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TARGETED MAXIMUM LIKELIHOOD ESTIMATION FOR DIRECT AND INDIRECT EFFECT ANALYSIS IN THE COMBINE (COMBINING MEDICATIONS AND BEHAVIORAL INTERVENTIONS FOR ALCOHOLISM) STUDY. *M. Subbaraman, S. Lendle, M. van der Laan (UC Berkeley, Berkeley, CA, 94720)

COMBINE investigators aimed to determine whether naltrexone, a drug alleged to reduce cravings for alcohol, combined with a behavioral intervention (CBI) alleged to change stress and coping behaviors, improves drinking outcomes more than either alone. After 16 weeks, only naltrexone alone and CBI alone significantly increased percent days abstinent (PDA) in models controlling for baseline PDA and site of treatment administration. Unexpectedly, the naltrexone + CBI combination did not offer any advantage over either naltrexone alone or CBI alone. To understand moderating and mediating factors, and to help explain the combination's lack of improvement over each monotherapy, controlled and natural direct effect analyses were performed using targeted maximum likelihood estimation (TMLE). TMLE offers several advantages over traditional direct effect analytic approaches such as double-robustness and allowance of treatment moderation by potential mediators. Cravings and stress were examined as theoretically informed mediators/moderators. Controlled direct effect results show that naltrexone, CBI, and the combination all work best when cravings are high, while none work when cravings are low. Similarly, naltrexone and the combination work better when stress is high. Natural direct/indirect effect results show that all three treatments' effects are at least partially mediated by cravings, and that craving reduction explains 50-67% of treatment effects. Furthermore, naltrexone appears to affect cravings earlier while CBI works later. Taken together, the set of results suggests the possibility of a threshold effect; if naltrexone reduces cravings early on and CBI is not effective when cravings are low, then the combination's lack of improvement over either monotherapy should not be surprising.

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ENSURING POSITIVITY WITH PROPENSITY SCORES GENERATED FROM MULTINOMIAL LOGISTIC REGRESSION. *JI Rosenbloom, MA Mittleman (Beth Israel Deaconess Medical Center, Boston, MA, 02215)

The optimal way to create and use propensity scores with more than two exposure groups is uncertain. Recently new methods to create exposure propensity scores have been proposed, in particular using multinomial logistic regression to simultaneously create propensity scores for all exposure groups, and then running one Cox proportional hazards (or other appropriate) model with all the propensity score variables as covariates. This method is pragmatically easy to implement and may require less computing power than other methods. However, this method is prone to violate the criterion of positivity. With two groups, it is simple to trim the propensity scores to ensure overlap and thus ensure the positivity. However, with three or more groups, defining the overlap and the correct way to trim is uncertain. Using alcohol consumption and mortality data from the Determinants of Myocardial Infarction Onset Study, we will create propensity scores for three ordinal exposure groups relative to abstainers, using multinomial logistic regression, and then will examine how we can trim to areas of overlap, thus ensuring positivity.

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MULTIPLY ROBUST MODELS FOR DISAGREEING COLLABORATORS. *DerSarkissian, Maral and Arah, Onyebuchi (University of California, Los Angeles, LA, CA)

Introduction: In assessing the relationship between chronic disease and self-rated health, researchers may disagree about which variables to control for from the following set: marital status, age, gender, employment, and education. The aim of this study is to extend the modern doubly robust estimation technique to multiply robust settings in which three estimators are combined allowing collaborators with competing confounding adjustments to build one final model. Methods: We used WHS data on 146,561 persons from 51 countries to assess the effect of the presence of chronic disease (diabetes, depression, or heart disease) on health. Three competing confounding adjustment schemes were considered and combined using an outcome regression, propensity score covariate adjustment, and a marginal structural model. Inverse probability weights were created for our exposure of interest, chronic disease, adjusting for all hypothesized confounders except employment in order to use a marginal structural model. A propensity score was also created adjusting for all hypothesized confounders except education. The inverse probability weight and propensity score were then used in a linear mixed regression of self-rated health scores on chronic disease and the confounders marital status, age, and gender. Results: The final estimate for the regression coefficient of chronic disease using our multiply robust model was 7.40. This can be compared to the estimated coefficient from the MSM of 7.39, that from the regression using propensity score adjustment of 7.69, or that from the outcome model of 7.90. Conclusions: Doubly robust estimation can be extended to multiply robust settings using more than two estimators. This allows investigators to obtain one set of results without being forced to agree on one model. Provided there is no further uncontrolled confounding and no bias is introduced, the estimated effect will be unbiased.

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INTERVENING TO REDUCE OBESITY: AN AGENT-BASED MODELING APPROACH TO ASSESS THE EFFICACY OF NETWORK-BASED INTERVENTIONS. *AM El-Sayed, P Scarborough, L Seemann, S Galea (Columbia University, New York, NY, 10032)

Obesity has nearly tripled in the past 30 years in high-income countries. Despite substantial investments, highly efficacious interventions to reduce obesity in the population remain elusive. Recent research has demonstrated that social networks may mediate the spread of obesity in populations, and therefore, may present important opportunities for intervention. We used a stochastic agent-based model parameterized from the 1999 and 2004 Health Surveys for England to assess whether interventions that targeted highly networked individuals could contribute to reducing obesity in populations. Agents were nested within a scale free social network with preferential mixing between demographically similar agents. We compared the effects of implementing obesity mitigation interventions targeted at (a) the most connected individuals in a social network and (b) individuals at random within the social network. We tested two separate simulations, one featuring an evidence-based parameter for the spread of obesity in a network, and another featuring an artificially high parameter, and two interventions, the first "prevented" obesity among 10% of the population at the simulation outset, and the second "treated" obesity among 10% of the obese population each year. Interventions that targeted highly networked individuals did not outperform interventions implemented at random in the population in the simulation featuring the evidence-based network spread parameter. However in the simulation featuring the artificially high parameter, the targeted prevention intervention outperformed the prevention intervention at random, while the treatment intervention implemented at random outperformed the targeted treatment intervention. Although descriptive epidemiologic studies have shown that networks influence the spread of obesity, interventions that target well-connected members in a social network may not reduce obesity any more than interventions that target network members randomly. Further study is needed to determine if network-informed obesity reduction experiments in human populations, informed by the observational data, are warranted.

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ISSUES IN THE REPORTING AND CONDUCT OF INSTRUMENTAL VARIABLE STUDIES: A SYSTEMATIC REVIEW. *Neil M Davies, Richard M Martin, George Davey-Smith, Frank Windmeijer (University of Bristol, United Kingdom)

Background: Instrumental variables, which are associated with exposures and do not directly affect outcomes, can be used to estimate causal effects of exposures in the presence of residual confounding. To interpret if an analysis using instrumental variables is valid, specific information about whether underlying assumptions are met must be presented. In particular, the association of instruments and exposures and associations of instruments and confounding factors. **Methods:** We investigated whether reporting of test statistics in instrumental variables studies was sufficient to prove the validity of the results, we systematically reviewed the epidemiological literature in Embase and Medline for papers containing the terms “instrumental variable” or “instrumental variables”. We extracted the information each study reported about their instrumental variables, including specification tests of important assumptions. **Results:** The search found 586 studies of which 61 were relevant and included. Only 19 studies reported appropriate tests of the associations of instruments and exposure. 29 studies reported the associations between the instrumental variables and observed covariates. 15 studies did not report the method used to estimate the standard errors. Studies using instrumental variables were frequently underpowered, based on samples that were too small to detect the expected effects of an exposure. **Conclusions:** We propose a checklist of information and specification tests that papers using instrumental variables should report. In particular, studies should report partial F-statistics or the reader to know the strength of the instrument variable to predict exposure and, therefore, the power of the instrument to detect effects of exposure.

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AREA-LEVEL SOCIOECONOMIC DISADVANTAGE AND TUBERCULOSIS SEVERITY. E. Oren*, M. Narita, C. Nolan and J. Mayer (University of Washington, Seattle, WA)

Lower socioeconomic status is associated with increased risk of tuberculosis, as well as with diagnostic delays, but the extent to which this reflects an underlying gradient in severity is unknown. We conducted a novel multilevel cohort analysis examining the relationship between socioeconomic disadvantage and disease severity, as measured via sputum smears and chest radiography results. 1,269 incident TB cases reported in King County, WA from 2000-2008 were included, representing 550 census block groups. A composite socioeconomic position (SEP) index was constructed consisting of a standardized z-score combining working class, unemployment, poverty, high school graduation, home value and median income. Multilevel logistic regression models were used to examine area-level fixed and random effects in addition to individual-level variables through merging of census-level, spatial, reporting and chart data. In multivariate models adjusting for individual demographic and socioeconomic measures, as well as area-based demographics, block-group SEP was not significantly associated with greater sputum smear grade, positive smears or more abnormal radiography results. Area-level variables likely explained very little between-block group variance (residual intraclass correlation: ~0). Lower SEP was not significantly associated with greater disease severity in this study cohort after controlling for individual age, race, sex and origin and block-group race, ethnicity and country of origin. These findings suggest that disease severity is not synonymous with delayed diagnosis and contrast with findings in other disease areas. Further research is needed to assess whether the SEP-severity association observed is further confounded by other area-level factors.

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INTRAUTERINE EFFECTS OF MATERNAL SMOKING ON LATER HEALTH OUTCOMES: CAUSAL OR CONFOUNDING? Keyes KM, Davey Smith G, Susser E (Columbia University, New York, NY)

Introduction: The relation between prenatal tobacco exposure and child/adolescent cognition, body mass index [BMI], and hyperactivity remains controversial. Reported associations are countered by sibling studies which suggest substantial family-level confounding. Sibling studies, however, also have limitations, e.g., using only mothers who changed their smoking habits. Another strategy is to compare the associations of maternal and paternal smoking. This strategy is enhanced if applied to populations where family-level confounding is less likely. **Methods:** We used data from the Child Health and Development Study, a population-based historical pregnancy cohort ascertained in 1961-1963 in California. A subsample of these women were prospectively followed >15 years (N=1,752). Maternal and paternal smoking were assessed at three time points by mother report; the three study outcomes were assessed in detail. There was little or no association between smoking and family socioeconomic position. **Results:** For proof of concept, we first documented that birth weight was related to maternal smoking rather than paternal smoking. Next, we found that mid-childhood BMI was associated with maternal ($\beta=0.52$, $p=0.04$) but not paternal smoking at the time of pregnancy, as was hyperactivity ($\beta=0.31$, $p=0.03$). Cognitive performance was not associated with maternal or paternal smoking in either childhood or adolescence. **Discussion:** Unlike sibling studies, these data suggest that prenatal maternal smoking may indeed be related to risk for high BMI and hyperactivity, though not cognitive performance. The interpretation of the results requires systematic examination of the advantages and disadvantages of sibling studies and maternal/paternal comparisons to detect confounding.

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DETECTING AND MEASURING CITATION BIAS: PROVENANCE ANALYSIS. *Eric Lofgren (University of North Carolina, Chapel Hill, NC)

The validity of many models in public health, such as transmission models of infectious diseases or cost-effectiveness models depend in part on their parameters being comprehensive effect estimates. As such, examining how reports of an effect of interest are cited and disseminated in the literature – and if any bias occurs in how different estimates of the same effect are propagated – is of interest. This type of bias can distort perceptions of the “state of the field” for all but the most diligent readers of the literature, and can be difficult to detect. The analysis of scientific papers as networks based on their citations is a well-established technique when evaluating journal impact, or studying an entire field. It is not however, commonly used to examine all papers estimating the same effect measure, as with a meta-analysis. We propose a type of analysis as an extension of a meta-analysis or systematic review termed “provenance analysis”. Papers estimating the same effect and their citations are treated as a directed network, similar to links between webpages. Network centrality measures are then used to examine how heavily cited a given paper is, and if the distribution of citation between papers is unbiased and uniform or if there are some papers which clearly have a larger impact on the landscape. Four such citation networks are examined using two measures – betweenness (how many paths of citations pass through a given paper) and PageRank centrality (how Google ranks webpages). Three model networks, a perfectly balanced network, a network where citation is unbiased but random, and a biased network are used as examples. A fourth network from the infectious disease literature is also analyzed, and the evidence for heavily biased citation within this network is discussed.

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VALIDITY AND EFFICIENCY OF PROSPECTIVE DESIGNS WITH INTENTIONAL MISSING DATA. Anthony Nunes*, Gregory Wellenius, E Andres Houseman, Maureen Phipps, Elizabeth Triche (Women and Infants Hospital, Providence, RI)

Missing data is typically viewed as a nuisance in observational epidemiology. Recent methods may enable epidemiologists to exploit missing data to improve efficiency and reduce subject burden by randomly omitting collection of some measures within individuals and over time. We describe and evaluate designed missing data in scenarios encountered in observational epidemiology. Study designs with unique patterns of designed missing data were compared to cohort designs with complete exposure ascertainment. We use simulated data to quantify bias and relative efficiency in the presence of non-designed missing data due to non-compliance or loss to follow-up. We evaluate the performance of missing data designs in observational data by quantifying the association between smoking and birth weight using multiple prospectively collected missing data designs. Through our simulations, we observed that missing data designs were unbiased relative to the traditional cohort study. Efficiency was dependent on the between time correlation of the true exposure, the within time correlation between the proxy exposure and the true exposure, and the prevalence of non-designed missing data. Missing data designs were more susceptible to a loss of precision in the presence of non-designed missing data. In our analysis of the observational data, designed missing data led to increased precision, increased compliance with study protocols, and no systematic bias in the magnitude of association between smoking and birth weight. In conclusion, epidemiologists should consider missing data designs as a means to improve efficiency, reduce subject burden, and improve compliance.

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VISUALIZING EPIDEMIC MODELS: A CASE AGAINST CONFIDENCE INTERVALS. *Eric Lofgren (University of North Carolina, Chapel Hill, NC)

Increasing computational power has given rise to the increasing popularity, and feasibility of using stochastic epidemic models to study of infectious diseases. These models, which include stochastic compartmental models, network models and agent-based models, are appealing when compared to deterministic models, building their results as the aggregation of individual data, rather than population averages. This approach is more strongly supported for modeling small populations, and the use of stochastic models allows for the examination of scenarios that, while unlikely, are not impossible - model outcomes ignored in their deterministic cousins. Unlike deterministic models however, most stochastic models lack an approachable analytic solution, and instead rely on simulation of the model system many thousands of times, producing a tremendous amount of data. This leaves the researcher with a not inconsiderable challenge in presenting their results. One approach adapts the familiar technique of presenting a mean and 95% confidence interval of the model results, analogous to a statistical model. While it benefits from presenting complex results in a form most epidemiologists are comfortable with, this approach is not without its problems, especially in the interpretation of what these intervals represent. We present the results of an example network model, and discuss how several methods of constructing confidence intervals around the results can lead to differing interpretations, as well as tendency of these methods to ignore scenarios that may be of interest to public health planners. Several alternative approaches are suggested, all of which are based on visualizing model results in their entirety, rather than currently common reductionist techniques.

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RESULTS OF A PILOT SURVEY OF VIRTUAL PORTFOLIO IN A DEGREE NUTRITION COURSE. *Carmen Marin, Shirley Rodriguez (University of Costa Rica, San Jose, Costa Rica)

To investigate the use of Mahara as virtual portfolio software a pilot study was developed to test its use to evaluate learning in a nutrition course. It is an off campus nutrition practice with private or public enterprises. Monitoring, supervision from teachers is expected as feedback to students under schedule. Virtual portfolio was proposed to be useful to improve communication, interaction and feedback between students and teachers. Fulfillment of course objectives was expected. Results show responses of thirty students to a three question questionnaire based on their Mahara experience; 268 open-ended comments were added. Mahara was helpful to develop better communication in 18/30; to reexamine advances of their practice in 9/30 and to discover strengths and weaknesses in their tasks in 12/30. Content analysis of students' comments was done. Categories and dimensions were obtained using Excel 2007. Conditional formatting based in rules and colors was used to show results. Data presentation was user-friendly and show distinctively differences in responses. In contrast, teachers' considered useful only Mahara's blog. Blog option was considered the most important and valuable use of Mahara. Teachers' indicated low time spent in data was not unique to Mahara. Email as an alternative allowed collection, maintenance and restore of student impressions and events which merited inclusion in the blog. Teachers and students considered Mahara and email as equally useful for tasks monitoring and students' preparation of course reports. They agreed Mahara was underutilized as virtual portfolio; other applications already familiar, "best known", "no need to invest time", "easier".

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MULTI-LEVEL FACTOR ANALYSIS (MLFA): A NOVEL METHOD TO CAPTURE ENVIRONMENTS USING INDIVIDUAL-LEVEL DATA WITHOUT AGGREGATION. *E.C. Dunn and K.E. Masyn (Harvard School of Public Health, Boston, MA, 02115).

Epidemiologists increasingly study multi-level phenomenon or how environmental features are associated with individual outcomes. Researchers conducting these studies face one major challenge: how to best measure and create variables that capture both characteristics of individuals and their environments. One variable type – derived variables – has been widely used in multi-level research. Derived variables are created by summarizing the characteristics of individuals within an environment, using means, medians, proportions, or measures of dispersion (e.g., variances). Although popular, the limitations of derived variables are not always articulated. These limitations include: (1) the potential poor quality of the variable; (2) the often lack of attention to variability within the environment; (3) the lack of attention to measurement error, and (4) the tendency towards single-level conceptualizations of environment. Here, we present an illustration of an analytic method called multi-level factor analysis (MLFA) that enables epidemiologists to measure environments using individual-level data. MLFA estimates a measurement model based on the shared variance among groups of items; it does so by decomposing the total sample variance-covariance matrix into within-group (e.g., individual-level) and between-group (e.g., environment-level) matrices, and simultaneously modeling distinct latent factor structures at each level. Our example uses 22 items from 82,186 students within 126 schools in the AddHealth study. We found differences in intraclass correlation coefficients across items, suggesting a model that assumes the same factor structure at each level may be misleading. Using MLFA, we identified five latent factors at the within-level and three factors at the between-level. However, when we compared the MLFA to analyses focusing on school-level means (i.e., used a derived variable), a different latent factor structure emerged in addition to considerable measurement error. These findings illustrate the utility of MLFA methods for epidemiological research.

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MECHANISMS BY WHICH WEIGHT LOSS REDUCES ARTERIAL STIFFNESS. *JN Cooper, E Barinas-Mitchell, JM Buchanich, A Youk, MM Brooks, M Conroy, K Sutton-Tyrrell (University of Pittsburgh, Pittsburgh, PA, 15261)

Aims: Arterial stiffness decreases with weight loss in overweight/obese adults, but the mechanisms by which this occurs are poorly understood. We aimed to elucidate these mechanisms. Methods: We evaluated carotid-femoral (cf) PWV and brachial-ankle (ba) PWV in 344 young normotensive adults (mean age 38 years, 23% male, BMI 25-40 kg/m²) at baseline, 6 and 12 months in a behavioral weight loss intervention. Linear mixed models were used to evaluate associations between weight loss and arterial stiffness and examine the degree to which improvements in obesity-related factors explained these associations. Pattern-mixture models (PMM) using dropout time as a covariate and Markov Chain Monte Carlo multiple imputation were used to evaluate the influence of different missing data assumptions. Results: At 6 months (~7% weight loss) there were significant decreases of 6% in cfPWV ($p < 0.0001$) and 1% in baPWV ($p = 0.049$). At 12 months cfPWV remained significantly reduced ($p = 0.02$). Reduced BMI ($p = 0.01$) remained significantly associated with reduced cfPWV after adjustment for all measured obesity-related factors. Common carotid artery diameter ($p = 0.003$) was associated and heart rate ($p = 0.08$) and mean arterial pressure ($p = 0.07$) were marginally associated longitudinally with cfPWV. Reductions in heart rate ($p < 0.0001$) and C-reactive protein ($p = 0.02$) were associated with reduced baPWV; each removed the significance of the effect of weight loss on baPWV. PMMs revealed several differences between completers and non-completers, but marginal parameter estimates changed little from the original models. Conclusions: Weight loss improves arterial stiffness in overweight and obese young adults. Its effect on baPWV may be explained by concurrent reductions in heart rate and inflammation. Missing data did not appear to bias our findings.

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EPIDEMIOLOGIC METHODS TO ASSESS DISEASE OCCURRENCE IN LONGITUDINAL STUDIES: MEASURES OF CHANGE AND STABILITY. Nelís Soto-Ramírez*, Ali Ziyab, Wilfried Karmaus (University of South Carolina, Columbia, SC, 29208)

In settings in which events re-occur in individuals, there is little agreement on how to measure dynamics and stability in longitudinal studies. The lack of measures of transitions and trajectories (pattern) of disease occurrences hampers epidemiologic research. Traditional measures of disease occurrence do not address the dynamic and stability in disease pattern (e.g. cumulative incidence), or are limited to stable cohorts (incidence), and may lead to wrong conclusions. To illustrate the ability of different approaches of detecting dynamics and stability, we investigated gender differences in the occurrence of asthma (characterized by relapsing-remitting nature) using a population-based study cohort covering the first two decades of life. During adolescence, a gender reversal of asthma occurs from boys to girls. Prevalence, incidence, cumulative incidence, positive transition (change in the individual status from unaffected to affected, independent of whether this is the first occurrence), negative transition, and remission were determined at ages 1-or-2, 4, 10, and 18 years. Configural frequency analyses (CFAs) were employed to investigate typical pattern of asthma and wheezing across age. Latent transition analyses (LTAs) were applied to simultaneously identify classes of asthma/wheezing episodes and to characterize transitions probabilities over time. CFAs identified typical asthma/wheezing patterns (longitudinal phenotypes, stability). Transitions probabilities demonstrated sex-specific transitions differences. In conclusion, classical disease measures provide little information of time-specific changes and do not describe typical pattern. Transition and pattern analyses generate novel information and impose little restrictions on the data (e.g. stable cohort).

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DECOMPRESSION SICKNESS CLAIM RATES AMONG INSURED DIVERS ALERT NETWORK MEMBERS. *S. I. Ranapurwala #\$, P. J. Denoble \$, R. D. Vann \$, P. Vaithyanathan \$ (# University of North Carolina, Chapel Hill, NC, 27599-7435; \$ Divers Alert Network, Durham, NC, 27705)

Decompression sickness (DCS) in recreational diving is a rare injury although known to cause permanent disabilities. Prior studies have yielded inconclusive results to establish DCS incidence due to small study size and select diving populations. Authors collected data of over 200,000 insured Divers Alert Network (DAN) members from 2000-2007 adding-up to 1,304,358 insured member-years and 2,672 DCS claims. DCS claims rate (DCR) was estimated as a proxy for DCS incidence rate. Crude eight-year DCR was 20.5. DCR among males was 22.1(21.1, 23.1) and among females was 17.6(16.4, 18.8). Age (15-80 years) was categorized into 7 groups. Age-adjusted male to female Mantel-Haenszel rate ratio (RR_{mh}) was 1.28(1.19, 1.39), and age-adjusted rate difference (RD_{mh}) was 5.79 (4.34, 7.24). Year 2002 recorded highest age-adjusted DCR of 26.2(20.3, 32.2). Higher percentage of older population (>50 years of age) in the years 2005-2007 decreased the annual incidence of DCS in these years (Beta= -0.12, Wald chi-square=8.17, $p = 0.0043$). Insurance dropout rate was higher among those who had DCS in the first year of insurance compared to those who did not have DCS in the first year insurance ($F = 46.66$, $P = 0.0064$, $Df = 1$). Crude RR of claiming future DCS among these groups from 2004-2007 was similar [0.84(0.49, 1.48)]. Results imply that DCR declined steadily after 40 years of age. Distribution of older population modified annual DCR, which declined progressively after 2002. Males to females difference was greatest between ages 35 and 40, which gradually disappeared till the mid-fifties.

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UTILITY OF COUNTY-LEVEL POVERTY AS A PROXY FOR CENSUS-TRACT POVERTY: DOES THE LEVEL OF THE AREA MEASURE MATTER? Rachel E. Patzer*, PhD, MPH, Matthew J. Page, MPP, Michael R. Kramer, PhD (Emory University, Atlanta, GA)

Introduction: Prior research suggests that census tract poverty measures may be the most sensitive and robust area-based measures of contextual SES. However many health surveillance data sources—including End Stage Renal Disease (ESRD)—only allow identification of patient zip code or county. We assess consistency of area-based poverty measures aggregated at the census tract, zip code and county scale for ESRD patients seeking renal transplantation in Georgia. Methods: We calculated the proportion of the population living below the poverty level in census tracts, zip codes and counties for a cohort of 1,881 ESRD patients referred to the Emory Transplant Center between 2005-2009. We calculated area-based difference in poverty measures as the mean arithmetic difference in poverty measured at tract as compared to either zip code or county. Difference by area scale was compared across strata of county Urban-Rural classifications using analysis of variance to detect statistical differences among groups. Results: A total of 848 census tracts within 122 counties were represented within Georgia. The mean difference between county level and census tract poverty estimates was 0.17% ($\pm 2.7\%$) and between zip code and census tract was -2.0% ($\pm 8.8\%$). County-level estimates in large central metropolitan areas were on average higher than tract level estimates for the same person (0.26% $\pm 2.3\%$) but were lower than tract estimates in non-metro areas (-0.14% $\pm 4.0\%$) ($p < 0.0001$). Similar trends were noted when comparing zip code measures to census tract measures, but mean differences were larger—from 6.0% in large central metro areas to -2.1% in non-metro areas ($p < 0.0001$). Conclusions: County-level, but not zip code-level, poverty estimates were comparable to census-tract measures in a population of ESRD patients seeking renal transplantation in Georgia. Further research is needed to elucidate how these differences could impact measures of effect in epidemiologic studies, particularly for urban and rural areas.

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UV EXPOSURE AND CANCER . *S Lin, D Wheeler, C Abnet (NCI, Bethesda, MD 20850)

Background: Most previous studies of the association between UV exposure and cancer are ecologic studies that lack individual-level confounders and rely on geographic surrogates of exposure (latitude). We examined the association between measured ground-level UV exposure (erythemal dose) and risk of 30 site-specific and total incident cancers in a well-defined prospective cohort with individual-level confounders and accounted for residual spatial autocorrelation. Methods: Residential UV exposure for each individual in the NIH-AARP Diet and Health Study (n=450,936) was generated by linking the US Census tract of baseline residence to the Total Ozone Mapping Spectrometer grid from NASA satellites, averaged for all measured days in July (1979-1992, 1996-2005). We used generalized additive models to estimate odds ratios (OR) and 95% confidence intervals (CI) per 33.7 units of UV exposure (half of interquartile range), adjusting for multiple individual-level confounders, such as smoking, alcohol, exercise, and other dietary and lifestyle characteristics. We also included a smoothed function of the spatial coordinates using penalized thin plate regression splines when there was significant residual spatial correlation. Results: We identified 75,938 incident cancer cases over 10 years of follow-up. Residential UV exposure was associated with increased risk of melanoma (OR 1.08, CI 1.02-1.15) and decreased risk of esophageal squamous cell carcinoma (OR 0.76, CI 0.62-0.93), Non-Hodgkin's lymphoma (OR 0.93, CI 0.88-0.98), and pleural (OR 0.67, CI 0.54-0.82), pancreatic (OR 0.92, CI 0.86-0.99), and prostate (OR 0.97, CI 0.95-0.99) cancers. Residential UV was not associated with total incident cancer (OR 0.99, CI 0.97-1.00). Conclusions: Our novel approach found that residential UV exposure was not associated with risk of total incident cancer but was associated with altered risk of some specific cancer types.

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A NOVEL STATISTICAL APPROACH TO INVESTIGATE GENDER DIFFERENCES IN LUNG CANCER TREATMENT AND SURVIVAL. *Margaret A. Kowski, Ph.D., Thomas J. Mason, Ph.D., Heather G. Stockwell, Sc.D., Getachew Dagne, Ph.D., Tatyana Zhukov, Ph.D. (University of South Florida, St. Petersburg, FL)

The objectives of this research were to test treatment and survival differences between women and men with lung cancer utilizing a unique statistical approach for the overall interaction effect on the outcome. Reporting the "overall effect" for lung cancer gender specific treatment differences or survival has not been demonstrated in the literature to the author's knowledge. Data for 44,863 primary lung cancer cases were collected from eight US state-based cancer registries to investigate three research questions. The lung cancer incidence data included the morphological types of adenocarcinoma, squamous cell, large cell and small cell. Stage, grade, treatment type plus individual characteristics such as gender, age at diagnosis, marital status at diagnosis and race were other variables obtained and included in the statistical models. By convention, main effects and interaction effects are reported in the literature; without the evaluation of the "overall effect" for a variable on the outcome, possible misinterpretations could be made. For example, utilizing the Cox's Proportional Hazards model when the interaction effect of gender and treatment type received was examined, females were at an increased risk for death by as much 29% as compared to males (HR = 1.18, 95% CI 1.09 – 1.29). But when the gender effect on survival was assessed, there was an increase in females survivorship as compared to males by as much as 28% (HR = 0.80, 95% CI 0.72 – 0.97). Also by utilizing this approach, it was shown for early stage disease females versus males with stage I lung cancer were 1.71 times more likely to receive chemotherapy in combination with radiation therapy versus the standard treatment protocol of surgery (OR = 1.71, 95% CI 1.06 – 2.78). Without this unique statistical approach, statistically significant gender differences in the treatment received and survival would not have been demonstrated.

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TYPE 2 DIABETES MELLITUS AND DEMENTIA IN OLDER ADULTS AND THE COMPETING RISK OF MORTALITY. *E.R. Mayeda, M.N. Haan, J. Neuhaus (University of California, San Francisco, San Francisco, CA)

Previous epidemiologic studies evaluating the effect of Type 2 Diabetes (DM2) on incident dementia in older adults have used standard semi-parametric survival analysis techniques (Cox proportional hazards models). DM2 is associated with poorer age-specific survival, and since dementia is often diagnosed later in life than DM2, many people with DM2 may not survive long enough to develop dementia. This is of particular importance in longitudinal studies of older adults, in which mortality significantly contributes to attrition of study populations. Cox models consider people who die during the study period to be censored and assume that censoring is noninformative. However, people who die are no longer at risk of dementia. Accordingly, traditional approaches may lead to biased estimates. Methods that account for the competing risk of mortality may yield more valid effect estimates. We estimated the effect of DM2 on incident dementia and cognitive impairment no dementia (CIND) in a cohort of 1,789 Mexican Americans aged ≥ 60 from the Sacramento Area Latino Study on Aging using a competing risk model to account for the competing risk of mortality. From 1998-2007, there were 158 incident cases of dementia/CIND and 350 deaths. After adjusting for potential confounders, DM2 was associated with an increased risk of dementia/CIND; the competing risk model (HR 2.09, 95% CI 1.47-2.96) yielded a smaller effect estimate than the Cox model (HR 2.44, 95% CI 1.72, 3.47). In older Mexican Americans, DM2 is associated with an increased risk of dementia. Competing risk models yield significantly different effect estimates than traditional Cox models due to the competing risk of mortality.

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COMPARISON OF ADDITIVE AND POLYGENIC SCORE METHODS FOR BREAST CANCER RISK PREDICTION. *L Bessonova (University of California, Irvine, Irvine, CA)

Introduction: In the last 5 years, genome-wide association studies (GWAS) have contributed a wealth of data on single nucleotide polymorphisms (SNPs) that may contribute to breast cancer risk. Association studies were done to evaluate possible links between alleles at particular loci and breast cancer risk. Alone, each of these alleles conferred only a small amount of risk, and often led to underpowered analyses to detect statistically significant associations. Simple additive methods are often used to combine SNP data and analyze SNPs in groups. However, recent studies outline a novel way of combining SNP data into a "polygenic risk" (PR) score. We will compare the ability of the AM and PR scores to predict breast cancer risk in a cohort of California teachers. Methods: We will use the nested case-control data from the California Teachers Study (CTS) to construct AM and PR scores for inflammation tag-SNPs genotyped. AM scores will be constructed using the log-additive model and summing the number of minor alleles across SNPs within inflammation genes (where each locus is coded as 0, 1, or 2, based on the number of copies of minor (i.e., less frequent in controls) allele). PR scores will be constructed using the Nurses' Health Study case-control data available through the Cancer Genetic Markers of Susceptibility (CGEMS) initiative, and applied to the CTS data. We will conduct a sensitivity analysis by constructing ROC curves to compare the abilities of the AM and PR scores to predict breast cancer risk in the CTS case-control study. Implications: The presentation will compare two ways of using SNP data for complex disease risk prediction. We will discuss how genetic variants that alone contribute only a small amount of risk can be combined into a "bigger picture" that would better explain the genetic underpinnings of complex traits.