increased variance and MSE, as expected. In the presence of residual confounding, all estimates which included Z were more biased, including the DR estimator when Z was in one or both models. If Z was a near instrument, failing to include it in at least one of the models resulted in bias (up to 10%) in all estimators. This was offset by a decrease in variance; MSE was minimized by omitting Z. If Z was an EMM, all estimates which did not include Z were biased. Including Z in any DR component model eliminated bias. MSE was minimized by including Z, despite the decrease in efficiency.

Conclusions: Including Z in one or both models had similar effects on bias and efficiency of DR and conventional estimators, for better and worse. All of these estimators require analysts to weigh potential bias amplification, weak effects of Z on the outcome, and/or EMM by Z.

58. Evaluating Different Physician's Prescribing Preference Based Instrumental Variables in the Study of Beta2-Agonist Use and the Risk of Acute Myocardial Infarction

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Background: Instrumental variable (IV) analysis with physician's prescribing preference (PPP) as an IV has been used to control for unobserved confounding in pharmacoepidemiology. PPP can be defined in several ways, but it is unclear how different PPPs perform across databases.

Objectives: To assess the validity of the IV PPP in two general practice (GP) databases in the study of inhaled long-acting beta2-agonist (LABA) use and the risk of acute myocardial infarction (AMI).

Methods: Information on adult patients with a diagnosis of asthma and/or COPD and at least one prescription of an inhaled short-acting beta2-agonist (SABA)/LABA/muscarinic antagonist (MA) was extracted from the British Clinical Practice Research Datalink (CPRD, n = 490499), and the Dutch Mondriaan (n = 27459) GP databases. Conventional Cox model and two-stage IV analysis were applied to estimate the effect of LABA vs. non-LABA (SABA/MA) on the risk of AMI. PPPs were defined by the proportion of LABA prescriptions per practice (PLP) or previous single (PPP1), or five (PPP5), or ten (PPP10) prescriptions by a physician. Quantitative methods (e.g. correlation (r), odds ratio (OR), standardized difference (SDif)) were used to assess the validity of the IVs. 95% confidence intervals (CI) for IV estimates were estimated using bootstrapping.

Results: LABA was not associated with an increased risk of AMI, adjusted hazard ratio 0.96 [95%CI 0.89-1.02] (CPRD) and 1.18 [0.97-1.43] (Mondriaan) in conventional Cox model and 0.95 [0.55-1.63], 1.24 [0.40-3.60], and 1.24 [0.47-3.09] in IV analyses with PPP10 for CPRD, and PPP5 and PPP10 for Mondriaan, respectively. PLP, PPP1 and PPP5 in the CPRD and PPP1 in Mondriaan were weakly associated with LABA ($r < 0.15$ or $OR < 2$). Also, observed confounders were imbalanced ($SDif > 0.10$) across PLP levels in Mondriaan.

Conclusions: LABA use was not associated with an increased risk of AMI compared to non-LABA. Validity of IV depends on the definition of IV and the database in which it is applied. We recommend researchers to generate several possible IVs, assess their validity, and report the estimate(s) from the most valid IV.

59. The Performance of Different Disease Risk Score Methods for Estimating Unbiased Odds Ratio in the Presence of Multiple Confounders

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Background: The disease risk score (DRS) is the probability of a specific outcome conditional on observed variables in the nonexposed population. The use of the DRS is aimed to result in balancing potential confounders between case and controls in a case-control study. Little is known about the performance of DRS methods for estimating odds ratios.

Objectives: To find out the performance of different disease risk score methods for estimating unbiased odds ratio in the presence of multiple confounders.