1.00		1715	1.00	
	Yes	346	1.34 (1.01 - 1.78)	0.04	330	1.15 (0.82 - 1.60)	0.4
Ln(creatinine)		1721	1.22 (0.90 - 1.65)	0.2	2045	1.29 (0.92 - 1.80)	0.1
Ln(INR)		1721	0.43 (0.26 - 0.70)	<0.01	2045	1.33 (0.83 - 2.12)	0.2
Albumin		1721	0.98 (0.96 - 1.00)	0.03	2045	1.01 (0.99 - 1.03)	0.2
Renal replacement therapy	No	1647	1.00		1929	1.00	
	Yes	74	1.99 (1.27 - 3.12)	<0.01	116	0.95 (0.54 - 1.65)	0.8
Patient location	Outpatient	1445	1.00		1752	1.00	
	Inpatient	276	1.36 (0.98 - 1.89)	0.06	293	1.13 (0.78 - 1.64)	0.5
<b>Donor</b>							
Donor age		1721	1.00 (1.00 - 1.01)	0.3	2045	1.01 (1.00 - 1.02)	0.02
History of diabetes	No	1632	1.00		1897	1.00	
	Yes	89	1.51 (0.96 - 2.37)	0.07	148	1.24 (0.79 - 1.94)	0.3

\* Transplants performed in Leeds were excluded due to a lack of follow-up beyond 12 months

30 Data on 39 NHS group 1 first super urgent split liver only transplants in the UK using livers from DBD donors between 1 April 2007 and 31 March 2017 were also analysed. Auxiliary and intestinal transplants were excluded from this cohort as were regrafts.



Transplants performed at Leeds (N=6) were also excluded due to a lack of follow-up beyond 12 months. Follow-up data were as recorded on the UKTR on 28 October 2017. Of these there were eight (24%) deaths or failed grafts in the 33 paediatric recipients, and three (50%) deaths or failed grafts in the six adult recipients. Due to these small numbers no survival analysis could be performed.

## SUMMARY

### ACTIVITY

- 31 There were 85 livers donated from donors who met the criteria for liver splitting between 1 April 2017 and 30 September 2017 (compared to 86 livers in the previous six months). Of these, 70 (82%) were available for splitting for elective recipients, having not been used in super-urgent, hepatoblastoma, intestinal or multi-organ recipients. Of these 70 livers, 35 (50%) were offered for splitting. Of the 35 livers offered for splitting, 12 (34%) were actually split (11 fewer than in the previous six months).
- 32 The percentage of livers split of those available for splitting increased from only 16 (16%) in 2014/15 to 18 (20%) in 2015/16, and finally to 44 (35%) in 2016/17, with the highest number of reported split livers. There were 12 (17%) livers split in the first half of 2017/18.
- 33 Donor history and abnormal liver function tests were common reasons why a liver available for splitting was not offered to be split. 23 livers were offered for splitting but instead used whole or reduced. Common reasons for not splitting these livers were donor related or a lack of suitable recipients.

### TRANSPLANT OUTCOMES

- 34 Transplants performed at Leeds were excluded from unadjusted and risk-adjusted survival analyses due to a lack of follow-up beyond 12 months. Note, however, that there is a plan of action in place to obtain outstanding follow-up data from Leeds.
- 35 Unadjusted analysis of transplant outcomes, 1 April 2007 – 31 March 2017, showed:
- For adult recipients, a significant difference in the overall survival curves up to five years post-transplant when comparing retained and imported livers ( $p=0.03$ ); with a 9% superiority in survival at 5 years for retained livers compared to imported livers.
  - For paediatric recipients, survival at 5 years post-transplant was superior for retained livers compared to imported liver, but this difference was not statistically significant ( $p=0.08$ ).
  - No significant difference in the overall survival curves up to five years post-transplant when comparing livers split by an adult or paediatric unit surgeon for both paediatric and adult recipients ( $p>0.3$ )
  - No significant difference between whole and split liver transplant survival at 3 years for earlier transplants (1 April 2007 - 31 March 2012),  $p=0.7$ , or more recent transplants (1 April 2012 - 31 March 2017),  $p=0.2$ .

- 36 Risk adjusted analysis of transplant outcomes within 3 years post-transplant, 1 April 2012- 31 March 2017, showed:
- A significant difference in outcomes for split liver recipients compared to whole,  $p < 0.01$  (HR for split=1.85, 95% CI 1.19-2.88)
  - Due to a low numbers after exclusion of transplants at Leeds, risk-adjusted analysis was not performed to compare the outcomes between retained and imported livers or between livers split by an adult or paediatric unit surgeon.

**ACTION**

- 37 Members are asked to note the reduction in the percentage of livers split in the first half of 2017/18, relative to percentages achieved in previous periods.
- 38 Members are asked to note the incompleteness of data reported to NHSBT in Split Liver Information form (see paragraph 18).

**Elisa Allen and Agne Zarankaite**  
**Statistics and Clinical Studies**

**November 2017**

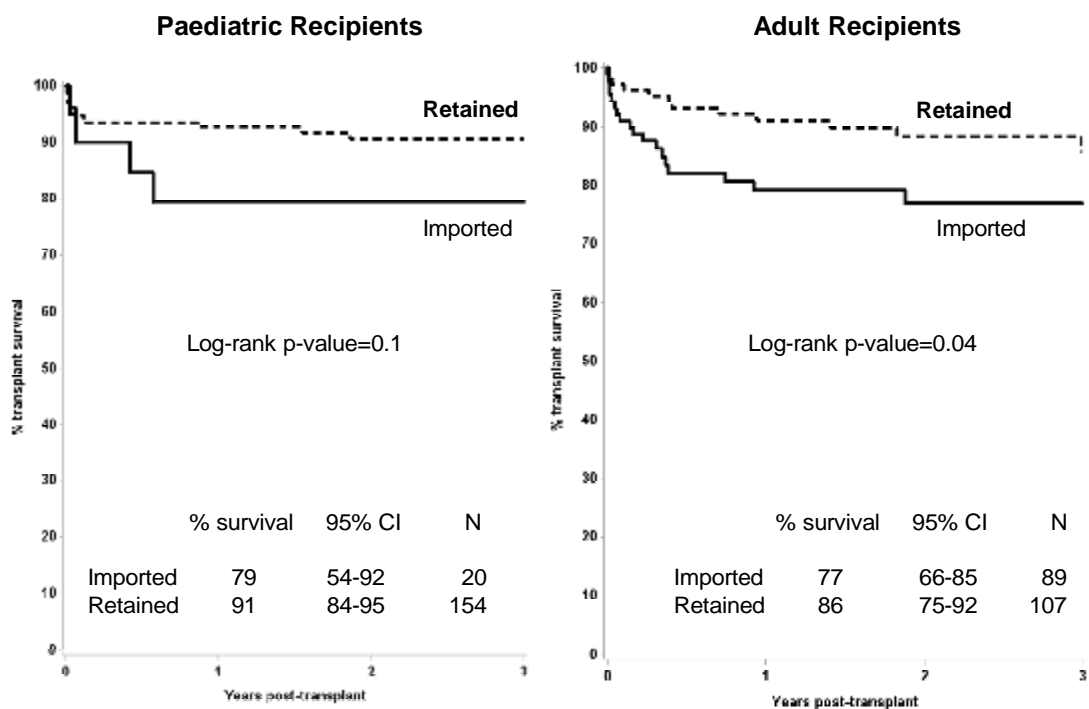
**Appendix I Causes of graft failure or patient death for NHS group 1 elective split liver only transplant recipients in the UK\* between 1 April 2007 and 31 March 2017 who died or whose graft failed within five years following transplant, by age group, whether the split liver was retained/ imported 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
<b>PAEDIATRIC PATIENTS</b>					
<i>Cause of graft failure - patient did not die</i>					
Hepatic artery thrombosis	8	3	9	2	11
Primary non-function	3	1	3	1	4
Chronic rejection	1	1	2	0	2
Biliary complications	1	0	1	0	1
Other	4	1	4	1	5
Not reported	1	0	1	0	1
<b>Total</b>	<b>18</b>	<b>6</b>	<b>20</b>	<b>4</b>	<b>24</b>
<i>Cause of death</i>					
Multi-system failure	6	3	9	0	9
Haemorrhage	1	2	2	1	3
Septic shock	1	0	1	0	1
Recurrent disease	1	0	1	0	1
Not reported	3	2	4	1	5
<b>Total</b>	<b>12</b>	<b>7</b>	<b>17</b>	<b>2</b>	<b>19</b>
<b>TOTAL</b>	<b>30</b>	<b>13</b>	<b>37</b>	<b>6</b>	<b>43</b>
<b>ADULT PATIENTS</b>					
<i>Cause of graft failure - patient did not die</i>					
Hepatic artery thrombosis	8	9	15	2	17
Chronic rejection	3	0	2	1	3
Other	2	3	5	0	5
<b>Total</b>	<b>13</b>	<b>12</b>	<b>22</b>	<b>3</b>	<b>25</b>
<i>Cause of death</i>					
Multi-organ failure	9	5	14	0	14
Non-lymphoid malignant disease	5	2	7	0	7
Haemorrhage	1	2	3	0	3
Pulmonary infection	1	3	3	1	4
Cerebro-vascular accident	4	0	4	0	4
Septicaemia	2	0	2	0	2
Myocardial ischaemia and infarction	2	0	2	0	2
Other	4	2	4	2	6
Not reported	0	2	2	0	2
<b>Total</b>	<b>28</b>	<b>16</b>	<b>41</b>	<b>3</b>	<b>44</b>
<b>TOTAL</b>	<b>41</b>	<b>28</b>	<b>63</b>	<b>6</b>	<b>69</b>

\* Transplants performed at Leeds were excluded due to a lack of follow-up beyond 12 months

## Appendix II

**Comparison of three year transplant survival of split livers transplanted in NHS group 1 elective patients in the UK\* between 1 April 2012 and 31 March 2017–  
RETAINED vs IMPORTED**



\* Transplants performed at Leeds were excluded due to a lack of follow-up beyond 12 months