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The role of causal inference in predictive modelling

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Clinical prediction models and what they are for.

Predictors
$X_1, X_2, \ldots, X_p$

Outcome
Y

E.g., age, sex, diagnosis, medical history, lifestyle, test results

statistical or machine learning model

continuous

binary

time to event

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Clinical prediction models and what they are for.

Predictors
$X_1, X_2, \ldots, X_p$ →  → Outcome
Y

- **Making decisions about interventions**
- Audit
- Counselling
- Patient selection for, e.g., RCTs

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Risk approach to intervening

- Example: Default approach to primary prevention of CVD: risk based
  - “consider anyone with QRISK > 10% for statins”
  - Based (informally) on the idea that those at higher risk have higher benefit

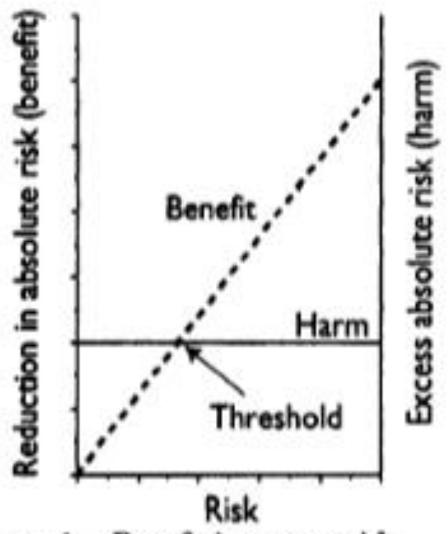

FIG 1—*Benefit increases with risk, but harm is constant. Net benefit occurs only when risk is above threshold*

Glasziou, Paul P., and Les M. Irwig. "An evidence based approach to individualising treatment." *Bmj* 311.7016 (1995): 1356-1359.

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Instead we would like to ask “What if I…” questions – causal inference.

50yr old male, white, heavy smoker, overweight, type 2 diabetes, elevated blood pressure

- Suppose Joe has a CVD risk of 17%.
- Joe might ask: “What if…
  - I stopped smoking?”
  - I lost some weight?”
  - I reduced my blood pressure?”
  - *I did nothing?*

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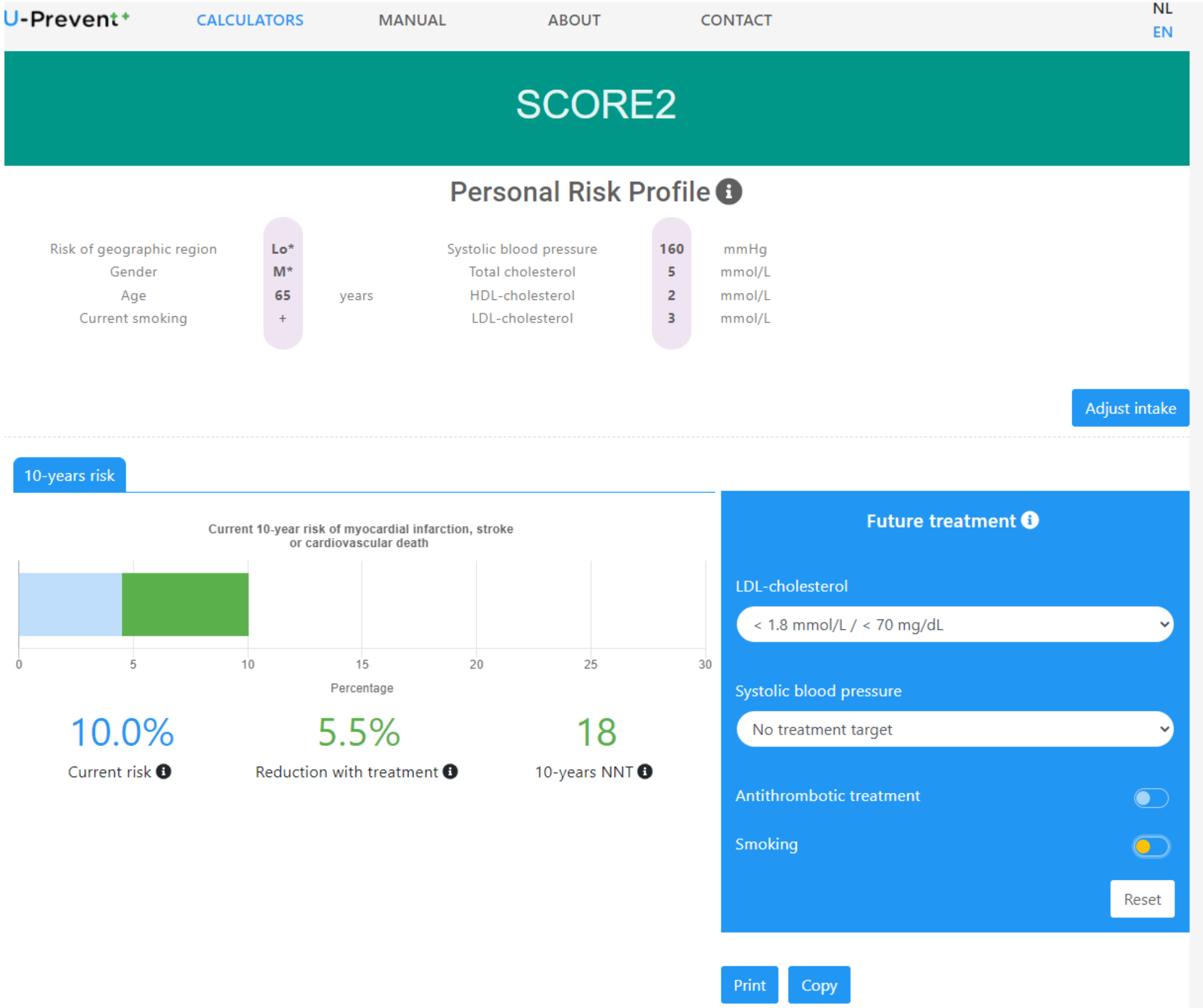
Benefit approach to intervening

- Calculate (individualised) benefit of an intervention(s) and make decisions based on that.
- Two basic approaches:
  - Plug-in / conditional - can be very bad.
  - Absolute risk x relative risk – better.



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Alternative approach: target estimands and use causal inference

- Causal inference for observational data gives us a clear framework for addressing this problem.

- We are always explicit about what any absolute risk we are calculating refers to, for example:

- ‘CVD risk if we do nothing for this patient’

- ‘CVD risk if this patient takes statins’

- ‘CVD risk if this patient takes statins and loses weight’

- ‘CVD risk if this patient doesn’t take statins now, but commences them if their risk goes above 10% in future’.

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van Geloven, N., Swanson, S. A., Ramspek, C. L., Luijken, K., van Diepen, M., Morris, T. P., ... & le Cessie, S. (2020). Prediction meets causal inference: the role of treatment in clinical prediction models. *European journal of epidemiology*, *35*(7), 619-630.

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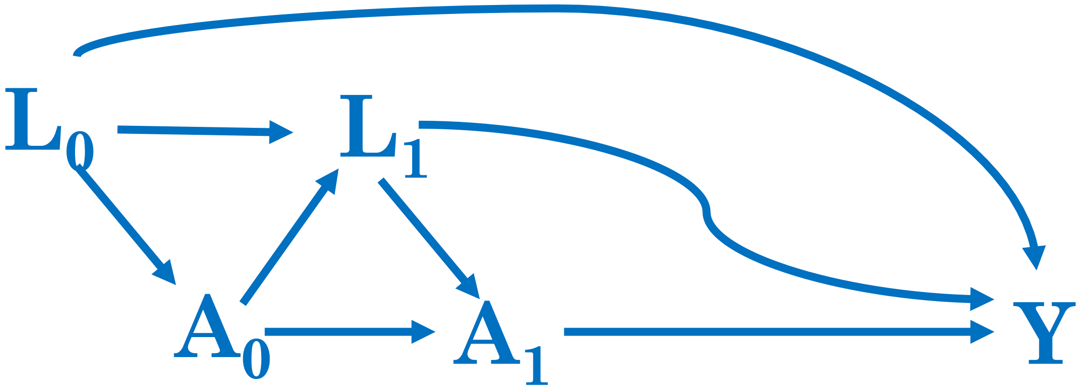
‘Treatment drop-in’ – why ‘doing nothing’ risk isn’t trivial.

- Suppose we’re interested in the ‘do nothing’ risk.
- Fit a time-to-event model
- How do we handle treatment naïve at baseline, who start taking treatment during follow-up?



Sperrin, M., Martin, G. P., Pate, A., Van Staa, T., Peek, N., & Buchan, I. (2018). Using marginal structural models to adjust for treatment drop-in when developing clinical prediction models. *Statistics in medicine*, *37*(28), 4142-4154.

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Other potential benefits of causal modelling in prediction

- Ensuring fairness of decisions based on prediction models
  - Through criteria such as counterfactual fairness.

- Improving generalisability of prediction models
  - Causal pathways more likely to be preserved than associations
    - Or explicitly rule out 'unstable' edges.
  - Apply counterfactuals to match different contexts

- Handling 'performative prediction'
  - Implementing a model changes things – feedback loops.

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