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Digital Futures

Theory & Methods Challenge Fortnight: Estimands and Feedback Loops

6 May 2020

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#TMCfturing

Prediction algorithms are used for decision support: first, a simple solution.

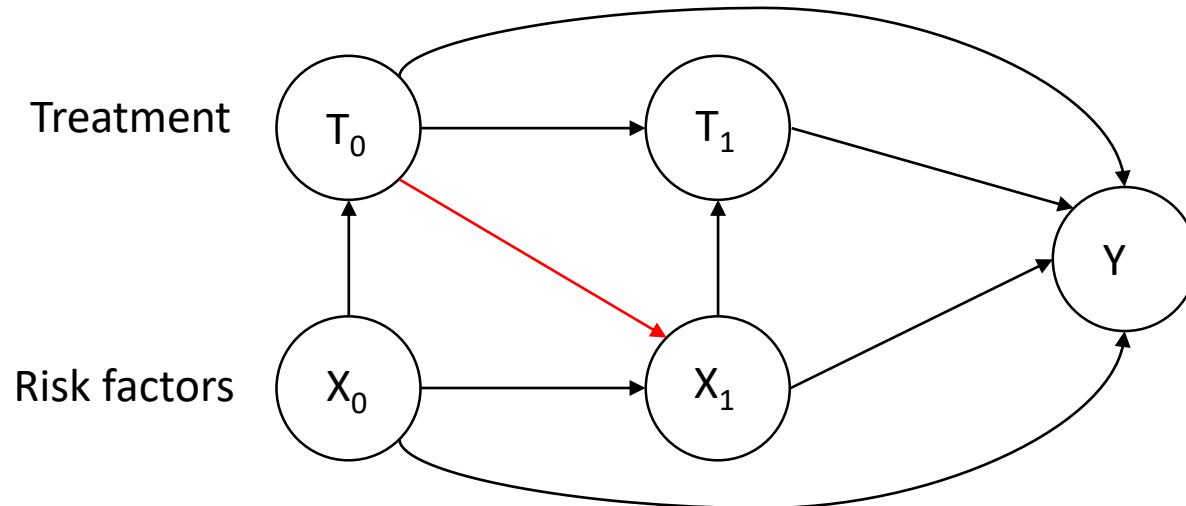
- Obtain the best covariate-adjusted estimate of relative treatment effect (e.g., odds ratio, hazards ratio) from an RCT.
- Develop a predictive model from complete, accurate observational data.
- Apply the relative treatment effects from the RCT to the estimated outcome risk from the observational data.

Clarity over estimands: what does our prediction mean?

- $E[Y|X, T] \neq E[Y(T = t)|X]$
- Treatment drop-in:
 - E[Y given we don't treat now]
 - E[Y given we don't treat now, or ever]?
 - E[Y given we don't treat now, or in next X years]?
- Distinguishing between *guided* and *background* treatments
- Pajouheshnia et al Diag. Prog. Res. 2017 <https://diagnprognres.biomedcentral.com/articles/10.1186/s41512-017-0015-0>
- Sperrin et al Stat. Med. 2018 <https://onlinelibrary.wiley.com/doi/full/10.1002/sim.7913>
- Van Geloven et al Eur. J. Epi. Forthcoming, <https://arxiv.org/pdf/2004.06998.pdf>

Treatment drop-in: a prediction problem requiring a causal resolution?

- Problem: modelling change in treatment after baseline.



- Failure to adjust for this leads to underestimate of risk
 - Additional 3.6% of population would be considered for statins (for CVD primary prevention) after correcting for this when predicting CVD risk with a 10% treatment threshold.

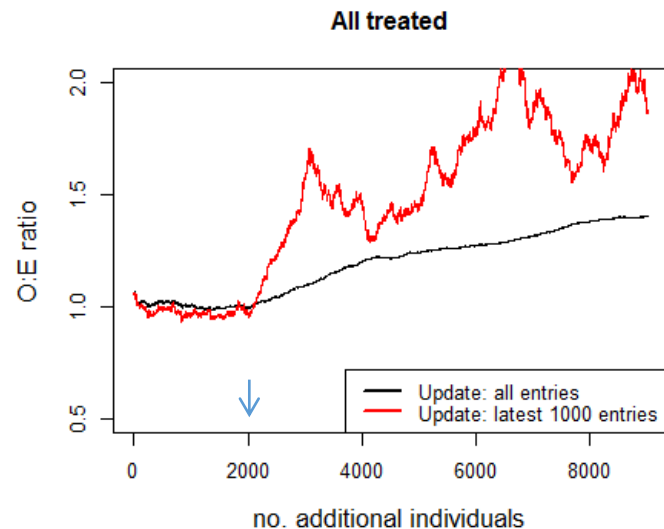
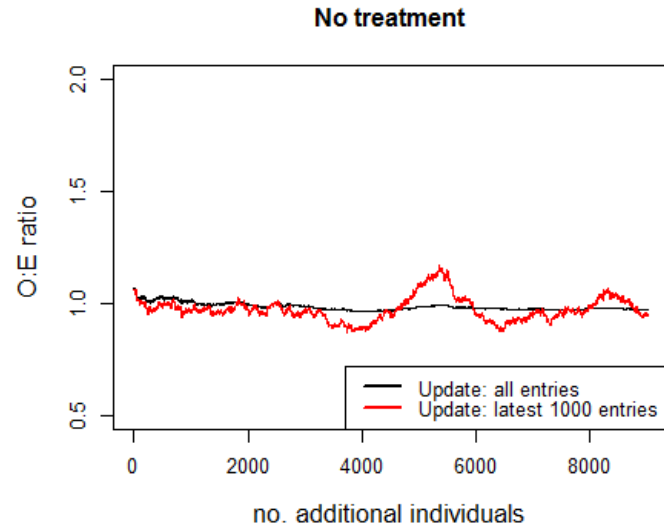
As soon as a risk model is deployed, behaviour changes.



- High risk patients receive intervention – and thus appear low risk.
- Missing data patterns (and general recording practices) change.

Hari Seldon, Isaac Asimov's *Foundation*

Prediction paradox: feedback loops



Results of small simulation

- Model was updated after every new patient entered database
- A new treatment was introduced after patient 2000.
- Treatment was prioritised to high-risk individuals according to the model being updated over time

Feedback loops and self-fulfilling prophecies

- Need solutions where treatment/intervention actions are modelled over time

* O:E (observed: expected ratio – model calibration)

Summary

- A simple solution to combine trial estimates with prognostic models exists to allow ‘what-if’ prediction.

But challenges remain in ‘what-if’ prediction:

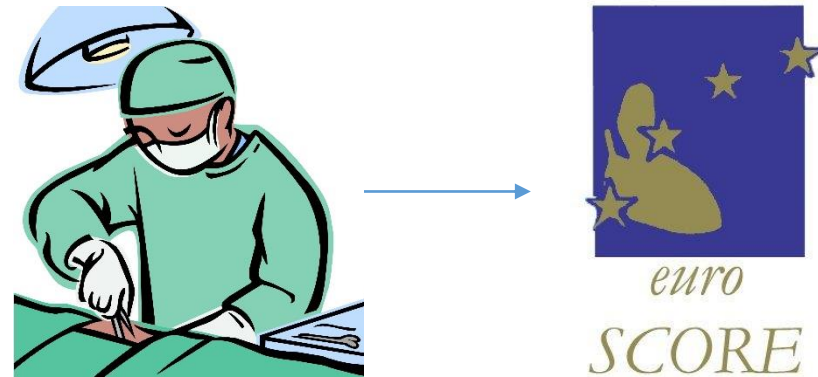
- Clarity over estimands (treatment naïve) and treatment drop-in.
- Selection bias.
- Validation challenges in treatment-naïve prediction
- Prediction paradox and feedback loops.

Development population may not reflect target for decision making.

Use:

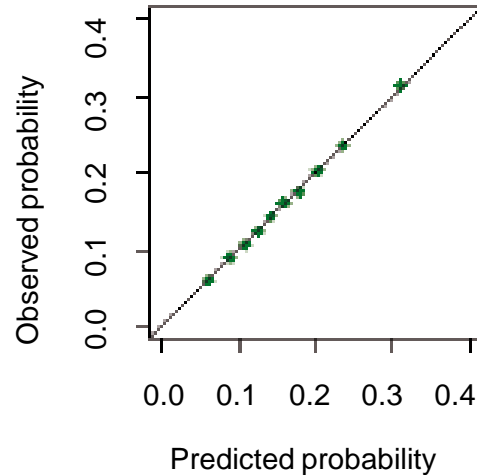
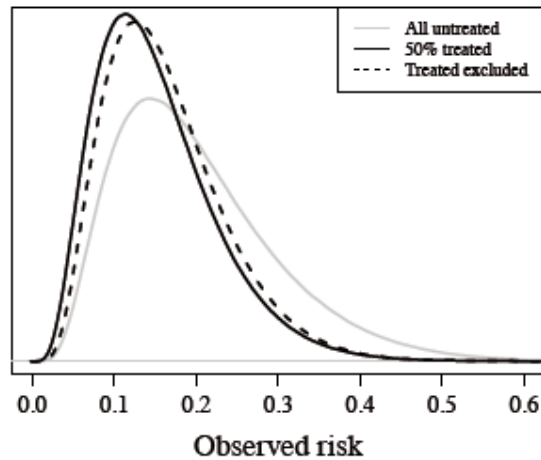


Development:



Standard validation/testing methodology do not estimate accuracy of predictions of $E[Y(T = t)|X]$ in treated patients.

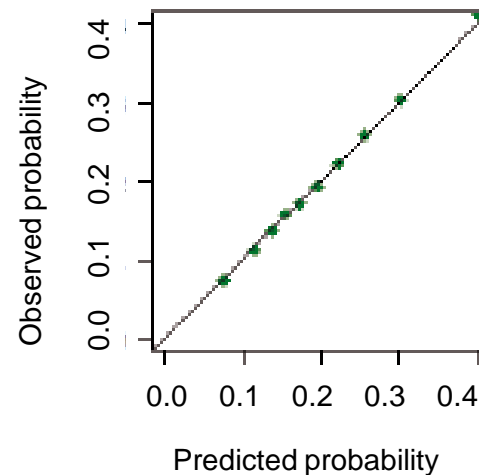
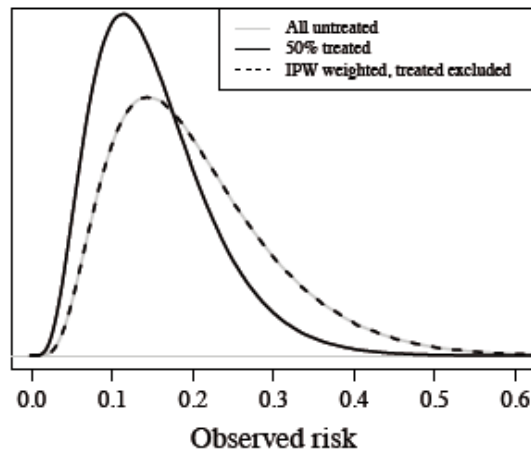
b) Non-random treatment



Exclude treated individuals

- Good calibration,
- Possible selection bias

d) Non-random treatment



Exclude and reweight with IPTW

- Good calibration,
- Corrects for selection

See Pajouheshnia et al
BMC Med Res Meth
2017