Appendix (to be published as supplementary material)

The formula for the survival probability at time t, S(t), is S(t)=exp(-H(t)). H(t) is the cumulative hazard that is calculated from the baseline hazard (H0) as H(t)=H0(t)\*exp(prognostic index). The prognostic index (PI) can be calculated by multiplying the values for the numerical predictors by the regression coefficient and to select the additional regression coefficients corresponding with the patient characteristics from the value list and taking the sum of all regression coefficients. The survival probabilities can be calculated with the formula shown above, using the prognostic index and the baseline hazards for the survival time.
To illustrate how the formula can be used to compute predicted survival consider the first example from the results section of the manuscript:

The first patient is a 59 year old male patient with renal vascular disease, a BMI of 25, smoking in the past, longer than 3 months before RRT start, no history of angina pectoris, peripheral vascular accident, malignancy and myocardinfarct, a charlson comorbidity score of 2, a Karnofsky score of 80, cholesterol level is 5 mmol/l, phosphate 1.8 mmol/l and albumin 36 g/l, starting on hemodialysis.
In the recalibrated ‘registry’ model this patient has a prognostic index (PI) of ((age\*0.064=)59\*0.064=)3.77)+((male=)0.069)+((renal vascular disease=)0.807+((hemodialysis=)0)=4.64.

The predicted 5-year survival for this patient is: exp(-(0.007\*exp(4.64)))=exp(-0.71)=49%. The 10-year survival for this patient is: exp(-(0.013\*exp(4.64)))=exp(-(1.36)=26%.

In the ‘easy’ model this patient has a prognostic index (PI) of (((age\*0.029=)59\*0.029=)1.69)+((renal vascular disease=)0.445+((smoking longer than 3 months ago=)0.013)+((BMI20-30=)-0.270)+((charlson score 2=)0.995)+((karnofsky 80=)-1.902)=1.78.

The predicted 5-year survival for this patient is: exp(-(0.123\*exp(1.78)))=exp(-0.73)=48%. The 10-year survival for this patient is: exp(-(0.257\*exp(1.78)))=exp(-(1.52)=22%.

In the ‘elaborate’ model this patient has a prognostic index (PI) of (((age\*0.031=)59\*0.031=)1.83)+((renal vascular disease=)0.485+((smoking longer than 3 months ago=)0.029+((BMI20-30=)-0.311)+((charlson score 2=)0.934)+((karnofsky 80=)-1.848)+(((chol 5=)5\*-0.060=)-0.3)+(((phosphate 1.8=)1.8\*0.189=)0.341)+(((albumin 36=)36\*-0.019=)-0.692)=1.28.

The predicted 5-year survival for this patient is: exp(-(0.188\*exp(1.28)))=exp(-0.67)=51%. The 10-year survival for this patient is: exp(-(0.4\*exp(1.28)))=exp(-(1.43)=24%.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Appendix table 1: calibration (measured by calibration in the large and calibration slopes) and discrimination (measured by c-index) for the 3 models for 3 periods of time**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|   | **recalibrated 'registry' model** | **'easy' model** | **'elaborate' model** |  |  |  |  |  |
| **CALIBRATION** |   |   |   |  |  |  |  |  |
|   |   |   |   |  |  |  |  |  |
| **\* calibration in the large** |   |   |   |  |  |  |  |  |
| observed 10 year survival: 0.353, vs predicted: | 0.352 | 0.352 | 0.350 |  |  |  |  |  |
| observed 5 year survival: 0.518, vs predicted: | 0.517 | 0.507 | 0.507 |  |  |  |  |  |
| observed 3 year survival: 0.653, vs predicted: | 0.664 | 0.652 | 0.653 |  |  |  |  |  |
|   |   |   |   |  |  |  |  |  |
| **\* calibration slope** |   |   |   |  |  |  |  |  |
| 10 year | 0.938 | 0.959 | 0.932 |  |  |  |  |  |
| 5 year | 0.872 | 0.984 | 0.955 |  |  |  |  |  |
| 3 year | 0.847 | 1.047 | 1.025 |  |  |  |  |  |
|   |   |   |   |  |  |  |  |  |
|   |   |   |   |  |  |  |  |  |
| **DISCRIMINATION** |   |   |   |  |  |  |  |  |
|   |   |   |   |  |  |  |  |  |
| **\* C-index** |   |   |   |  |  |  |  |  |
| 10 year | 0.724 | 0.784 | 0.788 |  |  |  |  |  |
| 5 year | 0.719 | 0.785 | 0.788 |  |  |  |  |  |
| 3 year | 0.715 | 0.793 | 0.798 |  |  |  |  |  |

**Appendix table 2: the integrated discrimination index (IDI)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|   | recalibrated 'registry' model |  'easy' model |   |  'elaborate' model |   |
|   | difference in predicted survival in patients with and without the event | difference in predicted survival in patients with and without the event | **IDI 'registry'-> 'easy' model** | difference in predicted survival in patients with and without the event | **IDI 'easy' -> 'elaborate' model** |
| 10 year survival | 0.339 | 0.421 | **0.082** | 0.428 | **0.007** |
| 5 year survival | 0.276 | 0.376 | **0.100** | 0.380 | **0.004** |
| 3 year survival | 0.197 | 0.311 | **0.115** | 0.317 | **0.005** |

The integrated discrimination index for the 10 year survival is the difference in the average predicted survival in patients with and without the event in two different models. The calculation of the IDI is further illustrated for the 10 year survival:In the ‘registry’ model the average predicted 10 year survival was 0.5585 in the group of patients with no event and 0.2194 in the group of patients that died; the difference between the predictions in the group with and without the event therefore is 0.5585-0.2191=0.3391.In the ‘easy’ model the average predicted 10 year survival was 0.6090 in the group of patients with no event and 0.1877 in the group of patients that died; the discrimination of the ‘easy’ model is better, as the difference between the predictions in the group with and without the event is 0.6090-0.1877=0.4212. The integrated discrimination improvement from the ‘easy’ model compared to the ’registry’ model is 0.4212-0.3391=0.0821.In the ‘elaborate’ model the average predicted 10 year survival was 0.6109 in the group of patients with no event and 0.1831 in the group of patients that died; the discrimination of the ‘elaborate’ model is only slightly better than the previous model as the difference between the predictions in the group with and without the event is 0.6109-0.1831=0.4278. The integrated discrimination improvement from the ‘elaborate’ compared to the ‘easy’ model is 0.4278-0.4212=0.0066.**Appendix table 3: Continuous Net Reclassification Improvement (NRI)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **10 year survival** | **5 year survival** | **3 year survival** |
|  **'Easy' model compared to recalibrated 'registry' model** |   |   |   |   |
|   | events with higher risk score  | 0.637 | 0.691 | 0.757 |
|   | events with lower risk score | 0.363 | 0.309 | 0.243 |
|   | *event NRI* | *0.274* | *0.381* | *0.514* |
|   | non-events with lower risk score | 0.725 | 0.678 | 0.639 |
|   | non-events with higher risk score | 0.275 | 0.322 | 0.361 |
|  | *non-event NRI* | *0.450* | *0.356* | *0.278* |
|   | total NRI | 0.723 | 0.737 | 0.792 |
|   |   |   |   |   |
|  **'Elaborate' model compared to 'easy' model** |   |   |   |   |
|   | events with higher risk score  | 0.577 | 0.578 | 0.588 |
|   | events with lower risk score | 0.423 | 0.422 | 0.412 |
|   | *event NRI* | *0.154* | *0.156* | *0.175* |
|   | non-events with lower risk score | 0.541 | 0.511 | 0.498 |
|   | non-events with higher risk score | 0.459 | 0.489 | 0.502 |
|  | *non-event NRI* | *0.082* | *0.022* | *-0.003* |
|   | total NRI | 0.235 | 0.178 | 0.172 |

 The continuous net reclassification improvement for the 10 year survival is the sum of the percentage of patients with the event that are reclassified to a higher risk score and the percentage of patients without the event with a lower risk score. The calculation of the NRI is further illustrated for the 10 year survival:For each patient the survival calculations for the 3 models are made and compared. If a patient with a lower survival chance in the new model versus the old model has died within 10 years this patient is counted in the events with a higher risk score; if a patient with a higher survival chance actually survived 10 years, this patient is counted in the non-events with a lower risk score. In the example in the results section of the manuscript the patient had a 10 year survival chance of 26% according to the ‘registry’ model; the survival chance is only 22% according to the ‘easy’ model, which indicates a reclassification to a higher risk score, and 24% according to the ‘elaborate’ model, indicates a reclassification to a lower risk score in the ‘elaborate’ versus the ‘easy’ model. If this patient has died within 10 years this patient is contributing to the events with a higher risk score in the ‘easy’ model and lower risk score in the ‘elaborate’ model. If the patient has survived 10 years the patient is contributing to the non-events with a higher or lower risk score. The percentages in this table represent the reclassification changes of all patients in the validation group. |  |  |  |  |
|  |  |  |  |  |  |  |