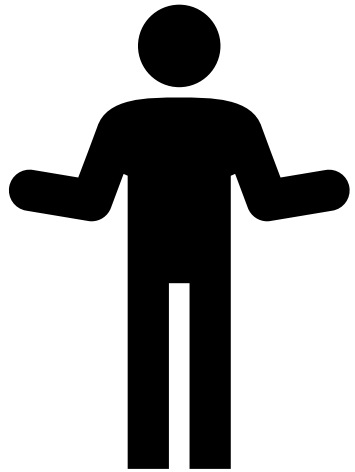
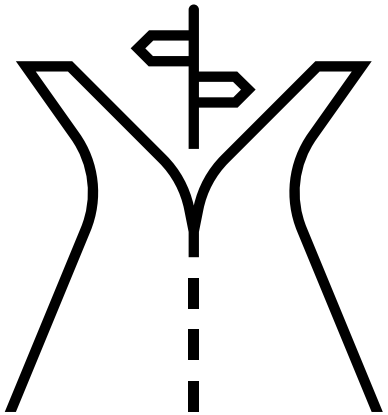
Causal prediction for medical decision making: Methods and practice



Introduction to causal prediction

Ruth Keogh

[Day 1, afternoon]



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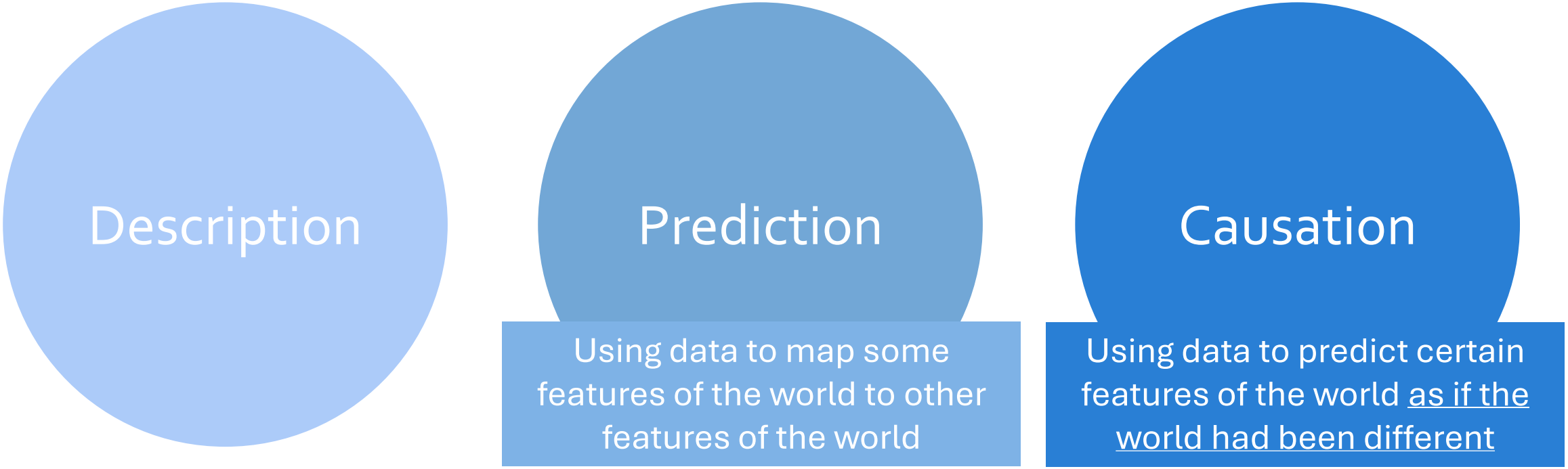

Clinical prediction models

Collins G S, Moons K G M, Dhiman P, Riley R D, Beam A L, Van Calster B et al. **TRIPOD+AI statement: updated guidance for reporting clinical prediction models that use regression or machine learning methods** BMJ 2024; 385 :e078378 doi:10.1136/bmj-2023-078378

- “Prediction models are used across different healthcare settings. They are used to estimate an outcome value or risk. Most models estimate the probability of the presence of a particular health condition (diagnostic) or whether a particular outcome will occur in the future (prognostic).

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- “Prediction models are used across different healthcare settings. They are used to estimate an outcome value or risk. Most models estimate the probability of the presence of a particular health condition (diagnostic) or whether a particular outcome will occur in the future (prognostic).

- Their primary use is to support clinical decision making, such as whether to refer patients for further testing, monitor disease deterioration or treatment effects, or initiate treatment or lifestyle changes.”

Use of prediction models for decision making

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What would my risk of the outcome be
… if I get referred for more tests?
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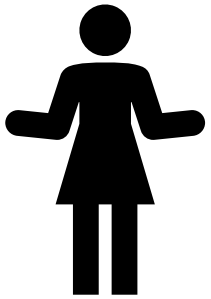

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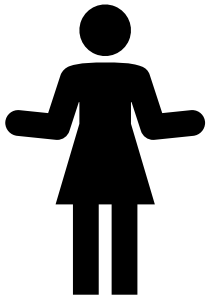

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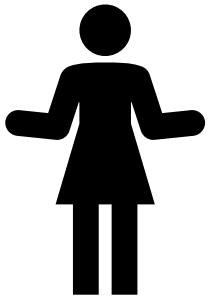

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What would my risk of the outcome be
… if I start exercising 3 times a week?
…if I continue my current activity levels?

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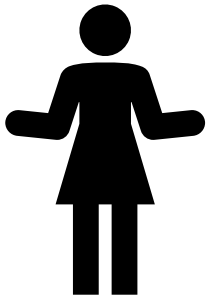

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These are causal questions, so causal thinking and techniques are needed...but prediction models are not usually developed using causal considerations

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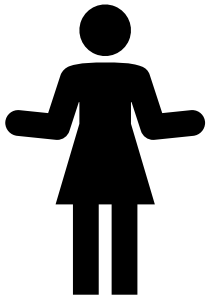

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What do we call this?

- Causal prediction
- Counterfactual prediction
- Prediction under interventions

Using standard prediction models to inform treatment decisions

Van Geloven, Keogh, van Amsterdam, et al**. The risks of risk assessment: causal blind spots when using prediction models for treatment decisions.** https://arxiv.org/abs/2402.17366

Three ways in which standard prediction models incorporate treatments:

1. Including treatment as a predictor in the model
2. Restricting to untreated individuals when developing the model
3. Ignoring treatment (even though it may be used in the population)

Standard prediction models:

1. Including treatment as a predictor in the model

Data used to develop the prediction model (training data):

- Includes treated and untreated individuals.

Prediction model:

- Includes treatment status A and additional predictors $X_1, \dots, X_p$

Prediction formula (e.g. if the prediction model was developed using a Cox model):

- $Risk(t|A,X) = 1 - S_0(t)^{\exp(\beta A + \gamma_1 X_1 + \gamma_2 X_2 + \cdots + \gamma_p X_p)}$

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Predicted risk if I take treatment?
Set $A = 1$ and using individual values for $X_1, \ldots, X_p$

Predicted risk if I <u>do not</u> take treatment?
Set $A = 0$ and using individual values for $X_1, \ldots, X_p$

Are these valid estimates of risk under the two treatment strategies?

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Conditions under which these risks have a causal interpretation

- If $X_1, \ldots, X_p$ includes all confounders of the association between treatment and outcome, and it does not include any mediators
- …and the model is correctly specified

Standard prediction models:

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Example: PREDICT study

- Used routinely collected primary care data to develop a model for predicting 5-year risk of cardiovascular disease.
- Model includes BP-lowering medication use, and a range of other predictors.

Predictions under interventions for a particular individual who has high BP

- **Setting BP med=1:** 11% risk of cardiovascular disease in the next five years.
- **Setting BP med=0:** 8% risk of cardiovascular disease in the next five years.

- According to the model, use of blood pressure lowering medication at baseline results in a higher predicted risk of cardiovascular disease.
- But this is unlikely to have a causal interpretation.

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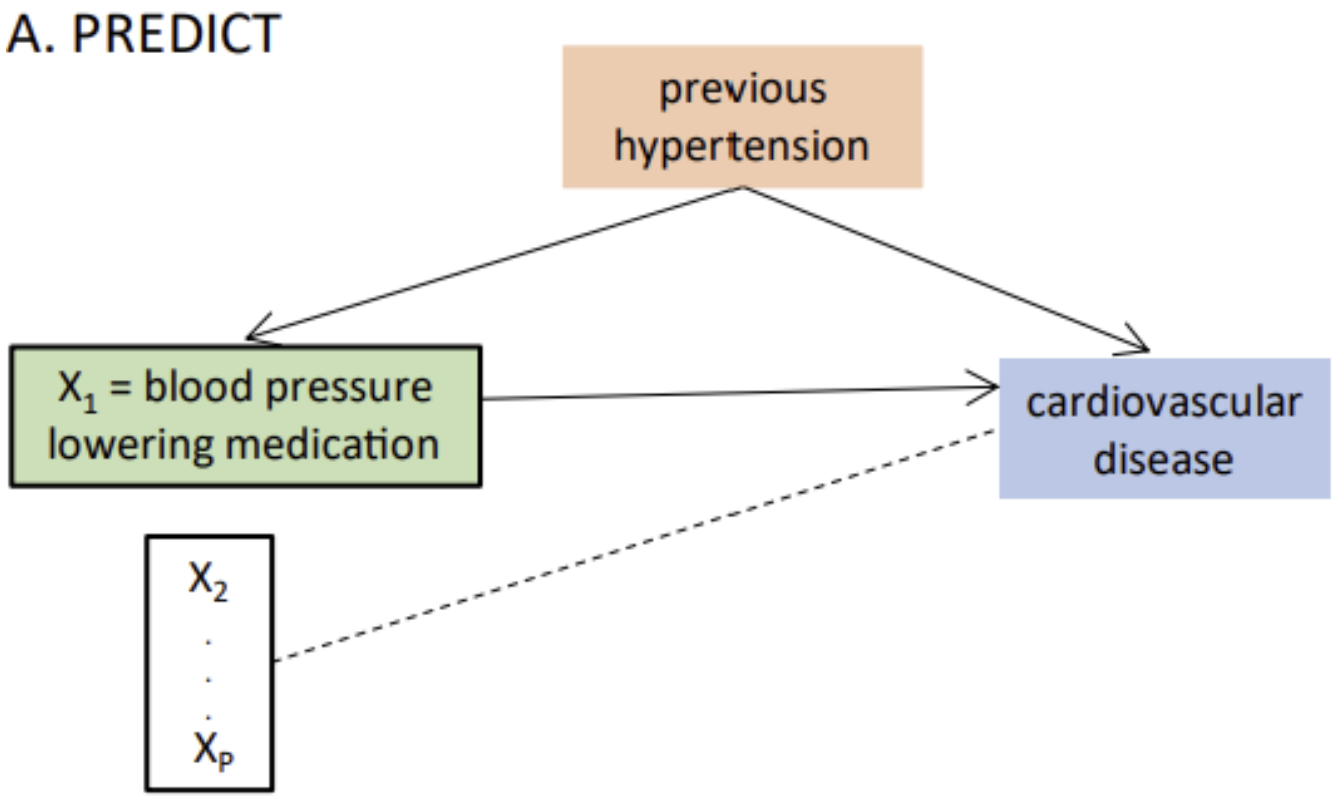

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We are still conditioning on treatment so similar issues arise as in the previous scenario

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Example: Cardiac surgery

- The EuroSCORE model predicts mortality after cardiac surgery
- The model was developed only using individuals who actually received surgery
- It has been suggested to use this to inform the decision about whether to proceed with the surgery

Example: Organ transplantation

- In organ transplantation prediction models have been developed for post-transplant survival
- It has been suggested to use this to inform the decision about whether to list a person for transplant or to inform the allocation of organs

Standard prediction models:

3. Ignoring treatment (even though it may be used in the population)

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Some people in the development data may be at low risk because they received treatment under standard care – that doesn't mean we should not offer treatment to those with low risk estimates

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- The **QRISK model** is used to inform whether a person should be prescribed statins, based on 10-year risk of CVD >10%.
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- Restricted to people not taking statins at baseline.
- People who contributed to the model could start statins during follow-up.
- Interpretation of risk derived from this model is difficult.
- A patient's predicted risk of lower than 10% may be driven by similar patients in the derivation cohort taking statins shortly after baseline.

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From tomorrow: how we can develop prediction models in a way that supports clinical decision making through combing causal thinking and methods with prediction modelling techniques