A two-stage prediction model for heterogeneous effects for many treatment options

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Background

A question of public health interest: “Which treatment is best for a specific patient?”. Different patients often have different health outcomes under the same treatment. It is essential to understand how different treatments vary across different patients, thus estimating Heterogeneous Treatment Effects (HTE)

1. Individuals’ characteristics influence the variation of HTE and their baseline risk score prior to treatment seems to be a determinant predictor for HTE [1]
2. Numerous treatments options available for each disease Network meta-analysis (NMA) is a key-tool for comparing many different treatment options [2]

AIM To develop a two-stage evidence synthesis prediction model to predict the most likely outcome under several possible treatment options while accounting for patients’ characteristics using individual participant data network meta-regression with risk scores

Data

- 3 randomized clinical trials (phase III), 2990 observations in total
- Disease: Relapsing-remitting Multiple Sclerosis (MS)
- Outcome: Relapse MS in 2 years

Methods

Stage 1 – Development of risk score prior to treatment

We fit five prognostic models with three shrinkage approaches and we select the one with the best discrimination and calibration Model’s output: The probability of Relapse MS in two years “blinded” to treatment, taking into account several prognostic factors

Stage 2 – Development of Treatment-effects prediction model

Prediction model with IPD Network meta-regression using the baseline risk score as the only predictor

Results

Stage 1 – Development of risk score prior to treatment

The best model (c-index=0.65, calibration-slope=1.03) is a model with 12 prognostic factors selected via lasso method and using penalized maximum likelihood estimation shrinkage approach.

Stage 2 – Development of Treatment-effects prediction model

Natalizumab seems to be the best treatment option on average. However this is not the case if we divide patients based on their baseline risks prior to treatment. Dimethyl fumarate is the best treatment option for low-risk patients (<30%), whereas Natalizumab is the best option for high-risk patients.

Conclusions

- The baseline risk score of patients moderates the absolute benefit of treatments
- This is the first prediction model that uses risk score from a nested prognostic model within a IPD Network meta-regression

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