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AN EPIDEMIOLOGICAL APPROACH TO THE EFFECTS SUBLUXATION-BASED CHIROPRACTIC CARE HAS ON MANAGING CVD RISK FACTORS: A CASE STUDY AND REVIEW OF THE LITERATURE. E.L. Zielinski and N.A. Blume. (Life University, Marietta, GA 30062)

Objective: We present the findings in which a 54 year old male experienced lipid panel normalization as a result of subluxation-based chiropractic care. Clinical Features: 54 year old male first presented into the office with a chief complaint of dyslipidemia. He had a past history of myocardial infarction and angioplasty. One month prior to care patient had a lipid panel drawn indicating that his total cholesterol levels were 124, LDL levels were 63, HDL levels were 38, and triglyceride levels were 116. Other complaints included anxiety, constipation, fatigue, irritability, mood swings, neck pain, and stiff neck. Occupational and personal stress levels were reported 8 out of 10. He also reported depression. Intervention and Outcomes: Paraspinal surface electromyography, range of motion, and thermography readings were taken on the initial visit, on the twelfth visit one month later, and fifteen days after his second blood draw (4 ½ months into care). In conjunction with the above findings, vertebral subluxations were confirmed at the levels of C1, C5, pelvis, and sacrum. Care plan included thirty one patient visits over a five month period before blood draw confirmed that his cholesterol levels decreased. No reportable lifestyle changes occurred beside chiropractic care. In response to the positive blood work results, the patients' cardiologist reduced his medications.

Conclusions: We offer a brief historical account of the role cholesterol has played in CVD and provide the most recent global data. Our review reveals that the "cholesterol is harmful" hypothesis is not ubiquitously supported by the literature. There appears to be a growing paradigm shift that subscribes to the theory that psychogenic stress-related inflammatory and hormonal responses are key components to atherosclerotic plaque build-up and subsequent CVD. A review of the chiropractic literature indicates that there is a well-documented relationship between subluxation-based chiropractic care and reduced psychological and physiological stress levels, reduced inflammatory markers, and normalized hormone levels. This suggests that chiropractic care may have a direct impact on lowering primary CVD risk factors. The results of this case study has warranted further research to substantiate these relationships.

1050

CROWD-SOURCED MAPPING OF SEXUALIZED VIOLENCE IN SYRIA. *J. Blachman-Forshay, L. Wolfe, & K.C. Koenen (Mailman School of Public Health, Columbia University, NY, NY 10032 & Women Under Siege Project, Women's Media Center, NY, NY 10018).

Background: The ongoing conflict in Syria began in March 2011 with widespread violence reported throughout the country. Sexualized violence is frequently reported months or years after a conflict, resulting in insufficient crime reporting and a delayed ability to prosecute perpetrators. This project is the first time that sexualized violence in conflict has been reported in real time. Methods: The project utilizes Ushahidi crowd-sourcing technology to map sexualized violence reports. Reports are ascertained through Twitter, email, or direct uploads to the website (women undersiegesyria.crowdmap.com) along with Google and YouTube searches in Arabic and English. Reports are uploaded to the crowdmap website. Crowdmapping enables each report to be geospatially plotted and categorized by victims' demographics, type of violence, perpetrator, and additional consequences. Results: We have analyzed 167 reports: 18% included multiple victims. Females aged 7-46 accounted for 80% of reports and 80% include rape. Twenty-one percent of reports included deaths with signs of sexualized violence, 8% anxiety/depression, and 4% pregnancy from rape. Among male victims aged 11-56, 50% of reports included rape and 74% were tortured by government forces within a detention center. Conclusion: Crowd-sourcing methodology enables sexualized violence in Syria to be tracked in real time. Data can be used to implement immediate interventions for victims as well as to determine whether crowd-sourcing is a valid data collection method to provide evidence for war crime prosecution.

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STRATIFIED REGRESSION MODELS FOR CASE-ONLY STUDIES. *Elizabeth Mostofsky and Murray A. Mittleman (Harvard School of Public Health, Boston, MA, 02115)

Case-only studies provide a useful approach for examining the impact of transient exposures on acute outcomes. Previously, it has been shown that for studies of a common exposure across individuals, such as environmental air pollution, a time-series study using unconditional poisson will provide identical results to a time-stratified case-crossover study using conditional logistic regression. If each individual can experience different exposure levels, such as behavioral factors, one must conduct a matched analysis of either all prior exposure information (conditional poisson) or a random sample of control times (conditional logistic). In the initial case-crossover design, self-reported history of behavioral exposures was ascertained for a random sample of control times. However, when information on the exact timing of exposure is available for each individual (e.g. registry data on vaccination dates), conditional poisson can be used to include the individual's entire exposure history. This approach, referred to in the literature as the self-controlled case series, can be shown to be identical to the case-crossover when exposure information is available for the entire control period. In this presentation, we will show that compared to conditional logistic regression using a sample of control times, conditional poisson using the total exposure history eliminates the problem of overlap bias and it allows for further adjustment for time and other covariates. Others have proposed that monotonic changes over time in case-only studies can be addressed by incorporating a control group or by using a discrete-time approach. We will show the relationship among these approaches using registry data on psychosocial stressors and the rate of cardiovascular events.

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MODELS APPROPRIATE FOR THE STUDY OF PATHOGENS EXHIBITING EXTRA-HOST POPULATION DYNAMICS. *Ayscue, P., Lanzas, C., Grohn, YT. (Cornell University, Ithaca NY)

Mathematical models have been used extensively to study infectious disease dynamics and typically track host characteristics as a proxy for the pathogen under study. These models generally function well in the study of disease transmitted primarily through contact, however, the formulation of a model at the host scale limits the researcher's ability to study salient pathogen-scale dynamics. As a result, host-based models have limited efficacy for the study of pathogens with more complex propagation dynamics, such as foodborne and environmentally transmitted diseases. Here we develop pathogen-scale models based in an ecological metapopulation framework, allowing us to study populations of organisms capable of moving between and growing in spatially segregated habitats. As an informative example, we consider Escherichia coli O157:H7 dynamics in cattle. By applying the above methods, we are able to disaggregate environmental and host contributions to E. coli maintenance in a farm environment and demonstrate that host-based contact is not an important driver in the system, a novel finding. We find that the pathogen-scale framework offers significant improvements over host-scale models for studying diseases with complex population dynamics by intuitively accounting for: extra-host population dynamics, transmission between heterogeneous environments, multiple high-dose challenge events to hosts, environmental stochasticity, quantifying bacterial loads in multiple habitats, and imperfect testing regimens that relate pathogen dynamics to common host-scale observations. The net effect is that researchers are able to examine the contribution of extra-host replication to the overall propagation of the pathogen. We conclude that the ecological metapopulation framework represents an important alternative for epidemiologists for the study of pathogens with substantial extra-host population dynamics.

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PARADOXES IN EPIDEMIOLOGIC RESEARCH: ARE THEY ALL JUST SMOKE AND MIRRORS? *H.R. Banack & J.S.Kaufman (McGill University, Montreal, QC).

The published medical literature is replete with examples in which authors report a "paradoxical" finding. A recent PUBMED search for "paradox* [ti]" returned 4000 publications from the past 10 years. One example of an apparent paradoxical finding is known as the "obesity paradox". Obesity is associated with a higher mortality risk in the general population, yet confers a survival advantage in certain disease groups. This so-called "obesity paradox" has been reported in a number of cardiovascular and non-cardiovascular disease populations including coronary artery disease, heart failure, stroke, renal disease, COPD, and diabetes. The objective of this presentation is to use data from the US National Health and Nutrition Examination Survey (NHANES) to demonstrate that the apparent "obesity paradox" is the result of a form of selection bias: stratification on a common effect. One of the most common manifestations of selection bias occurs as a result of conditioning on a variable affected by exposure and sharing common causes with the outcome (known as a "collider" in DAG terminology). Conditioning on a collider distorts the association between exposure and outcome among those selected for analysis and produces the spurious association between obesity and mortality. We will use causal diagrams to provide a conceptual framework for the interpretation of the "obesity paradox" and propose appropriate analytic approaches to reduce this bias including deterministic or probabilistic bias analysis using selection proportions and inverse probability weighting.

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APPLICATION OF HIERARCHICAL REGRESSION IN AN EPIDEMIOLOGIC STUDY OF CORRELATED EXPOSURES. *Upson, K, Holt, VL, De Roos, AJ (University of Washington, Seattle, WA)

Correlated exposures frequently occur in epidemiologic studies. Estimating multiple exposure effects using maximum likelihood estimation (MLE) may result in unstable coefficients or lack of model convergence, motivating use of separate models for each exposure. However, this practice does not allow for controlling for correlated exposures. We describe the application of Semi-Bayes hierarchical regression (HR) using SAS macro GLIMMIX to simultaneously evaluate multiple exposures. The method uses information about relationships between multiple exposure effects to adjust estimates towards a prior distribution to improve accuracy and precision over MLE. Using data on 93 cases and 198 controls from the Women's Risk of Endometriosis study, we investigated endometriosis risk in relation to correlated urinary phthalate metabolite concentrations using a mixed effects logistic model, combining models from two levels, and compared results to conventional MLE. The first-stage logistic regression model included 8 phthalate metabolites and 3 covariates (conventional analysis). In the second-stage linear regression model, we regressed first-stage model coefficients on prior covariates, grouping phthalate metabolites by parent phthalate diester with expected similar direction and magnitude of effect. We specified a prior variance corresponding to 95% certainty that true residual effect parameters lie in a 10-fold range. Although the appropriateness of our prior distribution is unknown, several HR model effect estimates had lower confidence limit ratios and were more reasonable (e.g., highest vs. lowest quartile, MEHP: OR 0.5, 95% CI: 0.2-1.2; MEHHP: OR 0.8, 95% CI: 0.3-2.1) compared to conventional MLE estimates (MEHP: OR 0.1, 95% CI: 0.03-0.7, MEHHP: OR 0.2, 95% CI: 0.006-5.7). Using multiple levels of information, HR may improve precision and accuracy of estimates over MLE, while adjusting for correlated exposures.

1056

THE ROLE OF HEAVY PRECIPITATION EVENTS IN WATERBORNE DISEASE OUTBREAKS IN THE UNITED STATES. *S Mekaru, S Stuver, A Ozonoff (Boston University, Boston, MA, 02118)

In the face of climate change, environmental risk factors for disease outbreaks are increasingly important. While heavy rainfall has reportedly contributed to waterborne disease outbreaks (WBDOs), little epidemiologic research on a broad association between heavy precipitation events (PEs) and WBDOs exists. Study of this association epidemiologically is limited by the poor fit of traditional study designs which evaluate outcomes at the individual level. Here, we present a novel approach to the case-crossover design, treating locations as individuals. "Cases" are locations which have had a WBDO and the exposure of interest is the presence of a heavy PE. For each of 92 locations with a CDC-documented WBDO meeting inclusion criteria (1989-2000), we evaluated NOAA rainfall data for the outbreak year and ten years before and after. We identified PEs exceeding defined rainfall thresholds in 24 or 48 hour periods. Repeated conditional logistic regression analysis performed on Monte Carlo sampled control years (n=1000) produced a median OR of 0.50 (95% CI 0.25-0.90) for a one-day rainfall exceeding 1.5" in the four weeks preceding the outbreak date. Overall, years with a heavy PE had lower odds of a WBDO than those without a heavy PE, strongly contrasting with the only other broad analysis of US WBDOs and PEs. This study's use of WBDOs after 1970s environmental legislation could suggest that the WBDO-PE relationship is modified by clean water infrastructure. While more research is needed on this specific association, this epidemiologically grounded design provides a framework for exploring environmental risk factors for diseases with important public health implications.

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NON-DIFFERENTIAL ERROR IN AGGREGATED MEASURES OF NEIGHBORHOOD CONTEXT. Stephen J Mooney*, Catherine A Richards, Andrew G Rundle (Columbia University - Mailman School of Public Health, New York, NY)

Background: Studies of neighborhood health frequently aggregate individual level data to create contextual measures. For example, percent of residents living below the poverty line and median household income are both aggregations of individual-level measurements of household income. These individual-level measures may be error-prone, yet we know of no exploration of the effect of aggregating erroneous individual-level data for use in multi-level health studies. Methods: Using both GEE and mixed models, we modeled the relationship between neighborhood socioeconomic status and individual level BMI using survey data from New York City and from simulated datasets. We assessed the effect of non-differential measurement error at the individual level on parameter estimates for resulting aggregated contextual measures. Results: For neighborhood variables aggregated from dichotomous individual-level measures (e.g. % of residents living below the poverty line), non-differential misclassification at the individual level inflates the group-level parameter estimate to 1/(individual-level sensitivity + individual-level specificity - 1) times its true value. For neighborhood variables aggregated from continuous individual-level measures (e.g. median household income), measurement error at the individual level does not cause bias in the neighborhood-level parameter estimate. Discussion: When using contextual measures created through the aggregation of individual level data, the effect of measurement error at the individual level depends on the specification of the contextual variable. Bias away from the null occurs when a non-differentially misclassified dichotomous individual-level measure is aggregated to reflect the proportion of people with that characteristic.

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AUTOMATED VARIABLE SELECTION PROCEDURES TO IDEN-TIFY STATISTICAL INTERACTION BETWEEN CORRELATED ENVIRONMENTAL EXPOSURES: THE CASE OF PHTHALATE METABOLITES AND BODY MASS INDEX. *Candace Robledo, Julie Stoner, Hélène Carabin, Linda Cowan, Jennifer D. Peck (NICHD, Rockville, MD)

Epidemiological studies of the association between a health outcome and urinary concentrations of several correlated environmental chemical metabolites are increasingly common. We propose that multiple linear regression automated variable selection procedures can be practical tools to identify interactions between a large number of correlated environmental chemical exposure values when modeling a continuous health outcome. A series of simulations were conducted to assess the performance of Backward Stepwise/Elimination, Forward Stepwise, Forward Stagewise, Least Angle Regression, and Least Absolute Shrinkage and Selection Operator methods at identifying interactions in linear regression models for pre-pregnancy body mass index (outcome) and a large number of correlated phthalate metabolites and their pair-wise interactions as independent factors in settings with small or moderate sample sizes. Measures of performance, including bias, mean squared error, and the true positive and false positive proportions, were calculated for the specified model. Simulations indicated that forward stepwise, modified to adhere to the hierarchical interaction/main effect principle, and unmodified least angle regression performed well (high true positive proportion and low false positive proportion) at identifying interaction among urinary phthalate metabolites. Automated variable selection procedures can efficiently identify a subset of potentially interacting co-exposures that can then be evaluated more thoroughly.

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A PROBABILISTIC SENSITIVITY ANALYSIS TO ESTIMATE THE IMPACT OF DATA ERRORS IN A RANDOMIZED TRIAL. Elisa L. Priest*, DrPH ; Lori A. Fischbach, PhD (UNT SPH , Ft Worth TX)

This study quantified the bias from data processing errors on the estimate of effect in a randomized clinical trial of the effectiveness of two different drug regimens on eradication of H. pylori. Data management can impact the frequency of data errors in clinical trials. However, there is little epidemiology literature showing the impact of data errors on the accuracy and precision of the estimates of effect in clinical trials. This study used data from a published randomized clinical trial and a probabilistic sensitivity analysis to correct the raw data for multiple data errors. This produces a simulation interval that reflects the range of potential estimates of effect. The simulation was performed with 10,000 repetitions each for non-differential errors in exposure (treatment), outcome (H. pylori eradication), stratification variable (histology), and all three combined. The original point estimates were compared with the simulation interval to examine the potential bias in the original analysis. The overall results comparing the two treatments showed a bias in the original analysis towards the null. In the simulation with all three errors, the original analysis biased towards the null (Risk Difference 1.5 [-9.7, 12.7]) compared with the mean simulation interval (Risk Difference 1.8 [-11.0, 14.0]). In contrast, when stratified by histologic diagnosis, the original results were biased away from the null in all strata compared with the simulation. This sensitivity analysis showed that nondifferential errors in data processing can bias the risk difference in a randomized clinical trial. Use of sensitivity analysis can correct for multiple biases in study data and show a more complete picture of the study results than a single point estimate.

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DATA MANAGEMENT IN EPIDEMIOLOGY STUDIES WITH LIM-ITED RESOURCES. Elisa L. Priest*, DrPH ; Lori A. Fischbach, PhD (UNT SPH , Ft Worth TX)

The goal of epidemiologic research is to accurately estimate the frequency of disease or the effect of an exposure on the occurrence of disease. This relies on study design, analysis methods, research conduct, handling and processing of the data and the resulting data errors. Two areas that are limited in the epidemiologic literature are project management and data management. Project management can provide epidemiologists with the knowledge, skills, tools, and techniques to manage the scope, quality, schedule, budget, resources, and risk of a research study. Data management includes handling, monitoring, and controlling data as it is collected, processed, combined, and interpreted. Data management processes may impact both the expense of a study and the validity and precision of the estimates of effect in primary and secondary analyses. There are no practical resources to assist epidemiologists with planning and implementing data management processes in a non-regulated study with resource constraints. I created a pragmatic, project-management based, framework that an epidemiologist can use to plan and implement data management. This framework is based on the principles found in the US government regulations for data management in research and is targeted towards those study types commonly encountered by researchers with limited resources: non-FDA regulated studies. The framework has three components: a visual outline of outputs (deliverables), a guide for planning data management, and a comprehensive set of customizable tools for planning and executing data management. Together with the guide, these tools lead an epidemiologist through a standardized, documented approach to planning data management for an epidemiologic study with limited resources.

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APPLICATION OF NONLINEAR MIXED MODELS WITH HAR-MONIC TERMS FOR ANALYZING LONGITUDINAL DATA. *K Schliep, S Mumford, P Albert, E Yeung, A Ye, E Schisterman (NICHD, Rockville, MD 20852)

Many physiological functions follow a cyclical pattern. Epidemiologists researching disease affected by biological rhythms typically conduct studies with repeated measurements. Several flexible models have been proposed for characterizing cyclic patterns but often require uniform measurements or are limited in their ability to study covariate effects. We propose application of a parametric nonlinear mixed model with harmonic terms approach, which allows for irregularly timed measurements, produces minimally biased estimates for small samples, and can be easily implemented in standard software packages. Moreover, in addition to allowing for estimation of differences in the mean effect of a covariate, this approach allows for estimation of differences in the amplitude and phase shift of the cyclical pattern. We present the nonlinear mixed model methodology, including how to model time, choose the number of harmonic terms using penalized likelihood, and how to estimate the effect of covariates on the cyclical pattern using a motivating example: the effect of sweetened soda intake on reproductive hormones in the BioCycle Study (n=259 women followed for up to 16 time points across 2 menstrual cycles). Women who consumed on average ? 1 cup/day of sweetened soda had 13.3% (P=0.04) higher mean free estradiol levels compared to woman who consumed < 1 cup/day after appropriate adjustment. Example code for running these analyses in R and SAS will be provided. The harmonic model offers a unique approach for studying cyclic patterns with few limitations. This work will help bridge the gap between methodological advancements and practical applications in research settings by providing a real-world example and tools for implementation.

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MARGINAL STRUCTURAL MODELS FOR CONTINUOUS EXPO-
SURES IN THE LONGITUDINAL SETTING: AN APPLICATION TO
REPRODUCTIVE EPIDEMIOLOGY. *Katherine Ahrens (Eunice Ken-
nedy Shriver National Institute of Child Health and Human Development,
Bethesda, MD)

Marginal structural models (MSMs) are an appropriate model choice
when adjustment for time-varying confounding affected by prior exposure
is necessary. In early applications, MSMs were primarily applied to ana-
lytical settings with a dichotomous exposure measured at two points over
time. MSMs can also be applied in the setting of continuous exposures
measured repeatedly over time; however such examples are limited in the
epidemiologic literature. The objective of this analysis is to present an
application of MSMs for estimation of etiologic effects in the context of
repeatedly measured continuous variables, such as that encountered when
reproductive hormones are measured multiple times over the course of the
menstrual cycle. These hormones, such as estrogen, follicle stimulating
hormone, leptin, luteinizing hormone, and progesterone follow a cyclical
pattern, driven by a complex process involving intricate feedback loops
and coordinated by the hypothalamic-pituitary-ovarian axis. Given the
complex feedback mechanisms traditional regression adjustment is inade-
quate. Using data from the BioCycle Study, which collected reproductive
hormone levels at up to 8 time-points per cycle over up to 2 menstrual
cycles from 259 healthy regularly cycling women, we will first describe
this feedback process and rationale for utilizing MSMs using directed
acyclic graphs (DAGs). We will then demonstrate how to estimate the
inverse probability weights for a continuous exposure in the longitudinal
setting with a focus on checking the underlying assumptions, evaluating
the model fit for both the weights and the final model, and interpretation
of the results. We will show how MSMs can be easily implemented in
standard software packages, and offer a straightforward approach for mak-
ing inferences about causal effects in the presence of time-dependent t
confounding in the longitudinal setting with continuous exposures.