Theory & Methods Challenge Fortnight:
Estimands and Feedback Loops

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Matthew Sperrin, Romin Pajouheshnia

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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.

- Paraphrased from: https://www.fharrell.com/post/ehrs-rcts/

Clarity over estimands: what does our prediction mean?

- $E[Y|X,T] \neq E[Y(T=t)|X]$

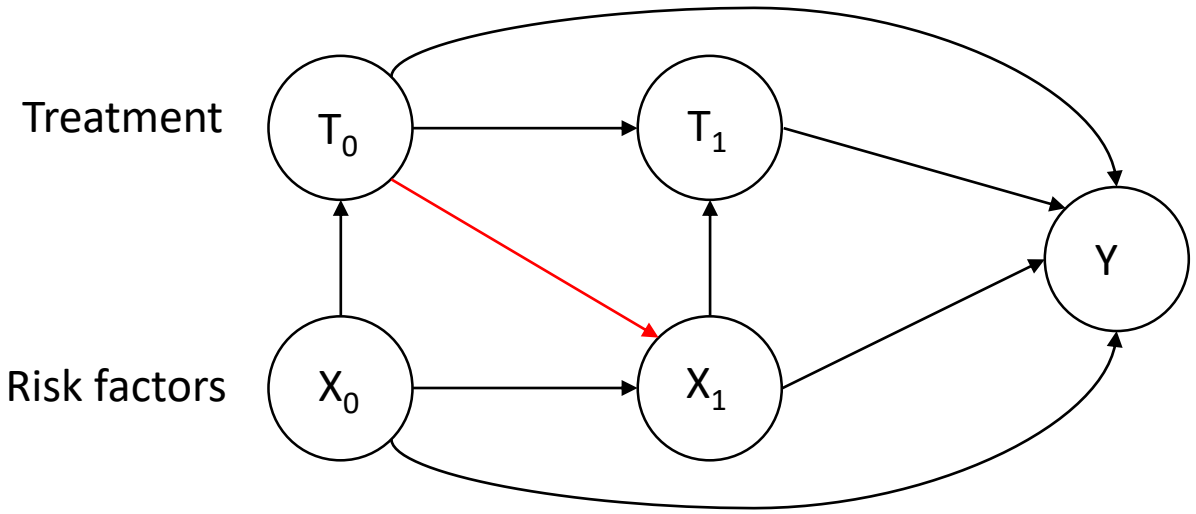
- Treatment drop-in:
  - E[Y given we don't treat now]
  - E[Y given we don't treat now, or ever]?
  - E[Y given we don't treat now, or in next X years]?

- 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.



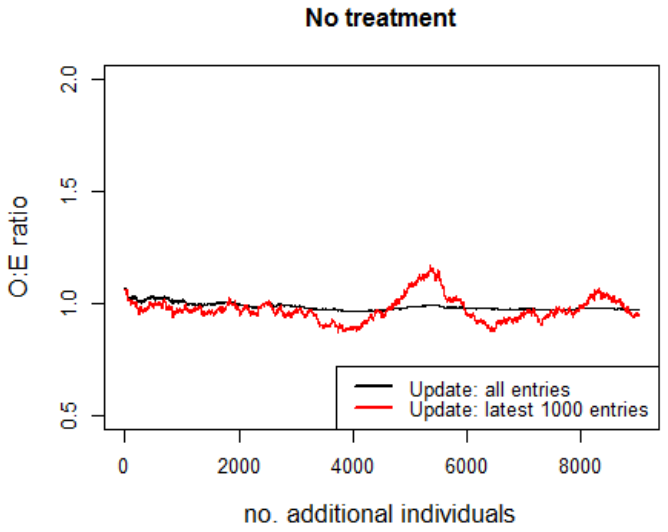
- Failure to adjust for this leads to underestimate of risk
  - Additional 3.6% of population would be considered for statins (for CVD primary prevention) after correcting for this when predicting CVD risk with a 10% treatment threshold.

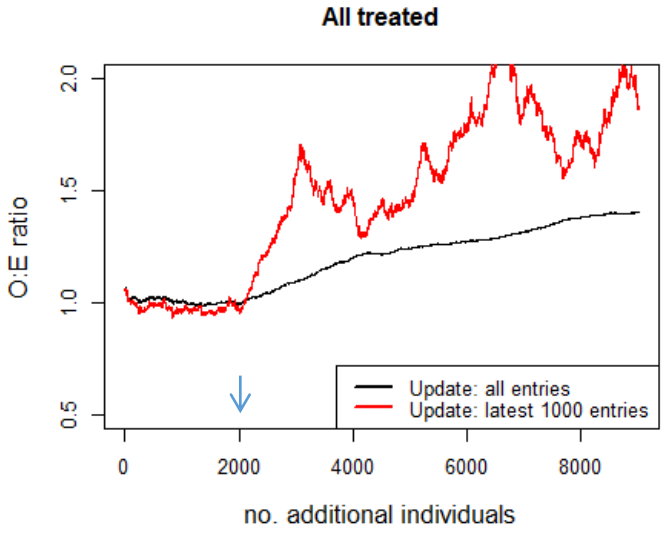
As soon as a risk model is deployed, behaviour changes.

Hari Seldon, Isaac Asimov's *Foundation*

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

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.

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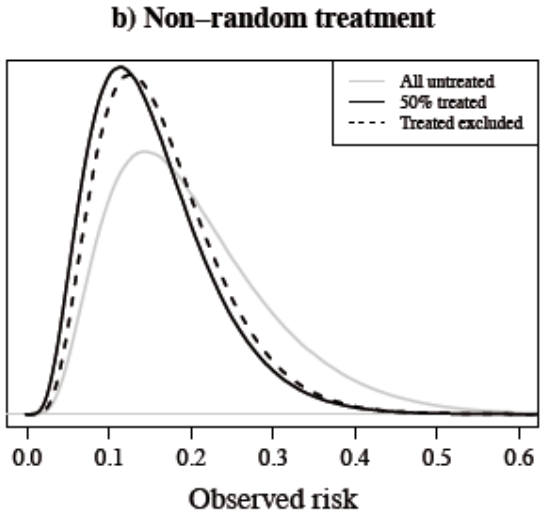
@MatthewSperrin
@pajouheshnia

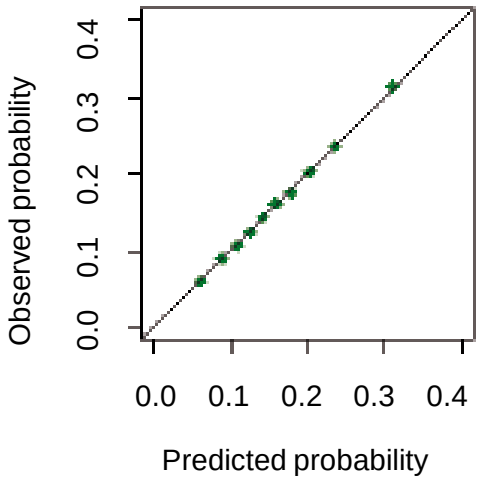
Development population may not reflect target for decision making.

Use:

Development:

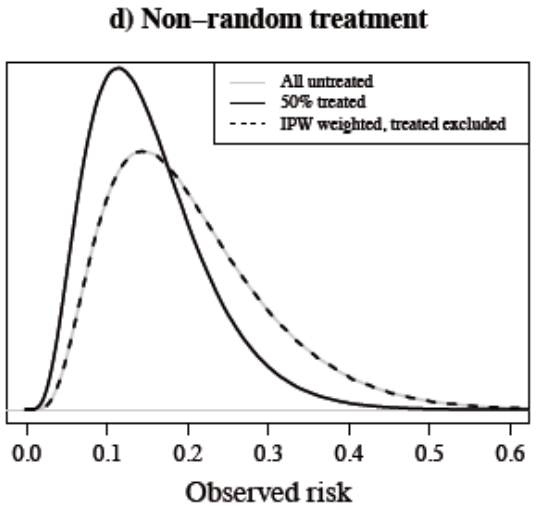
Standard validation/testing methodology do not estimate accuracy of predictions of $E[Y(T = t)|X]$ in treated patients.

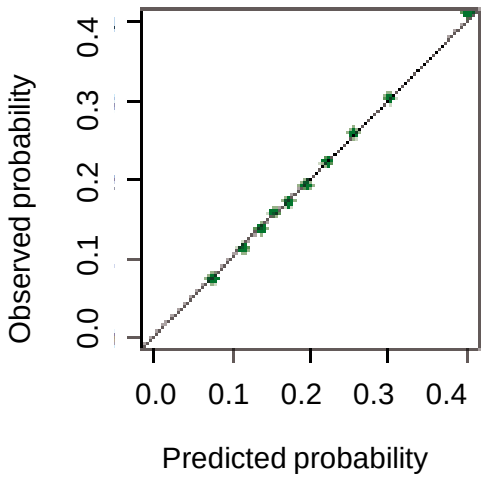




Exclude treated individuals

→ Good calibration,
→ Possible selection bias





Exclude and reweight with IPTW

→ Good calibration,
→ Corrects for selection

See Pajouheshnia et al BMC Med Res Meth 2017