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G-COMPUTATION AND INVERSE PROBABILITY OF TREATMENT WEIGHTED ESTIMATION OF AVERAGE TREATMENT EFFECTS AMONG THE TREATED AND THE UNTREATED. Aolin Wang*, Roch A. Nianogo, Onyebuchi A. Arah (Department of Epidemiology, The Fielding School of Public Health, University of California, Los Angeles, Los Angeles, California, USA)

Average treatment effects among the treated (ATT) and the untreated (ATU) are of interest in the presence of treatment heterogeneity or when projecting potential outcomes in a new subpopulation (using ATU for example). There are still no accessible demonstration of g-computation of ATT and ATU. Furthermore, although there are inverse-probability-of-treatment-weights (IPTW) for fitting marginal structural models of ATT and ATU, those weights analytically double the number of treated or untreated respectively, without normalizing back to the observed sample size. For students and practitioners, the link between g-computation and IPTW is also underappreciated and how different estimation approaches influence the standard errors remains unclear. In this study, we demonstrate the steps involved in the g-computation as well as IPTW fitting of ATT and ATU using real and simulated data. We derive and apply new inverse-probability-of-treatment weights that analytically maintain the observed sample size of the total (treated and untreated) population. For the g-computation, we implement an easy-to-use Monte Carlo simulation protocol that simulated the potential outcomes and a new treatment variable. By regressing the potential outcome on the simulated treatment variable, we obtained consistent point estimates and standard errors that matched those from IPTW fitting of marginal structural models of the ATT and ATU using both unstabilized and stabilized weights. G-computation and IPTW both break the link between confounders and treatment but via different means, namely simulated randomization of a new treatment variable and weighting of the observed treatment variable respectively. Given its flexibility in dealing with both time-varying confounding and effect heterogeneity, g-computation should be seen as a powerful tool for estimating ATT, ATU and projecting potential outcomes and should be included in routine teaching and practice.

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BOUNDING THE PER-PROTOCOL EFFECT OF COLORECTAL CANCER SCREENING. Sonja A. Swanson*, Oyvind Holme, Magnus Loberg, Mette Kalager, Michael Bretthauer, Geir Hoff, Eline Aas, Miguel A. Hernan (Department of Epidemiology, Harvard School of Public Health, Boston, MA)

When there is non-compliance in a randomized trial, the per-protocol effect – i.e., the effect that would have been observed had everybody followed the protocol – may be of interest. Unfortunately, a point estimate for the per-protocol effect is only achievable under similar untestable assumptions as those used to identify causal effects in observational studies. However, it is possible to sometimes attain lower and upper bounds for the per-protocol effect under weaker but more plausible assumptions. These strategies for obtaining bounds consistent with data and a set of assumptions, known as "partial identification" methods, are rarely used by epidemiologists. Here we present an example of the estimation of bounds for the per-protocol effect. Specifically, we estimated bounds for the effect of colorectal cancer screening on cancer incidence in the Norwegian Colorectal Cancer Prevention Trial, a randomized trial of sigmoidoscopy screening including 98,792 men and women aged 50-64 years. In this trial, 62% of those randomized to screening were screened; nobody in the control arm received screening. Under the assumption that randomization had no effect on the outcome except through screening, we obtained bounds for the risk difference (RD): $-0.64\% \leq RD \leq 36.98\%$. These bounds appear helpful for quantifying the maximum possible effectiveness, but are less helpful in quantifying the minimum effectiveness or to rule out harm. On the other hand, these bounds are valid without resorting to untestable "no confounding" assumptions. We will further show that these bounds can be viewed as summarizing partially-identifiable effects in subgroups of the population, and that for 62% of the population we can obtain a point estimate (RD=-0.36%) while for the remaining 38% we have less informative bounds ($-1.24\% \leq RD \leq 98.86\%$). We will describe narrower bounds that can be obtained under additional assumptions, and will discuss the application of this methodology to observational studies.

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MEDIATION ANALYSIS FOR HEALTH DISPARITIES RESEARCH. Ashley I Naimi*, Mireille E Schnitzer, Erica EM Moodie, Lisa M Bodnar (McGill University)

A large body of research is devoted to understanding mechanisms that underlie racial health disparities. This work is often based on mediation procedures that may not be justified with race as the object of study. We explore the consequences of using this common approach, often referred to as the difference method. We compare the difference method to more general methods including inverse probability weighted marginal structural models, the structural transformation method (also known as sequential g-estimation), doubly robust g-estimation of a structural nested model, and doubly robust targeted minimum loss based estimation. We use simulation data, and an empirical dataset of nearly 1 million pregnancies to assess the role of pre-pregnancy obesity in explaining the racial disparity in infant mortality. Using the difference method, we estimated that pre-pregnancy obesity explained between 6.5% and 10.5% of the racial disparity in infant mortality. In contrast, using more general methods, these estimates increased to between 12.9% and 18.8%. Our findings suggest that inappropriate use of the difference method can have important consequences on empirical findings.

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AUGMENTING CAUSAL DIAGRAMS WITH EFFECT MODIFICATION, INTERACTION AND OTHER PARAMETRIC INFORMATION. Onyebuchi A. Arah* (Department of Epidemiology, UCLA Fielding School of Public Health, Los Angeles, CA, US)

Causal diagrams have become ubiquitous in epidemiology. Despite this widespread use, students and researchers have not been able to use them to depict effect modification and interactions. This study introduces and demonstrates how to augment directed acyclic graphs (DAGs) with parametric information on product terms typically used in modeling effect modification and interactions. Guiding principles for expanding or suppressing edges and nodes are also developed. Several applications illustrations are developed to depict total effects, effect decomposition, joint effect models, and longitudinal data settings with time-varying interactions. Existing graphical rules continue to be applicable to augmented DAGs. Several important implications can be read off the augmented DAGs. For example, one result shows when and how effect modification requires only uncontrolled confounding of the main exposure. The augmentation also allows for an intuitive visual depiction of the structural classification of effect modification. Augmented DAGs are also used show how the total effect of an exposure in the presence of mediation and interaction decomposes in the controlled direct effect, mediated interaction, reference interaction and pure natural indirect effect that can be traced along specific directed paths. Finally, parametric augmentation is shown to extend to different functional forms for in path diagrams and their implications for confounding control and residual confounding.