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Editorial: Special Issue on "Causal Inference"

Jason Roy and Dylan Small

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Matching Methods for Observational Studies Derived from Large Administrative Databases

Ruoqi Yu, Jeffrey H. Silber and Paul R. Rosenbaum

Abstract. We propose new optimal matching techniques for large administrative data sets. In current practice, very large matched samples are constructed by subdividing the population and solving a series of smaller problems, for instance, matching men to men and separately matching women to women. Without simplification of some kind, the time required to optimally match T treated individuals to T controls selected from $C \geq T$ potential controls grows much faster than linearly with the number of people to be matched—the required time is of order $O\{(T + C)^3\}$—so splitting one large problem into many small problems greatly accelerates the computations. This common practice has several disadvantages that we describe. In its place, we propose a single match, using everyone, that accelerates the computations in a different way. In particular, we use an iterative form of Glover's algorithm for a doubly convex bipartite graph to determine an optimal caliper for the propensity score, radically reducing the number of candidate matches; then we optimally match in a large but much sparser graph. In this graph, a modified form of near-fine balance can be used on a much larger scale, improving its effectiveness. We illustrate the method using data from US Medicaid, matching children receiving surgery at a children's hospital to similar children receiving surgery at a hospital that mostly treats adults. In the example, we form 38,841 matched pairs from 159,527 potential controls, controlling for 29 covariates plus 463 Principal Surgical Procedures, plus 973 Principal Diagnoses. The method is implemented in an `R` package `bigmatch` available from `CRAN`.

Key words and phrases: Causal inference, fine balance, Glover's algorithm, observational study, optimal caliper, optimal matching, propensity score.

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Comment: Matching Methods for Observational Studies Derived from Large Administrative Databases

Fredrik Sävje

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Comment: Matching Methods for Observational Studies Derived from Large Administrative Databases

Mark M. Fredrickson, Josh Errickson and Ben B. Hansen

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Commentary on Yu et al.: Opportunities and Challenges for Matching Methods in Large Databases

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Rejoinder: Matching Methods for Observational Studies Derived from Large Administrative Databases

Ruoqi Yu, Jeffrey H. Silber and Paul R. Rosenbaum

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Linear Mixed Models with Endogenous Covariates: Modeling Sequential Treatment Effects with Application to a Mobile Health Study

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Abstract. Mobile health is a rapidly developing field in which behavioral treatments are delivered to individuals via wearables or smartphones to facilitate health-related behavior change. Micro-randomized trials (MRT) are an experimental design for developing mobile health interventions. In an MRT, the treatments are randomized numerous times for each individual over course of the trial. Along with assessing treatment effects, behavioral scientists aim to understand between-person heterogeneity in the treatment effect. A natural approach is the familiar linear mixed model. However, directly applying linear mixed models is problematic because potential moderators of the treatment effect are frequently endogenous—that is, may depend on prior treatment. We discuss model interpretation and biases that arise in the absence of additional assumptions when endogenous covariates are included in a linear mixed model. In particular, when there are endogenous covariates, the coefficients no longer have the customary marginal interpretation. However, these coefficients still have a conditional-on-the-random-effect interpretation. We provide an additional assumption that, if true, allows scientists to use standard software to fit linear mixed model with endogenous covariates, and person-specific predictions of effects can be provided. As an illustration, we assess the effect of activity suggestion in the HeartSteps MRT and analyze the between-person treatment effect heterogeneity.

Key words and phrases: Linear mixed model, endogenous covariates, micro-randomized trial, causal inference.

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Comment: Clarifying Endogeneous Data Structures and Consequent Modelling Choices Using Causal Graphs

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Moving Toward Rigorous Evaluation of Mobile Health Interventions

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Abstract. Qian, Klasnja and Murphy provide an assumption that allows for unbiased estimation of treatment effects in microrandomized trials when the data are modeled using linear mixed models with endogenous covariates. In this discussion, the validity of the assumption in the context of the HeartSteps microrandomized trial is reassessed. The utility of a marginal interpretation, versus the proposed conditional-on-the-random-effect interpretation, is also discussed.

Key words and phrases: Linear mixed model, endogenous covariates, microrandomized trial, causal inference.

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Comment: Diagnostics and Kernel-based Extensions for Linear Mixed Effects Models with Endogenous Covariates

Hunyong Cho, Joshua P. Zitovsky, Xinyi Li, Minxin Lu, Kushal Shah, John Sperger, Matthew C. B. Tsilimigras and Michael R. Kosorok

Abstract. We discuss "Linear mixed models with endogenous covariates: modeling sequential treatment effects with application to a mobile health study" by Qian, Klasnja and Murphy. In this discussion, we study when the linear mixed effects models with endogenous covariates are feasible to use by providing examples and diagnostic tools as well as discussing potential extensions. This includes evaluating feasibility of partial likelihood-based inference, checking the conditional independence assumption, estimation of marginal effects, and kernel extensions of the model.

Key words and phrases: Linear mixed models, partial likelihood, conditional independence test, marginal effects, kernel mixed models.

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Rejoinder: Linear Mixed Models with Endogenous Covariates: Modeling Sequential Treatment Effects with Application to a Mobile Health Study

Tianchen Qian, Predrag Klasnja and Susan A. Murphy

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Invariance, Causality and Robustness

2018 Neyman Lecture

Peter Bühlmann

Abstract. We discuss recent work for causal inference and predictive robustness in a unifying way. The key idea relies on a notion of probabilistic invariance or stability: it opens up new insights for formulating causality as a certain risk minimization problem with a corresponding notion of robustness. The invariance itself can be estimated from general heterogeneous or perturbation data which frequently occur with nowadays data collection. The novel methodology is potentially useful in many applications, offering more robustness and better "causal-oriented" interpretation than machine learning or estimation in standard regression or classification frameworks.

Key words and phrases: Anchor regression, causal regularization, distributional robustness, heterogeneous data, instrumental variables regression, interventional data, Random Forests, variable importance.

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Comment: Invariance, Causality and Robustness

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Comment: Invariance and Causal Inference

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Rejoinder: Invariance, Causality and Robustness

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Abstract. We sincerely thank Vanessa Didelez and Stefan Wager for their insightful and inspiring comments. Their views and thoughts on the topic of my article are of great value and truly contribute to put it into greater perspective.

Key words and phrases: Anchor regression, causal regularization, distributional robustness, heterogeneous treatment effects, instrumental variables regression, random forests.

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Outcome-Wide Longitudinal Designs for Causal Inference: A New Template for Empirical Studies

Tyler J. VanderWeele, Maya B. Mathur and Ying Chen

Abstract. In this paper, we propose a new template for empirical studies intended to assess causal effects: the outcome-wide longitudinal design. The approach is an extension of what is often done to assess the causal effects of a treatment or exposure using confounding control, but now, over numerous outcomes. We discuss the temporal and confounding control principles for such outcome-wide studies, metrics to evaluate robustness or sensitivity to potential unmeasured confounding for each outcome and approaches to handle multiple testing. We argue that the outcome-wide longitudinal design has numerous advantages over more traditional studies of single exposure-outcome relationships including results that are less subject to investigator bias, greater potential to report null effects, greater capacity to compare effect sizes, a tremendous gain in the efficiency for the research community, a greater policy relevance and a more rapid advancement of knowledge. We discuss both the practical and theoretical justification for the outcome-wide longitudinal design and also the pragmatic details of its implementation, providing publicly available R code.

Key words and phrases: Causal inference, confounding, multiple testing, sensitivity analysis, bias, longitudinal data.

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Comment: On the Potential for Misuse of Outcome-Wide Study Designs, and Ways to Prevent It

Stijn Vansteelandt and Oliver Dukes

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Comment: Outcome-Wide Individualized Treatment Strategies

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A New Template for Empirical Studies: From positivity to Positivity

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Rejoinder: The Future of Outcome-Wide Studies

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A Nonparametric Super-Efficient Estimator of the Average Treatment Effect

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Abstract. Doubly robust estimators are a popular means of estimating causal effects. Such estimators combine an estimate of the conditional mean of the outcome given treatment and confounders (the so-called outcome regression) with an estimate of the conditional probability of treatment given confounders (the propensity score) to generate an estimate of the effect of interest. In addition to enjoying the double-robustness property, these estimators have additional benefits. First, flexible regression tools, such as those developed in the field of machine learning, can be utilized to estimate the relevant regressions, while the estimators of the treatment effects retain desirable statistical properties. Furthermore, these estimators are often statistically efficient, achieving the lower bound on the variance of regular, asymptotically linear estimators. However, in spite of their asymptotic optimality, in problems where causal estimands are weakly identifiable, these estimators may behave erratically. We propose new estimation techniques for use in these challenging settings. Our estimators build on two existing frameworks for efficient estimation: targeted minimum loss estimation and one-step estimation. However, rather than using an estimate of the propensity score in their construction, we instead opt for an alternative regression quantity when building our estimators: the conditional probability of treatment given the conditional mean outcome. We discuss the theoretical implications and demonstrate the estimators' performance in simulated and real data.

Key words and phrases: Causal inference, average treatment effect, asymptotic linearity, efficient influence function, collaborative targeted minimum loss estimation, super efficiency.

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Comment: Increasing Real World Usage of Targeted Minimum Loss-Based Estimators

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Comment: Automated Analyses: Because We Can, Does It Mean We Should?

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Comment: Stabilizing the Doubly-Robust Estimators of the Average Treatment Effect under Positivity Violations

Fan Li

Abstract. Doubly-robust estimators within the one-step and TMLE frameworks could exhibit finite-sample bias and excess variability under positivity violations. We comment on how the application of a stabilization factor may improve the efficiency property of one-step estimator and TMLE, and the comparisons with their collaborative counterparts using the adaptive propensity scores.

Key words and phrases: Efficient influence function, overlap weighting, trimming, one-step estimation, targeted maximum likelihood estimation.

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Rejoinder: A Nonparametric Superefficient Estimator of the Average Treatment Effect

David Benkeser, Weixin Cai and Mark J. van der Laan

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On Nearly Assumption-Free Tests of Nominal Confidence Interval Coverage for Causal Parameters Estimated by Machine Learning

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Abstract. For many causal effect parameters of interest, doubly robust machine learning (DRML) estimators $\hat{\psi}_1$ are the state-of-the-art, incorporating the good prediction performance of machine learning; the decreased bias of doubly robust estimators; and the analytic tractability and bias reduction of sample splitting with cross-fitting. Nonetheless, even in the absence of confounding by unmeasured factors, the nominal $(1-\alpha)$ Wald confidence interval $\hat{\psi}_1 \pm z_{\alpha/2}\widehat{\mathsf{s.e.}}[\hat{\psi}_1]$ may still undercover even in large samples, because the bias of $\hat{\psi}_1$ may be of the same or even larger order than its standard error of order $n^{-1/2}$.

In this paper, we introduce essentially assumption-free tests that (i) can falsify the null hypothesis that the bias of $\hat{\psi}_1$ is of smaller order than its standard error, (ii) can provide a upper confidence bound on the true coverage of the Wald interval, and (iii) are valid under the null under no smoothness/sparsity assumptions on the nuisance parameters. The tests, which we refer to as Assumption Free Empirical Coverage Tests (AFECTs), are based on a U-statistic that estimates part of the bias of $\hat{\psi}_1$.

Our claims need to be tempered in several important ways. First no test, including ours, of the null hypothesis that the ratio of the bias to its standard error is smaller than some threshold δ can be consistent [without additional assumptions (e.g., smoothness or sparsity) that may be incorrect]. Second, the above claims only apply to certain parameters in a particular class. For most of the others, our results are unavoidably less sharp. In particular, for these parameters, we cannot directly test whether the nominal Wald interval $\hat{\psi}_1 \pm z_{\alpha/2}\widehat{\mathsf{s.e.}}[\hat{\psi}_1]$ undercovers. However, we can often test the validity of the smoothness and/or sparsity assumptions used by an analyst to justify a claim that the reported Wald interval's actual coverage is no less than nominal. Third, in the main text, with the exception of the simulation study in Section 1, we assume we are in the semisupervised data setting (wherein there is a much larger dataset with information only on the covariates), allowing us to regard the covariance matrix of the covariates as known. In the simulation in Section 1, we consider the setting in which estimation of the covariance matrix is required. In the simulation, we used a data adaptive estimator which performs very well in our simulations, but the estimator's theoretical sampling behavior remains unknown.

Key words and phrases: Causal inference, assumption-free, valid inference, U-statistics, higher-order influence functions.

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Discussion of "On Nearly Assumption-Free Tests of Nominal Confidence Interval Coverage for Causal Parameters Estimated by Machine Learning"

Edward H. Kennedy, Sivaraman Balakrishnan and Larry Wasserman

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Rejoinder: On nearly assumption-free tests of nominal confidence interval coverage for causal parameters estimated by machine learning

Lin Liu, Rajarshi Mukherjee and James M. Robins

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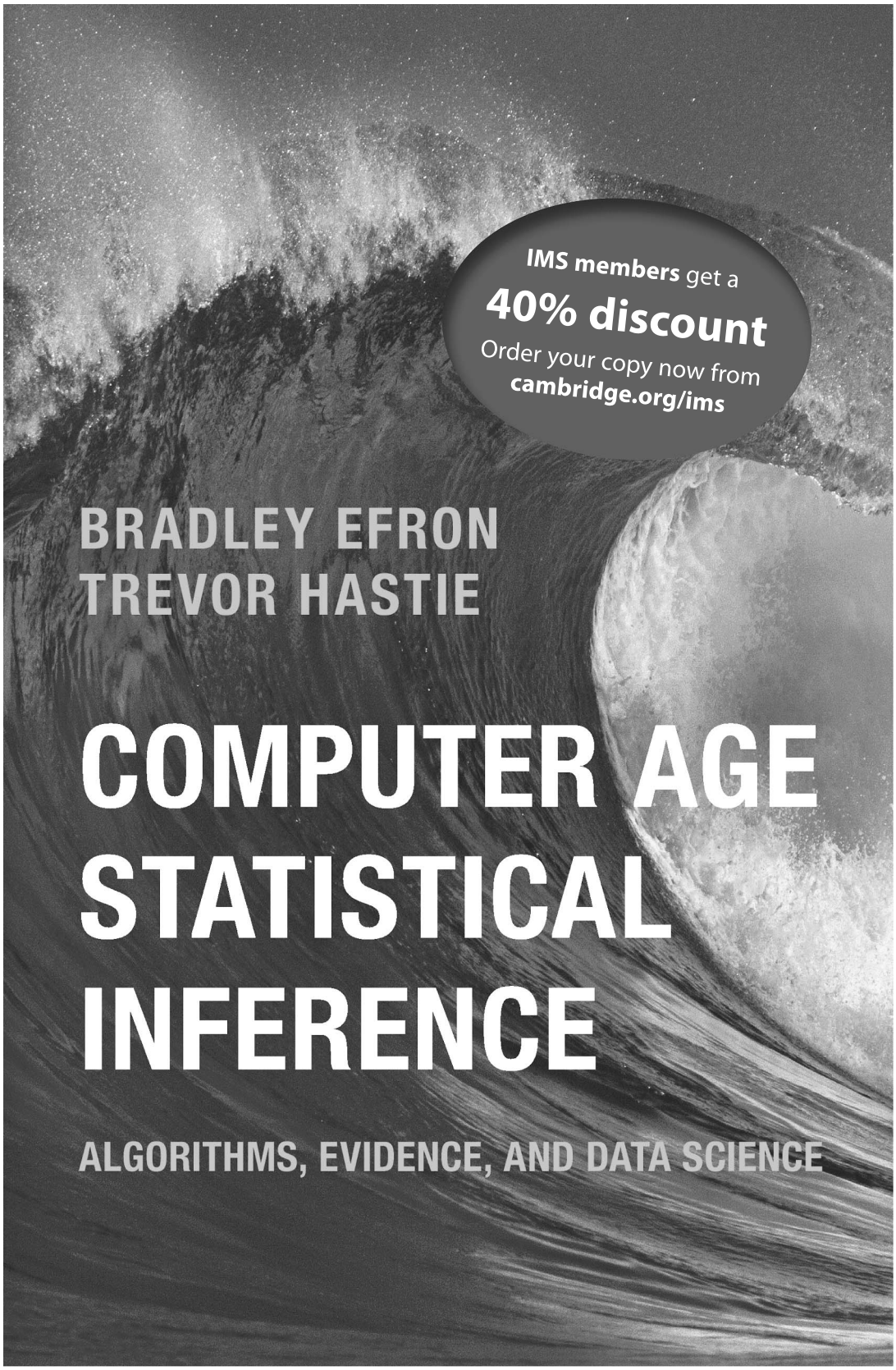
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