NHS BLOOD AND TRANSPLANT

LIVER ADVISORY GROUP

LIVER TRANSPLANT RISK COMMUNICATION TOOL

INTRODUCTION

1. NHSBT have been collaborating with the Winton Centre for Risk and Evidence Communication, at the University of Cambridge, to design an online risk communication tool to aid clinicians and patients in decision-making at different points in the transplantation process, using data from the UK Transplant Registry (see Appendix for other tools that the Winton Centre have developed).
   Specifically:
   - To communicate clinically relevant and statistically significant factors which influence patient and graft outcomes following listing for transplantation.
   - To help develop patients' understanding of the risks and benefits associated with transplantation and convey possible outcomes in an understandable way to a wide variety of patients via a user-friendly interface.
   - To provide useful information to clinicians when consenting patients, using NHSBT data to ascertain modelled outcomes.

2. The tools will be organ specific, incorporating data relevant to that specific organ. The lung and kidney risk communication tools recently went live and are available from the ODT website: https://www.odt.nhs.uk/transplantation/tools-policies-and-guidance/. This work will be extended to the other organs with the aim for the liver transplant tool used in clinical setting by the end of 2021.

3. This paper summarises the analysis undertaken to develop a communication tool for liver patients. The tool requires statistical models for outcomes on the liver transplant waiting list and outcomes post-transplant. The post-transplant model will be based on the risk model used in the Annual Report on Liver Transplantation. For the former, work is required to develop the model, using data from the transplant registry and importantly, using data that is contemporaneous with the National Liver Offering Scheme.

COHORT AND ANALYSIS

4. Data on 1905 adult NHS Group 1 elective registrations on the UK deceased donor liver only transplant waiting list from 20 March 2018 to 19 March 2020 were extracted from the UK Transplant registry as at 9 September 2021. Paediatric patients were excluded along with super-urgent patients, living donor liver transplants and multi-organ patients.

5. Thirty-five patients were registered twice during the time period and the second registration were excluded leaving a cohort of 1870 first registrations during the time period. Note that this is not first ever registrations and may include patients.

6. **Table 1** shows, separately, the 1 year post-registration outcome for non-cancer, cancer (including HCC downstaged patients) and variant syndrome patients. 1411 of the 1870 registrations were for non-cancer patients, of whom, 77% (N=1081) were transplanted during the first year of registration. *The rest of the paper focuses on the non-cancer cohort.*

Table 1 **One year registration outcome as at 9 September 2021 by type of patient**

	Transplanted	Died on the list	Removed due to condition deterioration	Removed due to other reasons	Still active/ suspended	Total
Non-cancer	1059 (75%)	54 (4%)	37 (3%)	44 (3%)	217 (15%)	**1411 (100%)**
HCC (including HCC downstaged)	276 (75%)	7 (2%)	29 (8%)	14 (4%)	43 (12%)	**369 (100%)**
Variant syndrome	35 (39%)	0 (0%)	5 (6%)	2 (2%)	48 (53%)	**90 (100%)**
Total	**1370 (73%)**	**61 (3%)**	**71 (4%)**	**60 (3%)**	**308 (16%)**	**1870 (100%)**

7. **Table 2** shows the one year registration outcome by transplant centre for non-cancer patients. The one-year transplant rate ranged between 62% and 84% by transplant centre while the death/ removal rate ranged between 3% and 13%. The cohort would be ideally split into a modelling cohort (70%) and a validation cohort (30%) and stratified by centre. However, due to the death/removal rates, it was agreed the initial analysis would be performed on the full cohort.

Table 2 **One year registration outcome by transplant centre for non-cancer cohort**

	Transplanted	**Died/ removed due to condition deterioration**	**Still active/ suspended or removed due to other reasons**	**Total**
Newcastle	38 (62%)	8 (13%)	15 (25%)	**61**
Leeds	116 (73%)	13 (8%)	29 (18%)	**158**
Cambridge	148 (80%)	8 (4%)	29 (16%)	**185**
Royal Free	148 (84%)	5 (3%)	24 (13%)	**177**
Kings College	241 (76%)	26 (8%)	51 (16%)	**318**
Birmingham	262 (71%)	28 (8%)	81 (22%)	**371**
Edinburgh	106 (77%)	4 (3%)	27 (20%)	**137**
Total	**1059 (75%)**	**92 (7%)**	**256 (18%)**	**1407**

8. Cox proportional hazards regression modelling, stratified by transplant centre, was used to determine the factors that affect one-year survival from listing for the non-cancer cohort and separate models were built for time to transplant and time to death or removal due to condition deterioration. **Table 3** shows all the factors examined and those identified as statistically significant at both 5% and 10% significance levels in the two multivariate analysis.

9. **Table 4** show the hazard ratios and confidence intervals for factors identified as statistically significant at a 5% level in either analysis. Harrell's c-statistic was calculated to assess the predictive accuracy of both models and were 0.74 for time to transplant and 0.83 for time to death or removal due to condition deterioration.

10. **Figure 1** and **Figure 2** show the baseline survivor functions for time to transplant and time to death or removal respectively.

Table 3	**Factors tested stratified by centre**	
	Time to transplant	**Time to death/ removal due to condition deterioration**
Age	<0.05	<0.05
INR	<0.05	<0.05
Sodium	<0.05	<0.05
Bilirubin	<0.05	<0.05
Albumin	5-10	<0.05
Inpatient status	5-10	<0.05
Disease group	<0.05	X
Creatinine	<0.05	X
BMI	<0.05	X
Blood group	<0.05	X
Previous abdominal surgery	<0.05	X
Gender	<0.05	X
Encephalopathy	X	<0.05
Diabetic	X	5-10
Renal status	X	X
HCV	X	X
Potassium	X	X
Ethnicity	X	X
Ascites	X	X

Table 4 **Hazard ratios for factors found to be statistically significant predictors, at a 5% significance level, of either time to transplant or time to death or removal due to condition deterioration**

			Time to transplant			Time to death/ removal due to condition deterioration		
Variable	**Levels**	**N**	**HR (95% CI)**	**p-value**		**HR (95% CI)**	**p-value**	
				Wald	**Overall**		**Wald**	**Overall**
INR	<1.2	251	0.58 (0.46, 0.73)	<.0001	<0.0001	0.44 (0.19, 1.06)	0.07	0.10
	1.2-1.3	412	0.56 (0.46, 0.67)	<.0001		0.51 (0.26, 0.97)	0.04	
	1.4-1.5	308	0.76 (0.64, 0.91)	0.003		0.50 (0.26, 0.97)	0.04	
	≥1.6	436	1	-		1	-	
Age	17-29	117	0.99 (0.75, 1.31)	0.96	<0.0001	1.05 (0.35, 3.18)	0.93	0.0002
	30-39	141	0.66 (0.52, 0.85)	0.001		0.63 (0.26, 1.54)	0.3	
	40-49	225	0.59 (0.48, 0.72)	<.0001		0.78 (0.41, 1.5)	0.5	
	50-59	498	1	-		1	-	
	60+	426	1.94 (1.67, 2.27)	<.0001		3.1 (1.79, 5.36)	<.0001	
Serum Bilirubin	≤30	353	0.30 (0.24, 0.37)	<.0001	<0.0001	0.42 (0.21, 0.82)	0.01	0.03
	31-50	320	0.40 (0.33, 0.48)	<.0001		0.38 (0.19, 0.76)	0.007	
	51-70	182	0.52 (0.42, 0.64)	<.0001		0.74 (0.35, 1.59)	0.4	
	71-90	121	0.72 (0.58, 0.90)	0.004		0.37 (0.12, 1.13)	0.08	
	>90	431	1	-		1	-	
Blood group	O	626	1	-	<0.0001	1		0.4
	A	559	1.52 (1.33, 1.75)	<.0001		1.22 (0.74, 2.01)	0.4	
	B	148	0.90 (0.72, 1.12)	0.4		1.72 (0.91, 3.27)	0.1	
	AB	74	2.32 (1.78, 3.02)	<.0001		0.98 (0.22, 4.40)	0.98	
Sodium	<133	284	1.48 (1.23, 1.77)	<.0001	<0.0001	1.99 (1.06, 3.76)	0.03	0.006
	133-135	314	1.22 (1.03, 1.45)	0.02		1.56 (0.86, 2.83)	0.14	
	136-138	437	1	-		1	-	
	≥139	372	0.86 (0.73, 1.03)	0.09		0.61 (0.32, 1.19)	0.15	
Aetiology (using Roberts grouping)	HCV/ HBV	71	0.97 (0.72, 1.32)	0.9	<0.0001	0.86 (0.31, 2.35)	0.8	0.15
	ALD	495	1	-		1		
	PSC	189	0.73 (0.56, 0.93)	0.01		0.48 (0.17, 1.32)	0.15	
	PBC	125	1.12 (0.85, 1.47)	0.4		0.75 (0.23, 2.42)	0.6	
	AID	118	1.11 (0.87, 1.42)	0.4		0.38 (0.12, 1.18)	0.09	
	Metabolic	223	1.41 (1.16, 1.70)	0.0004		1.37 (0.72, 2.60)	0.3	
	Other first	64	0.44 (0.30, 0.65)	<.0001		0.48 (0.13, 1.79)	0.3	
	Retransplant	122	0.69 (0.48, 0.98)	0.04		1.43 (0.48, 4.24)	0.5	
BMI at registration	<18.5	28	0.76 (0.46, 1.25)	0.3	<0.0001	1.35 (0.37, 4.95)	0.7	0.86
	18.5-24	441	1.06 (0.90, 1.24)	0.5		0.82 (0.43, 1.56)	0.5	
	25-29	475	1	-		1	-	
	30+	463	0.64 (0.55, 0.75)	<.0001		0.91 (0.52, 1.61)	0.7	
Serum Creatinine	≤70	672	1	-	0.0015	1	-	0.89
	71-90	379	1.07 (0.92, 1.26)	0.4		0.94 (0.53, 1.69)	0.8	
	91-110	197	1.19 (0.97, 1.46)	0.10		1.00 (0.53, 1.90)	0.99	
	111-130	80	1.63 (1.23, 2.16)	0.0007		0.61 (0.23, 1.63)	0.3	
	>130	79	1.57 (1.19, 2.07)	0.0015		1.00 (0.35, 2.84)	>0.99	
Prev abdominal surgery	No	1074	1	-	0.006	1	-	0.86
	Yes	333	0.78 (0.65, 0.94)	0.008		0.94 (0.49, 1.81)	0.86	
Gender	Male	828	1		0.03	1	-	0.4
	Female	579	0.86 (0.74, 0.99)	0.03		0.79 (0.47, 1.31)	0.3539	

Albumin	<27	348	0.85 (0.70, 1.04)	0.11	0.07	2.98 (1.46, 6.08)	0.003	0.01
	27-30	313	0.91 (0.76, 1.10)	0.3		2.37 (1.16, 4.84)	0.02	
(per 5g/l	31-34	342	0.79 (0.67, 0.95)	0.01		1.47 (0.73, 2.95)	0.3	
increase in AR)	≥35	404	1	-		1	-	
Inpatient status	Outpatient	1212	1	-	0.08	1	-	<0.0001
	Inpatient	195	1.19 (0.98, 1.46)	0.08		3.43 (1.94, 6.07)	<.0001	
Encephalopathy	Absence	814	1	-	0.88	1	-	0.05
	Prescence	593	1.01 (0.88, 1.17)	0.88		1.67 (0.99, 2.83)	0.05	

Figure 1 Baseline survival function for time to transplant for non-cancer cohort

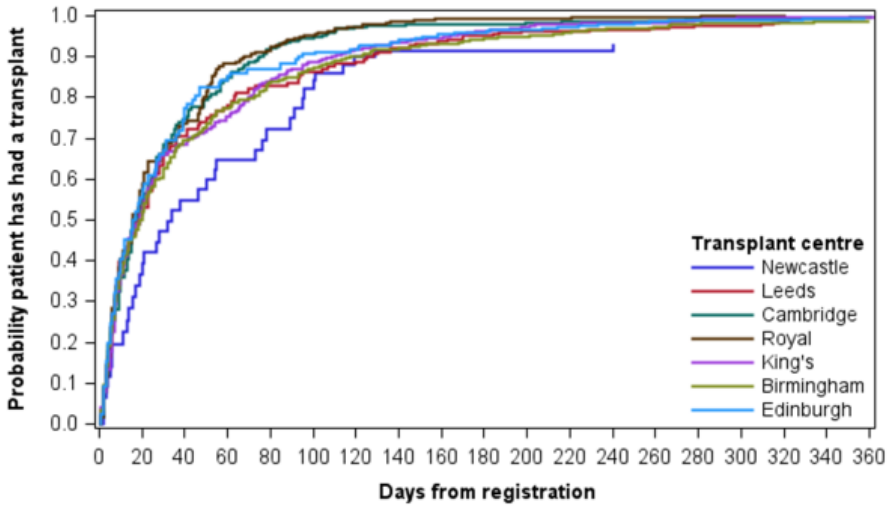
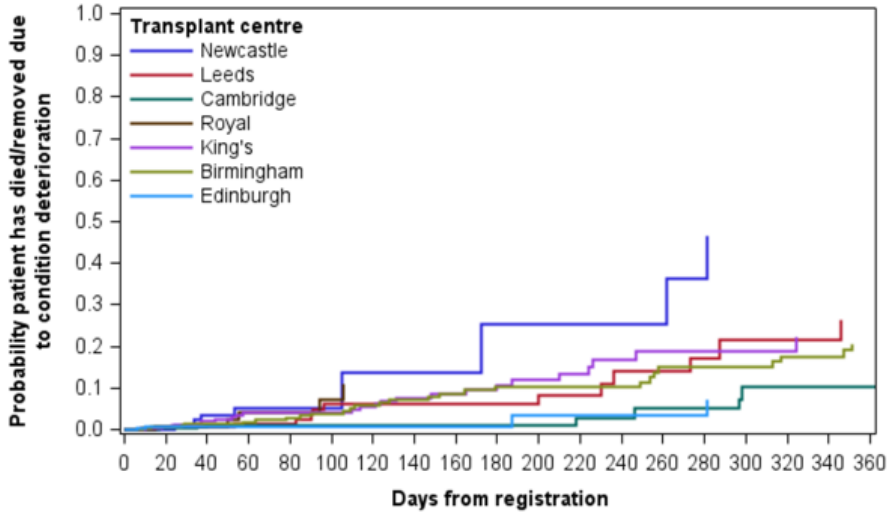


Figure 2 Baseline survival function for time to death or removal due to condition deterioration for non-cancer cohort



ACTIONS

11. Members are asked to note the final model to be used in the Liver Risk Communication Tool.

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APPENDIX

Previous tools that the Winton centre have been involved in developing:

https://breast.predict.nhs.uk/

https://prostate.predict.nhs.uk/