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Response to why the donor risk index and Eurotransplant donor risk index may also be applicable in France; reply to Winter et al. and statistical perspective

We read the comments of Blok et al.[1] related to our article.[2]

As stated by Royston:[3]"In all cases, the guiding principle is to apply the model in exactly the same way in the validation data as in the derivation data, or at least to be aware of any differences."

We maintain that, in the Eurotransplant validation study, "the model used in the validation dataset was not based on the same covariates as in the construction dataset" and that "the ET-DRI score was built by changing the coefficients of the DRI and adding variables", which is not recommended.[2,3]

Firstly, we adapted Royston's methodology[3] to the Donor Risk Index (DRI)[4] which contains only donor covariates, but which is adjusted on recipient covariates. Feng's model[4] is therefore the following simplified form:

$$\beta_{donor}X_{donor} + \beta_{recipient}X_{recipient}$$

To correctly validate this model, according to,[3] it would have been necessary to know $\beta = (\beta_{donor}, \beta_{recipient})$.

Unfortunately, such information was not available in.[4] We made therefore the assumption that Feng's $\beta_{recipient}$ = our $\beta_{adjustment}$. We then tested model 1.[2] Of note, testing only $\beta_{DRI} = 1$ is not adapted and presupposes that $\beta_{recipient} = 0$, which is false.

Secondly, the purpose of checking model misspecification is to test the adjustment of one or more covariates included in the DRI. Testing $\beta_{adjustment} + \beta^* = 0$ does not answer this question. Thus, in this step, we estimated the $\beta_{adjustment}$ using model 1,[2] set at the estimated value in model 2.[2] Again, the optimal way would have been to know Feng's $\beta_{recipient}$.

Thirdly, the purpose of the survival curves and hazard ratios was to test the discrimination of the different DRI risk groups, which were built only with the DRI (i.e. β_{donor}) (table 6 in[4]). Here, only the score is relevant and not the $\beta_{adjustment}$.

Concerning the c-index, it is not possible, in our opinion, to do much better for post-transplantation models because other covariates, not known at the time of transplantation, predict post-transplantation survival. This problem is well known and doesn't depend of the size of the dataset.[5]

Finally, Blok et al. proposed the Eurotransplant-DRI because of obvious differences in allocation systems between Eurotransplant and the American Organ Procurement and Transplantation Network; the same logic also holds true from one country to another.

CONFLICTS OF INTEREST

The authors do not have any disclosures to report.

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