**Text around TRAC (kidney)**

**What is TRAC?**

TRAC is an online Transplant Risk/Benefit assessment tool that can help clinicians and patients visualise possible outcomes for them from the point of listing for deceased donor kidney transplantation.

**What does TRAC do?**

This is a communication tool designed to aid discussions between patients and clinicians. It will help clinicians and patients to visualise how outcomes for patients with similar characteristics in the past have looked.

TRAC asks for some details about the listed recipient and/or details about the donor who donated their kidney. It then used past data about the outcomes of patients in the past to show likely outcomes for patients with different characteristics.

**Who is TRAC for?**

TRAC tool has been designed to be used by clinicians, patients and their families. It is a communication tool and should not be used by itself to make decisions.

**Patients should use TRAC in consultation with a medical professional.**

Data from adult patients only have been used to develop these tools, and they are not suitable for paediatric patients. The data used to develop this site has been developed patients registered for deceased donor kidney transplants in the UK, or who have received a deceased donor kidney-only transplant in the UK so will not be suitable for patients from other countries.

**Who built TRAC?**

Development of the statistical models was undertaken by the NHS Blood and Transplant statistics and clinical studies team.

The website has been built by the [Winton Centre for Risk & Evidence Communication](https://wintoncentre.maths.cam.ac.uk/) at the University of Cambridge who are funded by a generous donation from the David and Claudia Harding Foundation and the Winton Charitable Foundation.

**Technical**

**Model development**

This model was created using UK Transplant Registry (UKTR) data which is held by NHS Blood and Transplant (NHSBT). The UKTR database contains information on all patients who are listed for transplantation in the UK, and all patients who are transplanted with a solid organ transplant in the UK with follow up data.

Each of these variables are tested and kept in the model if found to have an important relationship with the outcome of interest (e.g. post-transplant survival). These variables are referred to as ‘risk factors’. Some of the models used by the TRAC tool are also used regularly by NHSBT in their organ specific annual reports (<https://www.odt.nhs.uk/statistics-and-reports/organ-specific-reports/>) and in other analyses.

At the end of the modelling process values were obtained called ‘parameter estimates’ which quantify the estimated impact of each risk factor upon the outcome of interest. There will be an estimated baseline risk curve plotted over time that represents an ‘average’ patient in the study cohort. The parameter estimates are then used by the TRAC tool to essentially shift this baseline curve when the values of the risk factors are changed from the ‘average’ values. This way, the patient can plot a curve for values of the risk factors that are relevant to their own circumstances.

Although the TRAC tool is based on reputable models, it cannot say what the outcomes for a particular patient will be. It can only provide a summary of survival and waiting list outcomes for people in the past with similar characteristics.

This tool has been developed using retrospective registry data. Therefore, changes to the Kidney Offering Scheme in 2019 are NOT reflected in these models.

All statistical analyses for this website were generated using SAS Enterprise Guide software, Version 7.1. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA.

**Outcomes from listing model**

The patient cohort for this model comprised all adult (aged ≥18 years) first kidney-only registrations (i.e. people joining the transplant waiting list) between 1 January 2010 and 31 December 2015.

Receiving a transplant is one of three competing events (transplant, death on the list, removal from the list) that a patient is ‘at risk of’ upon entering the kidney transplant list. Therefore, a model for each of these outcomes was developed using Fine and Gray methodology.1 This type of competing risks modelling has been used for survival analysis in kidney transplantation previously in other countries.2 Details of the mathematical form of these models are given in the [mathematical description](https://www.predict.nhs.uk/predict-mathematics.pdf).

Each patient in the cohort was assigned to 1 of 4 categories:

1) patients who were transplanted with either a living or deceased donor transplant

2) patients who died on the list whilst awaiting transplantation

3) patients who were removed from the list prior to transplantation. This could occurs for a number of reasons including patient choice or a deterioration in health such that a transplant was no longer suitable.

4) patients who were still waiting on the list. Patients who were suspended were classed as still waiting on the list.

A Fine and Gray regression model was developed which each produced a Cumulative Incidence Function (CIF), one for each of the three competing risks of interest.

The covariates used in the model were those which have previously been shown to have an impact on outcome and those which were thought to be clinically significant.

Do we want to include the parameter estimates for each outcome here?

Explanation of recipient input covariates:

**Age (years) -** Age at point of being actively listed onto the National Kidney Transplant List**.** This has been divided into categories by decade.

**Sex -** Male or female. Note this refers to sex, not gender**.**

**Ethnicity** – These have been categorised as per data collected by NHSBT**.**

**Graft number -** If the patient has had any previous solid organ transplants.

**Primary renal disease - diabetes -** Whether diabetes is the cause of renal disease of not. This does NOT mean ‘is the patient diabetic?’

**Highly sensitised (cRF >85%)** - any antibodies in the blood – e.g. as a result of pregnancy or a previous organ transplant.

**Blood group** – Patient’s blood group: O, A, B, AB

**Dialysis at registration** – Refers to any form of dialysis (peritoneal or haemodialysis) at the time of listing for transplantation.

**Matchability -** Whether due to a range of factors, such as blood group, it will be ‘easy’, ‘moderate’, or ‘difficult’ to find a matching organ. The ODT provides further details on how this is calculated and a tool for calculating matchability for individual patients: <https://www.odt.nhs.uk/transplantation/tools-policies-and-guidance/calculators/>

**Centre –** This refers to which of the 23 UK adult kidney transplant centres the patient will be receiving their transplant. (This is not always their dialysis centre).

**Post-transplant patient and graft survival models**

The patient cohort for these models comprised all adult (aged ≥18 years) first kidney-only transplants that occurred in the UK between 1 January 2010 and 31 December 2017.

Cox proportional hazards models were built where the following 22 factors were tested for inclusion in the models:

Donor age, type, cause of death, sex, cmv status, hypertension, BMI, height, weight retrieval creatinine, recipient age, ethnicity, sex diabetic nephropathy as a cause of renal failure, waiting time, matchability, blood group, cold ischaemia time and HLA mismatch.

Factors tested were those collected by NHSBT and available on the database and thought to potentially be clinically relevant. The model was built using a forward-step approach. Transplant centre was added to the model as a strata.

The post-transplant survival proportional hazards model operates such that each risk factor multiplies the baseline cumulative hazard by a fixed amount known as the hazard ratio or relative risk - essentially the proportional change in mortality risk. This means the cumulative hazard is the product of two components: the baseline hazard (chances of death or graft failure for a patient with a baseline set of characteristics at time of transplant) and the hazard ratios for the risk factors (the increased/decreased risk of death due to changes in these risk factors compared to the baseline characteristics). The cumulative hazard is then translated in to a survival function as described in the[mathematical description](https://www.predict.nhs.uk/predict-mathematics.pdf).

**5-year patient survival**

Post-transplant survival was defined as the time from transplant until the time of death. These data were censored at the last known follow-up date post-transplant if this was within 5 years of transplantation.

The following factors were found to be significant and included in the model; recipient age, recipient ethnicity, waiting time, recipient primary renal disease, donor age, donor hypertension, HLA MM level.

The baseline characteristics and effect of each risk factor is shown in the table below:

|  |  |  |
| --- | --- | --- |
| **Risk Factor** | **Factor level** | **Parameter estimate** |
| Recipient Age (years) | 18 - 29 | -0.56443 |
|  | 30 – 39 | -0.0144 |
|  | 40 – 49 | Baseline |
|  | 50-59 | 0.60208 |
|  | 60 – 69 | 1.18271 |
|  | 70 + | 1.62701 |
|  |  |  |
| Recipient ethnicity | White | Baseline |
|  | Non-white | -0.18166 |
|  |  |  |
| Recipient waiting time (years) | <=1 | -0.18491 |
|  | 1 to <=3 | Baseline |
|  | 3 to <=5 | 0.04909 |
|  | 5 to <=7 | 0.32106 |
|  | >= 7 | 0.69479 |
|  |  |  |
| Recipient primary renal disease - Diabetes | No | Baseline |
|  | Yes | 0.68609 |
|  |  |  |
| Donor Age (years) | 0 - 29 | -0.50465 |
|  | 30 – 39 | 0.15711 |
|  | 40 – 49 | -0.12827 |
|  | 50-59 | Baseline |
|  | 60 – 69 | -0.01357 |
|  | 70 + | 0.09648 |
|  |  |  |
| HLA MM level | 1 (000) | Baseline |
| 2 (100, 010, 110, 200, 210, 001,101, 201) | 0.29717 |
|  | 3 (020, 120, 220, 011, 111, 211) | 0.39373 |
|  | 4 ((021, 121, 221, 002, 102, 202, 012, 112, 212, 022, 122, 222) | 0.26281 |
|  |  |  |
| Donor Hypertension | No | Baseline |
|  | Yes | 0.28452 |

This model was tested for goodness of fit using a concordance statistic (c-statistic) which was found to be 0.71.

**Five-year post-transplant graft survival**

‘Graft survival’ refers to death-censored graft survival and was defined as the time from transplantation to return to long-term kidney replacement therapy or re-transplantation, whichever occurred first. Data were censored at the time of death or at last known follow-up.

The following factors were found to be significant and included in the model; recipient age, waiting time, graft number, recipient primary renal disease, donor age, donor BMI, donor hypertension, HLA MM level.

The baseline characteristics and effect of each risk factor is shown in the table below:

|  |  |  |
| --- | --- | --- |
| **Risk Factor** | **Factor level** | **Parameter estimate** |
| Recipient age (years) | 18 - 29 | 0.84483 |
|  | 30 – 39 | 0.29385 |
|  | 40 – 49 | Baseline |
|  | 50-59 | -0.07373 |
|  | 60 – 69 | -0.14067 |
|  | 70 + | -0.10022 |
|  |  |  |
| Recipient waiting time (years) | <=1 | Baseline |
|  | 1 to <=3 | 0.21323 |
|  | 3 to <=5 | 0.31039 |
|  | 5 to <=7 | 0.45953 |
|  | >= 7 | 0.83033 |
|  |  |  |
| Recipient graft number | First kidney transplant | Baseline |
|  | Re-graft | 0.22099 |
|  |  |  |
| Recipient primary renal disease - Diabetes | No | -0.3411 |
|  | Yes | Baseline |
|  |  |  |
| Donor Age (years) | 0 - 29 | -0.52485 |
|  | 30 – 39 | -0.31482 |
|  | 40 – 49 | -0.17204 |
|  | 50-59 | Baseline |
|  | 60 – 69 | 0.42198 |
|  | 70 + | 0.5792 |
|  |  |  |
| Donor BMI | <25 | -0.04701 |
| 25 to <=30 | Baseline |
|  | > 30 | 0.0478 |
|  |  |  |
| Donor Hypertension | No | -0.2105 |
|  | Yes | Baseline |
|  |  |  |
| HLA mismatch level | 1 (000) | Baseline |
|  | 2 (100, 010, 110, 200, 210, 001,101, 201) | -0.00426 |
|  | 3 (020, 120, 220, 011, 111, 211) | 0.17315 |
|  | 4 ((021, 121, 221, 002, 102, 202, 012, 112, 212, 022, 122, 222) | 0.25438 |

This model was tested for goodness of fit using a concordance statistic (c-statistic) which was found to be 0.63.

Explanation of donor recipient input covariates:

**Recipient age (years) -** Age at point of transplantation**.** This has been divided into categories by decade.

**Recipient ethnicity –** White or non-white.

**Recipient waiting time (years) –** Time waiting on deceased donor kidney waiting list until time of transplant (active and suspended). This can serve as a proxy for ‘time on dialysis’ as most patients are either already on dialysis or due to commence dialysis within 6 months at the time of listing for transplantation.

**Graft number -** If the patient has had any previous kidney transplants.

**Primary renal disease - diabetes -** Whether diabetes is the cause of renal disease of not – does NOT mean ‘is the patient diabetic?’

**Donor age –** The age at which the donor donated their organs.

**Donor BMI** – Donor BMI as recorded at the donating hospital site. Calculated as weight (kilograms) divided by height (m2)

**Donor Hypertension –** Whether the donor suffered from high blood pressure as recorded by NHSBT on data collection forms at the time of listing.

**HLA MM level –** Human Leukocyte Antigen (HLA) matching level. HLA are proteins located on the surface of white blood cells and other tissues. When people share the same HLA’s, they are said to be a ‘match’. There are may different types of HLA, and the matching can occur to different degrees, hence the different levels of matching.

**Centre -** This refers to which of the 23 UK adult kidney transplant centres the patient will be receiving their transplant. (This is not always the centre at which they are followed up).

**Mathematical section**

**Outcomes from listing model**

The Fine and Gray regression model3 directly models the subdistribution hazard such that:

where:

* is estimated using the Breslow (1972) estimate
* is estimated using the Newton-Raphson algorithm to maximise the partial likelihood function for the parameters in .
* represents the set of characteristics for the ith individual.

The subdistribution hazard, , is the instantaneous risk of event *k* occurring given that the patient has not yet experienced risk event k. Therefore importantly, patients that experience a risk event other than risk k (i.e. a competing risk event), are retained in the risk set for the calculation of , and hence , after this event. Weights are incorporated into the partial likelihood function such that patients who experience no event before time t are given a weight of 1, whereas patients who experience competing events before *t* are given a weight that reduces with time.

For the competing risks model, the baseline CIF’s for each of the competing risks (transplant, death on the list, removal from the list) from time of listing as well as the parameter estimates which are used to shift the baseline obtained. The formula for doing this is:

Where is the baseline CIF and ‘’ is the CIF that relates to a patient of particular characteristics (X).

The phreg function in SAS V.7.1 (SAS Institute, Cary, North Carolina, USA) was used to compute these estimates.

**Cox proportional hazards model**

This model was used to develop 5-year post transplant patient and graft survival models.

The estimated cumulative hazard for the ith individual for mortality after receiving a deceased donor kidney transplant, *t* days post-transplantation has the form:

where:

* is estimated using the Breslow (1972) estimate
* is estimated by constructing a partial likelihood function, independent of , which is maximised with respect to the parameters in .
* represents the set of characteristics for the ith individual.

This is translated into the survival functions presented in the TRAC tool through the following equation:

The phreg function in SAS V.7.1 (SAS Institute, Cary, North Carolina, USA) was used to compute these estimates.

**Model validation**

The models once developed will undergo statistical validation tests. The post transplant outcome models have been developed on 70% of the dataset and tested on the remaining 30% using a risk sore method. In addition, factors have been checked for proportionality, and residuals have been assessed. The ‘predictive ability’ of the models will also be ascertained using various statistical methods.

**Contact**

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**Future versions**

The data inputted will be inputted and updated annually. The parameters included in the model will be updated every 3-5 years.

**Legal disclaimer**

TRAC uses an algorithm based on information from many thousands of patients on the UK transplant registry. However, it can only provide a 'best guess' of likely outcomes based on past data, and it can never provide an accurate prediction for an individual. Patients should always consult their own specialist, who will be able to discuss the results in a more personalised context.

**Privacy**

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**References**

1. Annual Report on Pancreas and Islet Transplantation 2017/2018. NHS Blood and Transplant. <https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/12251/nhsbt-pancreas-and-islet-transplantation-annual-report-2017-2018.pdf>. Published 2018. Accessed 14/05/2019.

2. Sapir-Pichhadze R, Pintilie M, Tinckam KJ, et al. Survival Analysis in the Presence of Competing Risks: The Example of Waitlisted Kidney Transplant Candidates. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons.* 2016;16(7):1958-1966.

3. Jason Fine RG. A Proportional Hazards Model for the Subdistribution of a Competing Risk.

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