HealthCore | University of Maryland School of Pharmacy

MSR11

A step-by-step guide for causal study design when estimating treatment effects using real-world data

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Background

- Causal inference (CI) is an innate part of scientific research.
- While inherently challenging using real-world data, CI in observational research is growing more important due to the need for generalizable and rapidly delivered real-world evidence (RWE) to inform regulatory, payer, and patient/provider decision-making.[1-5]
- CI with observational data combines numerous theoretical and technical concepts, necessitating specialized training and competency.
- Existing methodological literature on this topic is rich but can be complex and daunting to navigate.

Objective

To develop a step-by-step guide to help researchers conduct high-quality CI studies using observational data.

Methods

Context

HealthCore conducts health services research to support decision-making both at life sciences companies and at its parent company Anthem Inc., one of the largest US health insurance companies. This CI guide emphasizes analytic techniques (such as propensity scores) that are used most frequently within our research.

Scope

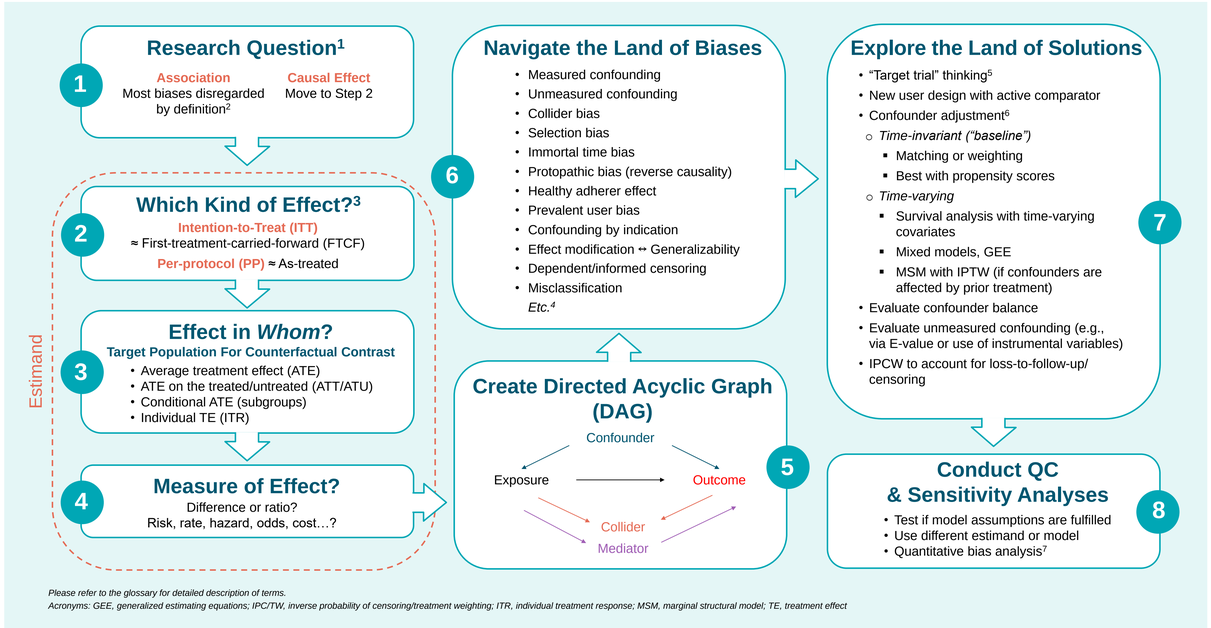
"Causal inference" was approached as a broad overarching concept defined by the totality of the research, from start to finish, rather than focusing on a particular analytic technique.

Process

A multidisciplinary team with research expertise primarily in epidemiology, biostatistics, and health economics, developed a step-by-step guide to causal study design and a corresponding glossary.

Results

Figure 1. A step-by-step guide to causal inference using real-world data



Please refer to the glossary for detailed description of terms.
Acronyms: GEE, generalized estimating equations; IPC/TW, inverse probability of censoring/treatment weighting; ITR, individual treatment response; MSM, marginal structural model; TE, treatment effect

[1]Ensure that the exposure and outcome are well-defined based on literature and expert opinion.
[2]More specifically, measures of association are not affected by issues such as confounding and selection bias because they do not intend to isolate and quantify a single causal pathway. However, information bias (e.g., variable misclassification) can negatively affect association estimates, and association estimates remain subject to random variability (and are hence reported with confidence intervals).
[3]"Trial ≈ real world data" parallels are inexact. PP especially can be expanded within the target trial framework.
[4]This list is not exhaustive; it focuses on frequently encountered biases.
[5]To assess bias in a nonrandomized study, use of the ROBINS-I tool is recommended (Sterne 2016; http://www.bristol.ac.uk/population-health-sciences/centres/cresyda/barr/riskofbias/robins-i/resources/).
[6]Only a selection of the most popular approaches is presented here. Other methods exist; e.g., g-computation and g-estimation for both time-invariant and time-varying analysis. There are also program evaluation methods (e.g., difference-in-differences, regression discontinuities) that can be applied to pharmacoepidemiological questions.
Conventional outcome regression analysis is NOT recommended for causal estimation due to issues determining balance, correct model specification, and interpretability of effect estimates.
[7]Online tools include, among others, an E-value calculator for unmeasured confounding (https://www.evalue-calculator.com/) and the P95 outcome misclassification estimator (http://apps.p-95.com/ISPE/).

Notes on the step-by-step-guide

- The guide addresses key conceptual issues that researchers should be aware of when implementing CI methods using real-world data.
- Every study can be subject to one or more biases, each of which can be addressed using one or more methods. For example: (1) to prevent prevalent user bias, employ an incident/new-user design; (2) to reduce misclassification bias, use validated measures of exposure, outcome and confounding factors or, in the absence of validated measures, plan a sensitivity or quantitative bias analysis.
- Copies of the guide and glossary are available using the QR codes at the bottom right of the poster.
- **Limitations of this guide** include the following: information was sourced widely, but no systematic literature review was conducted; space and useability constraints necessitated simplification of the complex source material and selections among many available methodologies; information about the relative importance of each step is not currently included.

*Please join our workshop on this step-by-step guide on **Tuesday, May 17th, from 1:30-2:30 pm EST** as part of **ISPOR Session #219**: Best Practices for Causal Study Designs Using Real-World Data*

Conclusions

- We outlined steps and described key conceptual issues of importance in designing CI studies, and created a visually appealing, user-friendly resource to help researchers clearly define and navigate these issues.
- We hope this guide serves to enhance the quality, and thus the impact, of RWE from observational research. We intend to update the documents based on community feedback. For comments and questions, please contact us at RWE@HealthCore.com.

References

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Disclosures

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