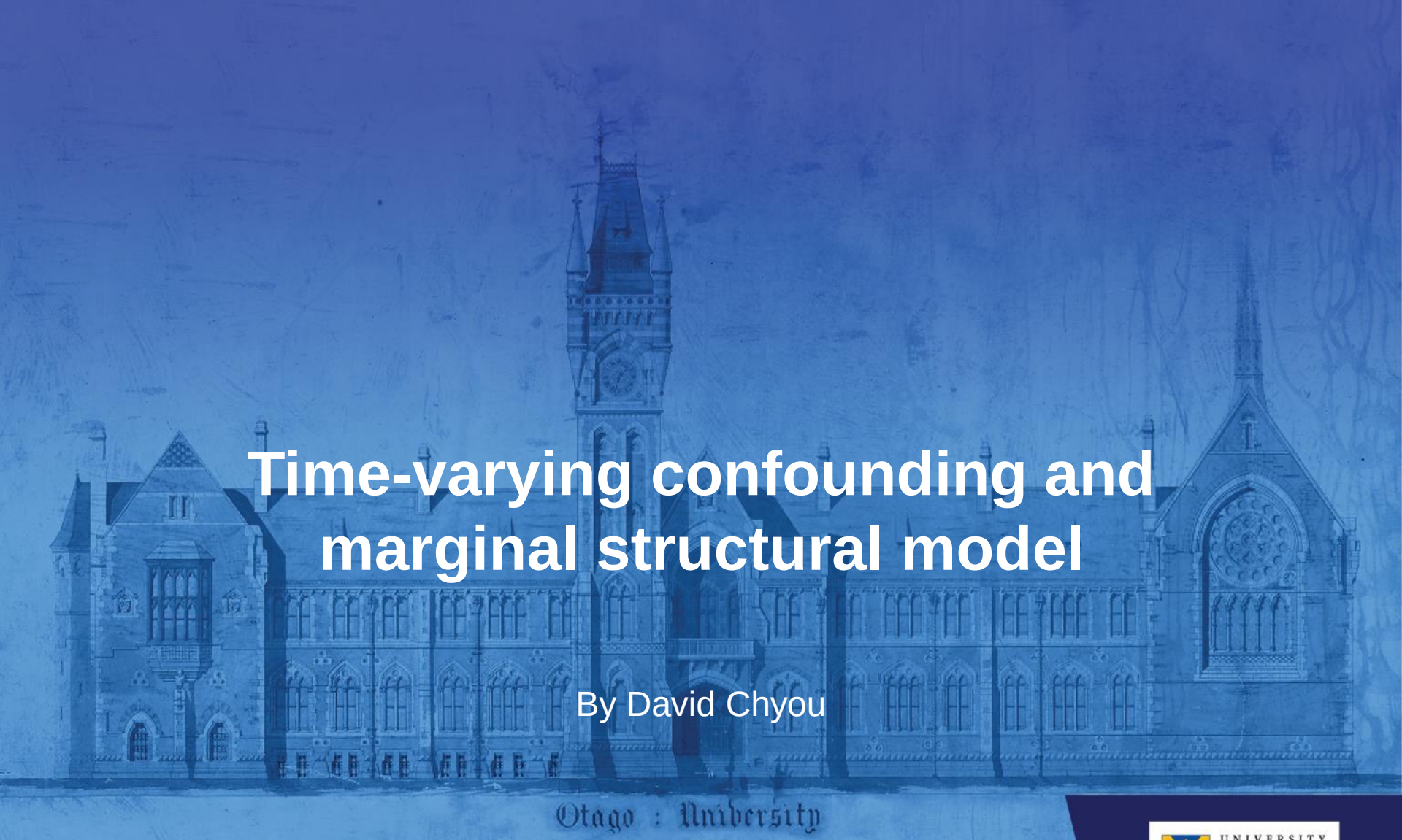
Time-varying confounding and marginal structural model

By David Chyou



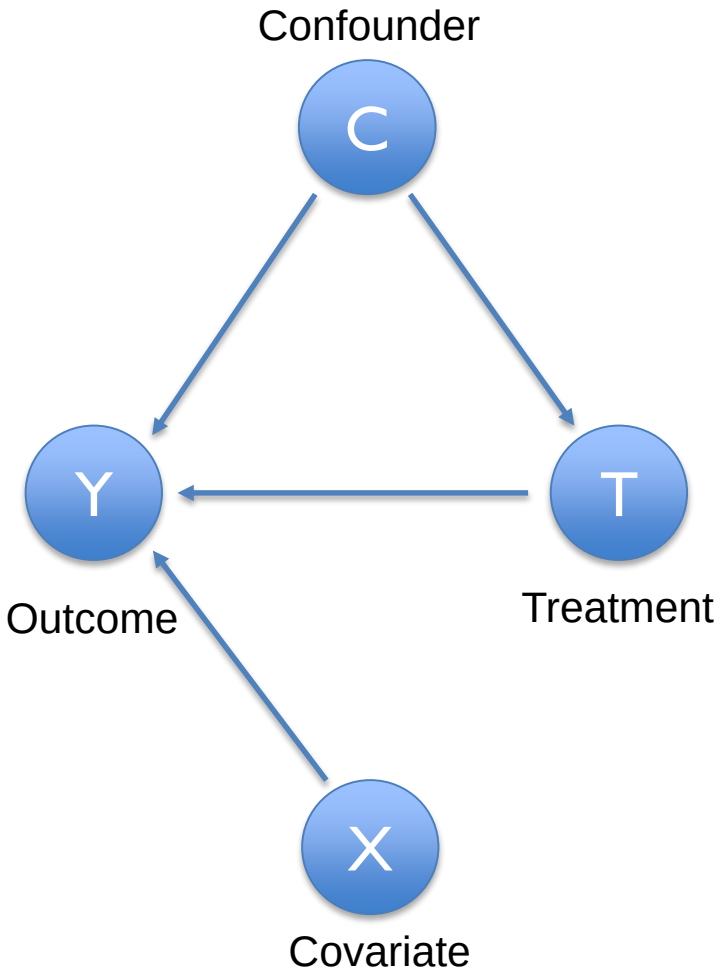
Overview

- An overview of time-varying confounding.
- Marginal structural model.
- Weighing regression by propensity score.
- Future prospective.

Confounder variables (recap)

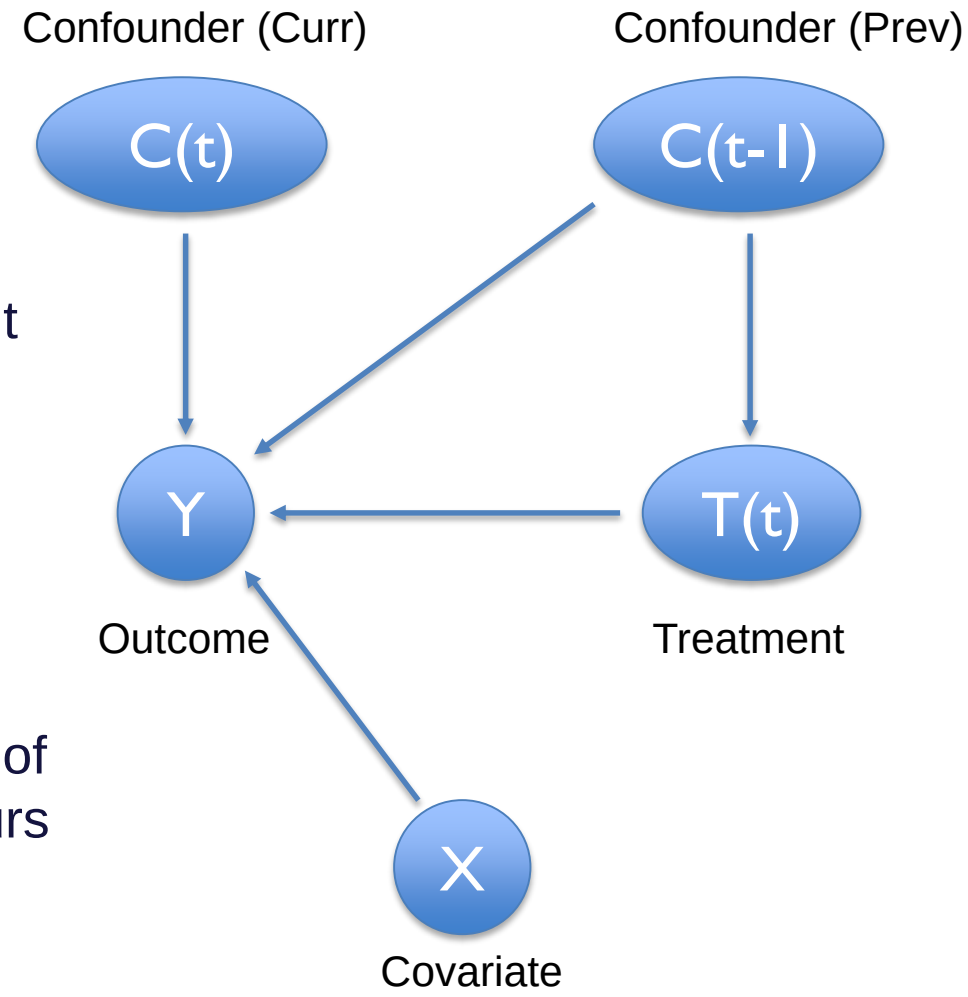
- Definition: Confounder variables are covariates that have effects on both the outcome variable and the grouping (treatment) variable.

- Example: liver cancer vs gender → alcohol consumption can be a confounder variable.



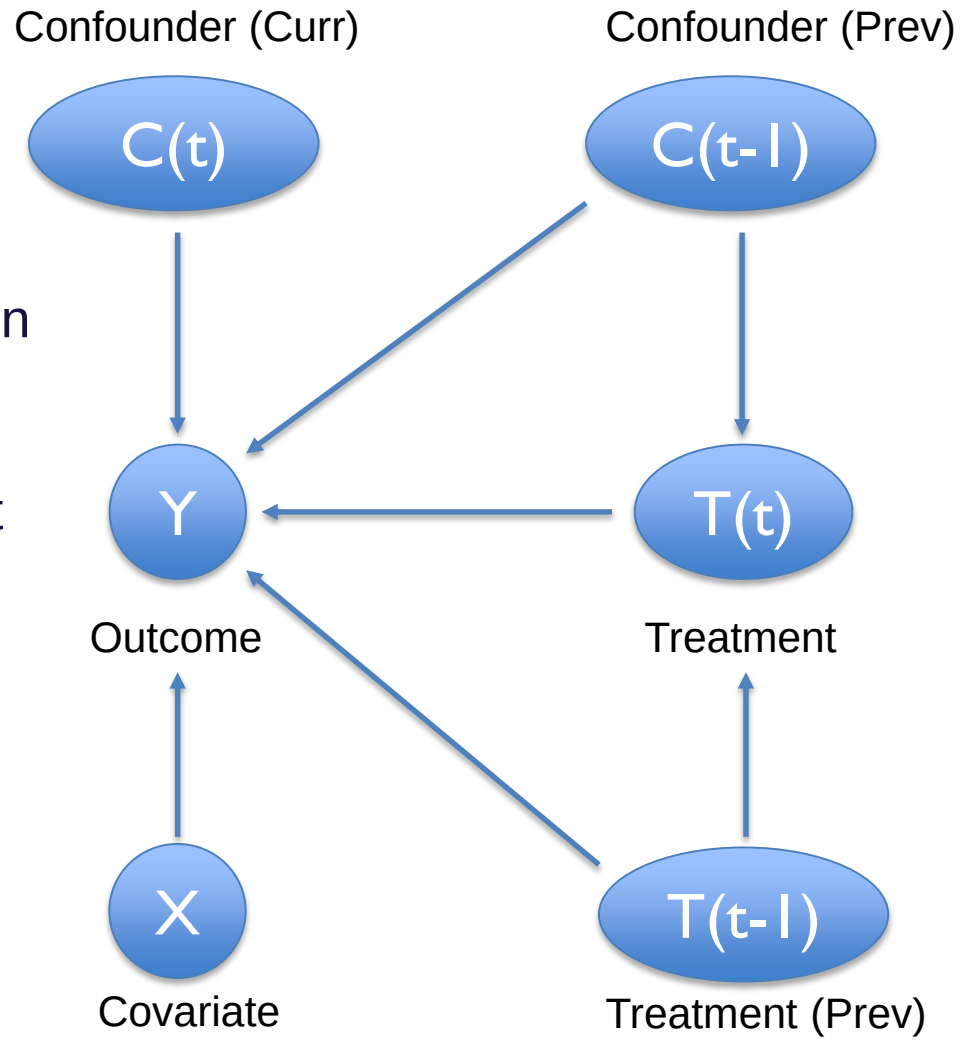
Time-varying confounding

- Treatment assignment is a decision process.
- The previous state of an individual will dictate the current treatment. The current state does not matter
- There is a decision lag.
- Example: A previous diagnosis of a cardiovascular problem favours the use of statin therapy at the present time.



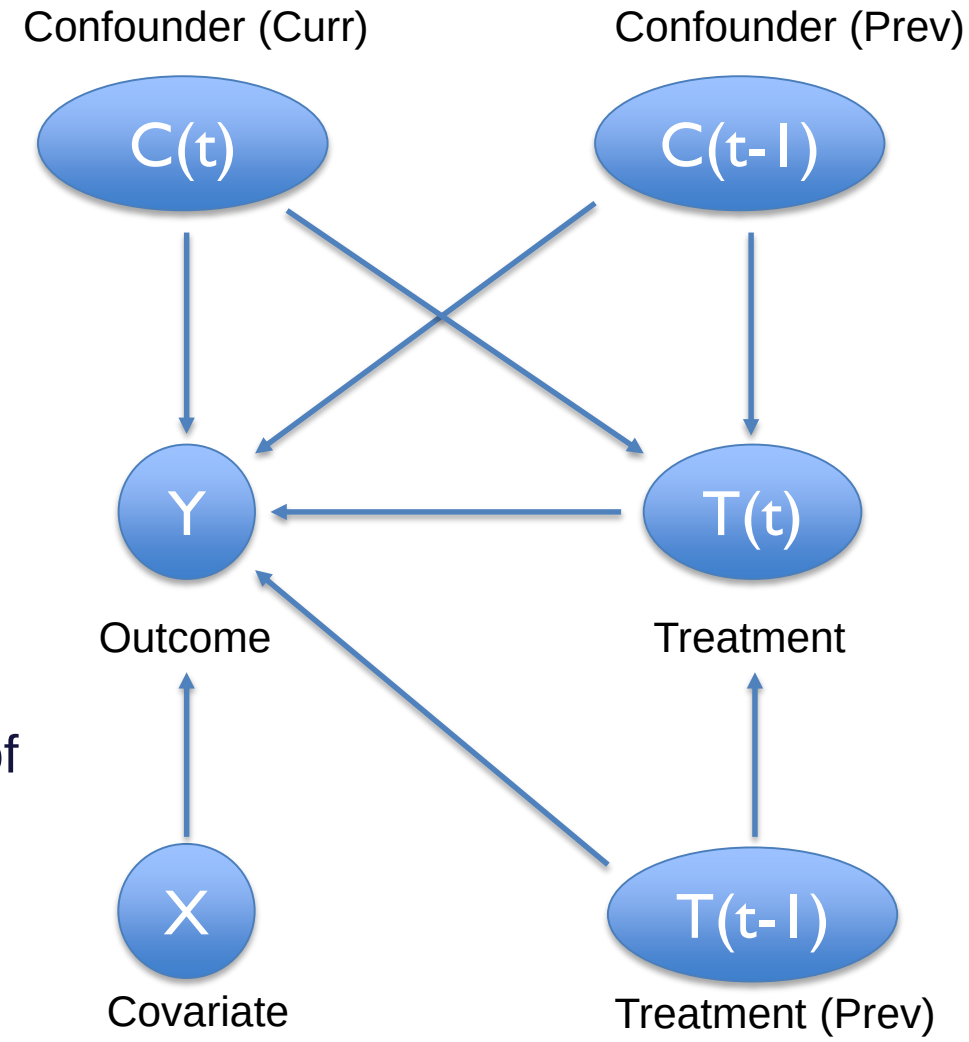
Time-varying confounding

- Also, previous treatment assignment can dictate the current treatment assignment.
- Example: An individual had been previously using antiplatelet therapy, but to avoid the risk of bleeding, the individual may not be prescribed anticoagulant at the present time.



Time-varying confounding

- Not all confounders are time varying.
- For example, gender and ethnicity
- So the current state of an individual can also dictate the current treatment.
- Overall, after taking the effect of time into account, the model of confounding is as shown in the diagram.



Summary

- Past treatments received by an individual can dictate the treatment the individual receives at the present time.

- Time-varying confounders can dictate the current, or the next treatment the individual receives.

- In this situation, the confounders dictate the entire treatment history, not just the treatment received at a specific time point.

Marginal structural model propensity scores

- The conditional probability the treatment history of an individual (H_i) up to the current time ($H_i[t \leq s]$) is observed given the observed values of all confounders (constant or time-varying) up to the time point.

- Given a set of possible treatments $\{a_1, a_2, \ldots, a_k, control\}$:

$$\Pr(H_i[t \leq s]|C_i) = \prod_{t=0}^{s} \Pr(T_{it} = a_{it}|T_{it-1}, C_{it}, C_{it-1})$$

- Conditional probability that an individual receives the treatment of interest at time t given the confounders and the previous treatment: $\Pr(T_{it} = a_{it}|T_{it-1}, C_{it}, C_{it-1})$

Marginal structural model propensity scores

- To calculate the probability that an individual receives the treatment of interest at time t given the confounders and the previous treatment, $\Pr(T_{it} = a_{it} | T_{it-1}, C_{it}, C_{it-1})$:
  - Multinomial time-series regression, stratified by ID.
  - Independent variable: lag of treatment histories (within each stratum), lag of confounders (within each stratum), and confounders.
  - Dependent variable: Treatment histories.

- To calculate the MSM PS ($PS_i = \Pr(H_i[t \leq s] | C_i)$):
  - Multiply together $\Pr(T_{it} = a_{it} | T_{it-1}, C_{it}, C_{it-1})$ for all $t \leq s$.

- R: IPW package can do the job.

After getting the propensity scores…

- In marginal structural modelling, confounding is usually handled by weighing the data by a weight proportional to the inverse of PS.
- Weighing results in a bigger “pseudo-population”, in which each case is duplicated according to the weights.
- If the PS model is the true treatment probability model, confounders will be balanced → no bias due to confounding.
- In reality, the PS model is only an approximation of the probability of treatment. Need to check for bias.

Propensity score weight for MSM

- Firstly calculate the unconditional probability that a treatment history (H_i) up to the current time ($H_i[t \leq s]$) is observed, $\Pr(H_i[t \leq s])$.
  - Given a set of possible treatments $\{a_1, a_2, \ldots, a_k, control\}$,
  - $\Pr(H_i[t \leq s]) = \prod_{i=1}^{s} \Pr(T_{it} = a_{it} | T_{it-1})$.
  - Use multinomial time-series regression to calculate each $\Pr(T_{it} = a_{it} | T_{it-1})$.

- The propensity score weight:

$$w_i = \frac{\Pr(H_i[t \leq s])}{PS}$$

- In R: IPW package.

Checking confounder balance after weighing

- Recap:
  - If the PS model is the true treatment probability model, confounders will be balanced after weighing → no bias due to confounding.
  - In reality, the PS model is only an approximation of the probability of treatment.

- Need to quantify the bias by calculating the weighed population standardized bias (PSB) for each covariate over each treatment group (a_i).

$$PSB = \frac{E[X_{weighed}|T = a_i] - E_{pop}[X_{unweighed}]}{\sigma_{pop}[X_{unweighed}]}$$

- PSB less than 0.2 means good confounder balancing.

Regress analysis on weighed data

- Recall that weighing results in a bigger “pseudo-data”, in which each case is duplicated according to the weights.
- We can treat weighed data as ordinary data and do regression analysis on them (linear, non-linear, GLM, Cox PH, etc.).
- If all confounders are balanced after weighing, we can just do a univariate regression between outcome and treatment.
- Otherwise, imbalanced confounders are usually handled by treating them as covariates.
- Statistical parameters are interpreted in the same way as in ordinary regression analysis.

Summary

- We need to consider the time-varying nature of the confounders.
- Previous treatments can confound the relationship between the outcome and the treatment.
- Marginal structuring modelling can control for this type of confounding.
  1. MSM propensity score calculation.
  2. Weigh the data using MSM PS.
  3. Compute population standardized bias to assess covariate balancing after weighing.
  4. Formulate the regression model. Include any imbalanced covariates in the model.
  5. Do the regression on the weighed data, and interpret the result.

Thanks for listening