NHS BLOOD AND TRANSPLANT

PANCREAS ADVISORY GROUP

PANCREAS RISK COMMUNICATION TOOL

INTRODUCTION

1. NHSBT have taken advice from 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. 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/. A liver transplant tool is being developed with the aim to be used in a clinical setting by the end of 2021, with the pancreas transplant tool following in early 2022.

3. This paper summarises the analysis undertaken to develop a communication tool for pancreas patients. The tool will require statistical models for outcomes on the pancreas transplant waiting list and outcomes post-transplant. For the latter, this will be based on the risk model used for patient and graft survival in the Annual Report on Pancreas and Islet Transplantation. For the former, work was required to develop the model, using data from the transplant registry available at registration.

COHORT AND ANALYSIS

4. For the outcomes on the pancreas transplant list, the cohort was adult patients registered on the UK deceased donor whole pancreas or simultaneous pancreas and kidney (SPK) transplant waiting list from 1 April 2013 to 31 March 2018.

5. The three possible patient outcomes within three years of pancreas registration were: transplanted; died or removed from the list; remained on the list. Patients who died on or were removed from the list have been grouped together due to the small numbers of events at some centres in the two groups, see **Appendix Table A1**. Two Cox proportional hazards regression models were fitted: time to

transplant (with all other outcomes treated as censored) and time to death or removal (with all other outcomes treated as censored). Both models were stratified by transplant centre so each centre has its own baseline hazard function but covariate effects are assumed to be the same across all centres.

6. The overall data set had 1182 observations. Seventy percent of the cohort (n=828) was used to develop the risk-adjusted models while the remaining 30% (n=354) was used to validate the models. Missing values were imputed as the largest factor level group if there was less than 3% missing in the overall cohort. Where there was more than 3% missing an "unknown" group was used.

7. **Table 1** shows the candidate variables considered in the analyses with the factor levels and those found to be statistically significant at the 5% level in each model. Models for the two outcomes (time to transplant and time to death or removal) were selected independently, and so contained different sets of covariates. The final models both contained all variables present in either of the independently-selected models.

Table 1 Candidate variables for predicting outcomes on the pancreas waiting list and whether statistically significant in either model.

		Model	
Candidate variable (for recipient at registration)	**Groups**	**Time to transplant**	**Time to death/removal**
Age (years)	18-29,30-39,40-49,50-59, ≥60		✓
Gender	Male, Female		
Registration year	2013-14, 2015-16, 2017-18	✓	
Ethnic group	White, BAME		
Blood group	O, A, B, AB	✓	
Sensitisation (cRF)	≤85%, >85%	✓	
Matchability Score	Easy, Moderate and Difficult		
Dialysis status	On dialysis, Not on dialysis		✓
Kidney required	Yes, No		
Cause of diabetes	Type 1, Type 2/other		
Years since diabetes diagnosis	<15, 15-<30, ≥30		
BMI	underweight, healthy, overweight, obese		
HbA_{1C} (mmol/mol)	≤53, ≥53, unknown		
Severe hypoglycaemic events	0, 1, 2-9, ≥10, unknown		
Insulin dose at registration (units/day)	0-29, 30-39, 40-49, ≥50, unknown		
Weight at registration (kg)	<65, 65-<76, 76 to <87, ≥87		✓
Height at registration (cm)	<170, 170-179, ≥180		
First graft	Yes, No	✓	
✓=significant at 5% level			

8. **Table 2** shows the hazard ratios for each model with all significant factors included in the model. In the **Appendix, Figures A1** and **A2** show the baseline survival

curves for each centre for the time to transplant and time to death/removal models, respectively.

Table 2 Hazard ratios from both final models

		Hazard ratio (95% CI)	
Variable	**Category**	**Model for time to transplant**	**Model for time to death / removal**
Age (years) (baseline = 40-49)	18-29 30-39 50-59 ≥60	1.22 (0.90, 1.66) 1.11 (0.92, 1.35) 1.19 (0.95, 1.49) 1.35 (0.66, 2.77)	0.31 (0.12, 0.79) 0.52 (0.32, 0.82) 1.07 (0.66, 1.75) 1.09 (0.25, 4.74)
Registration year (baseline 2013-2014)	2015-16 2017-18	0.80 (0.67, 0.97) 1.00 (0.80, 1.25)	0.99 (0.63, 1.54) 1.07 (0.64, 1.78)
Blood group (baseline = O)	A B AB	1.85 (1.55, 2.22) 1.55 (1.20, 2.01) 4.22 (2.90, 6.14)	0.63 (0.40, 0.99) 0.62 (0.33, 1.18) 0.91 (0.27, 3.03)
Sensitisation (cRF) (baseline ≤85%)	>85%	0.28 (0.18, 0.44)	1.87 (1.04, 3.37)
Dialysis status at registration (baseline = on dialysis)	Not on dialysis	1.11 (0.94, 1.31)	0.53 (0.36, 0.77)
Weight at registration (kg) (baseline=<65)	65 - <76 76 - <87 ≥87	1.04 (0.85, 1.27) 0.95 (0.76, 1.19) 0.82 (0.62, 1.07)	0.50 (0.30, 0.83) 0.63 (0.37, 1.06) 0.75 (0.43, 1.33)
First graft (baseline =yes)	No	0.41 (0.23, 0.72)	0.46 (0.19, 1.09)

9. To assess the predictive accuracy of these models, Harrell's c-statistic was calculated for both the original model-building dataset (in-sample) and the separate validation dataset (out-of-sample). These are shown in **Table 3**.

Table 3 Harrell's c-statistic for both final models

	Model time to transplant	Model time to death/removal
In-sample c-statistic	0.66	0.69
Out-of-sample c-statistic	0.50	0.62

ACTIONS

10. Members are asked to review the factors included in the analysis and approve the final model to be used in the Pancreas Risk Communication Tool.

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APPENDIX

Table A1	Summary of patient outcomes at 3 years, by transplant centre in the whole data set				
Centre	**Transplanted**	**Died**	**Removed***	**Still on list**	**Total**
Newcastle	33	3	6	11	**53**
Cambridge	105	9	7	10	**131**
Guy's	143	17	10	20	**190**
Oxford	291	25	20	27	**363**
Manchester	138	13	16	32	**199**
Edinburgh	85	10	15	13	**123**
WLRTC	39	3	7	9	**58**
Cardiff	46	4	7	8	**65**
TOTAL	**880**	**84**	**88**	**130**	**1182**
* includes due to condition deteriorated, condition improved, or unknown reason					

Figure A1 Baseline survival curves: time to transplant

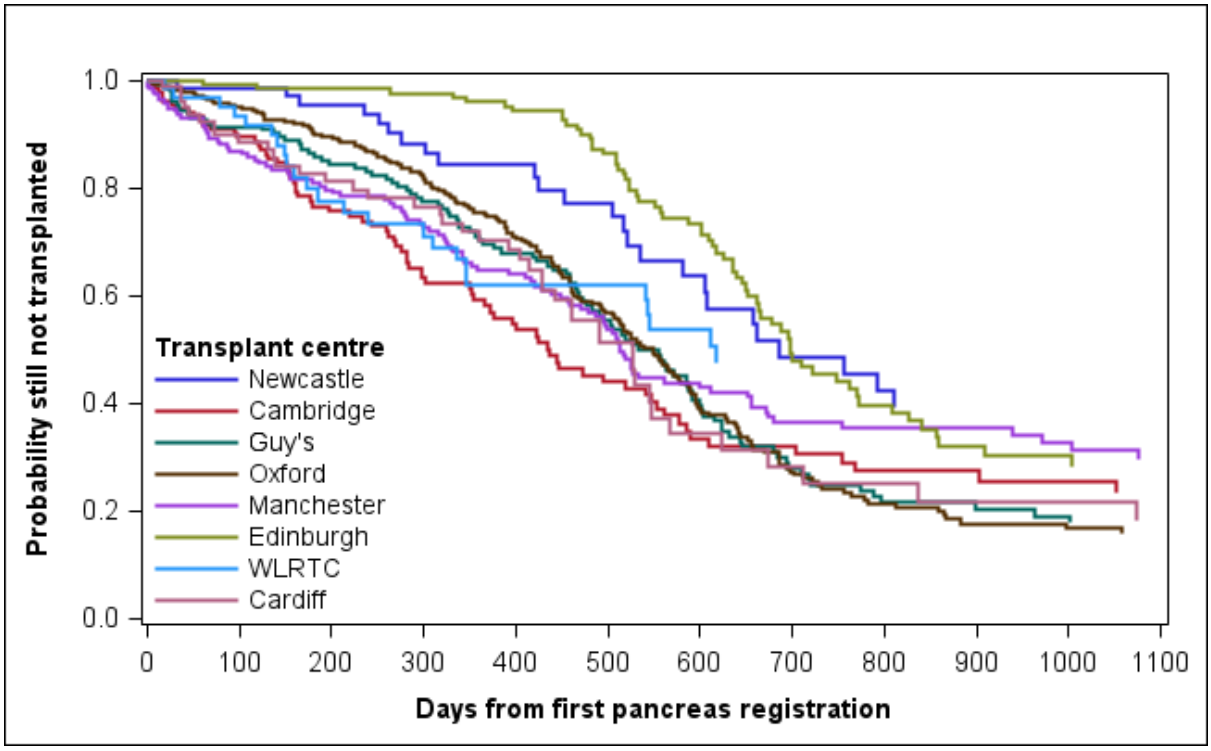

Figure A2 Baseline survival curves: time to death/removal