

The Metabolic Consequences Of Adverse Early Life Conditions And Subsequent Risk For Adult Type 2 Diabetes

Luke W. Johnston
 Department of Public Health, Aarhus University and Steno Diabetes Center Aarhus

- Background: Early life adversity is known to influence the risk for type 2 diabetes (T2D), but how metabolic processes mediate this link is unknown. Two recent advances eliminate some historical barriers in this area (i.e. difficulty in collecting and analyzing the data). First, can link cohort studies (with metabolic data) to national register databases (with demographic and medical data). Second, emergence of mediation analysis and causal structure learning techniques to help identify pathways between early life adversity, adult metabolism, and T2D risk.

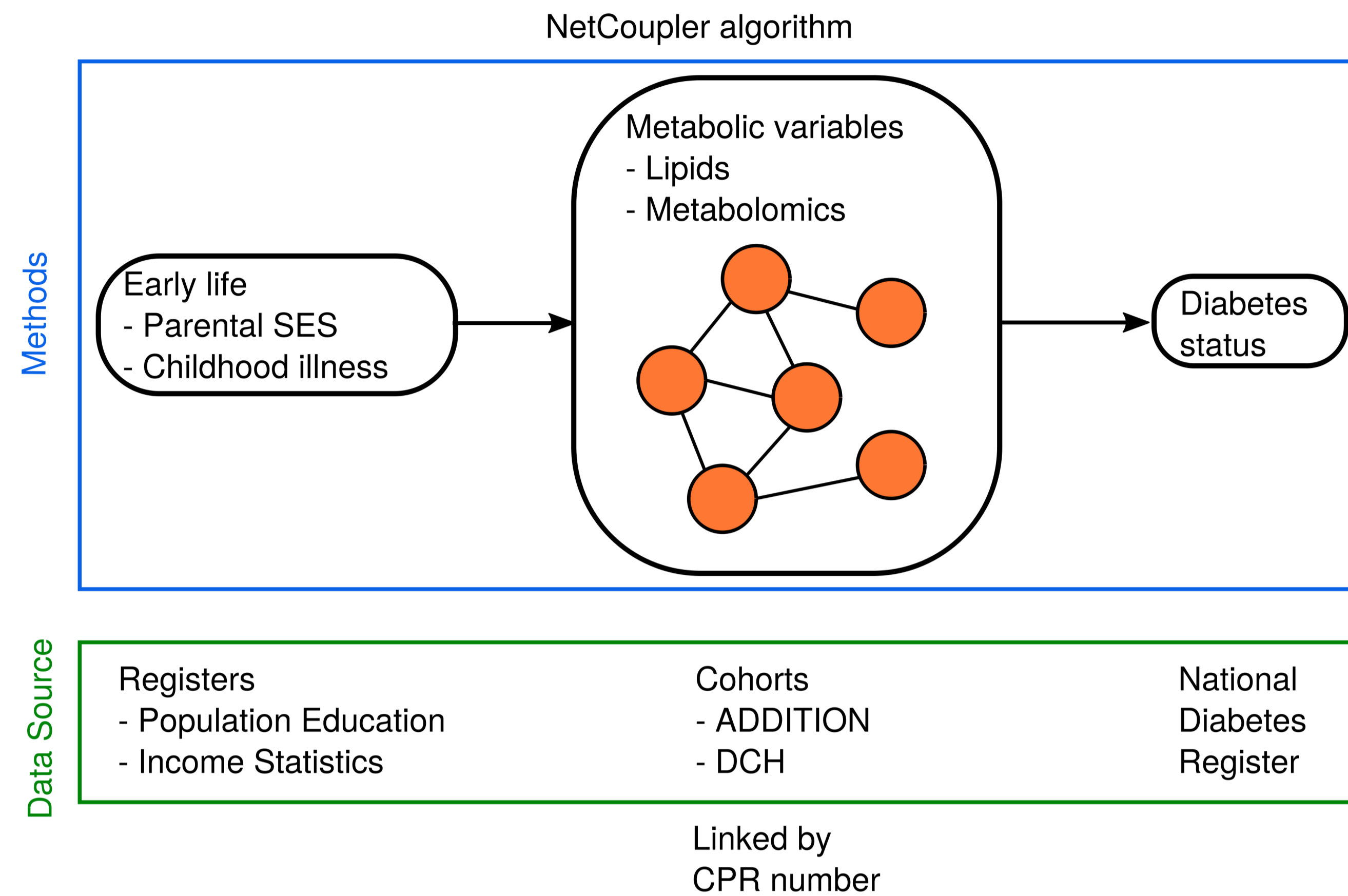
- Aims: Overarching aim is to better quantify and understand the impact that early life conditions have on adult metabolic capacity and the risk for incident T2D in adulthood. There are three primary objectives:

1. Investigate how specific early life conditions affect risk of T2D at national level.
2. Identify mediating pathways of adult metabolic capacity between early life adversity and T2D. Requires objective 3.
3. Extend and generalise NetCoupler algorithm (developed github.com/NetCoupler). It estimates direct and mediating pathways in high dimensional metabolic data.

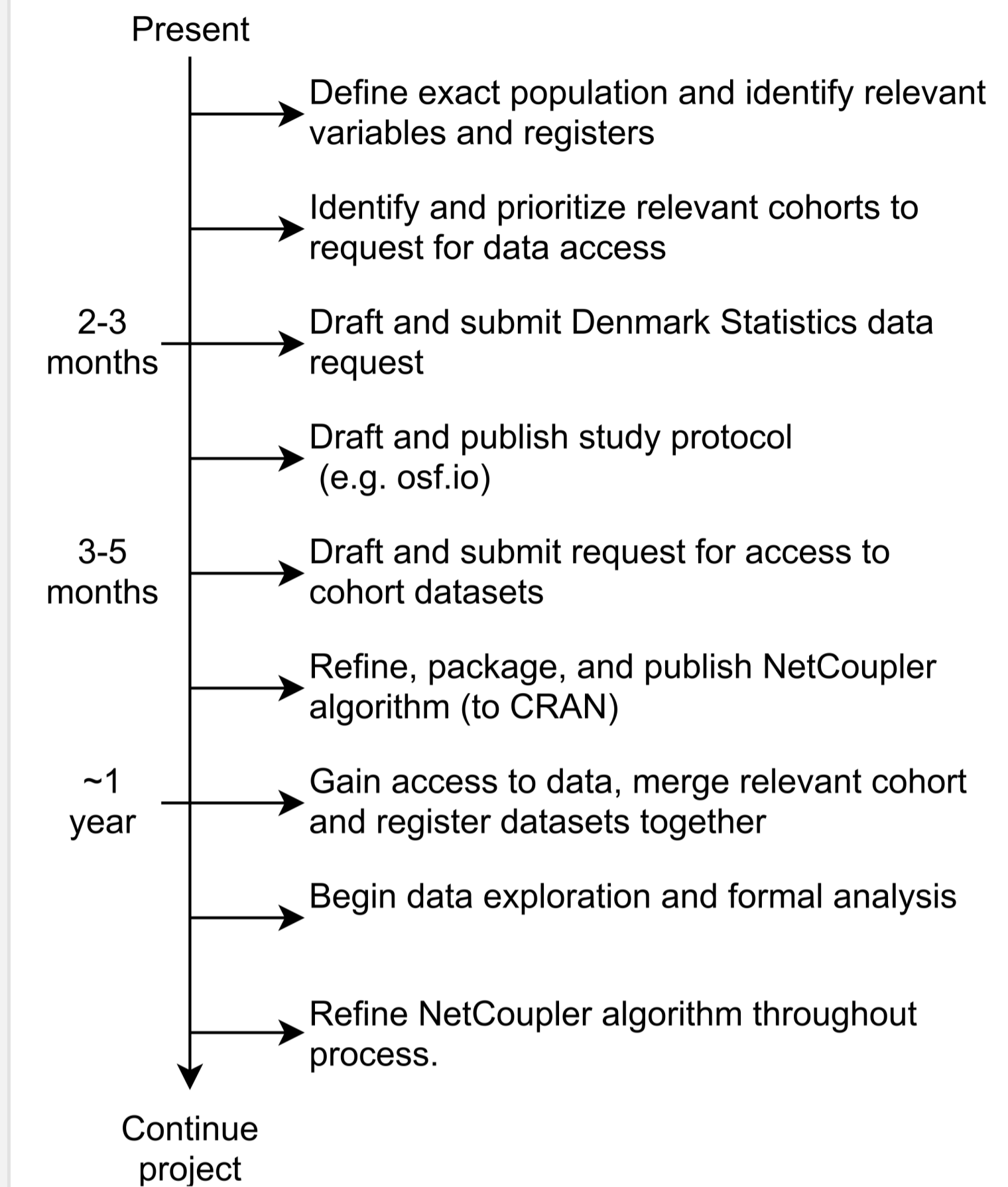
- Data sources: Danish register databases and Danish cohorts.

- Methods: Develop and apply a “causal structure learning” algorithm to identify potential pathways between early life conditions, metabolic variables, and diagnosis of T2D.

Overview of analysis process

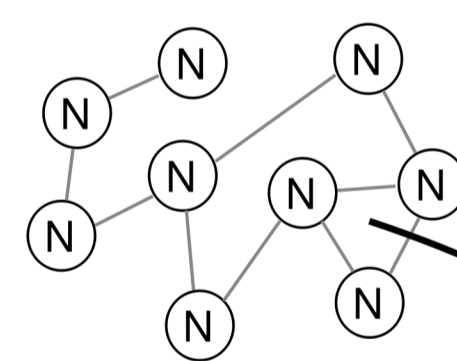


General timeline



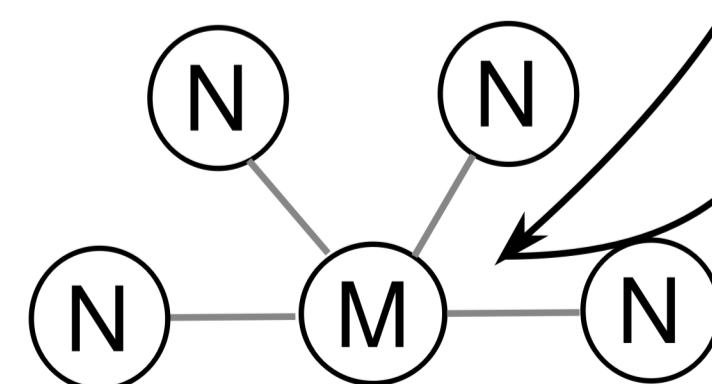
NetCoupler algorithm (github.com/NetCoupler)

1) Estimate causal graph



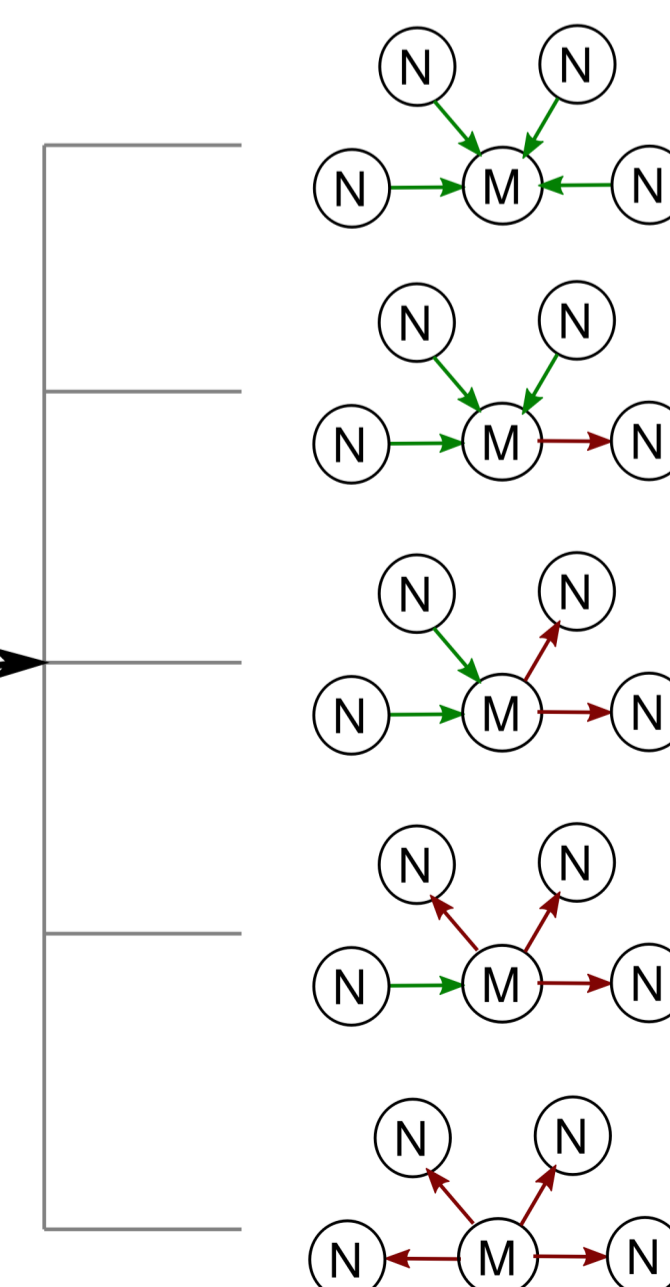
2) Select adjacency set.

Markov parents are a subset of direct neighbors.

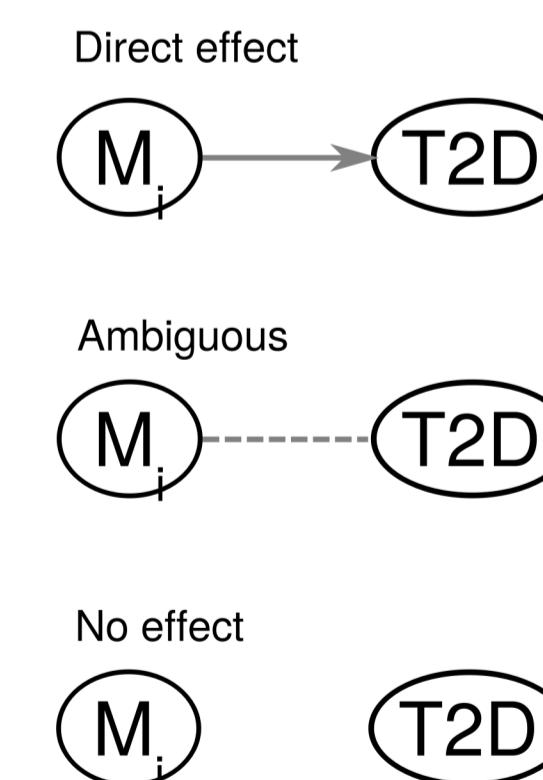


3) Calculate all possible causal effect estimates.

n neighbors = 2^n models



4) Classification of direct effects for each model.



5) Adjust for all direct effects and repeat until no more classification.

Contact:

Luke W. Johnston, MSc, PhD
 Email: lwjohnst@ph.au.dk
 ID 0000-0003-4169-2616



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