

confounder that affects the mediator and outcome that is itself affected by exposure.

Objectives: To extend causal mediation methods to the sibling study context, using the example of prenatal antidepressant exposure on childhood neurodevelopment, considering gestational age as a mediator.

Methods: Data were generated for A (dichotomous exposure to antidepressants), M (dichotomous mediator, low birth weight), Y (dichotomous neurodevelopmental outcome), and C (covariates), for correlated sibling pairs. An additional covariate, L, which affects M and Y, was also investigated. In this simulation set up, all associations between factors were positive. We fit regression models to estimate the controlled direct effect (CDE) and natural indirect effect (NIE), and included an intercept for each sibling cluster to account for shared sibling factors. We carried out a Monte Carlo simulation study and calculated bias for estimates of the CDE and NIE, for naïve models and models adjusting for family effects, and for scenarios where assumptions 2 and 4 were violated.

Results: Estimates of the total effect were comparable for the naïve and sibling analyses when all assumptions were met, and sibling estimates of the total effect outperformed naïve estimate when unmeasured confounding assumptions were violated. Sibling models also outperformed naïve estimates on measures of the controlled direct effect when assumptions 2 and 4 were violated, although estimates of the natural indirect effect were equally biased for sibling and naïve models.

Conclusions: Conducting mediation analyses in sibling studies may provide some protection against bias due to unmeasured confounding of the outcome-mediator association.

143. The Risk of Acute Myocardial Infarction Associated with Non-Steroidal Anti-Inflammatory Drugs Users: Impact of Additional Confounding Control for Variables Collected from Self-Reported Data

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Background: Several observational studies have employed electronic health databases to study the association between non-steroidal anti-inflammatory drugs (NSAIDs) and myocardial infarction. Because some important potential confounders might not be routinely collected in such data sources, patients' reports could be utilized additionally.

Objectives: This study evaluated the impact of using additional information from patients' reports when assessing the association between use of NSAIDs and the risk of acute myocardial infarction (AMI).

Methods: A case-control study was conducted among adult patients with hypertension and/or hypercholesterolemia in the Utrecht Cardiovascular Pharmacogenetics study. Information was collected from the Dutch PHARMO Database Network (Pharmacy and hospitalization records) and patients' questionnaires (body mass index, alcohol use, smoking, physical activity, and familial history of cardiovascular diseases). For each case, up to 13 controls were matched based on age and gender at the date cases were hospitalized (index date). Conditional logistic regression analysis was applied to estimate odd ratios (ORs) and 95% confidence intervals (95% CI).

Results: We identified 970 AMI cases and 2,974 controls during 1985–2005. Of all cases, 140 patients (14.4%) were exposed to conventional NSAIDs and 9 patients (1.0%) were exposed to selective COX-2 inhibitors at the index date. Compared to nonuse, neither conventional NSAIDs [(Adj. OR 0.98, 95% CI: 0.91–1.06) nor selective COX-2 inhibitors (Adj. OR 1.00, 95% CI: 0.74–1.36) were associated with an increased risk of AMI after adjustment for confounders routinely collected in pharmacy records. Additional adjustment for confounders collected from patients' reports did not change the risk estimates [(Adj. OR 0.97, 95% CI: 0.90–1.05) and (Adj. OR 1.01, 95% CI: 0.75–1.35)], respectively.

Conclusions: This study showed that additional potential confounders collected from patients' reports did not significantly change the risk estimates.

144. Bias Due to Selective Inclusion of Variables, Not Related to the Exposure nor to the Outcome, into a Propensity Score Model – A Simulation Study