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Subject: Data for lung TRAC tool
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JM

Hi Mike,

I am pleased to (finally!) send you the complete set of information you require to put together the Lung TRAC tool.

1. I have attached 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 up or down. The formula for doing this is:

$$CIF(t) = 1 - (1 - CIF_0(t))^{\exp(X\beta)}$$

Where CIF_0 is the baseline CIF and 'CIF' is the CIF that relates to a patient of particular characteristics (X).

How to calculate $X\beta$ in order to shift the baseline CIF:

Imagine we have only three variables in our model for time to transplant: sex (male/female categorical variable), height (linear continuous variable) and age (non-linear continuous using a spline). Then the linear predictor is:

$$X\beta = \beta_1 sex + \beta_2 height + \beta_3 age + \beta_4 F_1(age) + \beta_5 F_2(age)$$

The latter three terms of this expression make up the spline term where:

$$F_1(age) = \left(\frac{(x-k_1)_+^3 - (x-k_4)_+^3}{k_4 - k_1} - \frac{(x-k_3)_+^3 - (x-k_4)_+^3}{k_4 - k_3}\right)$$

$$F_2(age) = \left(\frac{(x-k_2)_+^3 - (x-k_4)_+^3}{k_4 - k_2} - \frac{(x-k_3)_+^3 - (x-k_4)_+^3}{k_4 - k_3}\right)$$

Please note that the '+' in the equation $(x-k_1)_+^3$ just means to set this part of the equation to 0 if $(x-k_1)^3<0$. The k's are the knots which we have specified in the spreadsheet.

Imagine that the characteristics of the baseline CIF (CIF_0) are as follows: sex=male, height=150, age=45. Then to calculate the CIF for a female of height 160 and age 60, we would calculate the following:

$$CIF(t) = 1 - \left(1 - CIF_0(t)\right)^{\exp\{\beta_1 + \beta_2(160-150) + \beta_3(60-45) + \beta_4\left(F_1(60) - F_1(45)\right) + \beta_5\left(F_2(60) - F_2(45)\right)\}}$$

If the patient had been male, we would exclude β_1 from the above calculation.
You will notice that $X\beta$ is a constant whereas $CIF_0(t)$ and hence $CIF(t)$ varies over time so once you have calculated $X\beta$, you simply apply this constant 'conversion factor' to the baseline CIF.

2. For completeness (you have already seen this), I have also attached the a) survival from listing and b) post-transplant survival spreadsheets. These come from Cox Proportional Hazards regression models. Each spreadsheet contains the baseline survival function as well as the parameter estimates which are used to shift the baseline up or down. The formula for doing this is:

$S(t) = S_0(t)^{\exp(X\beta)}$

Where $S_0(t)$ is the baseline survival and $S(t)$ is the survival function that relates to a patient of particular characteristics (X).
In order to shift the baseline survival in order to calculate $S(t)$ for a patient of particular characteristics (X), you apply exactly the same principles as described above to calculate $\exp(X\beta)$.

3. I have also attached a word document which summarises how the TRAC tool works in exactly the same format as the Predict tool. This can be used on the website under the same headings ('How it works', 'the technical section' and 'the algorithms'). I have also included the email address for questions and descriptions of each variable for the 'i's' (I would recommend asking Jas to review the i's).

Before the tool goes live, I suggest that we test the estimates of $CIF(t)$ and $S(t)$ for a set of 'test cases' (patients). If Mike could send us his calculated $CIF(t)$ and $S(t)$ for each model for an agreed set of test cases, we can then compare these with our estimates to make sure we're happy with what values are being plotted/displayed.

My last day is Monday (25^{th} Feb) so I will leave you in the capable hands of Lisa (cc'd) to coordinate things but I believe you have everything you need now to put together a first full draft. I would love to see the final version up and running so have asked Maria to send me a link when it is ready! Amongst all the nappies and feeding, I shall feel proud to see this tool up and running! ☺

Maria is working on the kidney models and Lisa will liaise with you regarding sending the data. The models are formulated in exactly the same way as described above so the same principles can be applied in programming (and similar text for the website, only slightly amended from the lung version).

Best wishes to you all,
Jenny

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$X\beta S(t) = S_0(t)^{\exp(X\beta)} (x - k_1)^3 S_0(t) CIF CIF(t) = 1 - (1 - CIF_0(t))^{\exp(X\beta)}$

$X\beta = \beta_1 sex + \beta_2 height + \beta_3 age + \beta_4 F_1(age) + \beta_5 F_2(age) CIF(t) X\beta (x - k_1)^3 X\beta$

$$CIF(t) = 1 - (1 - CIF_0(t))^{\exp(X\beta)}$$

$$F_2(age) = \left(\frac{(x-k_2)_+^3 - (x-k_4)_+^3}{k_4 - k_2} - \frac{(x-k_3)_+^3 - (x-k_4)_+^3}{k_4 - k_3}\right) X\beta$$

$$F_1(age) = \left(\frac{(x-k_1)_+^3 - (x-k_4)_+^3}{k_4 - k_1} - \frac{(x-k_3)_+^3 - (x-k_4)_+^3}{k_4 - k_3}\right)(x-k_1)^3$$

$$CIF(t) = 1 - \left(1 - CIF_0(t)\right)^{\exp\{\beta_1 + \beta_2(160-150) + \beta_3(60-45) + \beta_4(F_1(60) - F_1(45)) + \beta_5(F_2(60) - F_2(45))\}}$$

$$F_2(age) = \left(\frac{(x-k_2)_+^3 - (x-k_4)_+^3}{k_4 - k_2} - \frac{(x-k_3)_+^3 - (x-k_4)_+^3}{k_4 - k_3}\right) X\beta CIF_0(t) CIF_0$$

$$S(t) = S_0(t)^{\exp(X\beta)}$$

$$CIF(t) = 1 - \left(1 - CIF_0(t)\right)^{\exp\{\beta_1 + \beta_2(160-150) + \beta_3(60-45) + \beta_4(F_1(60) - F_1(45)) + \beta_5(F_2(60) - F_2(45))\}}$$

$$\exp(X\beta)\ S(t)\ F_1(age) = \left(\frac{(x-k_1)_+^3 - (x-k_4)_+^3}{k_4 - k_1} - \frac{(x-k_3)_+^3 - (x-k_4)_+^3}{k_4 - k_3}\right)$$

$$X\beta = \beta_1 sex + \beta_2 height + \beta_3 age + \beta_4 F_1(age) + \beta_5 F_2(age) CIF_0 CIF(t) CIF_0(t)(x-k_1)_+^3$$

$$CIF(x-k_1)_+^3 X\beta = \beta_1 sex + \beta_2 height + \beta_3 age + \beta_4 F_1(age) + \beta_5 F_2(age) CIF_0 (x-k_1)_+^3 \beta_1$$

$$\beta_1 (x-k_1)_+^3 CIF(t) X\beta = \beta_1 sex + \beta_2 height + \beta_3 age + \beta_4 F_1(age) + \beta_5 F_2(age) S(t) \beta_1 X\beta$$

$$CIF(t)\beta_1 \exp(X\beta)\ X\beta\ CIF(t) = 1 - (1 - CIF_0(t))^{\exp(X\beta)}\ CIF_0(t) X\beta$$

$$F_2(age) = \left(\frac{(x-k_2)_+^3 - (x-k_4)_+^3}{k_4 - k_2} - \frac{(x-k_3)_+^3 - (x-k_4)_+^3}{k_4 - k_3}\right) CIF_0$$

$$CIF(t) = 1 - \left(1 - CIF_0(t)\right)^{\exp\{\beta_1 + \beta_2(160-150) + \beta_3(60-45) + \beta_4(F_1(60) - F_1(45)) + \beta_5(F_2(60) - F_2(45))\}}$$

$$CIF\ F_1(age) = \left(\frac{(x-k_1)_+^3 - (x-k_4)_+^3}{k_4 - k_1} - \frac{(x-k_3)_+^3 - (x-k_4)_+^3}{k_4 - k_3}\right)$$

$$F_2(age) = \left(\frac{(x-k_2)_+^3 - (x-k_4)_+^3}{k_4 - k_2} - \frac{(x-k_3)_+^3 - (x-k_4)_+^3}{k_4 - k_3}\right)(x-k_1)^3$$

$$CIF(t) = 1 - (1 - CIF_0(t))^{\exp(X\beta)}$$

$$F_1(age) = \left(\frac{(x-k_1)_+^3 - (x-k_4)_+^3}{k_4 - k_1} - \frac{(x-k_3)_+^3 - (x-k_4)_+^3}{k_4 - k_3}\right)$$

$$CIF(t) = 1 - \left(1 - CIF_0(t)\right)^{\exp\{\beta_1 + \beta_2(160-150) + \beta_3(60-45) + \beta_4(F_1(60) - F_1(45)) + \beta_5(F_2(60) - F_2(45))\}}$$

$$CIF_0(t) S_0(t) CIF$$

Competing risks CIF inf...on.xlsx

Survival from listing i...on.xlsx

Post-transplant information.xlsx

About the TRAC tool FINAL.docx