Meta-analysis of observational studies can yield similar results to meta-analysis of RCTs when the SLIC index is used in meta-regression to adjust for confounding by indication or severity due to selection bias.

The Problem

Randomized controlled trials (RCT) provide the most rigorous evidence for comparative effectiveness, but most research studies remain observational due to issues of ethics, feasibility, & generalizability. The main limitation of observational studies is selection bias, leading to confounding by indication or severity which limits their utility as evidence of comparative effectiveness. The meta-analytic pooling of data from these studies is challenging due to residual confounding, inclusion of different confounders across studies & absence of outcome effect size data across confounders.

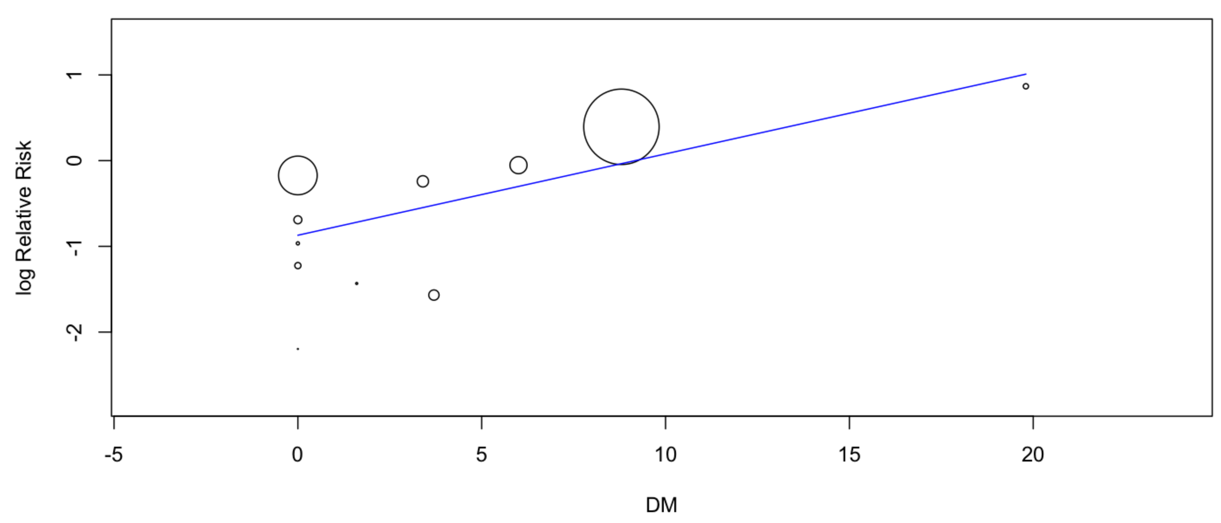
This study sought to improve the diversity of methodologies that can be validly incorporated into comparative effectiveness evidence-informed decision-making, by testing a novel statistical meta-analytic approach to control for confounding by indication or severity across multiple studies of similar & different designs.

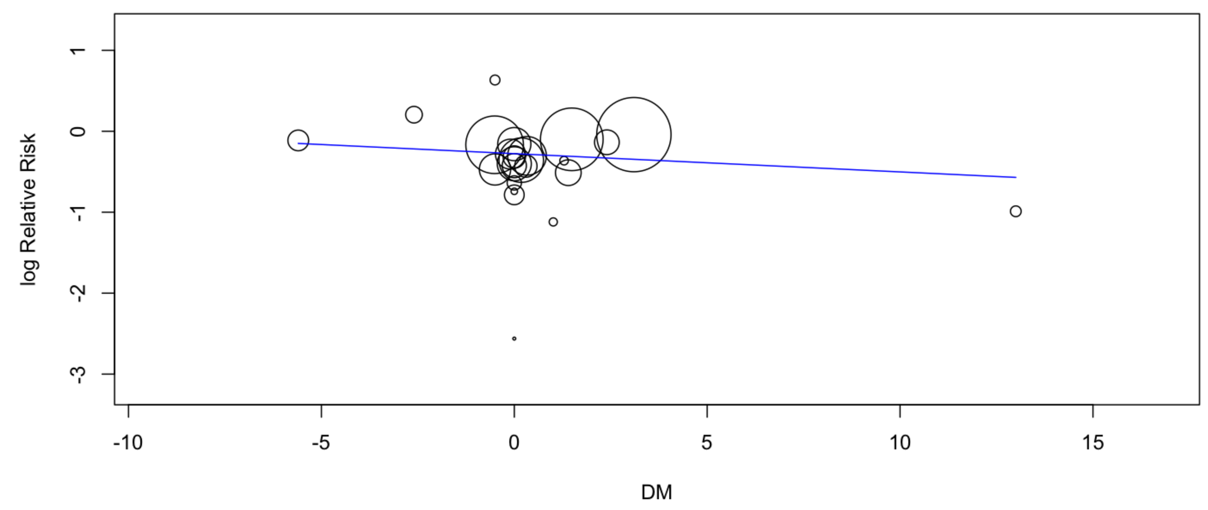
Methods

1. This study used the case of preventive statin therapy and its plethora of studies to test the proposed analytic approach.
2. PICO: adults; statins; non-statins; myocardial infarction (MI) and stroke.
3. Systematic review methods as recommended by the National Academy of Medicine were used to find, select, assess & synthesize effectiveness evidence from these studies.
4. 90 relevant research studies were included in the analysis, among 9,962 articles identified.
5. Data was extracted for a variety of confounders, & meta-analyses were performed for the RCTs & observational studies, pooled separately.
6. In each meta-analysis we included a de novo study level index of confounding (SLIC index) as a covariate for each confounder of interest.
7. SLIC index value for each study = (proportion or mean of a confounder in the exposed or treatment group) – (proportion or mean of a confounder in the unexposed or control group).
8. Alpha level set at 0.05 for statistical significance for all analyses.

Key Results

- For primary and secondary preventive statin therapy and the outcomes of MI and stroke, the pooled effect size for the observational studies suggested a larger benefit than the corresponding body of RCTs before regression analysis with the SLIC index.
- After regression analysis with the SLIC index for diabetes mellitus (figures 1 and 2), chronic kidney disease and coronary artery disease, the benefit suggested by the pooled effect size was similar for the observational studies and RCTs.





CONCLUSION

- The SLIC index when used in meta-analysis helps quantify the degree of confounding by indication or severity.
- It is a potential method to statistically tackle selection bias, the major limitation of observational research.
- Validation of the SLIC index may improve the utility of observational data for comparative effectiveness.

FUTURE RESEARCH

- As this method has only been tested on a single topic in health and healthcare research, a future project will replicate this method across a broader variety of well-researched topics.
- Data imputation & performance of sensitivity analyses & Monte Carlo simulation modeling should be used to evaluate analytic robustness of the SLIC index.
- This project was supported by grant number R03HS025025 from AHRQ.

Figure 1. Observational meta-regression of the SLIC index for DM against the log RR for the outcome of MI in primary preventive statin therapy. SLIC regression index = 0.101 (p = 0.002).

Figure 2. Experimental meta-regression of the SLIC index for DM against the log RR for the outcome of MI in primary preventive statin therapy. SLIC regression index = -0.023 (p = 0.306).

The Study Level Index of Confounding (SLIC): A Meta-Analytic Tool to Enhance the Utility of Observational Data for Comparative Effectiveness

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