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ADJUSTING FOR POOLED COVARIATES IN CASE-CONTROL STUDIES. Neil J Perkins*, Emily M Mitchell, Edwina Yeung, Enrique F Schisterman (NIH/NICHD)

Pooling designs offer a variety of benefits over analysis of individual samples in epidemiologic studies involving biomarkers, such as reducing assay costs and increasing efficiency compared to full and random sampling. When pooling a biomarker of an exposure of interest, current pooling designs seek to form pools that are homogeneous with respect to the outcome, in order to facilitate analysis. When this design is not implemented, such as when pools are formed before the outcome is observed, available statistical methods may not be directly applicable. This obstacle often discourages researchers from applying potentially significant cost-saving pooling techniques to measure biospecimens. In this study, we extend a multiple imputation framework for pooled, skewed biomarkers, focusing on logistic regression to adjust a main exposure measured individually for potentially costly covariates utilizing pools. The proposed methods readily permit analysis of pools that are heterogeneous with regard to outcome status. We perform a simulation study to quantify the benefit of adjusting for pooled measurements rather than complete individual measurements or a random sample of individual measurements. Polychlorinated biphenyls, both relatively costly and difficult to measure, were used to illustrate these methods. Adjusted main effect estimates using pooled covariates are similar with those using full individual data and standard errors are within 5% while drastically reducing the number of nuisance assays, at least half, necessary to achieve adjusted estimates.

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ROAD SEGMENT CHARACTERISTICS AND THE INCIDENCE OF FARM VEHICLE-RELATED CRASHES: A MULTI-STATE GIS-BASED MATCHED CASE-CONTROL STUDY. Shabbar I Ranapurwala*, Elizabeth Mello, Marizen Ramirez (Injury Prevention Research Center, The University of Iowa, Iowa City, IA)

Agricultural workers have the highest occupational mortality rate in the United States, and more than a third of the fatalities are attributed to transportation. Farm vehicle-related crashes (FVC) are hazardous for both farm and non-farm vehicle operators. In a matched case-control study, we measured gradient and sinuosity of road segments using ArcGIS, and evaluated their association with the incidence of FVCs from nine Midwestern states of the US during 2005-2010. A road segment with a FVC was defined as case (n=6,848), and a road segment without FVC was defined as control. The FVC data were collected from nine state departments of transportation, and road segment data from the Environmental Sciences Research Institute. Controls were matched by ZIP code, road type, and road segment length following 1:1 (controls=6,808) and 1:2 (controls=13,566) matching schemes. Using multivariable conditional logistic regression, odds ratios (OR) and 95% confidence intervals (CI) were computed. For sensitivity analyses, risk ratios for FVC incidence were calculated from the full cohort of road segments (n=6,491,811) using log linear regression. Compared to a leveled (<1% gradient) and straight (<1% sinuosity) road segment, increased gradient and sinuosity were associated with fewer FVCs. A road segment with >10% gradient was associated with 40% decreased FVC incidence (OR=0.60, 95% CI: 0.49, 0.75), and a road segment with >30% sinuosity was associated with 79% decreased FVC incidence (OR=0.21, 95% CI: 0.13, 0.36). Results were robust across all analyses. These associations may be due to cautious driving behaviors when maneuvering curvy or steep roads.

150-S/P

METHODS FOR ESTIMATING THE COMPARATIVE EFFECTIVENESS OF CLINICAL STRATEGIES THAT ADMINISTER THE SAME INTERVENTION AT DIFFERENT TIMES. Anders Huitfeldt*, Mette Kalager, James Matthew Robins, Geir Hoff, Miguel A. Hernan (Harvard School of Public Health)

In the absence of randomized trials, the generation of evidence to support clinical guidelines requires the emulation of trials using observational data. In this paper, we provide a methodology for emulating trials that compare the effects of different timing strategies, i.e., strategies that vary the frequency of delivery of a medical intervention or procedure. We review trial emulation for comparing (i) single applications of the procedure at different times, (ii) fixed schedules of application, and (iii) schedules adapted to the evolving clinical characteristics of the patients. For illustration, we describe an application where we estimate the effect of surveillance colonoscopies in patients who had an adenoma detected during the NORCCAP trial. We discuss methodological challenges that arise in the context of this surveillance intervention, such as confounding due to covariates that are only observed in those who undergo a colonoscopy, and the possibility of lead time bias.

151-S/P

EVALUATING INTERACTION IN THE METRIC OF TIME. Andrea Bellavia*, Matteo Bottai, Nicola Orsini (Unit of Biostatistics and Unit of Nutritional Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden)

Statistical interaction between two exposures of interest can be evaluated as a departure from additivity or multiplicativity, depending on the scale of the chosen model. The public health meaning and importance of presenting interaction according to both scales has been widely emphasized. In time-to-event analysis, however, given the popularity of the Cox proportional-hazard model, interaction analysis is usually limited to the multiplicative scale. Measures of additive interaction can be calculated using coefficients from a Cox regression, but these are seldom presented in epidemiological studies. In addition, all measures of interaction in time-to-event analysis, whether additive or multiplicative, are based on the hazard/rate scale, and a constant interaction during the follow-up period is typically assumed for simplicity. A possible approach for the analysis of time-to-event data is the evaluation of survival percentiles, defined as the time points by which different subpopulations reach the same fraction of events. In this approach the prospective is changed, with probability of the event of interest fixed to a specific proportion, and the time variable to be estimated. Statistical methods for the evaluation of conditional survival percentiles are available and their application in epidemiology is increasing. Evaluating interaction in this context assesses how the impact of one exposure on survival time is affected by another exposure. Moreover, this approach makes interaction dependent on the proportion of events considered, allowing an evaluation of how interaction is changing during follow-up time. The aim of this presentation is to introduce the concept of interaction in the metric of survival time, presenting the benefits of focusing on survival percentiles in its evaluation and estimation. With the proposed method interaction can be assessed both on the additive or multiplicative scales without assuming constant effects over time.

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