Table of Contents

The following abstracts are from the 2nd year Master of Science and Master of Public Health degree students in our Environmental Health, Occupational and Environmental Medicine, Occupational and Environmental Exposure Sciences, Toxicology, and Environmental and Occupational Health programs.

Comparing Apples to Apples: Developing Tools to Evaluate the Risk of Illness Due to Microbial Contamination of Tree Fruit

Jonathan Nagata
Environmental Health, MS
Preceptor: Scott Meschke

Introduction: Agricultural water, in particular irrigation and cooling water, has been identified as a potential route for introduction of microbial contamination to apples. However, a full understanding of the degree to which microbial contamination is introduced to fruit surfaces is limited by a lack of simple, efficient, and accurate methods to quantify microbial contamination on tree fruit. This study investigates a quick and easy-to-perform assay that incorporates surface elution and defined substrate technology to quantify E. coli on apples. This study aims to evaluate the efficacy of a surface elution method for the enumeration of E. coli on apples, utilizing IDEXX Colilert®-18 and QuantiTtray®/2000.

Methods: Unwaxed apple samples were inoculated with E. coli at low, medium, and high seeding levels, each differing by an order of magnitude. Inoculated apples were massaged in a Whirl-Pak® with 100ml of PBS for 5 minutes. The eluate was mixed with Colilert®-18 substrate and sealed in a QuantiTray®/2000. After incubation at 37o C for 18 hours, an MPN for E. coli was generated for each sample based on the number of positive wells (those that fluoresced under UV light).

Results: Using the surface elution method, the average recovery rate was 11.5% at the lowest inoculation level (~102 E. coli per sample; n=16). At the medium inoculation level (~103 E. coli per sample), the average recovery was 11.2% (n=16). Samples in the highest seeding level (~104 E. coli per sample) had an average recovery of 4.1% (n=10). Apple samples ranged in weight from 112.1g to 198.5g.

Significance: The E. coli enumeration method evaluated in this study will aid researchers in conducting quantitative microbial risk assessment studies on apple handling and processing. Future studies utilizing this method may inform food safety policies to minimize the risk of apple microbial contamination.

Contribution of the In-Vehicle Microenvironment to Ambient Source-Derived Personal NO2 Exposure Concentration in Multi-Ethnic Study of Atherosclerosis and Air Pollution Participants

Tyler Nicholas
Environmental Health, MS
Preceptor: Joel Kaufman

Background: Prior epidemiological and exposure assessment studies used outdoor nitrogen dioxide (NO2) concentrations as a surrogate for personal exposure to traffic-related air pollution (TRAP) but did not explicitly account for exposures within the in-vehicle microenvironment.

Objective: In this study, we assessed the contribution of the in-vehicle microenvironment to ambient source-derived personal NO2 exposure concentration in Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air) participants residing in Winston-Salem, NC (n=46).

Methods: We measured time-integrated microenvironmental (indoor, outdoor, and in-vehicle) and personal NO2 concentrations as surrogates of TRAP; time-location data was measured through a time-location diary. For our primary aim, we calculated microenvironmental contributions to ambient-source derived personal NO2 exposure concentration using a time-weighted model. Secondarily, we evaluated the correlations between microenvironmental NO2 concentrations and personal ambient-source derived NO2 exposure concentration using Pearson correlation coefficients. Our third aim was to predict in-vehicle NO2 concentrations using the time spent in different travel conditions using multiple linear regression.

Results: We found that the indoor and in-vehicle microenvironments were the highest contributors to ambient personal NO2 exposure concentration at 48.3±10.6 and 48.3±11.9%, respectively. Indoor and outdoor NO2 concentrations demonstrated stronger correlations (r=0.68) with ambient personal NO2 exposure concentration than in-vehicle NO2 concentrations (r=0.37). The percent of time-spent in-vehicle for the average trip was the most important predictor of in-vehicle NO2 concentrations, and explained 32% of their variation (R2=0.32).

Conclusions: These preliminary results indicate a high contribution of the in-vehicle microenvironment to personal ambient source-derived NO2 exposure concentration, suggesting the need to account for in-vehicle exposures in MESA Air and other air pollution studies.

Dermal Absorption of Benzo(a)pyrene from Weathered Soil and Implications for Risk Assessment of Contaminated Sites

Trevor Peckham
Environmental Health, MS
Preceptor: John Kissel

Soil cleanup standards and site-specific estimates of risk are based in part on predicted human exposure to soil contaminants. Chemicals in soil may be transferred to the skin surface via dermal contact, and from there, systemically absorbed. Because dermal absorption from soil is generally not rapid, characterization of the rate of uptake is important in predicting absorbed dose. For PAHs, USEPA currently recommends that risk assessments assume the dermal absorption from soils to be 13% of the total applied dose. However, fractional absorption is dependent on contaminant skin load, so dermal absorption is best described in terms of gradient-driven flux not percent absorption. To improve the general understanding of the potential for dermal absorption of PAHs from contaminated soil, experiments were conducted with four soils of varying organic carbon and black carbon content. Weathering of 14C-labeled benzo[a]pyrene (BaP) on the soils was conducted for eight weekly cycles in which soils were hydrated and dried. In vitro experiments were then conducted to investigate the effect of soil characteristics and BaP concentrations on flux into and through skin. Soils were applied to human cadaver epidermis at nominal initial concentrations of 3 and 10 ppm, and soil/skin contact was maintained for 8 or 24 h. Flux through skin was determined by the appearance of 14C-label in the receptor solution, and flux into skin was assessed from 14C-label recovered in skin after swabbing to remove residual soil and BaP. Experiments were also conducted with solvent-deposited BaP at a similar chemical load. Cumulative 24-h fluxes into and through skin from aged soils were lower than from solvent-deposited BaP, reflecting the reduced thermodynamic activity in soil. This research is particularly relevant in light of EPA's draft toxicity profile for BaP, which introduces a dermal cancer slope factor for use in risk assessment of BaP exposures, including exposures from soil.

Analysis of Prevalent Tuberculosis by Using Oral Swab PCR

Rachel Wood
Environmental Health, MS
Preceptor: Gerard Cangelosi

Background: Pulmonary TB is an airborne disease and a significant global health problem. The World Health Organization estimated that in 2012, 8.6 million people developed TB and there were 1.3 million deaths among both HIV positive and negative individuals. Exposure and transmission are associated with close contact, such as in workplaces and households. Locating and treating active TB cases is the best way to control exposure, though a limiting factor in case finding is the need for sputum as a diagnostic sample. This viscous material is difficult to obtain, limits test sensitivity, and drives up test costs. A more consistent sample and one that is easier to work with would enable simpler and cheaper polymerase chain reaction (PCR)-based diagnostics. A non-invasive sample would enable more active strategies for TB case finding, which would be beneficial to public health, clinical trials, and other research.

Aim: To validate PCR analysis of oral swab samples as a non-invasive means to assess pulmonary disease caused by Mycobacterium tuberculosis (MTB).

Methods: In this case-control study, oral swabs collected from humans were analyzed for the presence of MTB DNA using PCR. The case group consisted of 20 recently diagnosed South African TB patients and was compared to a group of 20 healthy control subjects in Seattle, USA who have had no known exposure to TB. Three oral swab samples were collected from each subject on 3 separate days within one week for a total of 60 swab samples per group.

Results: 16 of the 20 tuberculosis patients (80%) yielded at least one PCR-positive swab. In total, 35 of the 60 case samples were positive (58.3%). Healthy control swabs were 100% negative.

Discussion: With further development, oral swab PCR may become a valid alternative to traditional sputum testing as a means to detect active TB. It could improve the cost-effectiveness of TB diagnosis and impact TB epidemiology by facilitating real-time measurement of disease prevalence through active case finding.

Impact of Extreme Heat Events on Emergency Medical Services in King County, WA

Miriam Calkins
Occupational and Environmental Exposure Sciences, MS
Preceptor: Richard Fenske

Climate change is projected to have serious long-term consequences for public health. Numerous studies have established an association between extreme heat events and an increase in the risk of mortality and hospitalizations, but limited research is available on the effect of extreme heat on less severe health outcomes. This research partners with local health officials to define the association between Emergency Medical Service (EMS) calls and extreme heat in King County, WA. These data, along with Emergency Room visits, are thought to contain the next major, previously unexplored, category of health outcomes affected by extreme heat.

There are two primary aims of this research; characterize the relationship between extreme heat and EMS calls in King County and develop tools to assist in integrating the management of climate-related health risks into existing communication and emergency preparedness and response plans. The first aim is approached through a relative risk analysis of EMS calls on extreme heat days compared to non-heat days, as well as through a time-series analysis of the changes in EMS calls per degree increase in apparent temperature (humidex). The second aim is accomplished by translating scientific findings into materials suitable for use by local health officials, including constructing heat-risk maps and assessing the financial impact of heat-related calls on county resources.

The timeframe used for the analyses is May 1- Sept 30, 2007-2012. This seasonally abbreviated timeframe is consistent with our prior modeling, and was selected to exclude the effects of infectious diseases related to cold weather, such as influenza. Meteorological data provided by the UW Dept. of Civil and Environmental Engineering is used to calculate estimates of the apparent temperature (humidex), with extreme heat defined as the average King-county wide humidex for a given day above a specific threshold (the 99th percentile). Risk maps are created by combing the geocoded EMS call data with census tract population data and downscaled 1/16° meteorological data (~4 km x ~7.5 km grid). Publicly available average costs for different types of calls (e.g. Basic Life Support vs. Advanced Life Support) are used to calculate the difference in costs for the calls made on extreme heat days compared to non-extreme heat days. This research is in progress and will be completed by mid-summer.

Sociodemographic Differences in Perceptions of Occupational Safety Climate

Veatasha Dorsey
Occupational and Environmental Exposure Sciences, MS
Preceptor: Noah Seixas

Objective: To examine the impact of race, ethnicity, gender, and nativity (country of birth) on worker perceptions of occupational safety climate.

Methods: A cross-sectional analysis was performed on 182 worker self-report questionnaires administered across six metals processing industries. Questionnaires surveyed occupational safety climate, as measured by the 50-item Nordic Occupational Safety Climate scale (NOSACQ-50). The NOSACQ-50 tool addresses how workers perceive their management and co-worker's commitment to safety through seven subscales (management safety priority, empowerment, justice and worker safety commitment, safety priority/risk-non acceptance, safety communication and trust in safety ability). Respondents were also asked additional demographic information, and self-reported injury experience. Means comparisons (ANOVA) and proportions (Chi-square) testing were performed [STATA IC/12.1] to determine significant differences in associations between sociodemographics and NOSACQ-50 subscales as outcome measures. A combination of existing literature, and proportions testing (Chi-square) identified age, education, and injury experience as potential modifiers, and were adjusted for in multiple regression models.

Results: Occupational safety climate among all sites is relatively high (2.98, ± 0.04, n = 182) with respondents scoring their firm's safety communication the highest, and their co-worker's safety priority the lowest. Mean NOSACQ-50 response of Hispanic (2.83, ± 0.04, n = 39) and foreign-born workers (2.88, ± 0.04, n = 49) score under 3.00, indicating a "low" perception of occupational safety climate. African-American (3.02 ± 0.04, n = 17) workers surveyed experience among highest occupational safety climate perceptions, with Asians (2.99 ± 0.04, n = 15) and Whites (2.96 ± 0.04, n =137) experiencing the lowest among all NOSACQ-50 dimensions. Adjusting for age, education and self-reported injury, Hispanic and foreign-born workers experience statistically significant differences in their safety climate perceptions ($p < 0.001$). Among Hispanic and foreign-born workers who did not graduate high school, their NOSACQ-50 scores averaged 0.22 points less than those finished high school ($p = 0.029$, 95% CI: [-0.418, -0.022]) regardless of their age and injury experience. The findings suggest that ethnicity and nativity characteristics of workers influence perceptions of their firm's safety climate, but that these experiences are modified, either positively or negatively, depending on their educational status. The results also underscore the importance of developing diagnostic tools sensitive enough to capture potential safety barriers experienced by diverse worker populations.

A Comparison of Surface Sampling Techniques for Semi-Volatile Organic Substances in an Electronics Recycling Facility

Clara Jung
Occupational and Environmental Exposure Sciences, MS
Preceptor: John Kissel

Consumer products and building materials contain large numbers of semi-volatile organic compounds (SVOCs), which are consequently routinely detectable in indoor air and dust and in surface wipe samples. Biomarkers of SVOC exposure are commonly found in human blood and urine, and exposures implied by observed biomarker levels often cannot be explained by dietary ingestion and/or inhalation. The apparent missing dose is most likely explained by non-dietary ingestion and/or dermal absorption. However, translation of surface loads to dose remains challenging. Recent studies have determined the presence of an organic layer on indoor surfaces that can serve as a reservoir for SVOCs. Whether SVOCs on surfaces are primarily bound to particulate matter or are dissolved in an oily film might reasonably be expected to influence the mechanism(s) by which humans are exposed to them. The objective of this study is to compare surface sampling by vacuum and solvent-moistened wipes to assess the potential magnitude of the non-particle bound reservoir. Toward that end, an electronic waste recycling facility was selected as a target-rich environment for SVOC surface sampling. Collocated vacuum and wipe samples were collected and analyzed for selected SVOCs including flame retardants and phthalates.

Nanoparticle Deposition in an Air Liquid Interface Cell Culture Exposure Chamber

Sara Lien
Occupational and Environmental Exposure Sciences, MS
Preceptor: Michael Yost

Engineered nanoparticles represent one of the newest and fastest growing areas of exploration in both science and industry. However, the advances in material science also created a new and unknown hazard for those working with these materials. Ongoing nanoparticle toxicity research indicates that nanoparticles are not just smaller particles of the same material. Their small size and high surface area-to-volume ratio allow for unique properties and distinctly different toxicological effects than their larger counterparts. The overall goal of the research is to determine the effect of nanoparticle exposure on lung cells in culture. To accomplish this, an aerosol generation and delivery system is assembled to deliver particles on the nanometer scale via diffusion to the surface of the cells. The goal of this research project is to develop a reliable system of delivering nanoparticles to the cell culture surface. Salt nanoparticles generated by the system will be collected using a polycarbonate filter in place of lung cells and salt concentration will be measured by conductivity when the exposed filter is transferred to water.

1-Nitropyrene and Diesel Particulate Matter Exposures Among Workers in a Metal Mine

Christopher Pyke
Occupational and Environmental Exposure Sciences, MS
Preceptor: Christopher Simpson

Diesel engines are used all over the world in many different applications. Diesel exhaust (DE) is known to cause several adverse health effects, the most notable being lung cancer. Current methods of measuring exposure to DE use elemental carbon (EC) as an exposure surrogate, but EC is also formed by gasoline engines, biomass burning, and other sources. In addition, improved engine technologies have helped to reduce DE emissions which makes accurate measurement in environmental conditions difficult. 1-Nitropyrene (1-NP) is a chemical that is specific to DE, and with new analytical methods, can be detected at much lower concentrations. The goal of this study is to determine the relationship between personal 1-NP, and personal EC exposures, and how well personal exposures can be predicted from area monitoring in a metal mine. Exposures to 1-NP and EC were measured for a cohort of workers in a metal mine for 4 work days during March 2014. 1-NP samples were collected with GS-1 respirable cyclones, and EC was collected using SKC DPM impactors. Personal monitors for both 1-NP and EC were used during the work shift as well as 4 fixed location area monitors which were placed throughout the mine and in the above ground office space. In addition to the personal air monitoring, surveys were given to the miners which asked about the job tasks that the miners were performing throughout the day. The 1-NP filters were analyzed using a 2D HPLC MS/MS method and the EC filters were analyzed using evolved gas analysis (EGA) by thermal-optical analyzer. Improved surrogates such as 1-NP provide a more specific measure of diesel exhaust in situations with alternate sources of EC, as well as low exposure situations. In addition, the use of 1-NP also opens up the possibility of using metabolites of 1-NP as human exposure biomarkers.

Reducing Workers' Exposures to Chemicals and Dust in Nail Salons Using Local Exhaust Ventilation Systems

Nazila Shakibaei
Occupational and Environmental Exposure Sciences, MS
Preceptor: Martin Cohen

Objective: The goal of this study was to evaluate four local exhaust ventilation (LEV) systems to determine their effectiveness at eliminating vapors and dust from the breathing zone of nail salon technicians and their clients.

Methods: Four commercially available LEV systems were evaluated for their capture efficiency. For this purpose, acetone vapor and acrylic nail dust were generated at finger level using realistic work activities in a lab setting and exposures were measured in the technician's breathing zone using real-time air monitoring. The dust was generated by grinding acrylic nails using a standard salon tool and typical position and duration for the work. The technician's breathing zone dust exposures were measured in real-time using a Thermo PDR-1500. To assess the solvent capture efficiency, a bowl containing acetone was placed on the table for 10 minutes to simulate the exposure during the acrylic nail removal process. A MiniRAE 2000 photoionization detector was used to measure the acetone exposure during this process. Each scenario was measured with and without the LEV systems to compare the exposures.

Results: Without controls, the average acetone exposure was between 454 and 540 ppm. The different LEV systems were able to decrease the average exposure by at least 95%. Without controls, the average dust exposures ranged between 12 and 15 ug/m3. The different LEV systems were also able to reduce the dust exposures by 60-70%.

Conclusions: The LEV systems can significantly minimize the workers' and most likely their clients' exposures to particles and organic vapors in nail salons. The ability of the systems to reduce technician's exposures during real use will depend on the systems' usability and capacity.

Characterizing Lead Exposure at a U.S. Coast Guard Indoor Firing Range

Melvin Torres
Occupational and Environmental Exposure Sciences, MS
Preceptor: Martin Cohen

Exposure to airborne and settled dust at firing ranges is a well-known hazard that puts employees at risk for lead poisoning. Nine firearms instructors (FAIs) were studied over a 4-week period while working at a U. S. Coast Guard indoor firing range to determine if their work placed them at risk of overexposure to lead. Blood was collected at the beginning and end of the study to determine if a change in blood lead levels (BLLs) had occurred throughout the study. Questionnaires were also issued to obtain demographic, occupational, & extracurricular activity information to determine any other potential sources of lead exposure. Personal air lead exposures were measured for the instructors during weaponry qualification. To determine the effectiveness of range cleaning, surface wipes of lead dust before and after cleaning were collected from the floor. Mean BLLs from FAIs at baseline was 2.4 μg/dL compared to 2.3 μg/dL at the end of the study, more than 20 times below OSHA's standard of 40 μg/dL. Furthermore, the mean airborne lead was 2.7 μg/m3, also more than 20 times below OSHA's standard of 50 μg/m3. One of our hypotheses was to find a relationship between changes in BLL and mean airborne lead; however, no correlation was found. We also found no relationship between changes in BLL, mean airborne lead, the number of hours per month spent inside the range and the number of lead and jacketed rounds fired at the range. When evaluating the cleaning methods, paired t-tests were used to measure the post- to pre-cleaning differences for weekly and monthly cleaning practices. Statistically significant differences were found ($p<0.01$) for both, though weekly cleaning had lower surface concentrations after cleaning than before cleaning, while monthly cleaning had higher concentrations after cleaning than before. Our results show that a combination of controls, using jacketed bullets instead of lead and a well-functioning ventilation system, can be used to keep air and blood lead levels low. Additionally, although OSHA's surface contamination recommendation level of 21.5 μg/100 cm2 was not reached (highest value was 4.4 μg/100 cm2), we found that weekly cleaning is more effective than monthly cleaning at removing lead from the floor. A more robust cleaning procedure should be implemented to improve removal of lead from the range.

Bioaccessibility of Manganese in Welding Aerosols and Particle Size Distributions of Welding Fume

Christopher Warner
Occupational and Environmental Exposure Sciences, MS
Preceptor: Noah Seixas

Workers chronically exposed to manganese (Mn) are at increased risk for the development of a Parkinsonism syndrome called manganism. A longitudinal cohort study worked with students at a welding training school to investigate the viability of using Mn levels in various biological compartments to indicate exposure to Mn. However, Mn in welding fume exists as part of complex particles, from which it must dissolve in order to pass from the lungs into the blood. Therefore, the usefulness of welding fume exposure as an estimate of Mn dose could be improved by a better understanding of the solubility of Mn-containing fume in the lungs. Solubility depends on the physical characteristics of the particles, but is also a function of the location in the respiratory tract in which they are deposited. That location, in turn, is largely a function of particle size. To improve estimates of the potential systemic dose of Mn from welding fume, we measured particle size distributions and the solubility of Mn in fume from five types of welding (SMAW, GMAW, FCAW-dual shield, and FCAW-inner shield, and GTAW). Particle size distributions were measured by gravimetric analysis of PTFE substrates used in a 10 stage Micro-Orifice Uniform Deposition Impactor. Fume was collected for solubility tests on MCE filters. The filters were leached at 37 C in a simulated alveolar lining fluid (Hatch's solution) for time periods of 1, 24, 48, or 72 hours. Following centrifugal filtering, the rate of dissolution of the Mn from the particles was calculated by comparing, with ICP-MS, the Mn content of the solution and of the remaining filter. Mass median aerodynamic diameters (MMAD) were not statistically different between methods of welding. Average MMAD for each type ranged from 0.88 µm to 1.20 µm. Geometric standard deviation averaged between 3.5 and 4 for all welding methods except GTAW, for which average GSD was 6.56. All five welding methods showed a tendency toward a bimodal distribution, with one mode near 0.4 µm, and a less pronounced mode in the range of 2-5 µm. Forthcoming solubility data will be used in concert with particle size data to estimate the amount of Mn taken up into the bloodstream following inhalation of welding fume.

Glutathione Concentrations in Bronchoalveolar Lavage Fluids Induced by Diesel Exhaust Particles and Responsible Glutathione Transporters in Lungs in Mice

Eunmi Hwang
Toxicology, MS
Preceptor: Terrance Kavanagh

Inhalation of diesel exhaust particles (DEP) has been associated with adverse health effects. The most important and abundant antioxidant in the lung is glutathione (GSH), which can attenuate oxidative stress induced by DEP. GSH is present in the epithelial lining fluid of the lung and can be elevated when exposed to DEP. However, the transporters responsible for exporting GSH in the response to DEP are not well-known. Four candidate GSH transporters are ABCC2 (MRP2), ABCC12, ABCG2 (BCRP), and CFTR (ABCC7)*. In the previous study, it was observed that total GSH in the lung tissues was decreased when exposed to DEP. Thus, I hypothesized that the GSH transporters would be up-regulating in response to DEP in order to increase GSH levels in extracellular space. In this study, glutamate cysteine ligase modifier (GCLM) wild type, heterozygous, and knock-out mice were used. The GCLM is an important subunit of GCL which carries out the first step in GSH synthesis process. The mice were exposed to DEP via intranasal instillation and sacrificed 6 hours after being exposed for acute assessment. Total GSH levels in bronchoalveolar lavage fluids (BALF) were measured using 2, 3-napthalinedicarboxyaldehyde (NDA) which can produce fluorescence resulting from the reaction between GSH and NDA. The candidate GSH transporter genes were analyzed using real-time PCR. This study shows that the total GSH in BALF was slightly increased in the DEP exposure groups. Furthermore, it is observed that ABCC2 (except for GCLM knock-out mice), ABCC12, and ABCG2 were up-regulating when exposed to the DEP. It is not shown that the expression of CFTR was increased in response to the DEP. However, this study supports that CFTR is responsible to induce GSH from the result that basal CFTR expression level in GCLM knock-out mice was highest among three genotypes ($p < 0.05$). In summary, extracellular concentrations of GSH can be induced by DEP, and it is observed that the expression of ABCC, ABCC12, and ABCG2 was acutely increased. *ABCC: ATP-binding cassette (ABC) subfamily C protein ABCG: ATP-binding cassette (ABC) subfamily G protein MRP: Multidrug-associated resistance protein CFTR: Cystic fibrosis transmembrane regulator BCRP: Breast cancer-related protein

Effects of in Utero Diesel Exhaust Exposure on Development of Atherosclerosis in Hyperlipidemic Mice

Rebecca Ticknor
Toxicology, MS
Preceptor: Michael Rosenfeld

Coronary artery disease, commonly manifested as atherosclerosis, is the leading cause of death in western countries. There is significant evidence of the detrimental effect of particulate matter (PM) exposure on cardiovascular morbidity, and diesel exhaust (DE) is a substantial contributor to atmospheric PM levels in urban settings. However, there is little evidence of the impact of in utero exposure to PM and the long-term health effects. It is hypothesized that in utero exposures could permanently affect the health of the fetus through an epigenetic phenomenon termed “fetal programming”, in which fetal exposures alter gene expression through adulthood. The current study aims to elucidate the effect of in utero DE exposure on atherosclerosis development in adulthood in hyperlipidemic Apo E -/- mice. The study consisted of three treatment groups: a control group in which pregnant mice were exposed to filtered air (FA) during pregnancy and the pups were exposed to FA post-birth; a group in which pregnant mice were exposed to DE during pregnancy and the pups were exposed to FA post-birth; and a group in which pregnant mice were exposed to DE during pregnancy and the pups were exposed to DE post-birth until weaning, at which point they were switched back to FA. Thoracic aortas were analyzed for epigenetic changes (e.g. DNA methylation and histone acetylation) in male mice at 4 weeks of age. Histologic analysis of atherosclerotic plaque development and composition in the aortic sinus was conducted at 16 weeks of age. Results are pending and expected in August 2014. A previous pilot study suggests that DE exposure is associated with larger plaque areas in the aortic sinus (FA = 58 mm, DE = 77 mm), however, statistical power was limited due to a small sample size. Negative effects of in utero DE exposure could significantly impact secondary and tertiary healthcare and place a higher emphasis on primary healthcare in the form of public health policy reform and more stringent air pollution control requirements.

Relationship between Payment Schemes and Heat-Related Illness in Washington Agricultural Workers

Kristina Blank
Environmental and Occupational Health, MPH
Preceptor: June Spector

Aim: Previous studies in various sectors have indicated that piece rate payment is associated with increased rates of occupational injuries, compared to hourly pay. The relationship between payment type and heat-related illness (HRI) has not previously been studied. We aimed to examine the relationship between payment type and HRI in agricultural workers. We hypothesized that workers paid piece rates, compared to hourly workers, have an increased risk of engaging in behaviors that enhance their risk of HRI, and of developing HRI symptoms, and that this effect is more pronounced in hotter and more humid work environments.

Methods: A cross-sectional survey was administered to 100 agricultural workers in south central Washington using an audio computer-assisted self-interview instrument during the summer of 2013. Mean daily maximum heat indices over the week (HImax) preceding each participant's survey were computed from hourly temperature and relative humidity data obtained from nearby Washington State University AgWeatherNet weather stations. Associations between piece rate pay and workers' self-reported work effort (hard/very hard versus light/medium), frequency of hydration (less frequently than every 30 min. versus every 30 min. or more frequently), and specific HRI symptoms (heavy sweating and light-headedness versus no specific symptoms), adjusted for potential confounders, were examined using logistic regression.

Key Findings: The maximum HI ranged from 82°F to 90°F (median 85°F). The odds of greater work effort was higher in piece rate compared to hourly workers (adjusted OR= 4.08; 95% CI: 1.20, 13.80), and the odds of drinking water infrequently was lower in piece rate compared to hourly workers (adjusted OR= 0.31; 95% CI: 0.12, 0.79). The odds of experiencing specific HRI symptoms were higher in piece rate compared to hourly workers (adjusted OR= 3.93; 95% CI: 1.32, 11.67). We did not observe significant effect modification by HImax.

Conclusion: Piece rate workers may be at increased risk of HRI compared to hourly workers, and this increased risk may be mediated in part by increased effort at work. Results should be confirmed in larger, longitudinal studies that better address potential confounding by elements of work task and incorporate objective measures of hydration and heat health effects.

Safer Alternatives in Automotive Refinishing

Kristina Blank
Environmental and Occupational Health, MPH
Preceptor: Larry Brown

Background: The purpose of the project was to investigate safer alternatives in the automotive refinishing industry. Safer alternatives are chemical and non-chemical alternatives that replace chemicals or technologies of concern because they have less potential for human health and environmental impacts to employees and the community. Public Health -Seattle & King County strives to replace toxic chemicals or dangerous technologies with safer alternatives in order to protect health and the environment within King County. Specifically, this project attempted to determine if waterborne paint systems and alternative gun cleaners are a viable safer alternative for the Local Hazardous Waste Management Program (LHWMP) to promote to the auto body shops in King County.

Methods: Using an in-depth literature review, key informant interviews, and sampling/analysis of waterborne paint products and wastes, this project identified: the current state of technology for waterborne paint, the attitudes and barriers to using waterborne paints by King County shops, the key hazards of waterborne paints, and the processes of waterborne paint waste stream management.

Key Findings: There are no peer-reviewed occupational or public health studies of waterborne coatings from which to make informed conclusions about their safety. While waterborne paints have a decreased volume of solvents, they also use different, understudied solvents and often contain the same toxic and persistent chemicals that are of concern in solvent-based paints.

Recommendations: LWHMP should not move forward with promoting waterborne paints until more occupational exposure research and a comprehensive risk assessment have been conducted. LHWMP should analyze additional samples of waterborne paint wastes to more fully characterize them and determine how these wastes will designate if their use increases.

Affinity Purification of Bacterial Ribosomal RNA Precursors for Molecular Viability Testing

Herakles Li
Environmental and Occupational Health, MPH
Preceptor: Gerard Cangelosi

Background: Molecular viability testing (MVT) is a previously validated RT-qPCR based assay for rapid, sensitive, and specific detection of viable bacterial pathogens in samples. It is 5- to 10- fold more sensitive than standard DNA-targeted PCR for detecting bacterial pathogens in complex samples. It distinguishes viable from nonviable bacterial cells through ratiometric qPCR analysis of ribosomal RNA precursors (pre-rRNA) after a brief (≤1 generation time) nutritional stimulation. (Weigel et al. 2013) Traditional PCR assays require isolation and purification of the target DNA sequences from lysed cells through a multistep chemical process. Unique features of MVT analysis enabled a novel alternative method for capture of pre-rRNA.

Methods: Utilizing magnetic particle bound universal probes (UP-mag particles) we captured target pre-rRNA from lysed bacterial cells. These universal probes are oligonucleotides which hybridize to a conserved target region of the mature bacterial rRNA. Extraction of the target pre-rRNA for RT-qPCR was accomplished by magnetic separation of the UP-mag particles from the guanidine-lysed bacterial cell matrix.

Results: Capture and detection of pre-rRNA from *Staphyloccus aureus* and *Acinetobacter baumanii* was accomplished with detection levels comparable to the use of commercial RNA purification kits.

Conclusion: Compared to previously reported methods, magnetic capture of bacterial pre-rRNA improves the speed and efficiency of sample preparation for MVT analysis.

Assessment and Outcomes of the Duwamish River Cleanup Coalition Healthy Communities Project

Herakles Li
Environmental and Occupational Health, MPH
Preceptor: Gerard Cangelosi

A recent cumulative health impacts analysis of the 98108 zip code of the South Park and Georgetown neighborhoods of Seattle in the lower Duwamish River Valley found consistently lower health outcomes than the rest of the city. In order to address these underlying causes and improve the health of these communities the Duwamish River Cleanup Coalition (DRCC) launched the Healthy Communities Project. This initiative, funded by the EPA's Community Action for a Renewed Environment (CARE) grant program, awarded a series of smaller grants to local organizations to fund projects aimed at addressing some of the issues identified by the community as priority concerns. These projects, such as urban forest restoration, runoff and trash reduction, and home gardens, were designed to improve the environmental health of the 98108 zip code and empower local residents.

The roles of this practicum were to aid in the progress and analyze the efficacy of the DRCC Healthy Communities Project through: communication and coordination with the grantee organizations, site visits and interview of grantee projects, and evaluation of measurable improvements made to the overall environmental health of the lower Duwamish Valley communities. This practicum found that the Healthy Communities project was successful in reducing health risks of residents in the lower Duwamish River Valley on several indicators such as waste removed, trees planted, community members engaged, and families fed. While funding for the projects was ended after the 2013 calendar year, applications are being written for future funding and the DRCC continues to advocate for and work towards improving health outcomes in South Park and Georgetown.

Occupation and Computed Tomography Measurements of Chronic Obstructive Pulmonary Disease

Stanley Kimball
Occupational and Environmental Medicine, MPH
Preceptor: Sverre Vedal

Introduction: Occupational exposures have been linked to the development of chronic obstructive pulmonary disease (COPD). However, there are no studies reporting associations between occupation and computed tomography (CT) measures of COPD, such as airway wall thickness and lung density.

Methods: We analyzed data from a cross-sectional hospital and population-based study of current and past smokers conducted in Bergen, Norway between 2003 and 2005. 951 subjects completed an occupational questionnaire and underwent Chest CTs to evaluate lung density (% low attenuation areas - %LAA950) and airway wall thickness (AWT) as a measure of chronic bronchitis. An industrial hygienist derived a categorical dust exposure measure, 0 (none), 1 (low), 2 (medium) or 3 (high), based on job title and work type. We assessed the relationship between dust exposure and CT measures using multivariable regression, adjusted for age, sex, smoking and CT volume (airway obstruction-adjusted CT volume).

Results: When compared to no dust exposure, a dose response relationship remained for the low (N=308) and medium (N=129) categories, corresponding to 20% (0.99%, 46%) and 54% (18%, 102%) higher %LAA950, respectively, after adjusting for covariates. This suggests more emphysematous change, though only significant in the medium dust exposure. Occupations in the high (N=50) category showed a 33% (0.92%, 93%) higher %LAA950, though not statistically significant. When testing the association between dust exposure and AWT, the other COPD phenotype, the high dust category showed 0.092mm (.002, .181) greater AWT compared to no dust exposure, after adjusting for covariates.

Conclusion: Dust exposure, as defined by occupational title and work type, was associated with more areas of low lung density, reflecting more lung emphysema. Lack of power in the high dust category and perhaps precision in the low dust exposure estimate limited the study to detect a statistically significant dose-response relationship through all levels of dust exposure. The association of high dust exposure with airway wall thickness suggests that there is an association with chronic bronchitis at high dust levels only. Future studies using a job exposure matrix may allow more precise exposure estimation and quantification of the associations with CT measures of COPD.

Is there a Golden Hour in Combat Casualty Evacuation?

Scott Robinson
Occupational and Environmental Medicine, MPH
Preceptor: Joel Kaufman

Background: In robust civilian Emergency Medical Services trauma transport and treatment systems, large studies are showing that there is no relationship between relative increases in total pre-hospital time and mortality. Prior periods of research, notably that done in the late 1960s and 1970s showed a significant association between time and mortality. This relationship became popularly known as “The Golden Hour”. The new surprising and robust results contrast significantly with the historical data showing a relationship that drove the development of rapid response EMS systems in our nation and across the globe.

Purpose: The purpose of this study is to test the hypothesis that there is a relationship between total out of hospital time and mortality in the US military combat casualty care system, especially whether there is a “Golden Hour”. We will do this using data from the main data collection on casualty care and outcome within the military, the Joint Theater Trauma Registry, with the secondary aim of informing improvements to this data collection system.

Methods: The Joint Theater Trauma Registry collects data primarily at the point of surgical care on every patient evacuated to and treated at a theater surgical hospital. A data set of all patients with a known value for total pre-hospital time was requested and provided to the researchers. Data was available on evacuations occurring between 2003 to early 2012. Using logistic regression, adjusted odds ratios were calculated for the association of total out of hospital time and mortality. We also report adjusted odds ratios and prevalences for multiple other descriptors of interest.

Results: The Odds Ratio for association between total out of hospital time and mortality was consistently less than one. Using a time variable grouped by 20 minute intervals, we determined an odds ratio of 0.890 with a 95% CI of 0.823 to 0.963 and a p value of 0.004. In a sensitivity analysis, this relationship remained strong for the Iraq theater, but disappeared for the Afghan theater, with a OR 1.013168 and p value of 0.832. Other findings of interest were a consistent protective factor for blunt injury as compared to penetrating, and a strong increase in mortality for Afghan military (OR for mortality 2.91, p value < 0.001) that was not true of Iraqi military when compared to the US Military.

Conclusion: There is a negative association between time and mortality in the JTTR dataset for casualties evacuated in Iraq that contrasts significantly with a finding of no association between time and mortality in Afghanistan.

Vanadium in Fine Particulate Matter and its Association with Blood Pressure in the Multi-Ethnic Study of Atherosclerosis Cohort

Reema Sikka
Occupational and Environmental Medicine, MPH
Preceptor: Sverre Vedal

Background: Associations between estimates of long-term population exposure to fine airborne particulate matter (PM2.5) and cardiovascular endpoints, especially mortality, have now been reported in several population cohort studies. More recently, several studies have linked traffic-related pollutants with adverse cardiovascular outcomes. The components of PM2.5 that are primarily responsible for the cardiovascular effects of PM2.5 exposure have not been identified. Although a few studies have linked trace elements such as copper, zinc, and nickel with elevations in blood pressure, the effects of ambient vanadium on blood pressure are unknown. The purpose of this study is to determine if estimated PM2.5 vanadium exposure is associated with systolic and diastolic blood pressure.

Methods: The primary outcomes were cross-sectional measurements in 2005-2007 of seated systolic and diastolic blood pressure from 5517 participants aged 45-84 in the Multi-Ethnic Study for Atherosclerosis (MESA). Individual-level ambient exposure to vanadium was estimated using existing geospatial modeling predictions developed by MESA Air and the National Particle Components Toxicity (NPACT) Initiative. Incrementally richer regression models were used to adjust for the following covariates: age, gender, race/ethnicity, educational level, income, smoking status, alcohol use, blood lipids, body mass index, blood glucose, city region, and antihypertensive usage. Sensitivity analyses were conducted by restricting analysis to those not taking antihypertensive medications, and to those who had lived at one address since 1980. Additionally, some of the models included adjustment variables for other PM2.5 metals.

Results: In our primary model with adjustment for city region, mean systolic blood pressure (SBP) increased by 0.4 mm Hg per interquartile range (IQR) increase in vanadium (V) concentration, 95% CI [-1.1, 1.8]. There was no effect on mean diastolic blood pressure (DBP). The effect estimate for SBP was in the negative direction when there was no adjustment for city region. The effect estimates for SBP and DBP became larger (1.4 mm Hg [-0.5, 3.3] and 1.1 mm Hg [0.1, 2.0]), respectively, in city-adjusted analyses after excluding study subjects taking antihypertensive medications. The findings were somewhat sensitive to adjustment for other PM2.5 metals, depending on the metal.

Conclusion: These results indicate that exposure to vanadium may be associated with increases in both SBP and DBP. Because the findings were primarily seen in those not taking antihypertensive medications and were somewhat model-dependent, these findings need to be interpreted cautiously and replicated in other cohorts. Investigating potential effects of other PM2.5 components will also be of interest.

BEBTEH stands for Biostatistics, Epidemiologic and Bioinformatics Training in Environmental Health

The following abstracts are from PhD students whose research are funded by this training grant. The National Institute of Environmental Health Sciences federal training grant (ES015459) supports predoctoral and postdoctoral trainees from the Departments of Biostatistics, Environmental and Occupational Health Sciences, Epidemiology, and Genome Sciences who are pursuing quantitative training with environmental health science applications.

Pollutant Variability and Correlations in Mobile Monitoring Data as Compared to Central Site Monitoring

Elena Austin
Environmental Health, Post Doctoral Student
Preceptor: Michael Yost

Background: Mobile monitoring provides detailed temporal and spatial information on the distribution of traffic related pollutants in an urban environment. Spatiotemporal gradients are expected within the urban environment, however, the magnitude of these gradients as well as spatial and temporal distributions in the correlations between pollutants are not well understood. In this poster, the distribution and correlations of pollutants measured on the road are compared to the central site values in order to assess the added value of detailed on-road measurements.

Methods: The University of Washington mobile monitoring platform sampled 16 pollutants in 10 second intervals over 2-week periods in summer and winter 2012 in Baltimore, MD. Over the same time period, hourly AQS values of NO2, NOx, CO, O3 and PM2.5 were obtained from the STN monitoring site in Baltimore County, Md.

Results: The daily variability in the mobile measurements was much higher across all pollutants, and showed distinctive spatial structure. The correlation between NO2 and O3 was significantly different between the central site location and the mobile monitoring data. Season and local traffic density were found to modify the NO2 and O3 correlation. Daily median concentrations of O3 and PM2.5 were comparable between the central site and mobile monitoring data.

Conclusion: There are important spatial differences in the variability of pollutants and correlations between traffic related pollutants that are not captured by central monitoring. Developing a monitoring network that captures these important spatial differences may improve our understanding of the public health impacts of air pollution exposure.

Pathogenesis of Mortalin in Manganese-Induced Parkinsonism

Travis Cook
Toxicology, PhD
Preceptors: David Eaton & Jing Zhang

Parkinsonism (PS) is a movement disorder typically characterized by tremor, bradykinesia, rigidity, and postural instability. The number one cause of symptoms of PS is Parkinson disease (PD), although many other atypical parkinsonisms also exist, including those resulting from exposure to environmental agents such as pesticides and heavy metals. A particular metal of interest is manganese (Mn), which has long been known to be causative of acute onset PS termed manganism upon high intensity inhalation exposures for even short periods of time. More recent evidence indicates that some modern occupational populations chronically exposed to Mn experience a high prevalence of PS symptoms, demonstrating that more moderate exposures over long periods of time are also capable of inducing clinically significant outcomes. Persons occupationally exposed to modest Mn levels are of value in assessing potential risk to the greater population at large, who may be chronically exposed to low-level Mn in drinking water, ambient air, and/or food. Widespread low-level environmental exposure combined with the potential for neurotoxic effects therefore make the question of Mn-induced parkinsonism one of great public health concern, including increased risk of developing idiopathic PD in this population.

Mortalin, a 75-kDa mitochondrial heat shock protein heavily involved in stress response, has been implicated mechanistically in a wide array of neurological diseases, including PD. The role of mortalin in PD was initially identified in our laboratory several years ago in a study using a proteomic approach which found the protein to be decreased in the mitochondrial fraction of brain tissue isolated from PD patients as compared to similar tissue isolated from age-matched controls. A similar follow-up study found brain tissue levels of mortalin protein decreased as a function of disease severity, and several groups have reported a similar phenomenon in various PD model systems.

In the studies described here, we test the hypothesis that brain mortalin protein levels are modulated by Mn exposure. To date, we have discovered that in vitro Mn treatment of mouse primary astroglial cultures does indeed depress the quantity of mortalin in this cell type, and that this observation is not regulated at the transcriptional level. We have further found endpoints of neuronal health are adversely affected when co-cultured with astrocytes which have had mortalin expression knocked-down, perhaps related to perturbations of intracellular calcium levels resulting from elevated endoplasmic reticulum stress. To follow-up on these findings, the implications of Mn exposure on human brain mortalin levels are currently being studied on post-mortem tissue obtained from a cohort comprised of individuals who worked in Mn and non-Mn mines.

Characterizing the Effects of Lead on In Vitro and In Vivo Adult Hippocampal Neurogenesis

Anna Engstrom
Toxicology, PhD
Preceptors: Zhengui Xia

Adult neurogenesis is a process that influences hippocampal-dependent learning and memory through the generation and functional integration of adult-born neurons in the subgranular zone (SGZ) of the dentate gyrus (DG) in the hippocampus. The hippocampus is one of the earliest affected brain regions in Alzheimer's Disease (AD), and hippocampal neurogenesis can be modulated by physiological and pathological factors. Thus, the goal of this study was to assess how exposure to heavy metals, such as lead, may perturb adult neurogenesis and subsequently contribute to the cognitive decline associated with neurodegenerative diseases like AD.

Using adult neural progenitor/stem cells (aNPSCs) isolated from adult male C57BL/6J mice, I found that low concentrations (≤ 0.02ppm) of lead (II) acetate significantly decrease SGZ-aNPSC total cell number in vitro, with an EC50 of ~ 0.04 ppm. A significant increase in apoptosis and decrease in cell proliferation occurs, starting at 0.02 ppm and 0.04 ppm lead, respectively. To assess whether these effects are mediated through oxidative stress or activation of mitogen-activated protein kinase (MAPK) signaling pathways, I pre-treated SGZ-aNPSCs with either N-acetyl-cysteine (NAC, a precursor for glutathione), a broad c-Jun N-terminal kinase (JNK) inhibitor, or a p38 inhibitor. I found that pre-treatment with NAC and the JNK and p38 inhibitors significantly attenuated the decrease in total cell number and increase in apoptosis induced by 0.01 ppm lead.

In addition, I found that low lead concentrations (≤ 0.02 ppm) significantly decrease the percent of β-III tubulin+ (an immature neuron marker) cells and significantly decrease β-III tubulin+ neurite length, suggesting that lead impairs the spontaneous differentiation of adult SGZ-aNPSCs in vitro. In comparison, the median blood lead level for 1-5 year olds in the U.S. was 1.5 μg/dL (0.012 ppm) from 2009-2010, and studies using a developmental lead exposure paradigm to model human lead exposure report hippocampal lead concentrations of 246 ng/g tissue (0.246 ppm). Thus, my data suggests that environmentally relevant lead concentrations may lead to deficits in hippocampal neurogenesis.

Identification and Description of On-Road Emission Sources Using Mobile Monitoring Data

Jonathan Fintzi
Biostatistics, PhD
Preceptor: Lianne Sheppard

Identification and description of on-road emission sources in air pollution data collected using a mobile monitoring platform presents unique methodological challenges. Estimation of physically meaningful multivariate pollutant profiles is complicated by spatio-temporal sparsity, extreme non-stationarity, and inability to separate local, spatial, and temporal sources of variability. Interpretation of principal components anlaysis (PCA) of the complete dataset is difficult because the results are largely driven by spikes in the time series of the measured pollutants, but the components are interpreted as averages over the entire sampled space. We propose an analysis of a highly active subset of the data, admitting observations having two or more instruments reporting measurements that are outside of two standard deviations of the trimmed mean. PCA with varimax rotation is performed as a descriptive technique within this subset of the data to estimate multivariate pollutant profiles. Interpretation is aided by appealing to the video record from platform dashboard camera.

Estimation of the Mutation-Rate Parameter Using Sequence Data

Hojun Hwang
Biostatistics, PhD
Preceptor: Sharon Browning

Random mutation is a fundamental source of genetic variation in populations that may itself be affected by changes in environmental exposures. However, many earlier efforts to estimate the human rate of mutation have depended on indirect approaches based on observations of differential phenotypes. In this study, we investigate the viability of mutation-rate estimation using sequence data informed by patterns of genetic segments inherited identically by descent (IBD). The number of mutations accrued along a given IBD segment is modeled by a Poisson distribution conditional on the number of generations until the most recent common ancestor (MRCA), while the conditional density of pairwise times to MRCA given the lengths of IBD segments is estimated using the demographic history. Ten sets of sequence data for 2,000 individuals were simulated using MACS to match the demographic history, rates of heterozygosity, linkage disequilibrium, and IBD rates for chromosome 20 from the UK10K project. A constant mutation rate of 1.38 x 10^-8 and recombination rate of 1 cM per 1 Mb were used. Preliminary results are provided in this poster.

Spatial and Spatiotemporal Modeling of Long-Term PM10 Concentrations in the United States, 1990-2010

Joshua Keller
Biostatistics, PhD
Preceptor: Lianne Sheppard

Long-term exposure to particulate matter (PM10) has been associated with multiple adverse health outcomes. We compare spatial and spatiotemporal prediction models for predicting annual average PM10 concentrations across the contiguous United States from 1990 through 2010. Both approaches combine dimension reduction of a large geographic covariate dataset with spatial smoothing to borrow strength between neighboring observations. The spatiotemporal models use estimated time trends to borrow information between years, while the spatial models are fit separately for each year. Cross-validation R2 ranged from 0.41 to 0.63 for the spatial models and from 0.37 to 0.59 for the spatiotemporal models. For years with more data, the spatial models performed better, while the spatiotemporal models performed better in years with less data. Predictions from these approaches will be used in health-effect analyses across the two-decade period.

Insights into the Impact of Preferential Sampling on Health Analysis Using Data from Two Different National Monitoring Networks

Adel Lee
Biostatistics, Post Doctoral Student
Preceptor: Lianne Sheppard

Measurements of air pollution exposures are rarely available for participants in cohort studies. Consequently, when studying associations between air pollution and health outcomes, one typically has to rely on an existing network of spatially misaligned monitors to predict concentrations at subject locations. If the existing network was designed, for example, to preferentially sample areas with higher pollution levels, the network design may impact exposure predictions and ultimately the validity of the health effect estimate.

We use monitoring data from two regulatory networks and health data from the Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air) to study the association between components of fine particulate matter (PM 2.5) and carotid intima-media thickness (CIMT), a subclinical measure of atherosclerosis. The monitoring data was collected from the Interagency Monitoring for Protected Visual Environments (IMPROVE) network and the Chemical Speciation Network (CSN). The CSN and IMPROVE networks are intended to monitor air quality in urban and rural areas, respectively. These networks are preferentially sampled in areas where the components we study have high concentrations (CSN) and low concentrations (IMPROVE).

We investigate the impact of this preferential sampling by comparing the estimated health effect using monitoring data from the national network (CSN and IMPROVE) and from IMPROVE only. We find that there is a large difference in the sizes of the health effect estimates for the IMPROVE and national networks. Additionally, the health effect estimates are negative for the IMPROVE network and positive for the national network.

We use simulation studies to investigate whether this discrepancy in health analysis results is driven by preferential sampling. We find that placing monitors in areas with low concentrations could indeed result in negatively biased health effect estimates. This bias is in part driven by the spatial misalignment between the subject locations and the monitor locations that are preferentially sampled in areas with high and low concentrations, respectively. By designing our simulation study to match the settings for the IMPROVE network, we offer some insight into the differences in the health analysis results for this network compared to the national network.

Second Primary Cancers among Female Breast Cancer Survivors by Hormone Receptor Status from 1992-2010

Sabah Quraishi
Epidemiology, PhD
Preceptor: Christopher Li

Background: Incidence rates of second primary cancers following a first primary breast cancer may differ according to hormone receptor type given differences in etiology and treatment across estrogen (ER) and progesterone (PR) receptor subtypes. These differences have not been well characterized, thus the purpose of this study was to compare rates of second primary cancers across breast cancer subtypes.

Methods: Rates of second primary cancers among those with a first primary for ER+/PR+, ER+/PR-, and ER-/PR- breast cancer were extracted from the Surveillance, Epidemiology, and End Results Program (SEER) population-based cancer registry for 1992-2010. Standardized Incidence Ratios (SIRs) were calculated by cancer site.

Findings: Statistically significant SIRs of 1.2, 1.2, and 1.5 for any second primary cancer and 1.4, 1.3, and 2.2 for 2nd primary breast cancer were observed following ER+/PR+, ER+/PR-, and ER-/PR-, respectively. Myeloid and monocytic leukemia was among the highest increased risk (ER+/PR+, 2.0; ER+/PR-, 1.5; ER-/PR-, 3.4). Also observed were 1.6, 1.3, and 1.4 fold risk for endometrial and 0.5, 0.6, and 0.6 decreased risk for cervical cancers with ER+/PR+, ER+/PR-, and ER-/PR-, respectively. Thyroid cancers had increased risks with all subtypes (ER+/PR+, 1.4; ER-/PR-, 1.3), but was not significant for ER+/PR-. While certain second primary cancers have similar risks across subtypes, others vary. Ovarian cancer risk was increased with ER-/PR- (SIR=2.1). A 1.7 fold risk for bone and joint cancers was observed with ER+/PR+. Stomach cancer had a 1.4 fold risk with ER+/PR-. Among lymphatic and hematopoietic cancers, decreased risks of 0.6 for lymphocytic leukemia and 0.7 for Hodgkin lymphoma were observed with ER-/PR- and ER+/PR+, respectively.

Summary: This overview of second primary cancers among breast cancer survivors by hormone receptor type provides some clues as to what subsequent cancers women are at increased or decreased risk for following their first breast cancer. Some of the patterns seen among breast cancer survivors may provide additional insights as to shared environmental or other risk factors for subsequent cancers. Additional studies examining how risk factors and treatments influence these rates may provide clinically useful information that could impact management and follow-up of the growing population of breast cancer survivors.

Decoupling Regional and Local Sources in Mobile Monitoring of Air Pollutants

Erin Riley
Environmental Health, Post Doctoral Student
Preceptor: Christopher Simpson

A mobile monitoring platform developed by the University of Washington Center for Clean Air Research was deployed during summer and winter seasons of 2012 in Baltimore, MD to intensively sample 43 intersections dispersed throughout the metropolitan area. Sampling was performed during a two week period in the afternoons, with 1/3 of the total number of sites visited on any given day. One objective of this campaign is to determine if the mixtures and quantities of traffic related air pollutants varies spatially, and if those relationships are preserved across seasons. However, air pollutant concentrations for ozone, ultrafine particles, and PM2.5 are to a large extent impacted by regional pollutant levels, which change throughout the afternoon and across days. Decoupling local from regional sources is a central component to the analysis of any mobile platform data. Towards these ends a duplicate suite of instruments was deployed at a fixed location. However, the fixed site is also prone to detect local sources and, more importantly, the changes in pollutant concentrations owing to changes in meterological conditions do not necessarily occur across the city simultaneously or with the same magnitude. Herein we develop a methodology for decoupling the local pollutant concentrations of interest from the regional background, as well as identifying pollutants significantly impacted by regional sources.

Mobile and fixed site data are compared for the winter campaign in Baltimore, and the correlations between them are assessed. Anomalies in the data are examined to determine if they are correlated with meteorological events. The spatio-temporal relationship of these events is investigated using meteorological data collected by weather underground monitors to assess any time differences in the response of the fixed site and mobile site. A model is then developed for the regional background, and an investigation of the degree to which different pollutants manifest regional concentrations is made. This work advances the current state of the art in interpretation and pre-processing of mobile monitoring data for spatial analyses across a city over a two week time period.

Cerebrospinal Fluid α-Synuclein Predicts Cognitive Decline in Parkinson's Disease Progression in the DATATOP Cohort

Tessandra Stewart
Pathology, PhD
Preceptor: Jing Zhang

A majority of Parkinson's disease patients develop both cognitive and motor impairment, and biomarkers for progression are urgently needed. Although α-synuclein is altered in cerebrospinal fluid of Parkinson's patients, it is not known whether it predicts motor or cognitive deterioration. We examined clinical data and α-synuclein in >300 unmedicated Parkinson's patients who participated in the DATATOP study, with up to 8 years of follow up. Longitudinal measures of motor and cognitive function were studied before (Phase I) and during (Phase II) levodopa therapy; cerebrospinal fluid was collected at the beginning of each Phase. Correlations and linear mixed models were used to assess α-synuclein association with disease severity, and prediction of progression in the subsequent follow-up period. Despite decreasing α-synuclein (Phase I to Phase II change of -0.05 ± 0.21 log-transformed values, $p<0.001$), no correlations were observed between α-synuclein and motor symptoms. Longitudinally, lower α-synuclein predicted better preservation of cognitive function by several measures (Selective Reminding Test-Total Recall α-synuclein x time interaction effect coefficient -0.12, $p = 0.037$ and Delayed Recall -0.05, $p=0.002$; New Dot Test -0.03, $p=0.002$). Thus, α-synuclein, while not clinically useful for motor progression, might predict cognitive decline, and future longitudinal studies should include this outcome for further validation.

A National Prediction Model Based on Universal Kriging and Land-Use Regression Using Satellite-Based NO2 Measurements for Epidemiological Analysis of Long-Term Health Effects

Michael Young
Epidemiology, PhD
Preceptor: Joel Kaufman

Introduction: Epidemiological studies increasingly rely on exposure prediction models. Satellite data can improve performance for NO2 prediction using land-use regression (LUR). Predictions may especially be improved in regions with sparse monitoring data. Satellite data have not been evaluated in a combined LUR/spatial smoothing context.

Methods: We performed regionalized national land-use regression universal kriging on year 2006 annual average NO2 measurements from EPA monitoring sites in the contiguous US. This model combined spatial smoothing of monitor data and regression on geographic covariates such as distance to roadway. Partial least squares regression was used to select orthogonal components of 366 geographic covariates. Model performance was estimated using 20-fold cross-validation (CV) with both random CV groups as well as spatially clustered CV groups selected using a k-means algorithm. Ground-level NO2 was estimated from satellite OMI tropospheric NO2 column data via the GEOS-Chem model. These gridded satellite estimates were used as an additional input to the LUR-kriging model, and added performance was assessed by comparing cross-validation R2 values (R2cv) in models with and without the satellite NO2 data.

Results: R2cv using random CV groups were 0.86 for the model with satellite data and 0.85 for the model without satellite data. R2cv values using spatially clustered CV groups were 0.73 for the model with satellite data and 0.55 for the model without satellite data. For comparison, a prior national NO2 LUR (Novotny, 2011) reported an R2 of 0.78 including satellite data vs. 0.68 without satellite data.

Conclusions: Random cross-validation may not capture reduced performance far from monitoring locations, especially in the context of spatial smoothing. Clustered cross-validation may better estimate performance in unmonitored areas, and this method demonstrates model improvements from satellite data not shown by traditional cross-validation.

Genome-Wide Haplotypic Test Identifies Novel LDL-Associated Locus

Qian Zhang
Biostatistics, PhD
Preceptor: Sharon Browning

We performed genome-wide tests for association between haplotype clusters and each of 9 metabolic traits in a cohort of 5 402 Northern Finnish individuals genotyped for 330 000 single nucleotide polymorphisms. The metabolic traits were body mass index, C-reactive protein, diastolic blood pressure, glucose, high-density lipoprotein (HDL), insulin, low-density lipoprotein (LDL), systolic blood pressure, and triglycerides. Haplotype clusters were determined using Beagle. There were LDL-associated clusters in the chromosome 4q13.3-q21.1 region containing the albumin (ALB) and platelet factor 4 (PF4) genes. This region has not been associated with LDL in prior genome-wide association studies. The most significant haplotype cluster in this region was associated with 0.488 mmol/L higher LDL (95% CI: 0.361 - 0.615 mmol/L, p-value: 6.4 x 10-14). We also observed three previously reported associations: Chromosome 16q13 with HDL, chromosome 1p32.3-p32.2 with LDL, and chromosome 19q13.31-q13.32 with LDL. The chromosome 1 and chromosome 4 LDL associations do not reach genome-wide significance in single-marker analyses of these data, illustrating the power of haplotypic association testing.