Mendelian randomization (MR) continues to increase in popularity and is being applied in many different settings. However, while many MR study results are interpreted as vaguely-defined “lifetime effects” of sustained exposures, instrumental variable analysis, which is at the heart of MR, has historically been developed for and focused on the estimation of the effect of point exposures. This has led to some confusion about how to interpret MR estimates. We begin by providing one possible definition of a lifetime effect: the average change in outcome measured at time $t$ when the entire exposure trajectory from conception to time $t$ is shifted by one unit. Using simulations and an empirical example from a Rotterdam cohort, we demonstrate that MR analyses will only validly estimate this effect in certain settings: e.g., when the relationship between the genetic variant and the exposure is not a function of age and the effect of exposure on the outcome is linear. This is important because most MR studies use time-varying exposures and never investigate whether the relationship between the genetic variant and exposure varies with age. Previous studies have shown this type of age-dependent relationship in genetic variant/exposure pairs commonly used in MR. Finally, we explore cases in which valid estimation of the effect of a point intervention on the exposure could be achievable. We demonstrate with causal graphs and a derived bias formula that detailed substantive knowledge of the relevant exposure window for the outcome and of the longitudinal effects of the genetic variant on the exposure are required to determine whether valid estimation of the effect of a point intervention is possible. In sum, by using causal graphs, bias derivations, simulations, and empirical examples, we sought to bring clarity to different potential interpretations of MR effect estimates and the situations in which such estimates are particularly susceptible to misinterpretation or bias.

**Longitudinal Association Between Severity of Disaster Exposure and Subsequent PTSD and MDD Among a Prospective Cohort of Chileans**

Juan Carlos Nobrega*, Sorab Boga, Julie Hollenbeck, Karmel Choi, Kevin Moore, Emelie Wigdor, Allison Pellegrino, Jean-Patrick Menard, Benjamin Vicente, Sandra Saldivia, Karestan Koenen, Robert Kohn, Cristina Fernandez (University of Miami Miller School of Medicine)

**Purpose:** To determine whether the severity of disaster exposure increases the risk of developing posttraumatic stress disorder (PTSD) and major depressive disorder (MDD). **Methods:** Data from a prospective cohort study (2003-2011) of Chilean primary care attendees ($N=1,708$) was used. At baseline, participants completed the Composite International Diagnostic Interview (CIDI), a comprehensive psychiatric diagnostic instrument. In 2010, the sixth most powerful earthquake struck the coast of central Chile, which led to a 7.7-foot tsunami. Participants resided in cities closest to the epicenter of the disaster. One year later, survivors completed the PTSD and MDD modules of the CIDI, and were asked 22 questions about their experiences during the disaster (e.g., whether they were injured or displaced). Responses were summed to create a total severity score (range=0-14; mean=3.31; SD=1.93) and were categorized (0, 1, 2, 3, 4, 5+). **Results:** Marginal structural logistic regression models with inverse probability censoring and exposure weights indicated that, for every one-unit increase in the total severity score, the odds of developing post-disaster PTSD ($n=175$) and MDD ($n=315$) increased by 41% (OR=1.41; 95% CI=1.31-1.52) and 16% (1.16; 1.09-1.24), respectively. Results suggested a positive dose-response relationship between the number of disaster severity experiences and risk of post-disaster PTSD (OR range=1.19-8.22) and MDD (OR range=1.05-2.32).

For all analyses, restricting the sample to those with no pre-disaster disorder ($n=641$) did not materially change results. **Conclusions:** This study’s findings have the potential to inform targeted public health interventions and allocate resources to those at highest risk for developing post-disaster PTSD and MDD.

**Addressing Missingsness in the California Cancer Registry in the Form of Incomplete Dates**

Chelsea Obrochta* (SDSU/UCSD Doctoral Student, Epidemiology)

It has become commonplace to use modern imputation methods (e.g., multiple imputation – a distribution-based method) for missing character and numeric data, but little attention has been given to the problem of missing/incomplete dates. For research on the quality of cancer care, adherence to “guideline concordant treatment” (GCT) is defined as the initiation of proper treatment(s) in a timely manner (e.g., 60 or 90 days) following diagnosis, and in the correct order; both are outcomes that require complete dates for classification. We studied the relationship between patient race/ethnicity and GCT among patients diagnosed with colorectal cancer using data from the California Cancer Registry, and found that 11.13% of 21,550 patients had at least one incomplete date. Sociodemographic characteristics between patients with no incomplete versus incomplete dates significantly differed. To address missingsness in our data in the form of incomplete dates, we used multiple imputation via chained equations two ways: (1) we imputed the number of days from a known date (as an interval) and incomplete date and calculated the outcomes, and (2) we imputed the binary outcome (yes or no) for initiation of timely treatment and treatment in the correct order. Multiple logistic regression models were used to examine the association of race/ethnicity with adherence to GCT overall, and just for timeliness of care. Analyses results from imputing the date interval were comparable to the complete case analysis, but results from imputing the binary outcome variables differed greatly, resulting in a different conclusion. We will demonstrate which approach is valid using a pseudo simulation. Important measured and unmeasured characteristics between patients with missing data versus complete cases can significantly differ. In scenarios for which dates are required for a calculated outcome, it is important to determine an approach for handling missing data in the form of incomplete dates.

**Use of Splines and Consideration of Upstream and Downstream Metabolism to Study the Association Between Dietary Intake of Folate Pathway Cohort and Neural Tube Defects Risk**

Julie Petersen*, Samantha Parker, Allen Mitchell, Martha Werler (Boston University School of Public Health, Department of Epidemiology)

Daily intake of $>400$ µg of folic acid (FA) prevents neural tube defects (NTDs) in some but not all women. We investigated whether women with recommended FA intake might further reduce NTD risk with concurrent intake of the folate pathway cofactors (FPCs) vitamins B6 and B12, choline, betaine, and methionine, with consideration of where in the pathway each micronutrient affects FA metabolism. The Slone Birth Defects Study (1998-2015) interviewed case and control mothers 400 µg, ORs for high/ideal intake were below 1.0 for each FPC, ranging from 0.61 (B6) to 0.82 (methionine). High/ideal intake of 1, 2, or 3 upstream FPCs (B6, methionine) yielded ORs of 0.71 (B6) to 0.82 (methionine). High/ideal intake of 1, 2, or 3 upstream FPCs (B6, methionine) yielded ORs of 0.71 (0.37-1.39), 0.69 (0.34-1.39), and 0.26 (0.08-0.84), respectively. The corresponding ORs for 1 and 2 downstream FPCs (B12, methionine) were 0.99 (0.58-1.71) and 0.81 (0.42-1.56) overall; 0.81 and 0.56 among normal/underweight women; and not below 1.0 for obese/overweight women. Spine categorization appeared to be more sensitive because, when using quartiles, protective associations were not detected for choline, betaine, or methionine. Our findings support that neural tube development may be vulnerable to deficiencies in substrates for FA synthesis, which might be overcome with diets high in upstream cofactors.
EFFECTIVE STRATEGIES FOR TEACHING INTRODUCTORY EPIDEMIOLOGY TO UNDERGRADUATE STUDENTS: A PROTOCOL FOR A SYSTEMATIC SCOPING REVIEW
Nathalie Perez, Robert Hines, Adrian Specogna (University of Central Florida)

Purpose: Although usually taught at the graduate level, epidemiology courses are now being offered to undergraduate students in academic institutions. Recommendations for conducting introductory courses have been described, yet systematic summaries of evidence on effective strategies for undergraduate students with limited experience in statistics and medicine is lacking. Here, we present a protocol for a scoping review of the literature to identify and describe strategies for successful educational outcomes in undergraduate introductory epidemiology courses. Methods: The PRISMA-P reporting guidelines for review protocols was followed. We are interested in educational strategies, with or without a comparison group, displaying success in learning as measured by grades, surveys, and other valid performance indicators. Arkeys and O'Malley's methodological framework will be followed. PubMed, ERIC, Education Source, ProQuest Education Journals, and the Professional Development Collection online databases will be searched for published, peer-reviewed primary research studies of any design in academic journals. Inclusion and exclusion criteria will be iteratively developed, post-hoc, as we gain insight in the subject. Two independent reviewers will screen studies for eligibility and extract data from included articles using standardized electronic data abstraction forms. Results: Articles will be mapped based on the educational techniques used. We expect data, and study-level risk of bias, to be shown as a narrative summary in tables and diagrams for all included studies. The study will be disseminated in a peer-reviewed journal following the PRISMA reporting guidelines, at international scientific meetings, as well as to knowledge users through presentations within schools of medicine and public health. Conclusions: This review will contribute new knowledge on introductory, undergraduate epidemiology education and its development in emerging schools of public health and medicine.

“S/P” indicates work done while a student/postdoc