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CONTROL ID: 3356694
PRESENTER: Liangyuan Hu
PRESENTER (INSTITUTION ONLY): Icahn School of Medicine
TITLE: Causal comparative effectiveness analysis of dynamic continuous-time treatment initiation rules with sparsely measured outcomes and death
ABSTRACT BODY:
Abstract Body: Evidence supporting the current World Health Organization recommendations of early antiretroviral therapy (ART) initiation for adolescents is inconclusive. We leverage a large observational data and compare, in terms of mortality and CD4 cell count, the dynamic treatment initiation rules for HIV-infected adolescents. Our approaches extend the marginal structural model for estimating outcome distributions under dynamic treatment regimes (DTR), developed in Robins et al. (2008), to allow the causal comparisons of both specic regimes and regimes along a continuum. Furthermore, we propose strategies to address three challenges posed by the complex data
set: continuous-time measurement of the treatment initiation process; sparse measurement of longitudinal outcomes of interest, leading to incomplete data; and censoring due to dropout and death. We derive a weighting strategy for continuous time treatment initiation; use imputation to deal with missingness caused by sparse measurements and dropout; and define a composite outcome that incorporates both death and CD4 count as a basis for comparing treatment regimes. Our analysis suggests that immediate ART initiation leads to lower mortality and higher median values of the composite outcome, relative to other initiation rules.
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CONTROL ID: 3361269

PRESENTER: Katrina Leigh Devick

PRESENTER (INSTITUTION ONLY): Mayo Clinic

TITLE: Bayesian kernel machine regression--causal mediation analysis for environmental mixtures

ABSTRACT BODY:

Abstract Body: Greater understanding of the pathways through which an environmental mixture operates is important to design effective interventions. We present new methodology to estimate natural direct and indirect effects and controlled direct effects of a complex mixture exposure on an outcome through a mediator variable. We implement Bayesian Kernel Machine Regression (BKMR) to allow for all possible interactions and nonlinear effects of (1) the co-exposures on the mediator, (2) the co-exposures and mediator on the outcome, and (3) selected covariates on the mediator and/or outcome. From the posterior predictive distributions of the mediator and outcome, we simulate counterfactuals to obtain posterior samples, estimates, and credible intervals of the mediation effects. Our simulation study demonstrates that when the exposure-mediator and exposure-mediator-outcome relationships are complex, BKMR–Causal Mediation Analysis performs better than current mediation methods. We applied our methodology to quantify the contribution of birth length as a mediator between in utero co-exposure to arsenic, manganese and lead, and children's neurodevelopmental scores, in a prospective birth cohort in Bangladesh. Among younger children, we found a negative (adverse) association between the metal mixture and neurodevelopment. We also found evidence that birth length mediates the effect of exposure to the metal mixture on neurodevelopment for younger children. If birth length were fixed to its 75^{th} percentile value, the harmful effect of the metal mixture on neurodevelopment is attenuated, suggesting nutritional interventions to help increase fetal growth, and thus birth length, could potentially block the harmful effect of the metal mixture on neurodevelopment.

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CONTROL ID: 3367822

PRESENTER: Peng Wei

PRESENTER (INSTITUTION ONLY): The University of Texas MD Anderson Cancer Center

TITLE: Estimation of Total Mediation Effect for High-dimensional Omics Mediators

ABSTRACT BODY:

Abstract Body: Environmental exposures can regulate intermediate molecular phenotypes, such as gene expression, by different mechanisms and thereby lead to various health outcomes. It is of significant scientific interest to unravel the role of potentially high-dimensional intermediate phenotypes in the relationship between environmental exposure and traits. Mediation analysis is an important tool for investigating such relationships. However, it has mainly focused on low-dimensional settings, and there is a lack of a good measure of the total mediation effect. Here, we extend an R-squared (Rsq) effect size measure, originally proposed in the single-mediator setting, to the moderate- and high-dimensional mediator settings in the mixed model framework. Based on extensive simulations, we compare our measure and estimation procedure with several frequently used mediation measures, including product, proportion, and ratio measures. Our Rsq measure has small bias and variance under the correctly specified model. To mitigate potential bias induced by non-mediators, we examine two variable selection procedures, i.e., iterative sure independence screening and false discovery rate control, to exclude the non-mediators. We establish the consistency of the proposed estimation procedures and introduce a resampling-based confidence interval. By applying the proposed estimation procedure, we find that more than half of the aging-related variations in systolic blood pressure can be explained by gene expression profiles in the Framingham Heart Study of 1,711 individuals. We have implemented the proposed method in an R package ”RsqMed”.

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CONTROL ID: 3376717
PRESENTER: Lynne Billard
PRESENTER (INSTITUTION ONLY): University of Georgia
TITLE: Clustering of Intervals and Histogram Data
ABSTRACT BODY:
Abstract Body: The concept of symbolic data originates in Diday (1987). We consider two aspects of cluster methodology. First, while there has been a lot of activity in using regression-based algorithms to partition a data set into clusters for classical data, no such algorithms have been developed for a set of interval-valued observations. A new algorithm is proposed based on the k-means algorithm of MacQueen (1967) and the dynamical partitioning method of Diday (1973) and Diday and Simon (1976), with the partitioning criteria being based on establishing regression models for each sub-cluster. Second, we extend the Kim (2009) and Brito and Chavent (2012) (both of which extended the Chavent, 1998, work on intervals) divisive clustering for histograms based on the data midpoints to a double divisive monothetic method based on both the histogram means and their variances; see Kim and Billard (2018).
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CONTROL ID: 3387227

PRESENTER: Tugba Akkaya Hocagil

PRESENTER (INSTITUTION ONLY): University of Waterloo

TITLE: A Two-Stage Meta-Analytic Approach to the Synthesis of Evidence for Multiple Endpoints Across Multiple Cohorts

ABSTRACT BODY:

Abstract Body: Evidence from animal models and epidemiological studies has linked prenatal alcohol exposure (PAE) to a broad range of cognitive and behavioral deficits. However, there is virtually no information in the scientific literature regarding the levels of PAE associated with an increased risk of clinically significant adverse effects. The sample size in individual prospective longitudinal cohort studies may not provide sufficient power to examine effects associated with different levels and patterns of PAE. To address this critical public health issue, we propose to synthesize information regarding the effects of PAE and cognition across multiple endpoints using data from six major U.S. longitudinal cohort studies. We propose a two-stage meta-analytic approach which involves estimating the dose-response coefficients for each endpoint, and then pooling these correlated dose-response coefficients to obtain an estimated “global” effect of exposure. Specifically, in the first stage, we used individual participant data to derive the estimates of the effect of alcohol exposure by fitting a regression models which address confounding variables through adjusting for the propensity score. The correlation matrix characterizing the dependence between the endpoint-specific dose-response coefficients estimated within each cohort is then estimated, while accommodating incomplete information on some endpoints. We then discuss and compare inferences based on the two-stage approach to inferences based on a full multivariate analysis.

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CONTROL ID: 3387545

PRESENTER: Arman Oganisian

PRESENTER (INSTITUTION ONLY): University of Pennsylvania

TITLE: Nonparametric Bayesian approach for Causal Estimation and Adaptive Subgroup Discovery in Cost-Effectiveness Analyses

ABSTRACT BODY:

Abstract Body: Economists and policy analysts regularly compare treatments on the basis of both cost and effectiveness in order to inform resource allocation decisions and health policy. Several statistical challenges impede our ability to compare treatments on the basis of cost-effectiveness. First, these analyses are often conducted using observational data and, therefore, necessitate confounding control. Second, costs accumulated under a treatment and the treatment's efficacy (often defined as a survival outcome) tend to be censored. Third, cost and effectiveness are necessarily correlated - requiring joint modeling of a very complex, irregular distribution plagued with skewness, multimodality, and structural zeros. Our work has several contributions. We formally identify causal cost-effectiveness contrasts under modified ignorability and consistency assumptions. We then develop a flexible, nonparametric Bayesian model for the joint distribution that accommodates the complexity of these outcomes. This approach models the joint outcome via an adaptive mixture of simpler, parametric regression models. It is adaptive in the sense that the number of mixture components need not be pre-specified. Instead, as many components are introduced as the complexity of the distribution warrants. We incorporate this model into a Bayesian g-formula to compute the identified causal cost-effectiveness contrasts. Finally, we show how the model-based clustering of observations into mixture components can be used to automatically detect subgroups of the target population with heterogeneous cost-effectiveness profiles. This provides an advancement over standard methods which compute cost-effectiveness contrasts for pre-specified (not adaptively discovered) subgroups, then check to see which subgroup differences are meaningful. We outline an MCMC scheme for posterior sampling, assess frequentist properties our estimator under a variety of scenarios via simulation, and apply use our model to analyze the cost-effectiveness of various treatments among patients with endometrial cancer.

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