Causal Inference and Combining Sources of Evidence in Diabetes Studies

Emily Roberts, PhD
emily-roberts-1@uiowa.edu

Assistant Professor
Department of Biostatistics,
College of Public Health
University of Iowa

2025

Background

- Previous research on incorporating external data into Randomized Clinical Trials (RCTs) has shown promise, particularly when target group is small or disease is rare
- Downsides include potential confounding or selection bias
- Could research for Type 1 Diabetes (T1D) be strengthened through the combination of sources of information?

Motivating Studies

- T1D is a chronic disease that prevents the body from producing insulin via autoimmune destruction of beta-cells
- Clinical trials investigated treatment in new onset T1D patients assessing markers of residual functioning
- Trial 1: randomized patients to mono- or combination ATG therapy
- Repeated measures of C-peptide showed change for ATG
- Trial 2: Assessed ATG monotherapy in control vs active treatment

Mixed Models and Propensity Scores

- Mixed modeling approach for repeated measures
- Propensity score to match additional controls based on age, sex, ethnicity, race, and baseline C-peptide
- Results with or without inverse propensity weights: significance may be sensitive to specification of propensity score
- Requires further investigation

Conclusions and Next Steps

- Limitation: exploratory, secondary data analysis with small number of external controls, and not prespecified into the original design
- T1D research seems it could benefit from causal integration of data: existing set of external controls, tend to have similar inclusion criteria and measure similar primary endpoints

References

- Haller, M. J. et al. (2018). Low-dose anti-thymocyte globulin preserves β-cell function and improves HbA1c in new-onset t1d. *Diabetes care.*
- Haller, et al. (2019). Low-dose anti-thymocyte globulin preserves C-peptide, reduces HbA1c, and increases regulatory to conventional T-cell ratios in new-onset t1d. *Diabetes.*
- Krischer, Jeffrey (2023). ATG-GCSF in New Onset Type 1 Diabetes (V2) [Dataset]. NIDDK Central Repository.
- Gitelman, S. E., et al. (2013). ATG treatment for patients with recent-onset type 1 diabetes: 12-month results of a randomized, placebo-controlled, phase 2 trial. The lancet Diabetes endocrinology.