

## ISEE-448

## WHO IS SENSITIVE TO THE EFFECTS OF PARTICLES ON MORTALITY? A CASE-CROSSOVER ANALYSIS.

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We used a symmetric bi-directional case-crossover study design to identify characteristics that make an individual susceptible to sudden death in response to particulate air pollution exposures (PM10). We identified elderly subjects in Chicago with a history of Medicare reimbursed hospital admissions recorded between 1984 and 1991. These subjects were followed to identify deaths. We analyzed those deaths that occurred between 1988 and 1991. We measured the average PM10 exposure on the day of death and the day before death for each individual and compared it to their PM10 exposure on the days 6-14 days prior to death and 6-14 days following death. We controlled for weather covariates using natural splines with 4 degrees of freedom each.

The baseline effect of PM10 was an 11% increased risk of death per 100ug increase in PM10 (95% CI: 4-18). We found that the effect of PM10 was modified among those with a history of diabetes or myocardial infarction (MI) but not among those with a history of conduction disorders or heart failure. The effect of PM10 exposure on those with a prior diagnosis of diabetes was an increased risk of 25% (95%CI: 8%,44%) compared to 9% (95%CI: 1%,16%) in those without a diabetes diagnosis. The effect on those with a prior diagnosis of MI was an increased risk of 20% (95%CI: 0%,43%) compared to 10% (95%CI: 3%,18%) in those without an MI diagnosis.

We used individuals' zip codes to obtain information on socioeconomic factors from the 1990 census. We found no evidence that the effect of PM10 on mortality was modified by living in a zip code that was in the lowest quartile of median household income or the highest quartile of percentage of residents living in poverty.

## ISEE-449

## CASE-CONTROL STUDIES OF GENE-ENVIRONMENT INTERACTIONS: SAMPLE SIZE, POWER, MISCLASSIFICATION AND THE CASE-ONLY DESIGN ALTERNATIVE

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Studies of disease outcomes and the effects of genotype and of gene-environment interactions play an increasingly important role in epidemiology. Standard case-control and cohort designs are often used to evaluate risk with common genetic polymorphisms, and the variation of risk of exposure by genotype status. Methodological investigations of sample size and power indicate that epidemiological studies require large numbers of subjects to detect even moderate departures of a gene-environment interaction from the assumed null relationship. In addition, misclassification of either exposure status or genotype can further and markedly increase the required sample size. One option for increasing design efficiency is to include more than two categories of exposure or include exposure as a continuous variable. An alternative design has been proposed (the case-only design), in which an odds ratio for exposure and genotype is calculated among cases only. Assuming exposure and genotype are statistically independent and the joint odds ratio for exposure and genotype in the target population is multiplicative, the odds ratio computed among cases only is an unbiased estimate of the multiplicative odds ratio for interaction. Due to the strong assumptions, the case-only design often requires far fewer subjects. However, caution is recommended since validity of sample size calculations in achieving nominal power is compromised when assumptions are violated. An evaluation of the impact of misclassification and the modeling of multiple exposure categories on design of studies of gene-environment interactions, and the strength and limitations of the case-only design will help to identify feasibility of proposed studies.

## ISEE-450

## STUDY GENETIC POLYMORPHISM AND ASSOCIATION TO SOME PATHOLOGIES IN CENTRAL MOLDOVA POPULATION.

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Genetic investigations among farmers occupationally and residentially contacted to pesticide were performed in Central Moldova to evaluate possible genetic risk to some pathologies revealed during the clinical and epidemiological studies in 1991-1995. Polymorphism of ABO, Rhesus, MN, P, and Lewis antigen system, G1m, serum proteins Hp, Tf, Gc, erythrocytic isoenzymes AcP and EsD were studied in 1000 indigenous Moldovans. Allele frequencies, expected and observed distributions of genotypes and heterozygosity were estimated in total population and in groups of farmers with and without similar pathologies. Results were compared with Western Europe Romanic (WER) populations and with Russian of the FSU. Examined population was genetically closed to WER populations. At the same time high level of heterogeneity was found for the Hp, AcP, Gc, P, G1m and Lewis polymorphic loci. Significant decreasing of expected AcPa allele frequency and observed heterozygosity for AcP loci (deficit of ac and cc phenotypes) were established. It was shown that farmers with Tfc allele had approximately 6,5 and 2,6 times higher rate of chronic hepatitis, gastritis and cholecystitis respectively to those with Tf bc allele. It was also established association of AcPa allele with chronic hepatitis, cholecystitis and gastritis. Carriers of this allele suffered by these diseases approximately 3,4, 2,5 and 2 times more often than heterozygous phenotypes (ac, bc). Decreasing of Hp1 gene frequency and increasing Hp 1-1 phenotype were determined in farmers with chronic gastritis. The results showed the existence of relative genetic risk to some diseases in studied population. Thus, genetic factor may be one of competing risk together with environmental pollution and other confounders in this area.

## ISEE-451

## FALLOUT EXPOSURE IN KAZAKHSTAN AND THYROID DISEASE PREVALENCE

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**Purpose:** Villages near the Semipalatinsk Test Site (STS) in Kazakhstan were exposed to fallout from atomic bomb tests at the STS. Childhood radiation exposure is a risk factor for thyroid cancer, and presence of thyroid nodules is a marker for such exposure. We evaluated thyroid disease prevalence among the persons exposed at young ages and estimated the risk of radiation-related thyroid disease in a population with chronic exposure to mixed gamma and beta radiation from fallout.

**Methods:** The study population included 2998 current residents of 8 villages near the STS, <20 years of age at the time of exposure (in 1949, 1951, 1953), who had been present then or had migrated from relatively unaffected areas. Villages were selected based on accessibility and on published dose estimates. Screening included residential history and diet interview, thyroid ultrasound, and FNA biopsy of suspicious nodules with consequent cytopathology. Finger-stick blood samples were assayed for level of thyroid stimulating hormone.

**Results:** Thyroid nodules were detected in 920 participants, of whom 491 were recommended for biopsy; 27 patients had malignant thyroid tumors. Prevalence of nodules was positively and significantly related to exposure. Gamma-ray dose was used as an index of total dose from all sources, which has not yet been determined. Among exposed subjects, published estimates of gamma dose, adjusted on individual basis for a presumed inverse relationship between radiation sensitivity and age at exposure, were positively and significantly associated with disease prevalence.

**Conclusions:** Thyroid disease prevalence is positively associated with radiation exposure from fallout and inversely associated with age at exposure. Biodosimetry results will be used for dose validation.

## ISEE-452

## ENVIRONMENTAL POLLUTANTS AND MENSTRUAL CYCLE LENGTH IN A PROSPECTIVE PREGNANCY COHORT

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This study examined factors that relate to the duration of menstrual cycles. The study sample comprised 102 women aged 18-35 years who participated in a prospective pregnancy study of the New York State Angler Cohort Study (NYSACS). Reproductive histories were taken from women upon enrollment and information on sexual intercourse, menses, sport fish consumption, and other behavioral factors was collected. Recovery corrected values for blood samples taken at baseline are reported without adjustment for the LOD because of low level environmental concentrations.

Prospective menstrual information was gathered from the daily diary cards and was compared with the menstrual cycle information reported at baseline. To account for intra-individual variation in cycle length, the median cycle length was computed. Women were considered to have a normal cycle length if their median value was between 25-35 days (n=61) and a long cycle length if >35 days (n=22). Stepwise discriminant analysis revealed two variables that were significant (p<0.05) when examining cycle length differences between those with normal cycles and those with long cycles: PCB 25 and aldrin. Aldrin showed the stronger statistically significant interaction with cycle length (R<sup>2</sup>=.3156). Further, we employed a multiple stepwise linear regression looking at median cycle length and the environmental toxicants studied. Aldrin (R<sup>2</sup>=0.077), PCB 94 (R<sup>2</sup>=.122), PCB 194 (R<sup>2</sup>=.072), PCB 206 (R<sup>2</sup>=.055) and PCB 134 (R<sup>2</sup>=.037) contributed significantly to the total R<sup>2</sup>=.363. These findings suggest that the data from GLC-electron data capture laboratory methods on persistent low-level toxicants should be interpreted cautiously. We suggest prompt laboratory studies to clarify the reproductive effects of these chemicals.

## ISEE-453

## REFORMULATED GASOLINE CONTAINING 11% MTBE AND SYMPTOMS AMONG COMMUTERS

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Methyl Tertiary-Butyl Ether (MTBE) is added to gasoline to raise oxygen content and reduce tailpipe carbon monoxide emissions. In New Jersey, wintertime oxygenated fuel with a minimum of 2.7% oxygen by weight (15% MTBE by volume) was introduced in 1992, and later in 1995, reformulated fuel was introduced year-round with 2.0% oxygen (11% MTBE). Because many communities reported health complaints during the use of wintertime oxygenated fuel, this study was undertaken to look at symptom reporting and MTBE levels in the cars of commuters using reformulated fuel. Random samples of commuters participated at two different service stations (one in New Jersey where reformulated fuel was in use and one in Pennsylvania where it was not required). A total of 552 people completed questionnaires with demographic information and current health symptoms; of those, 321 allowed cabin MTBE levels to be measured: 18% nondetectable, 28% 1-45ppb, 27% 46-89ppb, and 28% >90ppb (range 0-931 ppb). Participants were asked to rate symptom discomfort from 0-4 for MTBE symptoms (headache, burning sensation of the nose or throat, dizziness or lightheadedness, gastrointestinal upset, sleepiness, cough and difficulty concentrating) and non-MTBE symptoms (fever, diarrhea, sweats or chills and muscle aches). Using multiple regression techniques, only complaints of muscle aches were statistically associated with MTBE levels (p=0.03), but were better correlated with the number of hours spent in the car prior to refueling (p=0.006). Overall symptom reporting was low. We conclude that those symptoms historically attributed to MTBE exposure in fuels were not correlated to automobile cabin MTBE levels.

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