NHS BLOOD AND TRANSPLANT

LIVER ADVISORY GROUP

NATIONAL LIVER OFFERING SCHEME - UPDATING TRANSPLANT BENEFIT SCORE PARAMETER ESTIMATES

BACKGROUND

1 The National Liver Offering Scheme (NLOS) was implemented on 20 March 2018 for all Donors after Brain Death (DBD) using models developed in 2014 to calculate the Transplant Benefit Score (TBS) for all patients active on the adult elective liver transplant list. It was agreed by the Liver Advisory Group (LAG) that the parameter estimates and baseline survivor functions for all models would be updated on a regular basis so that the calculated TBS was appropriate.

2 Concern was also raised by the NLOS monitoring committee regarding the number of named patient DBD offers for patients with hepatocellular carcinoma (HCC). It was agreed at the LAG meeting in November 2019 that access to liver transplantation for this group of patients would also be reviewed.

3 Following the last meeting, a working group was established and met on a regular basis to review and advise on the analyses performed and this paper provides an update since the last meeting.

DATA

4 The TBS for an individual patient is calculated as the difference between the estimated risk-adjusted five year post-transplant survival and the estimated risk-adjusted survival on the list. The parameter estimates and baseline survival functions utilised are dependent upon whether the patient had hepatocellular carcinoma (HCC) reported at registration.

5 The currently utilised parameter estimates and baseline survivor functions were based on adult registrations and transplants between 2006 and 2012 for non-cancer patients and 2009 to 2012 for HCC patients.

6 Data on all adult elective NHS group 1 registrations and transplants between 1 January 2010 and 31 December 2016 were extracted from the UK Transplant Registry for both cancer and non-cancer patients. Registrations ending in living or domino donor transplantation and multi-organ registrations were excluded along with eight HCC downstaging service evaluation registrations on or after 2 March 2015. Variant syndrome patients were also excluded as these patients are offered based on waiting time alone rather than TBS.

RESULTS

7 The number of CLD registrations included in the updated cohort was slightly higher to the cohort used for the currently utilised models (4476 and 3859 respectively). However, there were almost double the number of HCC registrations in the updated cohort relative to the previous cohort (1234 and 660 respectively).

8 **Figure 1** shows the unadjusted Kaplan-Meier survival on the list curves by registration year and aetiology and shows that there has been an increase in estimated survival on the list over time for the majority of aetiologies. Analysis of post-registration outcomes over time also indicated a decrease in mortality on the list for the majority of aetiologies. **Figure 2** shows the equivalent KM survival curves for survival post-transplant.

Figure 1 Unadjusted survival from listing by aetiology and registration year

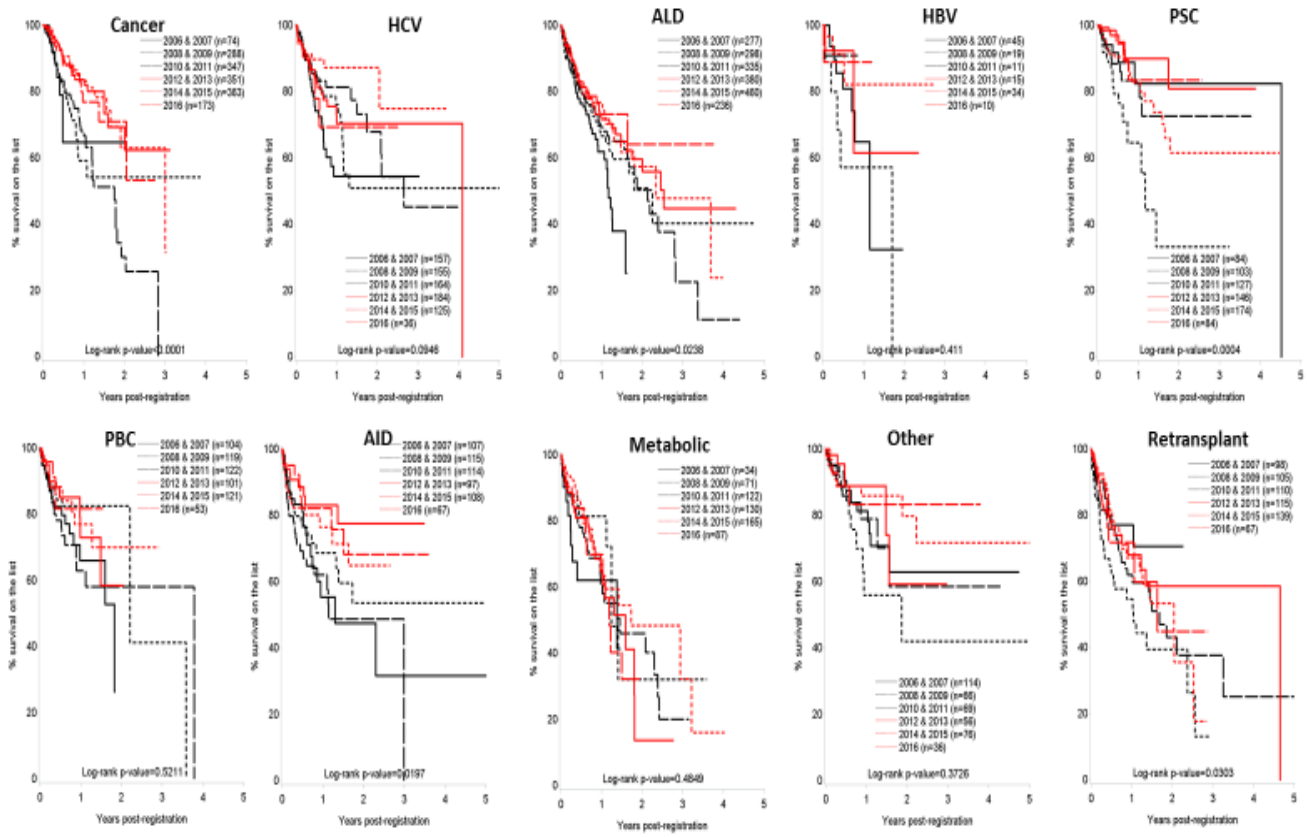
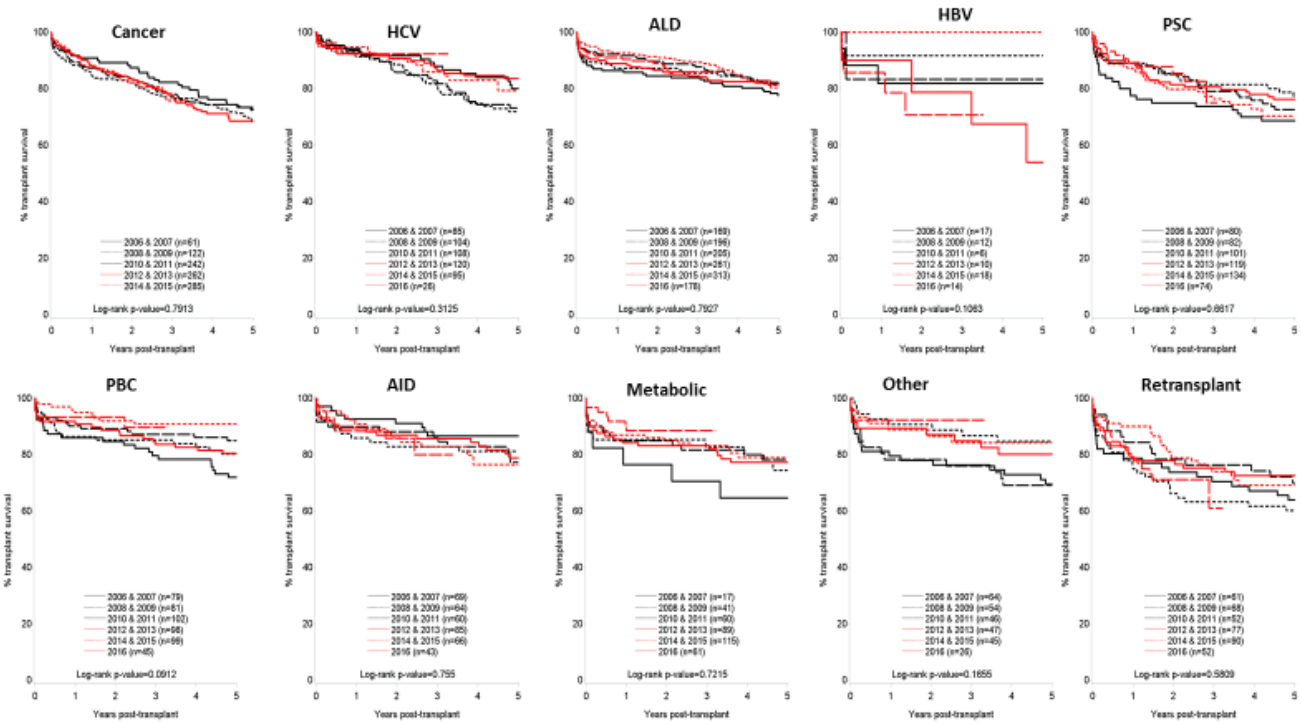


Figure 2 Unadjusted survival post-transplant by aetiology and registration year



9 Updated parameter estimates and baseline survival functions for both survival on the list and survival post-transplant were produced using the updated cohorts. The TBS using the updated estimates were calculated for all patients active on the list and compared to the equivalent TBS using the currently utilised estimates. Members of the working group agreed that the TBS score using the updated values for cancer patients was in line with clinical opinion but not for non-cancer patients.

10 **Figure 3** shows the survival on the list histograms using the updated estimates and the currently utilised estimates for non-cancer and cancer patients separately whilst **Figure 4** shows the equivalent for survival post-transplant. These histograms indicate that the difference in the TBS is potentially due to the estimated survival on the list for non-cancer patients which may be related to the reduction in deaths on the list. Further analysis of an extended cohort is ongoing (2006-2016 for non-cancer and 2009-2016 for cancer) to inform discussion.

Figure 3 Histogram of M1 for patients active on the list on 13 February 2020

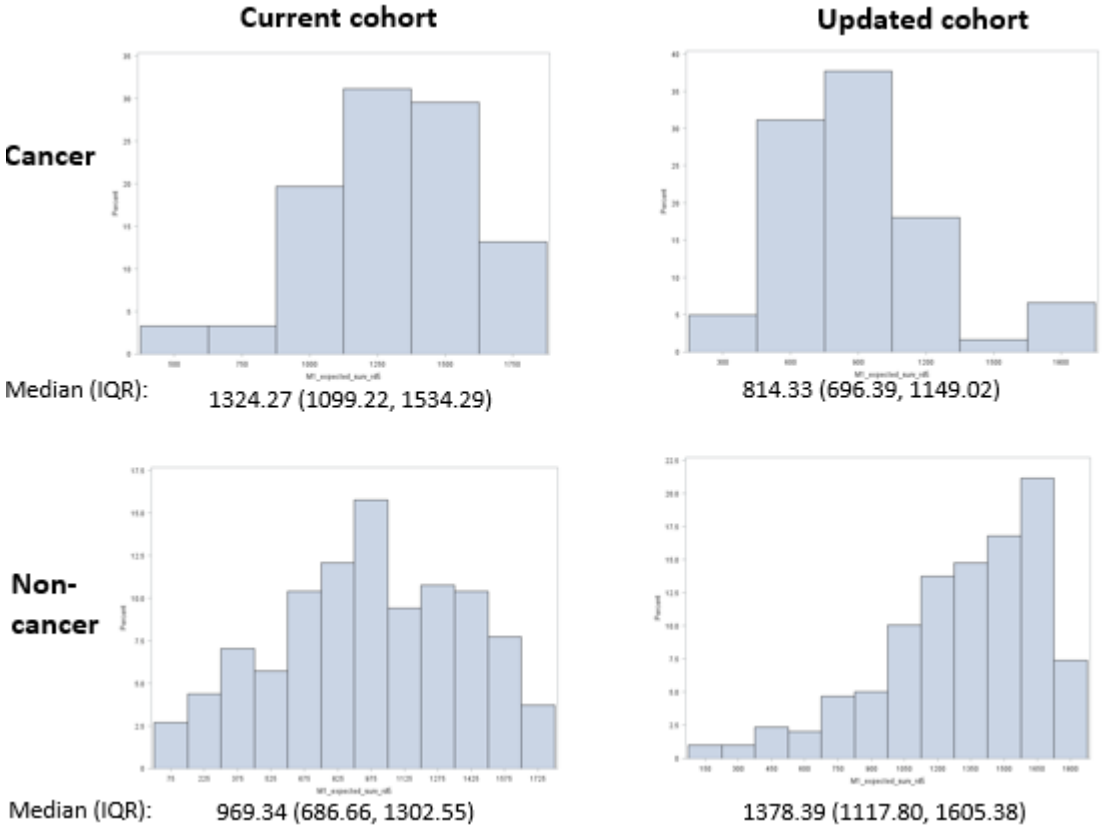
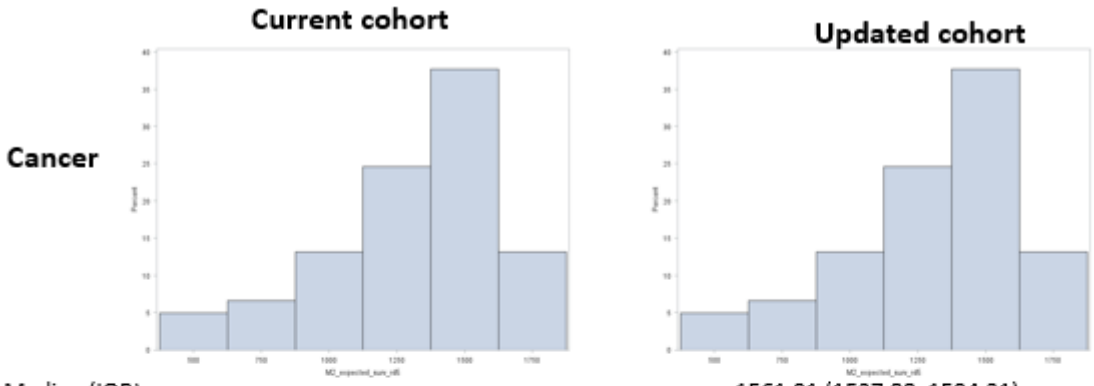
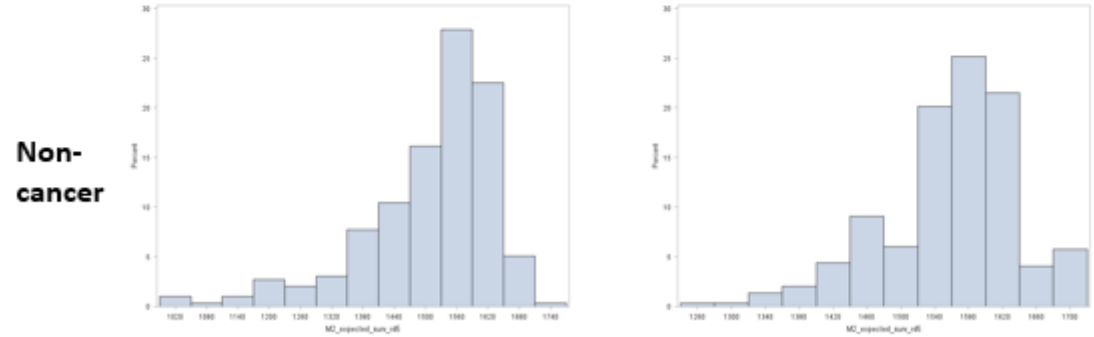


Figure 4 Histogram of M2 for patients active on the list on 13 February 2020





11 Changes in factors included in the non-cancer M1 over time were examined to evaluate the differences observed in the M1 estimate. Full details are not provided in this paper but could be provided on request.

12 The currently utilised models considered factors originally included based on clinical relevance alone rather than statistical significance. Analyses have now been performed to determine the factors that are statistically significant predictors of both survival on the list and survival post-transplant. **Table 1** shows the factors currently included in the non-cancer and cancer survival on the list (M1) and survival post-transplant (M2) models according to whether or not they were statistically significant in the updated cohort.

NEXT STEPS

13 Analysis involving an extended cohort (2006-2016 for non-cancer and 2009-2016 for cancer patients).

14 Simulations to evaluate the impact of updating the parameter estimates and the baseline survivor functions

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Table 1 **Factors included in current M1 and M2 models by whether the factor was found to be statistically significant in the updated cohort for non-cancer and cancer separately**

	M1		M2	
Recipient	**Non-cancer**	**Cancer**	**Non-cancer**	**Cancer**
Age	✓	✓	X	X
Age squared	X	✓	-	-
Sex	X	X	X	X
HCV	-	X	X	X
Disease group	✓	-	✓	-
Creatinine	✓	✓	✓	✓
Bilirubin	✓	✓	X	X
INR	✓	✓	X	X
Sodium	✓	✓	X	X
Inpatient	✓	X	X	X
Registration year	X	✓	-	-
Renal replacement therapy	X	X	X	X
Potassium	-	-	X	X
Albumin	-	-	X	✓
Encephalopathy grade	-	-	✓	X
Ascites	-	-	X	✓
Waiting time	-	-	X	X
Diabetes	-	-	X	X
AFP	-	✓	-	X
Maximum tumour size	-	✓	-	✓
No. of tumours	-	X	-	X
Donor				
Age	-	-	✓	✓
History of diabetes	-	-	X	✓
Donor type	-	-	✓	✓
Meets split criteria	-	-	X	✓
Cause of death	-	-	X	X
BMI	-	-	X	X
Blood group match	-	-	X	X
Interactions				
Bilirubin*sodium	✓	✓	-	-
Aetiology*sodium	✓	-	-	-
Donor type* creatinine	-	-	✓	✓
HCV* history of diabetes	-	-	X	X
HCV* donor age	-	-	X	X
Disease group * recipient age	-	-	X	X
Recipient age * creatinine	-	-	X	X
Disease group * donor type	-	-	X	X
Donor type * recipient age	-	-	X	X