Causal Inference in Life Course Research

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What do I mean by life course research?

- Understanding how exposures throughout the life-course impact late-life health outcomes

- Thinking about how exposures impact outcomes in terms of:
  - Disease initiation (biological)
  - Disease progression (biological)
  - Change impact of biological disease on outcomes (resiliency/reserve)

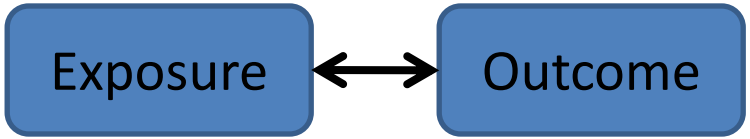
What do I mean by causal inference?

Does A cause B?

If I change A, would it change B?

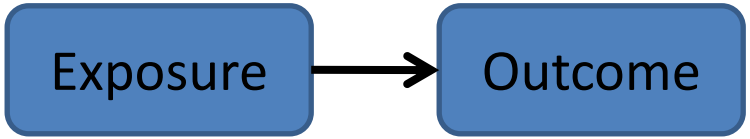
What do I mean by causal inference?

Estimate an association we think reflects a causal effect.



Association

- Present due to a causal effect, bias, chance, and/or reverse causation
- Estimated in studies



Causation

- Present due to a causal effect
- Inferred from study results

Causal inference in aging research poses methodological challenges

- What is our causal question?
- What/when is our exposure relevant?
- How do we remove non-causal explanations in this setting?
  - Confounding
  - Selection bias
  - Measurement error
  - Reverse causation

These are not unique challenges, but they are perhaps more important to consider in this setting than others…

What is our causal question?

- At its core, requires clearly identifying:
  - The exposure of interest
    - What exposure?
    - When during life course?
  - The outcome of interest
  - The population of interest

Does your question sound like it could be a randomized trial…?

What is our causal question?

Does hypertension cause dementia?

If I change blood pressure, would it change dementia risk?

- Does having an average SBP of 140 mmHg versus 120 mmHg from age 40 to age 50 increase risk of dementia at ages 70 to 90 in Americans?
- Are those who keep their SBP under 160 mmHg for the prior 20 years less likely to develop dementia this year than those whose SBP went over 160 mmHg in the prior 20 years?

What/when is our exposure relevant?

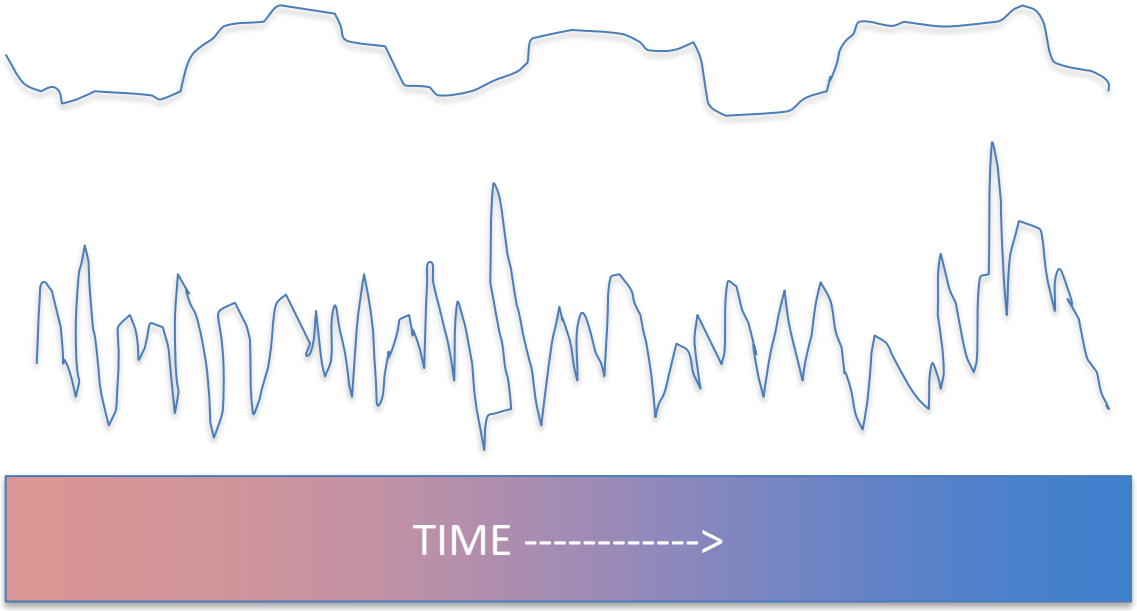
Are there critical windows of exposure?

Is it just that the time x years before onset is the relevant window?

Is cumulative exposure most relevant?

Or single acute events?

What/when is our exposure relevant?



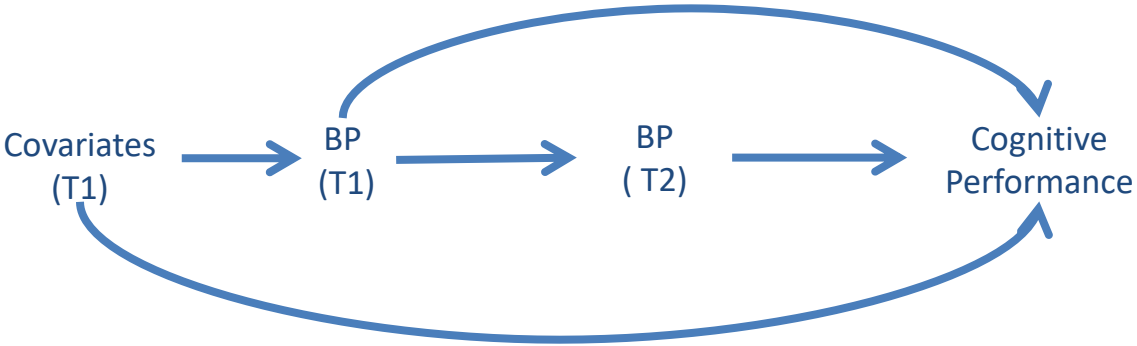
How do you summarize the relevant exposure?

- Area under the curve
- Number of “peaks”
- Number of “troughs”
- Time above a cut-off?
- Value at a single time
- Average value across time
- Etc….

How do we minimize likelihood of non-causal explanations?

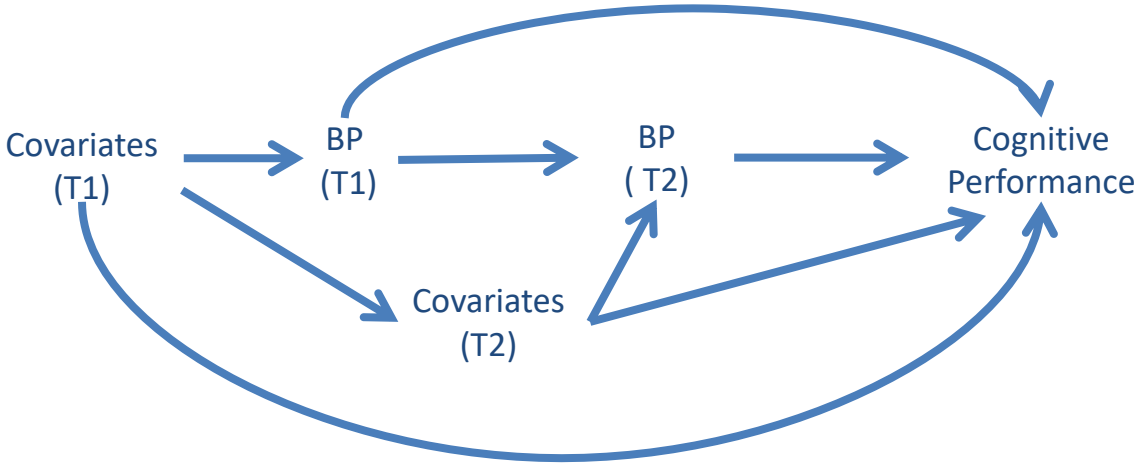
- Confounding
- Selection bias
- Measurement error
- Reverse causation

How do you adjust for confounding with a time-varying exposure?



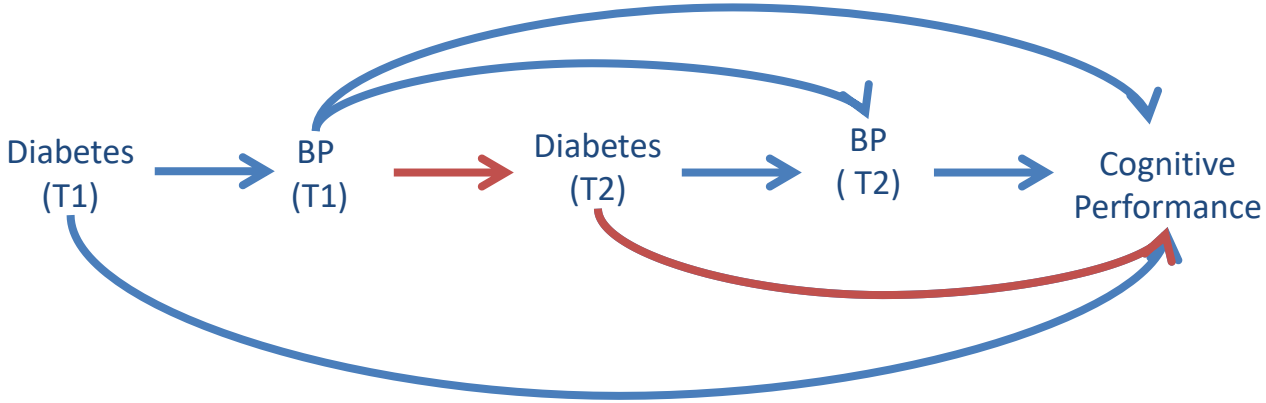
Past exposure can be a confounder of future exposure

How do you adjust for confounding with a time-varying exposure?



May need to adjust for confounders at multiple time points

How do you adjust for confounding with a time-varying exposure?



May need special methods to deal with "time-varying confounding", where a confounder is both a mediator and and a confounder – e.g. marginal structural models

How do we minimize likelihood of non-causal explanations?

- Selection bias
- Measurement error
- Reverse causation

Causal inference is possible!

But it isn't easy…

Thank you!

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