

OBSERVATIONAL DATA ARE ESSENTIAL FOR COMPARATIVE EFFECTIVENESS RESEARCH

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Observational data will often prove to be the most appropriate, timely, and cost-effective means of addressing important questions in comparative effectiveness research.

INTRODUCTION

Observational data, particularly from large claims databases, are a key resource for conducting comparative effectiveness research (CER) that is relevant to healthcare decision making. Yet there remains some resistance to the use of observational data on the grounds that only randomized controlled trials (RCTs) can ensure that treatment comparisons are unbiased.

Randomized controlled trials are the undisputed gold standard for establishing the efficacy of treatments for regulatory approval. However, a well-designed efficacy RCT targets a carefully selected patient population and implements a rigorous treatment protocol to ensure that the intervention being evaluated has the best possible chance of proving successful. The same features that ensure successful proof of efficacy limit the ability to generalize RCT results to clinical practice in ordinary care settings. Studies using observational data, on the other hand, have strong generalizability because the data used are typically collected through the normal process of medical care delivery.

This paper provides an overview of the advantages and challenges of CER using observational data. We argue that CER demands careful attention to study design by researchers, journal referees, and readers of published studies.

ADVANTAGES OF USING OBSERVATIONAL DATA

Studies using observational data, such as claims data from health plans and healthcare providers, fill a variety of potential gaps in the evidence base of CER. These studies:

- Reflect the **diversity** of medical practice, including the full range of physician treatment decisions (who gets treated), patient behaviors (how compliant they are), and financial incentives (physician reimbursement and patient out-of-pocket costs)
- Are timely and **efficient** because they do not require the logistical complexity and cost of prospectively designed and implemented patient recruitment and follow up
- Offer **large samples** of patients and thus have the statistical power to explore even rare diseases, to detect important treatment effects, and to explore variation in effect among subpopulations



Only the largest, longest, and most costly, pragmatic trials can match both the large samples available in observational datasets and the “real-world” diversity of practice, free from rigid protocols. However, by the time such studies have been completed, there is the risk that the information is no longer relevant due to changing medical technology and practice or entrenched attitudes among clinicians. Such undertakings only make sense if the stakes (potential costs and benefits) are exceedingly high and there are well-founded concerns about the feasibility of obtaining reliable estimates from observational data. Even then, an initial analysis of observational data may be required to confirm expectations and to provide data to inform trial design.

CHALLENGES OF OBSERVATIONAL DATA

The goal of CER is to make inferences from data about cause and effect, not just statistical associations. As noted, there are valid concerns about using observational data due to the possibility of biased comparisons in the absence of random treatment assignment. In fact, this analytic challenge is a consequence of one of the strengths of observational data; namely, that they reflect treatment choices doctors routinely make.

Since each doctor has his or her own preferred treatment options, a physician may provide Treatment A to most patients as the first option, and reserve Treatments B or C for those who do not respond well to Treatment A. In this example, one would expect to observe better outcomes with A because B and C are being used for more difficult cases. If all doctors practiced the same way, then it would be impossible to use observational data to make balanced comparisons among Treatments A, B, and C. But doctors, in fact, exhibit a wide range of practice patterns, so that an observational study can usually construct groups of patients getting either A, B, or C as their first-line treatment option.

THE SOLUTION: WELL-DESIGNED STUDIES

Given these considerations, careful study design is the first step in conducting CER using observational data. This means carefully thinking through what is known about how the treatments are intended to be used, which are well-established, and which are relatively new and still in limited use. If there are multiple specific indications for a particular medication, then the study should examine only those indications where each of the treatments is a similarly appropriate choice. If there are contraindications for any of the treatments, then such patients should be excluded from all treatment groups. The goal is to select only patients who, in principle, would have been good candidates for any of the treatments under comparison.

In addition to identifying comparable groups of patients, it is important to capture information about factors that might influence the outcome independent of treatment. These factors might include demographics, pre-existing diagnoses, prior interventions, and/or health insurance benefit design. Using this information, a variety of multivariate statistical methods, including matching, stratification, weighting, and regression, can be applied to further refine sample selection and estimate the magnitude of the treatment effect. Increased attention to study design issues when using observational data will contribute to the success of these studies and the value they bring to the CER community.

CONCLUSION

In CER, as in any other area of research, success depends on well-designed studies that are tailored to the objectives, and that are feasible within budget and timeline constraints. Choices about whether the study design should be prospective or retrospective, or whether it should be observational or protocol-driven, depend on the research question. However, it seems likely that retrospective observational data will often prove to be the most appropriate, timely, and cost-effective means of addressing important questions in CER.

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Mr. Huse has more than 25 years of experience conducting health economics and outcomes research projects sponsored by pharmaceutical, biotechnology, and medical device companies. He has worked on econometric analysis of retrospective databases, decision-analytic modeling, and design of clinical trial-based economic evaluations. He has served in senior consulting and management positions at several health economics and outcomes research firms and authored more than 50 professional journal articles, research monographs, and other publications. Mr. Huse holds both MA and BA degrees in economics from the University of Massachusetts in Amherst, MA.

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