MINUTES OF THE THIRTY SIXTH MEETING OF THE LIVER ADVISORY GROUP
HELD ON WEDNESDAY 8 MAY 2019 AT 12 BLOOMSBURY SQUARE, LONDON, WC1A 2LP

PRESENT:

Dr Douglas Thorburn
Mr John Isaac
Prof Derek Manas
Dr Ayesha Ali
Dr Varuna Aluvihare,
Mr Mark Aldersley
Mr Magdy Attia
Prof William Bernal
Mr Andrew Butler
Mr Chris Callaghan
Mr John Crookenden
Prof John Forsythe
Dr Alex Gimson
Dr Tassos Grammaticopoulos
Ms Pam Healy
Prof Nigel Heaton
Dr Andrew Holt
Dr Mark Hudson
Dr Joanna Leithead
Ms Wendy Littlejohn
Dr Aileen Marshall
Mrs Sarah Matthew
Ms Katie Morley
Ms Jacki Newby
Mr James Powell
Ms Katherine Quist
Dr Sanjay Rajwal
Ms Rhiannon Taylor
Dr Indra van Mourik
Ms Jacki Newby

IN ATTENDANCE:

Mrs Kamann Huang
Mr Lewis Downward
Ms Karen Mercer
APOLOGIES & WELCOME

Apologies
Prof Peter Friend, Prof Sue Fuggle, Mr Paul Gibbs, Mr Emir Hoti,
Dr Diarmaid Houlihan, Prof Joerg-Matthias Pollok, Ms Susan Richards,
Dr Ken Simpson, Mr Mick Stokes, Ms Sarah Watson and
Prof Stephen Wigmore.

Welcome
Members welcomed on board Mr John Isaac, the new Deputy Chair, and
Ms Pamela Healy, the new CE of the British Liver Trust.

1 DECLARATIONS OF INTEREST IN RELATION TO AGENDA - LAG(18)21

1.1 There were no declarations of interest.

2 MINUTES OF THE MEETING HELD ON 21 NOVEMBER 2018 - LAG(M)(18)2

2.1 Accuracy
2.1.1 The minutes of the previous meeting were agreed as an accurate record.

2.2 Action points – LAG(AP)(19)1
2.2.1 AP3 Response to matters arising from the NLOS and Monitoring Committee
Refer to minute 3.4.1 Reasons for fast track.

AP5 Compliance with sequential data submission
Refer to minute 3.5.

2.3 Matters arising, not separately identified
2.3.1 LAG Terms of Reference - LAG(19)2
The latest version of the Terms of Reference will be sent out with the Minutes
of this meeting for approval at next LAG meeting.

2.3.2 LAG Core Group update
Two issues to be addressed were:
(i) the Liver Advisory Group and transplant centres should be updated with
the work undertaken by the Core Group in a timely manner, and
(ii) notes and action points produced in the past to be replaced with formal
minutes and circulated to members in a timely manner.

The intention is for Core Group to be held monthly or every two months and
the membership of Core Group will be imminently reviewed.

3 NATIONAL OFFERING SCHEME

3.1 National Liver Offering Scheme (NLOS) (10 months data) - LAG(19)3
3.1.1 The NLOS was introduced on 20 March 2018 and the one year review was
looked at by the Monitoring Committee in April 2019. The results are
summarised below:

Registration Activity overall
- Although there has been an increase in both elective and super urgent (SU)
registrations since the introduction of the NLOS, there was no statistically
significant association between the two time periods and registration type.
Post registration outcome
- There was a statistically significant difference in the six months registration outcome in the six months post compared with the six months prior. In particular, the proportion of patients who died or were removed due to condition deterioration was 4% in the 6 months post compared with 8% in the six months prior.

Transplant list activity
- A higher proportion of new CLD and HCC registrations were transplanted in the first 12 months of the scheme compared to the same period prior. There was a decrease in mortality across all age groups.

Concern was raised regarding why there are patients who were on the list when the scheme was implemented who remain on the list. It was agreed that the demographics and aetiology of these patients would be examined.

3.2 Feedback from the Monitoring Committee

A summary of points made from the Monitoring Committee were:

- The overall mortality rate on the waiting list since the introduction of the NLOS is 5% compared to 8% in the year prior to the scheme. The overall median waiting time has fallen.

- Of the 417 adult patients registered on the elective list 19th March 2018, 53% have been transplanted as compared to 63% of new registrations. It is not clear why there should be this persisting difference in the proportion of patients receiving transplantation. Credit is given within TBS for time waiting. Further analysis of this to look at groups not being transplanted to include aetiology, blood group etc.

- Fast track is referred to in 3.4.1. However, 197 (57%) livers offered out to Fast Track have been declined. The Monitoring Group would recommend that this is looked at in more detail to ensure that potentially transplantable livers are not being lost.

- We have noted an increased trend in patients aged 60 to 69 years receiving DBD transplantation, 37% vs 30% in the preceding 12 months. There is also a reduction in DBD transplants in patients < 50 years, with an increase in DCD transplants in the 26 to 39 year group, 9.3% vs 5.3%.

- The most marked change has been in patients listed for HCC. The proportion of patients with HCC being transplanted with a DBD has fallen from 16.7% to 11.8%, with an increase in DCD transplants from 28.9% to 45.9%. Only 57 named offers to patients listed for HCC in 12 months of the scheme. A higher proportion of patients with HCC have been removed from the list as compared to patients with chronic liver disease or listed as variant syndromes. The removals of HCC patients are complex. However, it is concerning that survival in those patients transplanted for HCC with DCD grafts has fallen from 98.8% to 93.2%.

- For DCD blood group O recipients, the 90 day survival rate has reduced significantly from 98% to 89.5%.

- There has been no change in the proportion of re-grafts.

- There has been an increase in the workload in transplant activity following an increase in liver offers. Named offers account for 30% of all offers. The acceptance rate is 35% for first named offer; which is lower than predicted.
- The recommendation from the monitoring group is that review of the parameter estimates for the TBS and remodelling with larger numbers including a more contemporaneous population should be a priority, particularly in HCC.

J Forsythe commented that the NLOS is not set in stone and minor adjustments can be made to resolve issues; as has happened with previous organ allocation schemes. However, there needs to be sound evidence before performing the work required.

Feedback from transplant centres to the NLOS Scheme
- The waiting list was said to be falling at the time of the introduction of the NLOS which was proposed as a possible contribution to changes in the mortality rate after NLOS was implemented.
- More work is required to look at DCDs.
- Data for very long waiters has not been seen for those waiting within one year compared to those longer than one year.
- The fast track was reported to be operating poorly. The experience was that if the first three centres refuse an offer, the next centre gets a very short time to accept.
- These offers, mainly DCD, come from a range of regions from within the country and surgeons are being woken up throughout the night. Important decisions are being compressed into a shorter time frame. More time is required upfront to optimise implantation. There is a need to look at livers turned down and not retrieved.
- Low levels of splitting have led to unintended consequences with whole livers diverted to patients to selected as best suited to the right lobe as priority. If the whole liver had been offered upfront the intended recipient would have been very different.
- As mentioned above, the DCD survival rate has fallen. The suggestion was made to look at the previous 9 months eras to see if it is an outlier. The use of DCD livers has changed over the last five years and it could be that there is more pressure to use DCD in higher risk patients.
- The priority for HCC patients was said to go down and which seems a paradox as nationally we are seeking to shorten the waiting times for cancer treatment. There is a plan to update the parameter estimates using an updated cohort. It was highlighted that the NLOS is not a scheme to solely prevent people dying on the waiting list but needs to be regarded as a transplant benefit model. HCC patients may have a worse transplant benefit score due to lower anticipated post-transplant survival compared with other indications. However, currently the survival rate post-registration is potentially over estimated for HCC patients which further reduces transplant benefit and needs to be re-adjusted with updated parameter estimates.
- The majority (68%) of HCC patients are listed for tumours under 3 cm. The reasons for delisting are complex but in the new registrations, predominantly for disease progression which appears to occur early after registration reflecting unfavourable tumour biology or underestimation of tumour stage at the time of listing. A lot of work is required to investigate all these issues.
The request was made to provide data for declined named offers by centre for the next meeting.

**Actions:**
Core Group/Monitoring group to review:
- Review details of long waiters/prevalent patients on list at onset of NLOS who remain un-transplanted.
- Update parameter estimates to be updated based on a larger cohort of patient registrations.
- Monitor and investigate DCD outcomes and use of new technology.
- Further analyse centre behaviour and utilisation with regard to named offers and fast tracks.

**3.3 ODT Hub Update**

3.3.1 Issues raised were:
- There have been a few issues with liver splitting for paediatric and small adult patients in centres accepting the left lobe wanting more than a left lateral segment of liver. To avoid confusion such a situation needs a clear position to be taken rather than for two centres to discuss this on the night.
- There are Fast Track issues as mentioned in item 3.2.
- Two centres changed their decision, in the middle of offering, from a left segment lobe to a request for a full left lobe through changing the recipient. It was highlighted that this requires more anatomical decision making and that ideally the decision should be made upfront. The policy is the left lobe cases takes priority for liver splitting. The left lobe centre can decide how much of the lobe is to be used and for which patient.

**3.4 NLOS specific issues**

3.4.1 Reasons for fast track – LAG(19)4

3.4.1.1 The Liver Fast Track Scheme (FTS) was introduced on 1 November 1997 and five trigger points were revised when the NLOS was implemented on 20 March 2018.

There has been an increase in the number of livers being fast tracked (now 33% of all livers) with three quarters of livers accepted but later declined prior to being fast tracked.

NLOS Monitoring Group and core group have identified fast tracking as a significant issue. There is an opportunity to look at centre behaviour, i.e. if some centres have a higher number of offers declined, and data for organs declined and subsequently transplanted.

Questions raised were:
- Could fast tracked livers go to the patient with the highest TBS?
- What is the outcome of livers fast tracked?
- What are the demographics of those receiving fast tracked livers?
- What is the expected refusal rate for named patients? There is not a system for offering to technically difficult live patients; these can only access fast-track livers.
- Review triggers for fast track including:
  - the five hours of offering.
- Does it account for the low rate of acceptance for named patients?
- Is FT being precipitated by another organ being accepted?
- When there are no variants matching, the organ flips into FT.

A FTWU is to be set up asap led by D Manas, to review fast-tracks in depth. The aim is to complete this work within nine weeks.

D Manas

3.4.2 Updated parameter estimates
3.4.2.1 The new formulation of the transplant benefit score is in progress. Recalibration of M1 has been completed and work is underway on M2. This will be brought to LAG Core Group for approval. R Taylor will compare the new TBS scheme with the old allocation scheme which can be undertaken within 3 months. If the changes are a case of fine tuning then this would not likely need formal approval. If the changes are major then it will need to go through the whole approval process again. It was recommended that this should go to TPRC first to avoid any delays.

R Taylor

3.4.3 Review 1-year data on splitting and allocation in paediatric patients
3.4.3.1 There were 168 livers donated and transplanted between 20 March 2018 and 19 March 2019 which met the splitting criteria (compared to 149 livers in the previous year). Of these, 125 livers were offered for splitting and 30 were split (6 more than the previous year). Ten livers were declined for splitting. Overall there has been an increase in organs offered for splitting compared to organs split though there remains a low rate of splitting of livers within the current splitting criteria. It was noted that some livers outside the current splitting criteria were also split.

D Thorburn

3.4.4 Review criteria for splitting livers
3.4.4.1 In view of an aging population and obesity, the question was raised about reviewing the splitting criteria to establish what organs are suitable for splitting. Deemed consent under the Opt Out scheme will not apply to children under 18 years of age.

There was a discussion about how the current criteria might be refined to ensure higher rates of splitting of organs to meet the criteria. A question was raised that all donors under 50 years of age (this is currently 40 years of age) to be offered for splitting with no weight or time in ITU criteria. This would affect potentially one third of donors so some criteria would be required to reduce this number to ensure adult patients were not disadvantaged. It was stated that currently more than 2/3 of livers are split at night. The last time liver splitting was reviewed was through a WG 18 months ago chaired by P Friend. The time is right to review the splitting criteria again with the inclusion of both paediatric and adult clinician representation.

D Thorburn to establish a FTWU to review the criteria for offering organs for splitting to be chaired by Magdy Attia.

D Thorburn

3.5 Compliance with sequential data submission – LAG(19)6
3.5.1 NHSBT have received 3105 sequential data collection forms between 14 December 2017 to 28 April 2019 for all seven UK liver transplant centres. Of this number, for 331 patients on the elective CLD/HCC transplant list 59 forms had not been returned within the last 2 months and no forms have been received for 39 patients on the transplant list for more than one month.
Centres are reminded to return their forms on a regular basis so that the TBS score can be accurately recorded to reflect the patient's condition.

**4 ADULT TO ADULT LIVE DONOR TRANSPLANT – LAG(19)7**

4.1 The final report from the Fixed Term Working Unit (FTWU) was presented. The subject has been discussed at the British Liver Transplant Group (BLTG) last year. The Chair of KAG, C Watson, commented the scheme did not take into consideration developments in DCD, perfusion and split livers.

The FTWU acknowledged that adult to adult live donor transplantation should not be looked at in isolation and should be part of the liver donation strategy to include wider issues such as the reducing mortality rate, new technology and the increasing rate of DCD, which is higher than our European countries.

It was commented that the national 5 years patient survival is 70%. There is the opportunity to review indications for OLT and access more Living Donor Liver Transplantation (LDLT) in addition to changes such as the Opt Out Scheme and new technologies.

The post 2020 strategy for liver transplantation is not yet finalised. The suggestion is to expand the groups of patients and indications for adult to adult live donation with the inclusion of patient and Lay Member representation. It is proposed that the next step of the strategy is for discussion between NHSBT, NHS England and with patients.

J Crookenden raised the issue of risks to donors. It must be acknowledged that there will always be a greater risk to living liver donation than a living kidney donation. This issue will be discussed further outside of the meeting.

**5 SUSTAINABILITY**

5.1 NHSBT considers it is a requirement to inform a patient if an organ offered to a centre is declined due to logistical reasons e.g. no theatre being available. However, in these cases it must be fully evidenced that the transplantation has definitely been declined for this reason before the centre can relay this to the patient. There is strong feedback from patients that they want to know the reason why an organ has been declined.

NHSBT acknowledged this may be complicated logistically but a new process would be designed and it was felt that it is still the right decision to make. Centres highlighted that it should be made clear that the decline of an organ is not down to the clinician but is a result of the institution not being able to provide this. The other potential issue may be an increase in Adverse incident reporting. It was commented that the biggest problem is the start time of the transplant, which is dictated by the donor hospital and theatre availability.

Centre representatives to consider how they will handle these discussions within their units.
6 LIVER TRANSPLANT COMMISSIONING

6.1 NHS England

6.1.1 A Ali outlined the NHSE Aspirant Market Entrants process which potential liver transplant franchisees would need to apply to. This is an open process and if any centres are interested in putting in an application, details can be provided.

NHS England are already working with NHSBT on a model in preparation for the Opt Out Scheme.

7 CLINICAL SERVICE EVALUATIONS/PROPOSALS

7.1 HCC Downstaging – LAG(19)8

7.1.1 As at 28 April 2019, there have been 27 UK elective registrations for HCC down-staging since March 2015; from the 27 patients 25 have received a liver only transplant. Of the 25 patients, 17 were known to be alive at their last follow up and one patient had died. R Taylor to update the Elective Liver Recipient Registration Form to specify that the cancer information needs to be post-downstaging for HCC downstaging patient.

As there is currently no evidence of adverse outcomes in this pilot, it will continue to run until 40 patients have been listed with 2 years follow up.

7.2 Cholangiocarcinoma: MELD exception points

7.2.1 The joint proposal from Canada and Spain using liver transplantation for the treatment of early stages of intrahepatic cholangiocarcinoma in cirrhotics, to include the UK, has gone through the Ethics Group. There is a current delay from the insurers for the clinical trial. The number of participants are small but the indemnity is comparatively large to cover all the transplant centres.

The current protocol is for the patient to be transplanted within 3 months of listing with hepatoblastoma patients transplanted within two weeks. If there is not enough funding to cover all the centres then it will be a single centre.

Discussion regarding where these patients appear in a matching run to be held outside of the meeting with the decision fed back to all centres.

A discussion more widely on liver transplantation for hilar cholangiocarcinoma was undertaken with consensus that this should be considered for a pilot evaluation.

D Thorburn to establish a FTWU to be set up to consider a pilot of liver transplantation for hilar cholangiocarcinoma to be chaired by Nigel Heaton and John Isaac.

7.3 Extracorporal liver perfusion – LAG(19)9

7.3.1 A formal application from LAG to RINTAG to include extracorporal liver perfusion for livers for patients with acute liver failure was approved, with priority given before NHS group 2 patients and research. Any livers remaining at the end of this process can be used for NHS group 2 and research. J Newby, Hub Operations, will look at how this process will work logistically.

S Wigmore will Chair an external monitoring committee to oversee the process.
7.4 Neuroendocrine tumours – LAG(19)10
7.4.1 In the absence of P Gibbs, this paper will be presented at the next meeting.

7.5 Proposed pilot for transplanting patients with deteriorating cirrhotics – LAG(19)11
7.5.1 A paper was presented looking at critically ill patients with cirrhosis and those ending up in ICU.

It was stated that for Acute On Chronic Liver Failure (ACLF) patients at stage 2 or 3, the predicted survival was for 90 days; less than 50%. The first consideration is identifying suitable patients for transplantation within a window when OLT could be delivered. Secondly to identify a mechanism of ensuring such patients would receive offers after they were listed and a number of potential schemes for this were discussed.

D Thorburn to establish a FTWU, chaired by Will Bernal, with representatives from all centres to bring back recommendations to the next LAG meeting in November 2019.

D Thorburn/ W Bernal

8 SUPER-URGENT LISTING APPEALS MECHANISM – LAG(19)12
8.1 It was highlighted that the new process for SU appeals has been implemented when such cases should be approved first by the LAG Chair (or his/her Deputy) before the Hub Office then disseminates the appeal to the coordinators and on call teams in each of the units. LAG agreed that a SU appeal would be approved if a minimum of four positive responses are received from the centres.

9 USE OF HEPATITIS C VIRAEMIC DONORS IN TRANSPLANTATION – LAG(19)13
9.1 Funding from NHS England (NHSE) for DAAs for HCV negative recipients with HCV positive solid organs has been approved for Scotland, Wales and NI but not across the whole of the UK as hoped. Hepatitis C viraemic donation can be undertaken in a transplant centre in England from the three nations mentioned. A proposed policy is going through NHSE with the hope of a final policy by November 2019.

Post meeting note:
A T/C was held on 15th May to agree the Terms of Reference, membership, the check list, governance and frequency of meetings.

10 FTWU - CENTRALISED EXPLANT REVIEW, SU LISTING AND HCC
10.1 It is hoped that the paper from the FTWU will be completed in the next couple of months.

Abid Suddle in his capacity as Chair of this FTWU will submit a paper to LAG for the November meeting with recommendations.

A Suddle

11DECLINED OFFERS DUE TO LOGISTICAL REASONS
11.1 Refer to Minute 5.
12  GOVERNANCE ISSUES

12.1  Non-compliance with allocation
12.2.1 There have been no reports of non-compliance with allocation.

12.2  Governance Report – LAG(19)14
12.2.1 There has been an increase in the number of incidents relating to novel technologies and its impact on the retrieval process. Owing to the complex multi aspects feeding into this area, work is being undertaken to examine how novel technologies can work efficiently within the standard retrieval process.

Discussion took place regarding vessels required for other transplants and whether it would be feasible to use cryo-preserved vessels. This was not accepted owing to the safety aspects not fully understood.

12.3  CUSUM

12.3.1  Summary of CUSUM monitoring of outcomes following liver Transplantation – LAG(19)15

Over the last 6 months there have been 3 signals for adult elective liver transplantation and 1 signal for paediatric elective liver transplantation.

NHSBT have received reports of the actions taken for three of the signals.

12.3.2  Report on recent triggers
12.3.2.1 A 'Lessons Learnt' document highlighting the issues for shared learning has been circulated to centres between meetings.

Each centre will respond at end of the procedure whether it be an internal or external issue. One outstanding trigger within the timeline is yet to be followed up and will be reported at the next meeting.

12.3.3  Proposal for shared lessons learned following CUSUM triggers
12.3.3.1 The recommendation is for a standardised way of reporting these reviews, internal or external, via a template. The reporting needs to be open but anonymised.

D Thorburn to develop a template for Lessons Learned post CUSUM trigger for approval by John Forsythe and Core group.

13  STATISTICS AND CLINICAL STUDIES (SCS) REPORT

13.1  Summary from Statistics and Clinical Studies – LAG(19)16
13.1.1 A paper was presented outlining recent presentations, publications and current and future work in liver transplantation.

Key points for noting are the recruitment of three clinical fellows, Maria Ibrahim on organ utilization, George Greenhall on malignancy in transplantation and Gillian Hardman on cardiothoracic transplantation. One data application for liver transplantation as a treatment for hepatocellular carcinoma; a study using existing electronic data was approved.

Centres were informed that NHSBT will shortly be writing to request information on which transplants that involved machine perfusion can be
incorporated into the NLOS monitoring committee report and the Annual report on Liver Transplantation.

It was acknowledged that the statistical support provided to LAG was of a very high standard and greatly appreciated by members.

**13.2 Transplant centre profiles – LAG(19)17**

An Adult Liver Transplant profile for Birmingham Queen Elizabeth Hospital was presented to members, for information, showing data such as the number of patients transplanted, the number on the waiting list and those that had died, the median waiting time, and patient survival after a transplant. The information provided has included feedback from the Liver Patient Group and other patient groups.

**14 MULTI-VISCERAL & COMPOSITE TISSUE ADVISORY GROUP (MCTAG)**

**14.1 Report from the Multi-Visceral & Composite Tissue Advisory Group Meeting - 13 March 2019**

A key issue raised was regarding abdominal fascia being requested by non-intestinal transplant centres to aid abdominal wall closure in an isolated liver transplant. The retrieval of tissue (as opposed to organs) is not covered under the HTA licence for NORS teams. King’s and the Royal Free currently have a licence. Regarding rectus fascia and storage duration, this is being negotiated with the HTA currently. They have no specific objections but SOPs and permissions need to be obtained.

**15 ANY OTHER BUSINESS**

**15.1 Bile collection proposal for QUOD – LAG(19)18**

A request was made to LAG for the collection of bile samples from QUOD (Quality in Organ Donation). The question was raised as to how these samples would be different to all the other bile samples already being collected and what was the plan for them before the establishment of a further biobank.

There was no one available to respond to the questions and the recommendation was that as this is a retrieval issue this should be taken to NRG.

**16 Date of next meetings:**


**17 FOR INFORMATION ONLY**

The following papers were attached for information to members:

**17.1 Transplant activity report: March 2019 - LAG(19)19**

**17.2 Group 2 Transplants – LAG(19)20**

**17.3 Outcome of appeals – LAG(19)21**
ACTION

17.4 Activity and organ utilisation monitoring (dashboard) – LAG(19)22

17.5 Minutes of the Multi-Visceral & Composite Tissue Advisory Group meeting: 24 October 2018 - LAG(19)23

17.6 Minutes from the National Retrieval Group: 3 October 2018 - LAG(19)24

17.7 QUOD statistical reports – April 2019 - LAG(19)25

New Appointments

Ms Betsy Bassis has been appointed the new Chief Executive for NHSBT starting 4th March 2019, replacing Ms Sally Johnson.

Organ Donation & Transplantation Directorate

Administrative Lead: Kamann Huang

May 2019