



Samantha Alfonso

HUGEN

III-12

Universal Tumor Screening for Lynch Syndrome: Investigation of Patient Reported Distress Levels

Lynch syndrome is a hereditary cancer predisposition caused by pathogenic variants in mismatch repair (MMR) genes that confers an increased lifetime risk of colorectal cancer up to 70%. Many healthcare facilities have chosen to employ universal tumor screening (UTS) of colorectal tumors through pathologic microsatellite instability (MSI) testing or immunohistochemistry (IHC) staining for MMR protein expression. These screening tests identify individuals at risk to carry a germline mutation in a Lynch related gene. This case-control pilot study analyzed levels of patient distress among colorectal cancer patients who had UTS and subsequently underwent genetic counseling at the University of Pittsburgh Medical Center (UPMC) Hereditary GI Tumor Program, and patients who had UTS completed and were seen in the surgical oncology center without genetic counseling. The control group consisted of patients who received genetic counseling for diagnosis of colorectal cancer before 50 years old. Patients were asked to complete a series of validated questionnaires (PHQ-8, GAD-7, IES-R) to evaluate their levels of depression, generalized anxiety, and trauma associated with their diagnosis of cancer. To assess these levels over time, these measurements were taken at three points: prior to genetic counseling, two weeks after genetic counseling, and two weeks after genetic test results were reported. After receiving their genetic test results, participants also completed the MICRA questionnaire to evaluate impact of the results on distress. Given the small number of participants (n=23), nonparametric tests were used to assess the differences in patient distress over time. Levels of distress were measured in both groups' at all three time points. For a given individual, we did not identify statistically significant differences in any distress scores across the three time points within the case group using Wilcoxon-signed rank tests. Trends in respective group means demonstrate varied levels of anxiety after genetic counseling. Analysis of baseline distress between patients in the case group and the control group was not statistically significant, however the mean values of patient distress trended higher across the case population compared to the control population. The impact of test result type (positive or negative) on distress levels did not identify a statistically significant difference ($p=0.727$). The highest recorded value for distress after receiving genetic testing results was 5 (possible score range 0-30) and was identified in a case participant who received a negative result from genetic testing. However, patients in the case group reported higher levels of uncertainty following genetic testing. Understanding the impact of UTS on patient-associated distress has important public health implications and may assist in patient support to alleviate psychological distress.



Layden Alexander

EPIDEM

VI-4

The Conflicting Roles of Pre-Pregnancy Obesity and Excess Gestational Weight Gain on Placental Inflammation Risk in Term Pregnancies

Introduction: Obesity and excess gestational weight gain (GWG) may cause low level chronic inflammation during pregnancy. Inflammatory lesions, both acute and chronic, can occur in the placenta predisposing the neonate to birth complications. We hypothesize that pre-pregnancy obesity and excess GWG will increase the risk of both acute and chronic placental inflammatory lesions in term pregnancies. **Methods:** 8,239 women with a singleton term pregnancy and placental evaluation delivering at Magee-Womens Hospital in Pittsburgh, PA were grouped by pre-pregnancy BMI as lean (18.5 to <25kg/m²), overweight (25 to <30kg/m²), or obese (>30kg/m²). Frequencies of acute inflammatory lesions (chorioamnionitis, vasculitis, funisitis) and chronic inflammatory lesions (villitis) were compared across BMI classes by 2 tests. Modified Poisson regression estimated risk of placental inflammatory lesions associated with obesity and increasing GWG. Inverse probability weighting was used to adjust risk estimates for missing data bias. **Results:** Obese women compared to lean women had a lower frequency of acute chorioamnionitis (34.3% vs 42.0%, $p < 0.0001$) and a higher prevalence of chronic villitis (14.9% vs. 12.9%, $p = 0.03$). Pre-pregnancy obesity was associated with a decreased risk of acute chorioamnionitis (RR: 0.91, 95% CI: 0.84-0.99), and an increased risk of chronic villitis (RR: 1.23, 95% CI: 1.05-1.44) among labored pregnancies. Increasing GWG was associated with a mild increased risk of acute inflammatory lesions: chorioamnionitis (RR: 1.06, 95% CI: 1.01-1.09), vasculitis, (RR: 1.08, 95% CI: 1.02-1.14) and funisitis (RR: 1.09, 1.00-1.18); and an increased risk of chronic villitis among women delivering male babies (RR: 1.11, 95% CI: 1.01-1.23). **Discussion:** We report that maternal obesity may increase the risk of chronic maternal placental inflammation but be protective against acute chorioamnionitis in term pregnancies. Conversely, we found that excess gestational weight gain increases the risk of acute inflammatory lesions. The effects of gestational weight gain on inflammation and placental development warrant further study.



Renee Anderko

IDM

II-10

IL-18 defines exclusive memory-like NK cell populations

The success of ART is reflected in the aging population of people living with HIV-1. Although age is an important factor contributing to the increased incidence of cancer among HIV-1-infected individuals, HIV-1 infection itself is associated with a higher risk of both developing and dying from non-AIDS-defining cancers. NK cells are widely appreciated for their role in the immunosurveillance of virally transformed and malignant cells, but they also provide innate alarm signals that shape and regulate the adaptive immune response. In chronic HIV-1 infection, an expanded population of CD56dim FcRg deficient NK cells with poor direct reactivity toward tumor targets persists despite treatment with ART. The purpose of this study was to explore the phenotypic and functional relationship between FcRg- NK cells and the previously described IL-18-induced memory-like NK helper cells in the setting of HIV-1 infection. Utilizing HIV-1 seropositive participants of the Multicenter AIDS Cohort Study, we measured baseline frequencies of peripheral blood FcRg- NK cells and assessed the phenotypic and functional impact of treatment with IL-18 alone, or in combination with IL-12, on the FcRg- and FcRg+ subsets by flow cytometry. The frequencies of FcRg- NK cells varied widely in HIV-1 infected men. IL-18 drove the differentiation of CD25+/CD83+ NK helper cells, which produced IFN γ and strongly diminished CD16 expression in response to IL-12. In contrast, FcRg- NK cells did not respond to IL-18, illustrated by failure to express CD25 or CD83, to downregulate CD16 expression, and to produce IFN γ . FcRg deficiency was also characterized by an attenuated capacity to express IL18Ra upon IL-18 and IL-12 co-activation. Our results indicate that memory-like NK helper cells and FcRg- NK cells are exclusive populations. Furthermore, the inability of FcRg- NK cells to provide proper immune help in response to innate activation signals, coupled with their poor direct recognition of tumor targets, warrants further exploration of the relationship between FcRg- NK cells and the development of cancer in HIV-1-infected individuals.



Eli Andrade

BCHS

II-1

PreP awareness among Black MSM and transgender women involved in sex work: implications for HIV combination prevention in populations at highest-risk

In the United States the brunt of new HIV infections continue to take place among Black MSM and transgender women (TGW). Black MSM and TGW involved in sex work face additional conditions that place them at risk of HIV infection and other harms related to sex work, making access and awareness of HIV prevention technologies. Pre-exposure prophylaxis (PreP) in the context of HIV combination prevention can protect populations at highest risk of HIV infection. In the case of Black MSM and TGW involved in sex work, PreP can... Methods: Black MSM and TGW 18 years of age or older were recruited between 2014-2017 in Black Pride events across five cities in the United States (Atlanta, GA; Detroit, MI; Houston, TX; Philadelphia, PA; and Washington DC). An audio computer-assisted self-interview (ACASI) survey was implemented, all participants were tested for HIV on site. The survey included questions on sociodemographic characteristics, health care factors, sex behaviors and practices, HIV status and testing, psychosocial factors and PreP and PEP access, use and awareness. This analysis focuses on those MSM and TGW that reported involvement in sex work in the last 12 months (N=364). Results: Preliminary results show significant differences between Black MSM and TGW involved in sex work by PreP awareness (aware vs. unaware) and level of education, employment status, homeless status and sexual orientation. In addition, there are significant differences by having ever been tested, recent HIV testing, and presence of health insurance. Results of bivariate and multivariable analysis are in progress. Conclusions: Awareness of PreP among Black MSM and TGW involved in sex work is influenced by social conditions that may enhance vulnerability to HIV infection. Strategies that seek to deliver PreP to populations at highest-risk need to tailor these efforts to the specific needs of individuals with intersecting conditions related to HIV risk.



Kendra Bobby

BIOST

V-17

Spatial Association between Social Vulnerability and Overdose Mortality in Pennsylvania and its Adjacent States

The purpose of the current study is to investigate the spatial relationship between social vulnerability as given by the CDC's Social Vulnerability Index (SVI) and accidental poisoning mortality, or overdose deaths, in Pennsylvania and its adjacent states. This study explores the suggestion of Jalal et al. (Science, Sep. 2018), that the opioid epidemic is an aggregate of individual subepidemics. We evaluate this by local spatial distribution of overdose mortality rates and SVI factors, such as poverty, overcrowding, and unemployment. Our analysis local measures of spatial autocorrelation, county level clustering techniques, and visual analytics to study the spatial relationship between the socioeconomic landscape of regional clusters of overdose mortality rates.

Visualization of RVFV and inflammatory immune cell infiltration of pregnant Sprague-Dawley rat tissues using immunohistochemistry

Background: Rift Valley fever virus (RVFV) is endemic to the African continent and commonly infects domestic livestock via mosquito bite. Affected animals often develop fatal hepatic necrosis and undergo spontaneous "abortion storms" that result in loss of between 90-100% of pregnancies. Human infection occurs from contact with affected livestock and typically manifests as a febrile illness that can advance to hemorrhagic fever, liver disease, and encephalitic disease. Cases of human vertical transmission have been recorded and resulted in fetal viremia, fetal abnormalities, and fetal death. The first established rodent model of vertical transmission witnessed that pregnant rats were more likely to succumb to infection than non-pregnant rats and that RVFV was able to bypass the antiviral protections of the reproductive system and directly infect the placenta. Even asymptomatic mothers that survived to give birth produced stillborn pups or pups with severe abnormalities (McMillen and Hartman, 2018). Little is known about the mechanism of viral infection in the placenta and the resulting fetal pathology. We sought to follow the trajectory of RVFV from injection site to the reproductive organs of pregnant dams in a congenital model of RVF. Methods: We performed subcutaneous inoculation of pregnant Sprague-Dawley rats at embryonic day 14 (E14). Maternal and fetal tissues were processed for RNA in situ hybridization (RNA ISH) of RVFV RNA and immunohistochemical (IHC) staining of immune cell markers in order to identify inflammatory cell infiltrates and resulting pathologies of lethally infected and sublethally infected rat tissues compared to that of infected non-pregnant, pregnant uninfected, and non-pregnant uninfected controls. Results: RVFV-infected pregnant and non-pregnant rats were susceptible to liver inflammation and necrosis; however, tissues from survivors of infection displayed evidence of tissue repair. Infected pregnant rats were more susceptible to severe liver pathology even at lower inoculation doses than infected non-pregnant rats. Placental tissues from lethally and sublethally infected rats contained high amounts of infectious virus and displayed histological evidence of hemorrhaging and necrosis. Infection of trophoblast giant cells (TCGs) and infiltration of neutrophils were also determined using immunohistochemistry. RVFV was found in the brains and peritoneal cavities of pups from dams that succumbed to infection while pups from survivors exhibited fetal resorption or extreme deformities (fetal hydrops and stunted development). Conclusion: We found evidence of hemorrhage, necrosis, and leukocyte infiltration into placentas from RVFV-infected pregnant rats. This study gives insight into RVFV cellular targets during pregnancy which can be further investigated for development of antiviral therapies.

Correlating the Oral Microbiome with Nitrate Metabolism in Patients with PH-HFpEF

Background: In humans, commensal oral bacteria reduce nitrate to nitrite, which is ultimately further reduced to form nitric oxide (NO), a potent vasodilator. NO signaling is dysfunctional in pulmonary hypertension (PH). Evidence suggests that microbial bioactivation of nitrate may play a role in the prevention and treatment of systemic vascular pathology and PH. To date, no studies have examined the association between alterations in the ability to reduce nitrate to nitrite, the oral microbiome, and hemodynamics in patients with PH-HFpEF. **Objective:** To determine differences in conversion of oral nitrate to nitrite in patients with PH-HFpEF and healthy controls. **Methods:** Healthy controls and patients with PH-HFpEF (mean PAP > 25 mm Hg, PCWP > 15 mm Hg, TPG \geq 12, cardiac index >2.0 L/min/m² on clinical right heart catheterization) were administered 1000mg of sodium nitrate orally. Plasma nitrate and nitrite were measured at baseline and at 2- and 6-hours following drug administration. Saliva, stool and tongue scraping samples were collected before nitrate administration for bacterial DNA extraction. We amplified the V4 hypervariable region of the 16s rRNA gene for sequencing on the Illumina MiSeq platform. **Results:** Baseline (PH-HFpEF 78.28 μ M, Control 106.23 μ M), 2-hour (PH-HFpEF 401.16 μ M vs Control 648.31 μ M, p=0.32), and 6-hour (PH-HFpEF 545.83 μ M vs Control 340.11 μ M, p=0.25) plasma nitrate levels were similar in patients with PH-HFpEF (n=2) and healthy controls (n=3). Baseline plasma nitrite levels were also not significantly different in healthy controls and patients with PH-HFpEF (PH-HFpEF 0.08 μ M vs Control 0.10 μ M, p=0.64). Post-oral nitrate administration, plasma nitrite levels increased in healthy controls, but remained unchanged in PH-HFpEF patients (FIGURE) at 2 hours post oral nitrate administration (PH-HFpEF 0.17 μ M vs Control 0.96 μ M, p=0.03) and 6 hours post administration (PH-HFpEF 0.16 μ M vs Control 0.70 μ M, p=0.05). The taxonomic compositions of bacterial communities sampled on the tongue were significantly different between patients with PH-HFpEF (n=4) and healthy controls (n=3) (weighted Unifrac p-value=0.05) (FIGURE). In saliva samples, there were taxonomic differences between patients with PH-HFpEF (n=8) and controls (n=4) (weighted Unifrac p-value=0.02). Patients with PH-HFpEF were found to have significantly higher abundance of known nitrate reducing bacteria including Rothia, Prevotella and Streptococcus in saliva samples compared to controls (p<0.001). **Public Health Significance:** PH-HFpEF is a disease associated with the metabolic syndrome and obesity. The incidence of PH-HFpEF continues to rise as obesity rates continue to rise. There are currently no known effective treatments for PH-HFpEF. The oral microbiome may play a significant role in the effectiveness of potential therapies. **Conclusion:** In a pilot study of nitrate reduction in PH-HFpEF, we found a diminished ability to reduce nitrate to nitrite as measured by plasma levels after oral nitrate administration. Further studies may provide insight into whether variations in the microbiome contributes to the pathobiology of PH-HFpEF and suggest novel therapeutic possibilities. This abstract is funded by: 5P01HL103455-08 (AM, MTG, BAF), K24HL123342 (AM).



Melissa Bulik

HUGEN

III-20

Using Perturb-seq in primary human pulmonary fibroblast to better understand Systemic Sclerosis pathway pathologies

Introduction: Systemic sclerosis (SSc) is a complex disease with both genetic and environmental factors affecting approximately 300,000 individuals in the United States. Presentation of symptoms vary greatly however tissue fibrosis, autoimmunity, and vasculature changes are defining characteristics of SSc. Disease progression and severity are variable with lung fibrosis leading to mortality in the most extreme cases. Previous work in our lab has identified differentially expressed genes within myofibroblast populations between normal and scleroderma lungs. Understanding molecular pathways involved in tissue pathology may lead to novel treatment plans which can be specific for subtypes of scleroderma patients. Perturb-seq, the combination of CRISPR-Cas9 gene editing and single-cell RNA sequencing (scRNA-seq) techniques, should allow for deeper understanding of the molecular mechanisms involved.

Methods: Primary human lung fibroblasts were isolated from normal lung explants. These cells were grown in culture with complete DMEM/10%FBS. CRISPR-Cas9 Alt-R system was used to knockout FBXO32 and TCF12 in separate experiments. Following gene knockout, cells were grown for one week to allow for downstream effects, and then treated with TGF or PBS as a control for 24 hours. Samples were antibody tagged with unique hashtags, pooled, and ran for scRNA-seq to study downstream effects of the gene knockout. Ingenuity Pathway Analysis (IPA) has been used to identify pathways involved.

Results: We are in the process of analyzing CRISPR-Cas9 knockouts, anticipating that targeted gene deletion will occur in some of the cells within each sample. Using scRNA-seq and bioinformatics software, we will separate the cell types based on transcriptomic profiles. We anticipate identifying downstream gene regulation in both Transcription Factor 12 (TCF12) and F-Box Protein 32 (FBXO32).

Conclusion: Perturb-seq can aid in delineating important pathways in SSc pathology. IPA will aid in the process of recognizing downstream effects caused by gene alteration. Continued analysis of the data is necessary to identify additional genes and pathways of interest.



Sih-Ting Cai

HPM

III-1

The Challenges Ahead: The Burden of End-Stage Renal Disease in Taiwan and the United States to the Year 2040

Background. Care for end-stage renal disease (ESRD) imposes a substantial financial burden on health care systems worldwide. In this study, insights from epidemiological and health economics research were combined to explore the factors driving the demand for ESRD care in Taiwan and the US and to forecast incidence and prevalence of ESRD to the year 2040. **Methods.** Two models were constructed based on data from 2000 to 2014. The results of these models were combined with demographic forecasts through 2040 to produce ESRD forecasts. One model assumed that changes in ESRD would be driven only by changes in the size and age distribution of the population. The second model augmented this demographic forecast based on the forecast errors in the 2000-2014 period. **Results.** Demographic changes alone accurately predicted much of the change in ESRD incidence and prevalence in the US from 2000-2014, but substantially understate changes in both incidence and prevalence in Taiwan. After adjusting for these forecast errors, we estimate that the population over 85 living with ESRD by 2040 could be nearly 18 times as large as that today in Taiwan; the estimate for the US suggests that the population with ESRD will be 5 times greater than it is today. **Conclusions.** The effects of population aging, technological innovations, and their interactions will lead to rapidly increasing spending on ESRD treatment. To address this inevitable challenge, both countries need to be more effective in chronic kidney disease management and more responsive to growing expenditures.

BMP10 is the sole required ligand for endothelial ALK1 signaling

Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant vascular disorder characterized by development of high-flow arteriovenous malformations (AVMs) that can lead to stroke or high-output heart failure. HHT2 is caused by heterozygous mutations in ALK1, which encodes an endothelial cell bone morphogenetic protein (BMP) receptor. BMP9 and BMP10 are established ALK1 ligands. However, the unique and overlapping physiological roles of these ligands remain poorly defined. To probe spatiotemporal ALK1 ligand requirements, we generated zebrafish mutants in *bmp9* and duplicate paralogs, *bmp10* and *bmp10-like*, which encode putative Alk1 ligands expressed primarily in liver and heart, respectively. Combined loss of *bmp10* and *bmp10-like* results in embryonic cranial AVMs indistinguishable from *alk1* mutants, confirming functional redundancy of these paralogs during embryonic vascular development. In contrast, *Bmp10* is the only necessary Alk1 ligand in the juvenile-to-adult period, with mutants exhibiting hemorrhagic and/or enlarged vessels in anterior skin and liver, heart dysmorphology, and premature death. Heart dysmorphology correlates with severity of vascular defects and *bmp10* mutant hearts show increased cardiac output, suggesting that vascular defects lead to low systemic vascular resistance and high-output heart failure in *bmp10* mutants. Notably, this same phenotype occurs with low penetrance in *alk1* heterozygotes. Taken together, these data support *bmp10* mutants as a valuable model for AVM-associated high-output heart failure, which is an increasingly recognized complication of severe liver involvement in HHT.

Hepatitis C Testing at Drug and Alcohol Facilities in Allegheny County

Background: Hepatitis C is an infectious disease caused by the bloodborne hepatitis C virus (HCV) that leads to cirrhosis and liver cancer. The current epidemic of opioid use has led to an increase in new HCV infections transmitted by intravenous drug use. Allegheny County Health Department (ACHD) conducts sentinel surveillance of HCV testing at community organizations serving individuals at high risk for HCV infection. The objective of this analysis is to assess HCV testing practices and HCV positivity at drug and alcohol treatment facilities in Allegheny County.

Methods: ACHD contacted selected outpatient facilities including drug and alcohol treatment facilities, federally qualified health centers (FQHCs), HIV service providers, homeless service programs, dialysis facilities, corrections facilities, and a syringe service program to collect data for 2016 and 2017 on the number of 1) HCV antibody tests completed, 2) positive HCV antibody tests, 3) HCV RNA tests completed, 4) positive RNA tests, 5) referrals to care, and 6) clients treated. Data were submitted on a standard form by email or fax. Data were entered and analyzed in Excel.

Results: Of the 44 drug and alcohol treatment facilities contacted, 38 (86%) submitted complete data for 2016 and 2017 and were included in the analysis. Of the 38 facilities, 2 (5%) provided HCV testing in house, 13 (34%) provided HCV testing on site through an outside organization, and 23 (61%) did not offer HCV testing. In 2016, drug and alcohol treatment facilities reported 911 HCV antibody tests with 22.5% positive. In 2017, they reported 1,028 HCV antibody tests with 20.3% positive. HCV positivity was higher in the drug and alcohol facilities compared with all other facility types, with the exception of the syringe services program (27.8%). According to the survey for 2016 and 2017 combined, 76% of individuals who screened positive were referred for confirmatory RNA testing (results were not reported). Drug and alcohol treatment facilities did not report treating any clients for Hepatitis C.

Conclusions: Drug and alcohol treatment facilities serve a population at high risk for HCV infections. Less than half the drug and alcohol treatment facilities surveyed offer HCV screening and some only offer it through other organizations, so it may only be available intermittently. While there was a slight increase in HCV screenings at these facilities from 2016 to 2017 there is much room for improvement. Ideally, all people who use intravenous drugs who enter treatment programs would be screened for HCV. Positivity is high at drug and alcohol treatment facilities compared with other community settings emphasizing the need for increased testing. This analysis also identified a need for better follow-up for confirmatory RNA testing and linkages to care.



Nemin Chen

EPIDEM

II-3

Gray Matter Density Correlates with Gait Speeds from Different Walking Tasks in Older Adults

Background: Slow walking speed is associated with neuropathological changes in the brain, which can be used as an early marker for poor health outcomes among older adults. Complex walking tasks are often used to mimic the walking condition in the community setting. However, the neural correlates of complex walking tasks are unknown. **Objective:** Assess the association of gray matter density (GMD) with usual pace, fast pace, and narrow-path gait speed. **Methods:** We used a subset of Health, Aging, and Body Composition Study where participants returned to the Year10 or 11 visit and had magnetic resonance imaging (MRI) scan and gait measures. A total of 290 participants were included in our study. GMD was obtained from T1-weighted MRI. Walking tasks include a 20 m usual pace walking, a 20 m fast pace walking, and a 6 m narrow-path walking. Linear regression was used to assess the association between region of interest (ROI) GMD and gait speed. Bonferroni correction was used to adjust for multiple comparisons. Significant associations were further adjusted for age, sex, race, and education level. **Results:** The average age was 83. 57% of participants were women and 40% were black. We observed a positive correlation between middle frontal area GMD and all three gait measures. Usual pace gait speed was also positively correlated with anterior cingulum and hippocampus GMD. Fast pace gait speed was also positively correlated with anterior, middle, and posterior cingulum as well as supplementary motor area GMD. All the associations became insignificant after adjusting for the demographics. **Conclusion:** GMD of multiple ROIs were correlated with gait speed under different walking conditions.



Jon Chernus

HUGEN

I-2

A genome-wide association study of orbicularis oris muscle defects

Nonsyndromic cleft lip with or without cleft palate (NSCL/P) is one of the most common birth defects in humans (affecting about 1.7 in 1,000 live births). The etiology of NSCL/P is multifactorial, with environmental and genetic components. Although there has been considerable progress in identifying genetic risk factors, its complex genetic architecture is not fully understood. One complicating factor in the study of NSCL/P is the wide spectrum of severity – encompassing both “overt” clefts and milder manifestations such as notches or grooves in the lip. This broad range of severity raises the possibility that genetic studies of NSCL/P may suffer from lower power when the mildest versions of clefts (“subclinical phenotypes”) are categorized as unaffected. In particular, it has been hypothesized that defects in the orbicularis oris muscle (OOM, a muscle encircling the mouth) may be an important subclinical phenotype sharing a common genetic etiology, as these defects are more prevalent in relatives of individuals with NSCL/P. Furthermore, an understanding of the genetics of OOM defects and their relation to clefting may be useful in genetic counseling for families with a history of clefting. Here we performed the first genome-wide association study of OOM defects, testing about seven million common genetics variants for association with this trait. Study participants, recruited at several U.S. and international sites, were drawn from the larger Pittsburgh Orofacial Cleft Study. Two independent subgroups were analyzed. The first analysis ($n = 2,365$) included close relatives of individuals with cleft lip who did not have clefts themselves. The second analysis ($n = 1,874$) included only individuals with no family history of clefting. Our results include several genome-wide significant ($p < 5E-8$) and suggestive ($p < 1E-5$) associations. A number of these are located in or near plausible candidate genes for clefting, providing some evidence consistent with a shared etiology.



Jacqueline Cohen

HUGEN

IV-19

Relationship Between Cognition and Statin Use in the Long Life Family Study

In the United States, greater than one-third of adults aged 40 years or older are using cholesterol lowering medication, and 90% of these medications are statins. The relationship between statin use and cognition is unclear: some studies report that statin use is associated with cognitive impairment, whereas other studies report that statins may have a protective effect against cognitive decline. In this study, I investigated the relationship between measures of cognition and statin use by analyzing data from the Long Life Family Study (LLFS) comprising 1691 probands and their siblings (mean age=90yo), and their 2439 offspring (mean age=61yo). Cognitive outcome was measured by two quantitative and four verbal cognitive traits, as well as the Mini-Mental State Exam (MMSE) (in the proband generation only). Each cohort was examined separately. Statin use was 16% among probands and 11% among offspring. As expected, mean cognitive function scores for all measures were lower among probands than among offspring. Among probands, statin users had higher cognitive function scores overall, and this difference was significant for MMSE and the two quantitative cognitive traits (e.g., MMSE was 25.2 versus 26.3 units in statin nonusers and users, respectively; $p < 0.0005$). In contrast, among the offspring, statin nonusers had higher cognitive function scores overall, and this difference was significant for three cognitive measures (e.g., animal recall was 22.2 versus 21.1 units in statin nonusers and users, respectively; $p = 0.003$). Reasons for the opposite direction of effect in the proband versus offspring generation are unclear, but may be due, in part, to the differing dose or length of time that statins had been prescribed. For example, low to moderate dose, long-term statin use may reduce cognitive decline. Alternatively, individuals who take statins at a younger age may have more severe cardiovascular disease and require a higher dose. Given that cardiovascular disease and statin prescription are continually increasing in the U.S., further pharmacological and pharmacogenomic research on statins is warranted.



Stephanie Corey

EPIDEM

IV-8

Evaluating Differences in Human Papillomavirus and Related Cancer Prevention Measures Among the Lesbian, Gay, Bisexual, and Transgender Community and Heterosexual and Cisgender Individuals

Background: Lesbian, gay, bisexual, and transgender individuals (LGBT) are at unique risk for contracting Human Papillomavirus (HPV) and developing related cancers compared to their heterosexual cisgender peers. Incidence of HPV and late-stage cancer diagnoses can be reduced with HPV vaccines and routine screening. Therefore, this study examined gender and sexuality differences in HPV preventive measures to inform the understudied field of LGBT cancer prevention. **Methods:** From 2015-2016, the Allegheny County Health Department commissioned a health survey of 9,026 adults using probability-based sampling. We examined differences by gender identity (cisgender women versus cisgender men and transgender) and sexuality (heterosexual versus gay/lesbian, bisexual, and other) for lifetime receipt of HPV vaccine and number of HPV vaccines. Among cisgender women, we examined sexuality differences in HPV and Pap tests. Logistic and multinomial logistic regression analyses adjusted for age, race/ethnicity, education, marital status, and income. **Results:** Compared with cisgender women, transgender individuals had higher odds (AOR: 9.14; 95% CI: 1.12, 74.54) of never receiving an HPV vaccine. Compared with heterosexual cisgender women: bisexual women had higher odds (AOR: 1.85; 95% CI 1.06, 3.24) of not receiving a Pap test within the recommended guidelines; and cisgender women who reported their sexuality as "other" had higher odds (AOR: 5.73; 95% CI: 1.19, 27.50) of never receiving an HPV test. **Conclusion:** Transgender people as well as bisexual-identified and other-identified cisgender women are less likely to engage in some cancer preventive measures. These findings expand upon the limited evidence in cancer prevention among sexual and gender minorities.



Noelle Cornelio

HPM

IV-5

Examining the Impact of Asset Limits on Medicaid Eligibility and Enrollment for Seniors

Background: Low-income individuals who are > 65 years old can qualify for both Medicare and Medicaid coverage. If income and asset limits are met, these seniors can be categorically eligible for full Medicaid coverage that not only covers Medicare premiums and other cost-sharing (coinsurance, copayments) as well as benefits not covered by Medicare. However, asset limits can create barriers to Medicaid eligibility by preventing people who meet the income threshold from being eligible, making the eligibility rules more difficult to understand, and creating an administrative burden on Medicaid staff. In this study, we analyze how Medicaid asset limits have changed over time, assess how these limits impact Medicaid eligibility and enrollment, and estimate how changes to policy would change the number of seniors eligible and enrolled. **Methods:** This study has three objectives: 1) examine the variation in Medicaid income and asset limits in all states from 2006 to 2018, 2) assess the number of individuals who are not eligible or enrolled due to asset limits but who are eligible based on income, 3) project the number of seniors who would be newly eligible under different policy scenarios. For the first objective, we collected data from each state via interviews with state Medicaid program officials, published reports, and state websites. We then compiled this data into a state-by-year database which we examined for changes in policy between and within states from 2006 to 2018. For the two other objectives, our database was merged with restricted data from the Health and Retirement Study (HRS). The HRS is a longitudinal, nationally representative survey of adults in the United States who are over the age of 50, and contains high quality income and asset information, individual demographics, state identifiers, and the ability to link to Medicare enrollment data. **Results/Discussion:** Although most states increase Medicaid income eligibility limits for seniors annually, asset limits have stagnated at \$2,000 for individuals and \$3,000 for couples for most states since before 2006. In 2018, 38 states had the standard asset limit, while 9 states and DC had a higher limit, 2 had a lower limit, and 1 did not have a limit. Additional analysis will focus on the impact of asset limits and policy changes on Medicaid eligibility and enrollment. **Policy implications:** Medicaid asset limits have largely remained unchanged over time, which may limit low-income seniors' eligibility for and enrollment in Medicaid. Removing or increasing the asset limit, may not only reduce the administrative burden on state Medicaid programs, but help this population access care.



Tianyu Ding

BIOST

II-15

A reduced rank regression framework for interpretable image-on-scalar regression with application to Alzheimer's Disease

A key question to advancing our understanding of the multidimensional nature of Alzheimer's Disease, which is characterized by both neurological and cardiovascular pathologies, is how brain structure is linked to vascular burden. Reduced rank regression is a widely used technique for overcoming the high-dimensional nature of multivariate regression, such as the image-on-scalar regression of brain images onto vectors of vascular burden. Existing penalized extensions allow for the incorporation of smoothness and sparsity on reduced rank subspaces. However, sparsity and smoothness on reduced rank subspace do not directly translate into meaningful structures on image spaces, blurring biological interpretation. In this study, we propose a sparse reduced rank regression framework, which includes a novel fused group lasso penalty, combined with an encoder decoder, that ensures smoothness, sparsity and interpretability on the image space. An algorithm is developed for model fitting that uses alternating direction method of multipliers (ADMM) to perform optimization within low-dimensional subspaces. Empirical properties of the proposed approach are examined and compared to existing methods in simulation studies and the modeling of PET images from subjects in a study of Alzheimer's.

Cutis laxa mutations in fibulin-5 decrease elastin Deposition, specific signaling pathways, and decrease survival in vivo

Cutis laxa (CL) is a rare disorder of elastic fiber formation, deposition, and function, which produces a phenotype of loose and inelastic skin, and a variety of other systemic manifestations. Mutations in multiple genes can cause CL, however, it is not fully understood how the mutation of each gene affects cell signaling and function, elastic fiber deposition and formation. One cutis laxa gene is fibulin-5 (FBLN5), which is required for the deposition of elastin onto microfibrillar scaffolds. To further understand the molecular mechanisms of FBLN5-related cutis laxa, fibroblasts from 5 patients were studied, each homozygous for a different fibulin-5 (FBLN5) mutation: 2 previously reported (S227P, C217R) and 3 newly identified (P18fs*25, C320fs*76 and N63T). Colorimetric elastin assays indicated that mutant cells assembled significantly decreased ($p=0.0007$, Welch's t test) amounts of elastin with 82.07 ± 8.164 $\mu\text{g}/\text{million cells}$ in controls and 50.72 ± 3.568 $\mu\text{g}/\text{million cells}$ in mutants. When comparing individual patients to the controls, the reduction in elastin deposition correlated with the position of the mutation, with mutations close to the N-terminus having a more severe effect than those close to the C-terminus, with one exception. To investigate the consequences of FBLN5 mutations for cell signaling, we performed transcript profiling by mRNA sequencing. Pathway analysis of differentially expressed genes identified gene transcripts with significant fold changes both up (Nik related kinase (NRK); FC = 320.53) and down (steroid 5 alpha-reductase 2 (SRD5A2); FC = -3582.21) compared to control cells. RNA-sequencing analysis also showed a significant reduction in the FBLN5 transcript levels in one of the frameshift mutations (P18fs*25) and one of the missense mutations (C217R). Pathways analysis revealed alterations in G protein coupled receptor (GPCR) signaling, calcium signaling, and TGF- β^2 signaling. Consistently, immunoblotting showed significantly decreased ($p<0.0001$) pSMAD3 levels in patient cells. Thus, cutis laxa causing FBLN5 mutations impair elastic fiber deposition and decrease GPCR and TGF- β signaling but may also alter actin polymerization and steroid signaling. Preliminary in vivo data, using zebrafish as a model system, suggest that frameshift and early termination mutations in *fbln5* in zebrafish leads to decreased survival, the cause of which is still being evaluated. Mechanistic insights gained from determining how FBLN5 mutations lead to disease formation has the potential to have great impact on the lives of these patients and beyond.



Eric Edwards

EPIDEM

IV-20

The Effects of Thyroid Medication on Bone Mineral Density: A Study of Women's Health Across the Nation (SWAN) Pharmacoepidemiology Study

Background: As women progress through menopause, bone mineral density (BMD) slowly decreases due to estrogen loss. Several studies suggest that medications taken for hypothyroidism do not have a significant effect in the rate of BMD loss while others suggest that thyroid medication could decrease BMD and increase the risk of fractures, osteoarthritis and osteoporosis. **Objective:** To determine if women who initiate thyroid medication for hypothyroidism experience an increase loss in BMD at the femoral neck (FN), hip or spine compared to non -initiators. **Methods:** We investigated changes in BMD associated with new use of thyroid hormone therapy in a prospective longitudinal cohort of mid-life women. BMD and medication use were measured annually over a period of 16-years. Propensity score matching (PS) was applied to balance baseline characteristics of women who did and did not initiate thyroid medications. Mixed model regression was used to examine annualized change in BMD. Covariates with a known impact on bone health (age, race, body mass index (BMI), menopausal status, thiazide diuretic and hormone use) were included in all models. **Results:** Our cohort included 356 women (n=178 in each group) with a mean age of 52.9 (SD=5.6) years and BMI of 29.4 (SD 6.8). 64.3 % of the women were Caucasian, 19.9% African American, 9.6% Chinese and 6.2% Japanese. Median follow-up time was 9.5 years. After adjusting for the variables mentioned above, the annual rate of bone loss at the FN, hip and spine for the treatment and control groups were FN (-0.71% vs. -0.85% p= 0.22), hip (-0.57% vs -0.66% p=0.47), and spine (-0.59 vs -0.71% p=0.41). **Conclusion:** After employing a pharmacoepidemiology design and PS matching there were no significant differences in BMD between those who used thyroid medications and those who did not at either the FN, total hip, or spine.



Zeynep Erdogan-Yildirim , Hannah Guzolik,
and Ryan Hartmaier

HUGEN II-2

Functional Investigation of ESR1 Fusions Identified in Endocrine Therapy Refractory Estrogen Receptor Positive Breast Cancer

Metastatic estrogen receptor (ER)-positive breast cancer is an incurable disease that remains a clinical challenge and a public health burden. Over 40,000 women die each year from breast cancer and over 90% of these are due to metastatic disease. Although there has been great success with anti-endocrine treatment, most patients with metastatic disease develop resistance during the course of therapy. Loss of ER or missense mutations in the ligand-binding domain (LBD) of ER are reported as causal mechanisms of resistance. Recently, our laboratory showed that ESR1 fusions involving loss of LBD, play a role in lack of response to therapy. Only limited knowledge exists on the actual frequency and functional role of ESR1 fusions. Hence, I aimed to expand the search for further ESR1 fusions in advanced breast cancer disease and to characterize the functional role of ESR1 fusions (ESR1-DAB2, ESR1-GYG1 and ESR1-SOX9) our lab published earlier along with the ESR1-LPP fusion found in a PDX-model. Screening of RNA-seq data of primary-metastatic paired breast tumors (n=45) in UPMC cohort and metastatic BrCa (n=91) in the publicly available MET500 cohort revealed a total of five ESR1 fusions sharing identical breakpoint with ESR1-YAP1 fusion. ESR1-GYG1 was the only ESR1 fusion identified in the UPMC cohort. For functional assessment, the ESR1 fusions were transiently and stably transfected into cell lines. The immunofluorescence staining confirmed the predominant nuclear localization of the ESR1 fusions, while ESR1-LPP and ESR1-GYG1 fusions additionally displayed cytoplasmic localization. ER activity assays via luciferase assay and qRT-PCR demonstrated estrogen-independent constitutive activity of ESR1 fusions that is unresponsive to anti-endocrine treatment. While ESR1-DAB2 and ESR1-SOX9 fusions induced the transcription of estrogen-responsive genes, only ESR1-SOX9 demonstrated statistically significant estrogen-independent proliferation in stable expressing T47D cells. Overall, active ESR1 fusions may have a critical role in developing anti-endocrine resistance and promoting tumor progression. Since ESR1 fusions with loss of LBD are recurrent in therapy-refractory ER-positive breast cancer, further comprehensive studies are needed (1) to determine their true frequency, (2) to understand their mechanism of action and (3) to determine their value as prognostic and therapeutic biomarkers.



Leisure-time Physical Activity and Mental & Physical Health-Related Quality of Life Among Pregnant Women From the Behavioral Risk Factor Surveillance System (BRFSS) 2017 Survey

PROBLEM/CONDITION:

Depression during pregnancy, commonly referred to as antenatal depression, affects women with a prevalence rate that ranges between 10% to 25%. Antenatal depression increases the risk of preterm labor and low birth weight, and if left untreated, it can increase the risk for postpartum depression and suicidality. Additional risk of increased hospital visits and pregnancy complications such as preeclampsia (PE) are linked to untreated maternal depression. In addition to adverse effects on maternal health, antenatal depression can lead to adverse effects on the children born to affected mothers. Studies have shown that it can affect childhood development with higher rates of impulsivity, difficulty with social interactions, along with cognitive, behavioral, and emotional difficulties. Treatment of depression is a vital component of eliminating adverse pregnancy outcomes. Unfortunately, it has been widely reported that pregnant women underutilize existing treatments such as participating in support groups, using antidepressant medication, and psychotherapy, treatments that are more feasible, accessible, and acceptable such as physical activity can be tools to reduce the incidence and prevalence of depression among pregnant women.

Leisure-time physical activity (LPTA) is a potential solution to antenatal depression; however, we do not fully understand the benefits of physical activity in pregnant women. Physical activity has been shown to have a positive impact on reducing depression in other populations such as non-pregnant women, the elderly, and adolescents, with long-lasting effects.

The purpose of this analysis is to examine the association of LPTA with mental health in a nationally representative sample of pregnant women from the 2017 Behavioral Risk Factor Surveillance System (BRFSS) dataset.

REPORTING PERIOD:

2017

METHODS:

This is an analysis of the 2017 BRFSS dataset, which is a nationally-representative cross-sectional study. Our analysis utilizes the core component of the study only.

Dean's Day Competition 2019

Analysis: The BRFSS dataset contains a total of 450,016 individuals, of which 55.8% are women. We only included women who reported being pregnant during the time of the survey and reported information on both mental health and physical activity. Our final analysis consisted of 1,651 women.

A Poisson regression model was used to estimate the association between intensity of physical activity (inactive, insufficient, active, highly active) and levels of poor mental health days (0 days of poor mental health, 1-14 days of poor mental health, >14 days of poor mental health). We used pregnant women who were inactive in the last 30 days as our reference group. Our adjusted model assessed age, income level, race, and health coverage. Data has been weighted using appropriate measures provided by the CDC. All statistical analyses were carried out using SAS v9.4.

RESULTS:

The prevalence of poor mental health is 39.9% among women who were pregnant in this study. After adjusting for confounders, LTPA was significantly associated with days of poor mental health in the last 30 days among pregnant women. Our data suggest that pregnant women who are highly active have nearly 1.4 less day of poor mental health (margins 2.45 (1.8, 3.1), $p < 0.01$) compared to those who are not active (margins 3.39 (0.4, 6.4), $p=0.03$). Age groups of 25-29 years and 30-34 years are significantly associated with days of poor mental health compared to 18-24 years old with $p < 0.03$ and < 0.01 , respectively.

CONCLUSION:

Evidence exists that LTPA is beneficial for the reduction of poor mental health among pregnant women of all ages. Additional studies are needed to study the effect of duration, type, and intensity of physical activity on mental health.

Improving Type 1 Diabetes Management: Considerations for a Peer-Support Network in Kigali, Rwanda

Background: As non-communicable diseases rise in low-middle income countries, the problem of access to care and social support become significant global health concerns. In Rwanda, collaborative work between the International Diabetes Federation's Life for a Child (LFAC) program and the Rwanda Diabetes Association (RDA) improve access to treatment and insulin for type 1 diabetic youth (T1DY). These youth (age<26) in Rwanda however still face barriers in personal diabetes management. T1DY need reliable methods for communicating problems that are prohibiting their continued treatment. In addition, T1DY need consistent social and emotional support from people who understand living with diabetes. Drawing on LFAC/RDA data and stakeholder insights, this project explores barriers youth face in diabetes management. Peer-support networks are considered as one possible solution T1DY in Rwanda could use for their social, emotional and clinical needs. **Methods:** In June 2018, data collected between June 2009-February 2018 on 1,542 T1DY across the country were analyzed to generate an updated LFAC/RDA registry as a baseline for planned future intensive follow up. Youth were categorized as Kigali residents (n=267) or out of area (n=1262), and 13 have no residency data. Stakeholder interviews with the RDA and neighboring Tanzania Diabetes Youth Association (TDYA) are continuing and additional data will be examined from previous LFAC/RDA surveys. **Results:** Initial results suggest that of the Kigali youth for whom vital status is known (n=235), 8.5% (n=20) have died. Of the Kigali youth eligible for the LFAC registry (n=161), 14.9% (n=24) have been lost to follow up (LTF). The resulting LFAC/RDA registry total of 180 includes 43 out of area youth who use the RDA as their primary clinic. Additionally, stakeholder interviews suggest that barriers for diabetes management include stigma, job insecurity, transportation costs and access to medicine. **Conclusion:** This preliminary analysis describes LTF status of those eligible for the updated LFAC registry. As one objective of this registry is more rigorous follow up, it is significant that LFAC and the RDA consider additional methods for continuing their work towards resolving diabetes management barriers. Peer-support networks could be crucial for reaching this objective by encouraging T1DY engagement and communication while providing more direct social and emotional support.



Jessica Frankeberger

BCHS

VI-7

Spatial Access to Medication Assisted Treatment (MAT) and Reproductive Health Services for Opioid-Dependent Pregnant Women in Allegheny County

As opioid abuse continues to be a public health crisis in the United States, pregnant women who use opioids may be at particularly high risk of negative outcomes. Pregnant women who are opioid-dependent require access and utilization of public health services, specifically medication-assisted treatment (MAT) and regular prenatal visits, to minimize the effect of opioids on the woman and the child. Thus, the availability of services needs to be examined to ensure that these resources are accessible in regions most impacted by opioid abuse. MAT services, primary care facilities, and reproductive specialist centers were mapped alongside opioid overdose rates in Allegheny County, PA. Using a rook contiguity, global and local Moran's I tests were used to determine if clustering of these services occurred. Three spatial lag regression models were used to examine the spatial relationship between these services and opioid overdoses. The results indicated that while opioid overdoses did cluster ($p=0.029$), only MAT services significantly clustered ($p=0.048$) among the three types of health service locations. When adjusting for poverty, population density, and percent white, opioid overdose was a predictor for locations of MAT services ($p=0.023$) and primary care facilities ($p<.001$), but not for reproductive specialist centers ($p=0.112$). Corrections for spatial error improved model fit. While there is a lack of reproductive specialist services in areas most affected by opioid overdose, MAT and primary care facilities are proximately located within these areas. Thus, primary care facilities may serve as a first point of contact for pregnant women who are opioid-dependent and should be targeted for interventions to improve treatment for these populations, including being trained to provide buprenorphine prescriptions.

Genome-wide DNA Methylation Study of Preeclampsia within Pregnant Trimesters

Background: Preeclampsia (PE) is a hypertensive, multi-system disorder of pregnancy which has a significant impact on the maternal and infant health. It increases the risk of hypertension and cardiovascular diseases and it is a leading cause of mortality for mothers and babies. Although many risk factors such as hypertension and obesity have been identified to be associated with PE, there are no literature which formally explores clinical reliable biomarkers that can predict PE. Our pilot study has shown that endoglin-related (ENG) genes had significant association with PE. Our current study is focusing on analyzing relationships between PE and those ENG-related genes. **Public Health relevance:** Preeclampsia is a disease which threatens the health of millions of pregnant women and their babies across the world. Finding the clinical reliable biomarkers related to PE can largely minimize the risk of PE and improve the prognosis and prevention of PE. **Purpose:** to characterize and compare maternal blood DNA methylation profiles of the ENG-related genes in pregnant women who did or did not develop PE. **Design:** Our study is a longitudinal study which aims to analyze DNA methylation profiles across three trimester peripheral blood samples in pregnant women who did or did not develop PE. 91 cases and 98 controls were included in the study. Other health-related outcomes such as BMI, blood pressure and gestational age were also collected for potential analysis. **Methods:** Genome-wide DNA methylation data were collected using the Infinium Methylation EPIC Beadchip. ENmix and minfi package in R were used to perform data cleaning and quality control. Due to the mismatching of duplicate pairing with minfi functional normalization method, a new normalization method, which is included in funtooNorm R package, were implemented for getting better clustering by treating different trimesters as different tissues. Then surrogate variable analysis (SVA) was used for determining unknown surrogate variables and obtaining top hits within each trimester. Endoglin-related genes and summary statistics were extracted from top tables. Significant and suggestive results of interest could be obtained by calculating gene-level and CpG-level p-values. **Results:** funtooNorm normalization method resulted in much better clustering for duplicate pairs within each trimester using beta values compared to ENmix normalization. In SVA, QQ plots demonstrated that within trimester analysis was a better analyzing method which took consideration of trimester effects. Manhattan plots and top hits indicated that there were some significant signals related to preeclampsia. TRAF3IP2 was identified to be involved in inflammation and lipid metabolism and was associated with early onset preeclampsia. AQP11 expression was identified to become lower during fetal development and thus it was highly related to human pregnancy. **Conclusions:** Several endoglin-related genes and genes from top hits were associated with pregnancy and preeclampsia.



Alexa Furek

BCHS

V-5

Implementing Smoke-Free Laws in the Context of the Tobacco Retail Environment in Allegheny County: A Geospatial Analysis

Introduction: Low-income populations have a disproportionately high exposure to smoking and secondhand smoke. In 2018, a Department of Housing and Urban Development (HUD) federal rule required all local public housing agencies (PHAs) in the U.S. to implement a smoke-free policy. HUD's Public Housing Program is designed to provide rental assistance to low-income populations, and in theory, the smoke-free housing policies should increase smoking cessation and reduce secondhand smoke exposure. However, characteristics of the macroenvironment can affect residents' smoking behaviors and compliance. For example, the high concentration of tobacco retailers in Allegheny County poses challenges to smoke-free policy implementation.

Objective: To examine clustering patterns of tobacco retailers near public housing buildings, in comparison to clustering patterns near schools, in Allegheny County, PA.

Methods: Geocoded data of licensed tobacco retailers, public housing buildings, and schools (K-12) in Allegheny County were mapped in QGIS. Buffer zones of 500ft, 0.25mi, 0.5mi, and 1mi were created around each public housing building and each school. The number of tobacco retailers within each buffer was recorded. A Multi-Distance Spatial Cluster Analysis (Ripley's K-Function) was performed in ArcMap 10.6.1 to identify clustering of tobacco retailers in Allegheny County.

Results and Conclusions: (pending)



Kelly Gagnon

BCHS

VI-8

Facilitators and Barriers to Improving Primary Care for LGBTQ+ Patients at Federally Qualified Health Centers

Background: Lesbian, Gay, Bisexual, Transgender and Queer (LGBTQ+) people experience disparities in health care access and outcomes. Developing capacity to identify LGBTQ+ patients in order to monitor, evaluate and improve disparities in this vulnerable subpopulation requires structural changes in training, data collection, and care workflows. **Methods:** The Transforming LGBT Care quality improvement (QI) initiative was co-led by Weitzman Institute, Fenway Institute and the National Association of Community Health Centers (NACHC), with guidance from the Centers for Disease Control and Prevention (CDC). This initiative combined two evidence based programs, Project ECHO and Practice Improvement Collaborative (PIC), with the goal of improving primary care for LGBTQ+ patients at 10 federally qualified health centers (FQHCs) in nine States. To understand barriers and facilitators to providing affirming care to LGBTQ+ patients at FQHCs, we used a general inductive approach to conduct qualitative content analysis on Project ECHO (n=64) and QI LC transcripts (n=33). The research questions for this study were: what systems, cultural, and clinical practice factors arose during the synchronous Project ECHO and LC intervention? and to what extent did these factors act as barriers/facilitators to health centers' ability to improve primary care for LGBTQ+ people? **Results:** Content analysis indicated most topics discussed during ECHO were clinical, while LC session participants emphasized workflow changes and systematic barriers. Behavioral health (comorbidities, treatment and service needs) was the most common topic discussed during ECHO (86% of sessions), while health information technology (HIT) infrastructure and changes were discussed in 82% of LC sessions. Many factors emerged during content analysis that acted as both facilitators and barriers to implementation, including change acceptance and implementation team. Facilitators included staff training and community partners. HIT was the most frequently cited implementation barrier. **Conclusions:** Project ECHO and PIC sessions identified and addressed clinical and systematic barriers and facilitators. Both interventions were needed to improve data collection and address STD testing disparities among LGBTQ+ patients.

Impacts of rehabilitation after hospital discharge on functional and quality-of-life outcomes in children with severe traumatic brain injury (TBI)

Given the few studies on the effectiveness of traumatic brain injury (TBI) rehabilitation in children, we aimed to examine whether rehabilitation after acute hospitalization improves functional and quality-of-life (QoL) outcomes in children with severe TBI. We analyzed data collected at one-year follow-up from the Approaches and Decisions in Acute Pediatric TBI (ADAPT) trial, a multisite and multinational longitudinal study of children with severe TBI (Glasgow Coma Scale < 8). Rehabilitation use after hospitalization was measured by interviewing a primary caregiver. Functional outcome was assessed using the Glasgow Outcome Score Extended for Pediatrics (GOS-E Peds) to compare "poor" (GOS-E Peds 3-7) to "good" (GOS-E Peds 1-2) outcomes. Domain-specific QoL was measured using caregiver-reported Pediatric Quality of Life Inventory (PedsQL). We used a generalized boosted model to generate propensity scores (PS) for receiving rehabilitation as a way to adjust for confounding. Then we compared frequencies of poor functional outcome and QoL scores between children with and without rehabilitation using inverse probability of treatment weighting of the PS. A total of 399 children younger than 18 years were included in the analysis of functional outcomes. Most children (81.9%) were reported having received rehabilitation after hospital discharge. Rehabilitation was not associated with functional outcome in PS adjusted analysis (aOR=1.54, 95%CI 0.66-3.61). Among 209 children with domain-specific PedsQL scores, rehabilitation was associated with small and non-significant decreases in scores of physical functioning (aBeta=-1.46, 95%CI -10.84-7.92) and psychosocial functioning (aBeta=-3.95, 95%CI -13.69-5.80), as well as the total score (aBeta=-2.56, 95%CI -11.47-6.35). The lack of significant beneficial impacts of rehabilitation does not imply that post-discharge rehabilitation should not be given. The results might be constrained by limitations in measurement of rehabilitation and specific functional limitations at hospital discharge, and lack of data on pre-injury QoL. Larger studies with more precise measures of the type and amount of rehabilitation, as well as longitudinal measures of functional limitation and QoL outcomes will be essential to extend current results.



Xiaotian Gao

BIOST

V20

Inference on Mean Quality-adjusted Lifetime Using Joint Models for Continuous Quality of Life Process and Time to Event

Quality-adjusted lifetime (QAL) has been considered as an objective measurement that summarizes the quantitative and qualitative health aspects in a unitary and meaningful way. The idea is to account for each patient's health experience in adjusting the overall survival, with death at one extreme and perfect health at the other extreme. In existing literature, the health states are defined to be discrete and the number of states is taken to be finite. Therefore, QAL can be calculated as a sum of time spent at each health state multiplied by the corresponding weight. In this paper we propose an estimator of the mean QAL when the quality of life process is assumed to be continuous and observed with error over time at fixed time points via joint modeling of quality of life and time to event outcomes. We prove the asymptotic properties of the proposed estimator and study its finite sample performance through simulation. We illustrate its application with data from a breast cancer clinical trial study.



Kimberly Garrett and Kristin Frawley

EOH

I-17

The Antidotal Action of Some Gold(I) Complexes Toward Phosphine Toxicity

Phosphine (PH₃) is responsible for more human poisonings than any other toxic substance yet there is no antidote currently available. Because of the widespread availability of metal phosphide rodenticides which generate phosphine gas, this toxin poses a public health threat in terms of both individual poisonings (e.g. occupational exposure, suicide) and through its potential use as a bioterrorism agent. Phosphine is a mitochondrial poison that purportedly prevents oxidative phosphorylation through the inhibition of complex IV of the electron transport system (ETS). Additionally, phosphine executes toxicity through damage to hemoglobin, resulting in methemoglobinemia. This work investigates the usefulness of three commercially available Au(I) compounds in the amelioration of phosphine toxicity through scavenging activity. The selected Au(I) complexes have been used in the treatment of rheumatoid arthritis, so their pharmacologic activity has already been evaluated. Au(I) compounds are likely to decorporate phosphine because of PH₃'s propensity to bind to "soft" metal ions, of which Au(I) is the softest. The ameliorative effects of the Au(I) compounds were assessed via insect (*G. mellonella*) and mouse models. Results show that all three Au(I) compounds can effectively detoxify phosphine in biological systems. All three Au(I) compounds were effective prophylactically in both the insect and mouse models while only some were effective as post-exposure ameliorative agents.



Julia Gerow

HUGEN

I-3

Seeing Both the Forest and the Trees: Utilizing a Mixed Method Data Matrix Approach to Integrate Quantitative and Qualitative Data in a Large-Scale Evaluation Model

Large-scale evaluation projects include a range of challenges related to the scale of implementation, particularly when both implementation and process are valued as highly as outcomes. Mixed method approaches are useful for integrating these different lenses, and allow evaluators to address both process and outcome goals. In this poster, we will provide an overview of a tool developed by the Office of Child Development to integrate quantitative and qualitative process and outcome data in a large-scale evaluation. This Data Matrix was designed as a type of heat map, which allowed us to examine project impacts broadly, but that also provided information on higher impact or more intensive hot spots. As such, this tool highlights both the forest and the trees, metaphorically, documenting the breadth and complexity of implementation activities without losing sight of the process or big picture impacts the project is having on the County or the Commonwealth. The Data Matrix is rooted in a mixed-method framework and focuses on integrating quantitative and qualitative data sources (e.g., record reviews, surveys, count analyses, and guided interviews) into a multifactor impact score. Preliminary findings suggest that this approach successfully integrates quantitative and qualitative process and outcome data, providing a useful framework for considering large-scale impact. The goal of this tool is that it can be shifted to provide an evaluation method for other large-scale projects as well, capturing the nuances of implementation while giving a heat map of the overall project.



Jerome Givi

HUGEN

II-7

Factors Impacting Local Obesity Rates in Pennsylvania

To enable public health professionals to assess health issues within and among counties, the Pennsylvania Department of Health has compiled on a variety of health-related measures (at the county-level and regional level) and integrated them into an Enterprise Data Dissemination Informatics Exchange (EDDIE) tool. I investigated the relationship between local health-related factors and obesity rates in Pennsylvania counties and regions using data from EDDIE, as well as other publicly available data sources. Correlation analyses demonstrated the factors that had the strongest correlation with obesity were median income ($r=-0.6465$), population density ($r=-0.5666$), the percent of the population who smoke ($r=0.5820$), and the number and density of parks ($r=0.5018$ and $r=-0.4649$, respectively). A similar relationship was seen at the region level for population density ($r=-0.5753$) and the percent of the population who smoke ($r=0.6086$). Significant relationships were also seen between obesity and the percent of population who ate at least five fruits and/or vegetables every day for the past month ($r=-0.7421$), percent of the population with no leisure time physical activity in the past month ($r=0.6977$), and the percent of the population in poverty ($r=0.4528$). Forward and reverse stepwise regression were also done to create predictive models for obesity rate. The county-level regression models had adjusted R² values that ranged from 0.5763 to 0.5874 and included the variables median income, parks per square mile, percent of adults with no health insurance, and population density. The region-level regression models had adjusted R² values ranging from 0.5963 to 0.6732, and included the variables the percent of population who ate at least five fruits and/or vegetables every day for the past month, percent of the population with no leisure time physical activity in the past month, the percent of adults with no health insurance, and the percent of the population in poverty. In conclusion, numerous health-related factors are significantly associated with local obesity rates and programs aimed at impacting these factors could impact local obesity rates.

A Lifestyle Intervention in Older Adults Improves Physical Fatigability but not Mental Fatigability

Obesity and physical activity (PA) are associated with physical fatigability in older adults. It is hypothesized that weight loss and PA interventions will improve dimensions of perceived fatigability, physical and mental. **PURPOSE:** Examine the impact of a community-based healthy aging and behavioral weight management intervention on change in both physical and mental fatigability among obese community-dwelling older adults enrolled in the 13-month Mobility and Vitality Lifestyle Program (MOVEUP). **METHODS:** We measured perceived physical and mental fatigability using the validated Pittsburgh Fatigability Scale (PFS, range 0-50 for both physical and mental with lower score= less fatigability); self-reported light-moderate PA (LMPA, > 2.5 METs) using the CHAMPS questionnaire; and weight. **RESULTS:** At baseline, participants (N=92) were age 68.9 ± 4.1 years, 82.6% female, 25% African American, body mass index 34.2 ± 4.4 kg/m². Baseline PFS score for physical was 18.9 ± 8.2 and mental 11.3 ± 8.2 . After 13 months, participants lost 14.8 ± 13.0 lbs (7.3% of body weight) and increased LMPA by 2.3 hours/week. Concurrently, physical fatigability decreased by 3.2 points (16.9%) to 15.8 ± 8.3 ($p=.0005$); and mental fatigability had decreased by 0.9 (8%) to 10.4 ± 8.6 ($p=.29$). Physical, but not mental, fatigability was modestly correlated (-0.22 , $p=0.04$) with change in LMPA after age and sex adjustment; neither were correlated with change in weight loss. **CONCLUSION:** Lifestyle interventions may improve physical, but not mental, fatigability. These results provide further evidence that fatigability is multi-dimensional, suggesting that mental and physical fatigability have unique biological pathways. Future work will investigate underlying mechanisms to develop better interventions for reducing fatigability in older adults.



Sara Godina

EPIDEM

V-6

Neighborhood Socioeconomic Status and Cognitive Function in Older Adults: The Healthy Brain Project

Previous studies indicate an association between neighborhood socioeconomic status (nSES) and cognitive function, however the mechanism remains unknown. We examined cross-sectional associations of nSES and measures of cognitive function and brain integrity in 264 community-sampled adults (mean age 83, 56.82% female, 39.02% Black) from the Healthy Brain Project, a substudy of the Health, Aging, and Body Composition Study. Cognitive function was assessed using the Modified Mini Mental Exam (3MS) and the Digit Symbol Substitution Test (DSST), and magnetic resonance imaging was used to quantify white matter hyperintensities (WMH) and grey matter volume of specific brain regions. U.S. Census data was used to calculate a composite measure of nSES using six measures of income, education, and occupation. Linear mixed effects models were used to account for clustering by census block and adjusted for age, gender, race, income, and education. In fully adjusted models, nSES was not associated with 3MS score ($\hat{\tau}^2=0.048$, 95% CI: -0.122,0.218) or DSST score ($\hat{\tau}^2=0.151$, 95% CI: -0.234,0.535), cross-sectionally. White matter hyperintensities were not associated with nSES and gray matter volume analyses are pending. Results suggest the underlying mechanism driving the association between nSES and cognitive function is not present late in life, and occurs earlier in the lifespan.



Kathyayini Gopalakrishna

HUGEN

VI-15

Maternal IgA protects against the development of necrotizing enterocolitis in preterm infants

Neonates are particularly susceptible to infection by colonizing microbes, and mammals protect their offspring via antibodies secreted into breast milk. Necrotizing enterocolitis (NEC) is a disease of preterm infants characterized by intestinal epithelial damage and inflammation associated with the microbiota. The incidence of NEC is significantly lower in infants fed with maternal milk, though the mechanisms underlying this protective benefit are not clear. Here, we show that maternal Immunoglobulin A (IgA) is an important factor in protection against NEC. Analysis of IgA-binding of fecal bacteria from preterm infants indicated that maternal milk was the predominant source of IgA in the first month of life and that a relative decrease in the fraction of bacteria bound by IgA is associated with the development of NEC. Sequencing of IgA-bound and unbound bacteria revealed that prior to disease onset, NEC was associated with increasing domination of the IgA unbound microbiota by Enterobacteriaceae. Further, we confirmed that IgA is critical in preventing NEC in a murine model, where we demonstrate that pups reared by IgA deficient mothers are susceptible to disease despite exposure to maternal milk. This study illustrates the importance of maternal IgA in shaping the host-microbiota relationship of preterm neonates and provides evidence that IgA is a critical and necessary factor in maternal milk for the prevention of NEC.

Rest-activity rhythm timing and depression symptom severity in dementia caregivers

Study: Differences in rest-activity rhythms (RARs) are associated with depression. Few studies have explored how the timing of RAR characteristics relates to subclinical depression symptoms, a risk factor for major depression. The present study proposes three measures to identify associations of RAR timing on subclinical depression symptoms in dementia caregivers, a group at risk for developing depression. **Methods:** RARs were assessed using actigraphy from 57 participants (aged 50+) enrolled in the Aging Well, Sleeping Efficiently Caregiver study. Subclinical depression symptom severity was assessed using the Hamilton Rating Scale for Depression (non-sleep items). The three proposed measures, calculated in 4-hour time bins, included: absolute mean activity, standard deviation of mean activity across days, and relative activity. To account for differences in participant-specific chronobiology, 4-hour time bins were based on 'Person-Time' (clock-time minus participant's typical morning rise time, estimated using an extended cosine model). Spearman correlation and multiple regression (adjusted for age and sex) were used to assess associations between activity at each time bin and depression scores. **Results:** Multiple regression analyses showed that, four hours before typical rise time, both mean activity (standardized $\hat{\rho}^2 = 0.40$, P-value <0.01) and relative activity (standardized $\hat{\rho}^2 = 0.38$, P-value <0.01) were positively associated with depression symptoms. **Conclusion & Significance:** Results suggested that dementia caregivers who had more activity before their typical rise times had higher levels of subclinical depression symptoms. These results add important new information that sleep fragmentation late in the sleep period may be particularly related to caregiver's mood and may help inform where in the RAR activity- and sleep-based interventions should be applied.



Krista Grobelny

HPM

I-6

Analyzing the correlation between Neonatal Abstinence Syndrome (NAS) and average drive-time to methadone clinics providing pregnancy services for pregnant women in Pennsylvania Counties, 2016-2017

Objective: To analyze whether there is a correlation between average drive-time to methadone clinics that provide services (PPWs) to pregnant women in Pennsylvania and county-level Neonatal Abstinence Syndrome (NAS) rates. Methods: We used NAS rates provided by the Pennsylvania Health Care Containment Cost Council in each of Pennsylvania's 67 counties. PPWs were located using the Substance Abuse and Mental Health Service Administration's National Directory of Drug and Alcohol Abuse Treatment Facilities (2017). We then examined the drive-time from each county's population center to its three closest PPWs, using CDXGeodata's GeoRoute Service. This data was used to determine the average drive time from the population center to each PPW. An independent means T-test was performed to analyze the statistical significance of NAS rates in counties with the top 10 shortest and longest drive-times. Results: We found no association between the rate of NAS by county and the average drive-time from county population centers within Pennsylvania to PPWs ($R^2=0.0052$). Moreover, no statistical significance in NAS rates between counties with the top 10 shortest average drive times and the 10 longest average drive times were identified ($t(9) = -0.0124$, $p(p < .05) = 0.9660$). Conclusion: Our analysis failed to reveal a relationship between the rate of NAS by county and the average drive-time to the three closest PPWs to county population centers.

Assessing Genetic and Lynch Syndrome Goals within Comprehensive Cancer Control Plans

Introduction: Colorectal cancer is the third most deadly cancer in the United States and Lynch syndrome (LS) is the most common hereditary colorectal cancer. Current guidelines recommend screening all individuals with newly diagnosed colorectal cancer tumors for LS to reduce morbidity and mortality in relatives. However, states vary in their inclusion of genetic-related strategies in their cancer control plans and the relationship between inclusion of these strategies and incidence, and incidence-based mortality for LS is unclear. Methods: I categorized 51 state cancer control plans by five levels of evidence-based genetic strategies. For each state, I obtained incidence and incidence-based mortality for colorectal cancers diagnosed before age 50 through the National Program of Cancer Registries (NPCR) and Surveillance, Epidemiology, and the End Results (SEER) program from 2001-2015. Using ANOVA, I assessed possible relationships between cancer control plan categories and each state's incidence of colorectal cancer and incidence-based mortality for LS. Results: Six states (11%) had no genetics mentioned in their plan, 9 (17%) state plans included a genetics-related term, 13 (25%) plans had a genetics-related objective, 20 (39%) plans had a LS specific objective, and 4 (8%) of state plans had an objective related to screening all individuals with newly diagnosed colorectal cancers for Lynch syndrome. Overall, the inclusion of genetics in a state cancer control plan was not related to colorectal cancer incidence ($p=0.90$) nor incidence-based mortality ($p=0.50$) of colorectal cancer diagnosed before age 50. Conclusion: I observed no relationship between measures of colorectal cancer incidence or mortality and state cancer control plan objectives, most likely because most state cancer plans that incorporated genetic screening were only developed within the past 10 years. However, 78% of states included a genetics-related goal in their cancer control plans. Furthermore, plans developed after 2015 were more likely to include goals related to universal screening, genetic testing, or genetic counseling. Future analyses should focus on evaluating shorter term outcomes such as earlier age of colorectal cancer diagnosis, as well as the number of at-risk individuals identified via cascade screening of relatives.



Alyson Harding

EPIDEM

III-6

Assessing community opioid awareness using the Community Assessment for Public Health Emergency Response (CASPER) methodology in South Pittsburgh Neighborhoods

Background/Objective: Overdose rates in Allegheny County and throughout the United States have increased in recent years. While the average number of overdose deaths in Allegheny County in 2016 was 52.9 per 100,000, areas of the county have death rates as high as 80 per 100,000. This summer, I interned with the Allegheny County Health Department (ACHD), assisting in the coordination of a door-to-door community survey about opioid overdose awareness. Goals of this project included: 1) assessing community knowledge and sharing resources, and 2) practicing the Community Assessment for Public Health Emergency Response (CASPER) methodology and deploying surge capacity volunteers. **Methods:** The CASPER methodology was developed by the Centers for Disease Control and Prevention as a rapid needs assessment tool for post disaster situations. Using a two-stage cluster sampling design, we selected thirty random census blocks from the South Pittsburgh neighborhoods of Southside, Mt. Washington, and Mt. Oliver. We then selected seven random housing units per census block to survey, and developed a replacement scheme. We recruited and trained volunteers, who conducted door-to-door surveys in June 2018. The survey was developed in conjunction with the Allegheny County Department of Human Services, the City of Pittsburgh, and CONNECT Communities. Depending on the surveyor's preference, data were collected via paper survey or through an electronic app called Survey123. We conducted descriptive data analyses in Microsoft Excel. **Results:** Over four days, 51 volunteers approached 705 housing units to complete 100 surveys, and distributed 20 naloxone kits. The project engaged members of the Allegheny County Medical Reserve Corps, students and faculty from the University of Pittsburgh, as well as staff members from the ACHD. Of surveyed participants, 42% said that opioid overdose was a major problem in their area, 79% had heard of Narcan (Naloxone), and 97% reported they would call 911 if they saw someone overdosing. Nearly half of participants surveyed knew someone personally who has overdosed. **Conclusion:** The opioid crisis is a complex public health issue that will take the involvement and cooperation of community groups, law enforcement agencies, medical professionals, and public health practitioners to combat. This door-to-door survey allowed the ACHD to begin conversations about opioid overdose awareness with community members.



Emmett Henderson

BCHS

VI-10

Characterizing Patterns of Social Support Among Midlife and Older Men Who Have Sex With Men

Background: Gay, bisexual, and other men who have sex with men (MSM) in midlife (40-64 years) and older adulthood (65+ years) experience higher rates of social isolation compared to their heterosexual counterparts. There have been no longitudinal analyses of social support among MSM. The purpose of this study was to use a person-centered approach to understand how patterns of social support manifest and change over time among MSM. **Methods:** Data were from Understanding Patterns of Healthy Aging among Men Who Have Sex with Men a sub-study of the Multicenter AIDS Cohort Study (MACS). This study applied longitudinal latent class analysis across three waves of data collection on 1,120 individuals age 40 or older at baseline to identify subgroups who differ on multiple indicators of social support types over time. Classes of social support were characterized by the source of support (primary partner(s), biological family, created family, friends, acquaintances, people in your church, co-workers, other) and degree of support received (not at all, very little, somewhat, quite a bit, a great deal, prefer not to say). **Results:** Five substantive classes were identified: Low social support, i.e., low levels of support from all sources across time; Moderate friends and family support, i.e., low levels of support from all sources except friends and family; Dynamic support, i.e., inconsistent levels of support over time; friends and family centered, i.e., high levels of support from friends and family; and, high support, i.e., high levels of support from all sources across time. **Conclusions:** Unique social support types emerge among midlife and older MSM. This study highlights the importance of understanding heterogeneous social relations and developing tailored interventions to promote social connectedness in this population.



Brandy Hill

EOH

I-5

Acute impact of pollution control breach on asthma control in vulnerable populations near U.S. Steel's Clairton Coke Works following 2018 Fire

Rationale: Racial, socioeconomic, and geographic disparities exist in asthma. Previous studies relate exposure to sulfur dioxide (SO₂) with asthma exacerbations. We utilized the University of Pittsburgh Asthma Institute Registry (AIR) to study associations of asthma exacerbations between two populations of asthmatics. The objective was to examine if asthma symptoms worsened following a significant fire event that destroyed pollution control equipment at the factory. Participants' perceptions of their environment were also evaluated.

Methods: AIR is a volunteer asthma patient registry (n=2052). AIR was used to identify asthmatics in regions potentially impacted by the Coke Works fire, as compared to a more distant control group. Allegheny County Health Department (ACHD) identified "affected" locations. Of the 269 participants selected, 143 were from affected zip codes, and 90 from unaffected areas. Phone calls and emails were sent, of which 83 responded. An Institutional Review Board (IRB) approved questionnaire was administered via phone by the Asthma institute between February 1 and February 20, 2019. Participants were asked to recall health and environmentally-related events from the 4 weeks prior to survey administration. Survey data was analyzed with demographic, clinical, and physiologic data obtained during enrollment in AIR. Chi-Square statistics and the two-tailed Fisher Exact probability test were used to compare control and study groups. Concentrations of SO₂ were generated by Carnegie Mellon University's Real-time Affordable Multi-Pollutant (RAMP), and ACHD air sensor data. Mean hourly and daily SO₂ levels were examined and compared with historical data. Geographic information system (GIS), ArcGIS 10.6 software was used to geocode participants by residential address to model their estimated SO₂ exposure, proximity to air sensors, and Clairton Coke works.

Results: The cohort was predominantly females (84%), white (60%) with 54% having at least a college degree, and 47% resided in affected areas. Chi-square and F-Test analysis indicated groups were independent and no significant demographic difference existed between them. The study group reported a significant increase in asthma exacerbation (RR: 1.76, 95% CI 1.1-2.8, p<0.01). These patients had a historically lower mean FEV₁% Pred of (76%) contrary to control group (86%), and significantly reduced FEV₁% Pred (<60%) (RR: 3.39, 95% CI 0.99-11.6, p<0.05). Though not significant in this small cohort, an increased risk of medication usage (RR 1.38, 95% CI 0.96-1.99, p=0.07) was noted. Additionally, 72% of the study group indicated a smell in their outside air. The smell most reported was "rotten egg" (RR: 6.63, 95% CI 1.48-3.15, p<0.0001). The majority was aware a major environmental event occurred near their home (RR: 5.36, 95% CI 2.24-12.8, p<0.0001) and felt air pollution in their area sometimes worsens their asthma symptoms (RR 1.67, 95% CI 1.22-2.29, p<0.001). SO₂ data indicated several daily and hourly averages >75ppb following the fire.

Conclusions: In contrast with the control group, study group participants are concerned about the effects of air pollution in their community on their asthma. Study group participants felt that their communities' outdoor air quality impacts their asthma. The study group also increased their asthma medication beyond what they typically used following the fire. Historical lung function was also worse in the study group, suggesting that longer term exposures may have contributed to poorer lung function. Interestingly, 46% of people in "affected" areas were unaware of the fire this may reduce the impact of information bias. The study area is considered a non-attainment zone for SO₂, the nature of the factory accident may potentially increase exposure onto an already vulnerable population. These data suggest long term exposure effects may impact respiratory disease and require further study, as well as potential remediation.



Brandy Hill

EOH

VI-1

Geospatial Analysis of Asthma Severity and Traffic Pollutant Exposure in Urban and Suburban Allegheny County, PA

Department of Environmental and Occupational Health, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA1; Center for Atmospheric Particle Studies, Department of Mechanical Engineering, Carnegie Mellon University, Pittsburgh, PA2; University of Pittsburgh Medical Center (UPMC) Asthma Institute, Pittsburgh, PA3. Special acknowledgment to UPMC Asthma Institute Research Coordinators for their contributions to the AIR Registry.

Rationale: Racial, socioeconomic, and geographic disparities exist in asthma. Previous studies correlate exposure to traffic-related pollutants with asthma and episodic respiratory exacerbations. We analyzed the University of Pittsburgh Asthma Institute Registry (AIR) for associations between asthma severity, traffic-related pollutants, and residency in environmental justice (EJ, having >20% impoverished residents and/or >30% identified as non-white) versus non-EJ census tracts in Allegheny County.

Methods: AIR is a volunteer asthma patient registry (n >2,000) with a range of severity recruited from 2007 to the present within the Pittsburgh region. Asthma severity scores were based upon clinical (medication regimen) and physiologic (lung function) data obtained at time of enrollment. Exposure estimates for black carbon (BC) and nitrogen dioxide (NO₂) for Allegheny County census tracts were generated using a land use regression model and ranked into quartiles from low to high exposure (Q1 to Q4). AIR patients were assigned to quartiles based upon residential addresses. Relative incidence of severe asthma (SA) for participants in each quartile was calculated relative to the lowest. Patients in EJ and non-EJ tracts were compared to identify if subjects were disproportionately experiencing SA based on socioeconomic factors. Geospatial analysis was used to identify participant and SA clusters using a Euclidean nearest-neighbor distance method.

Results: The entire AIR cohort deviated from the overall county population with more females (70% vs. 51.5%), minorities (32% vs. 21.2%), and higher education level (48% vs. 39% with at least a college degree). Of the AIR Cohort, 47% lived within EJ tracts compared to only 28% of all county residents. AIR participants as a whole were over-represented in areas of higher pollution exposure. For example, over twice as many patients reside in the highest NO₂ quartile compared to the lowest. The number of SA cases relative to non-severe appeared unchanged across BC exposure, but increased with NO₂ exposure. Relative incidence of SA was not different between EJ and non-EJ areas. Nearest neighbor cluster analysis produced statistically significant ratios for entire cohort.

Conclusions: AIR study participants were disproportionately represented in EJ regions and areas of high pollution. This may reflect an increase in asthma prevalence in these areas and/or recruitment bias. A trend for SA to be associated with NO₂ exposure, but not EJ location suggests that environmental factors like air pollution may contribute to severe asthma independent of socioeconomic factors.



Megan Hoenig

HUGEN

I-7

Genetic Testing Outcomes in a Utilization Management Genetic Counseling Clinic Compared to Genetic Testing Ordered by Non-Genetics Providers

UPMC Children's Hospital of Pittsburgh started the Genetic Testing Clinic (GTC) in January 2018. The GTC is a genetic counseling-only clinic that offers same-day and scheduled appointments for referrals from non-genetic providers ordering a genetic test. This clinic is unique in that it incorporates utilization management (UM) for the requested genetic test while providing comprehensive genetic counseling. After one year and 459 patients, outcomes of the clinic, such as test order modifications, family history risk assessment and triage, and facilitation of familial testing were assessed. Upon IRB approval, retrospective chart review of the electronic medical record and internal databases were performed for 200 of the GTC patients to obtain detailed outcomes of the clinic. Additionally, chart review of genetic testing ordered by non-genetics providers in 2017 was performed for a comparison. Proportion analysis was performed and identified 13.5% (27/200) of the GTC patients had unrelated family history risk factors, for which a referral to cancer genetics or cardiogenetics was provided; 6.5% (13/200) of GTC patients had their test modified based upon genetic counselor review. Additionally, the average number of business days from appointment to insurance pre-authorization submission was 16 business days for GTC patients and 23 business days for patients seen by non-genetics providers (unpaired t test $p=0.0085$). Finally, non-genetics providers often lacked documentation of the informed consent process. 77/150 (51%) did not document any types of possible genetic testing results, 67/150 (45%) documented one type of possible genetic testing result, 112/150 (75%) did not document any risks, benefits or limitations, and 149/150 (99%) did not document the possibility of incidental findings. In contrast, review of possible results, risks, benefits and limitations of genetic testing were discussed and documented routinely for GTC patients. Genetic counseling is valuable for patients undergoing genetic testing; however, not every patient receives genetic counseling. This clinic represents a service delivery model that provides genetic counseling and utilization management to patients and has public health significance as it improves access to those who might not have received it otherwise, ensures comprehensive pretest counseling, and completes insurance authorization in a timely manner.



Beth Hoffman

BCHS

III-16

It's Not all About Autism: The Emerging Landscape of Anti-Vaccination Sentiment on Facebook

Background: Due in part to declining vaccination rates, in 2018 over 20 states reported at least one case of measles, and over 40,000 cases were confirmed in Europe. Anti-vaccine posts on social media may be facilitating anti-vaccination behaviour. This study aimed to systematically characterize (1) individuals known to publicly post anti-vaccination content on Facebook, (2) the information they convey, and (3) the spread of this content. **Method:** Our data set consisted of 197 individuals who posted anti-vaccination comments in response to a message promoting vaccination. We systematically analysed publicly-available content using quantitative coding, descriptive analysis, social network analysis, and an in-depth qualitative assessment. The final codebook consisted of 26 codes; Cohen's κ ranged 0.71-1.0 after double-coding. **Results:** The majority (89%) of individuals identified as female. Among 136 individuals who divulged their location, 36 states and 8 other countries were represented. In a 2-mode network of individuals and topics, modularity analysis revealed 4 distinct sub-groups labelled as "trust", "alternatives", "safety", and "conspiracy". For example, a comment representative of "conspiracy" is that poliovirus does not exist and that pesticides caused clinical symptoms of polio. An example from the "alternatives" sub-group is that eating yogurt cures human papillomavirus. Deeper qualitative analysis of all 197 individuals' profiles found that these individuals also tended to post material against other health-related practices such as water fluoridation and circumcision. **Conclusions:** Social media outlets may facilitate anti-vaccination connections and organization by facilitating the diffusion of centuries old arguments and techniques. Arguments against vaccination are diverse but remain consistent within sub-groups of individuals. It would be valuable for health professionals to leverage social networks to deliver more effective, targeted messages to different constituencies.

Physicians' opioid prescribing patterns after receipt of pharmaceutical payments related to opioids

Research Objective: Prescription opioids, which have been heavily promoted to physicians, account for 25% of opioid overdose mortality, and changing provider behavior to reduce inappropriate opioid prescribing is a major policy focus. Although pharmaceutical payments to physicians have been associated with increased prescribing, little is known about the nature of this relationship, such as whether the association is non-linear or if the association varies by specialty or other provider factors. Therefore, we evaluated for temporal associations between pharmaceutical payments related to opioids and subsequent opioid prescribing behavior. Study Design: To determine the relationship between pharmaceutical payments for opioids in a given year and physicians' opioid prescribing patterns in the subsequent year, CMS 2014-2015 Open Payments data was matched to the Medicare Part D 2015-2016 dataset. Open Payments includes all payments physicians receive from pharmaceutical companies and device manufacturers; Part D data includes outpatient prescription fills identified by prescribing physicians. We categorized providers into quartiles based on the proportion of a physician's Part D claims that were for opioids. Pharmaceutical payments included food and beverage, travel and lodging, education, and consulting (not research). Payment amounts were split into four groups: \$0, \$1 to <\$19, \$20 to <\$100, and \$100. Generalized ordinal logistic regression models were employed to account for a non-monotonically changing relationship between quartile of prescribing and payment amount. Models were stratified by physician specialty, and controlled for non-opioid related pharmaceutical payments, patient panel size, average patient age and risk score used to adjust Medicare Part D plan payments, physician gender, state overdose death rate, and year of prescribing. Population Studied: 238,988 providers who prescribed opioids in 2015-2016 who were matched to the Open Payments database in the year prior. Principal Findings: Approximately 12% of physicians received a payment from opioid manufacturers related to opioids. The association between amount of payment and the odds of being in a higher quartile of prescribing changed between levels of prescribing. For example, among primary care physicians, those paid \$100+ had double the odds (aOR=2.13) of being in the top three quartiles of opioid prescribers versus the bottom quartile, but triple the odds (aOR=3.62) of being in the fourth quartile versus the bottom three. This relationship varied between specialties. The strongest relationship was among psychiatrists and neurologists, whose odds of being in the highest quartile of prescribing compared to the bottom three were 11 times higher (aOR=11.62) for those receiving \$100+ versus \$0 and 2 times higher (aOR=2.03) for those receiving \$1-\$19 versus \$0. The weakest relationship was among surgeons, whose odds of being in the highest quartile of prescribing were 35% higher among those receiving \$1-\$19+ versus \$0 (aOR=1.35). Conclusions: The non-monotonic relationship between increased prescribing and payment amount varied between specialties. For some specialties, there may be a threshold effect at which the payment amount is no longer associated with prescribing. Implications for Policy or Practice: Our findings are informative to Medicare, health systems, and pharmaceutical firms in identifying factors influencing opioid prescribing.



Mara Hollander

HPM

VI-6

Adults and Youth Enrolled in Permanent Supportive Housing Experience Changes in Health Care Utilization and Spending

Research Objective: Housing is an important social determinant of health: people who are homeless typically have higher inpatient and emergency department (ED) use and lower average life expectancy than those who are housed. Permanent Supportive Housing (PSH) programs provide homeless individuals with non-time limited housing and access to case management and other health services, which may improve health outcomes and reduce downstream costs of care. In this study, we evaluated long-term changes in utilization and spending associated with the receipt of PSH among formerly homeless Medicaid recipients in Pennsylvania. Our analyses address limitations of prior research, which rarely explores outcomes more than 12 months beyond PSH entry or differential impacts of PSH on children versus adults. Study Design: We matched Homeless Management Information System (HMIS) data for 54 of Pennsylvania's 67 counties to Medicaid enrollment and administrative claims. We measured within-person changes in inpatient stays, emergency department (ED) visits (overall and non-emergent use), and community-based behavioral health service utilization from 1 year before and up to 3 years after PSH entry. Regression analyses, which were stratified by age (<21 vs. 21 years and older), controlled for pre-PSH individual characteristics (gender, race/ethnicity, region, rural residence, and baseline comorbidities), changes since baseline in individuals' health, and time trends. Population Studied: 1,670 adults (≥ 21 years at PSH entry) and 1,129 youth (<21) enrolled in both PSH and Pennsylvania Medicaid during the period 2008-2015. Principal Findings: The median length of stay in PSH in our sample was 942 days (25th to 75th percentile: 547 to 1,572 days). Three years after PSH entry, the adjusted number of acute care visits per 100 person-months declined 37.2% from baseline (95% CI: 7.8% - 66.7%) among adults. Adjusted adult monthly ED use declined 21.4% (95% CI: 5.5% - 37.2%) relative to baseline, and nonemergent ED use declined 24% (95% CI: 2.4% - 45.5%) from baseline. Residential SUD and mental health spending decreased by 89.5%, and inpatient spending decreased 51%. Among youth enrollees, we observed no significant changes in acute care or overall ED utilization following PSH entry, but large decreases in community SUD and mental health spending (37.4% from \$85.32) and in spending overall, which was \$363.60 at baseline and decreased 30.8% to \$251.58. Conclusions: PSH is associated with decreases in inpatient and ED use, as well as residential and inpatient spending, among adults, and decreases in community behavioral health spending. Although our estimates cannot be interpreted as causal effects of housing, our findings suggest the potential for Medicaid programs to benefit when unstably-housed adult beneficiaries with significant health needs are placed into PSH. Implications for Policy or Practice: A substantial body of research shows that homelessness contributes to high health care costs and poor health, which may perpetuate housing instability. States may be able to address avoidable acute care utilization and unmet behavioral health needs for homeless adults by providing PSH. Because homeless populations are disproportionately served by Medicaid, particularly in expansion states, there may be short and long-term financial benefits to Medicaid programs from providing housing to homeless enrollees. These findings can inform current CMS efforts to integrate Medicaid and housing services.



Mallory Hudson, Trinity Sprague and Makenzie White

BCHS

I-4

An Interdisciplinary Collaboration in International Engineering Projects

As early as 1970, interdisciplinary work has been discussed in scholarly literature as an approach for addressing complex problems. Recent research shows that interdisciplinary approaches are crucial for achieving project success and sustainability. In 2012, the University of Pittsburgh Chapter of Engineers Without Borders identified a need for public health problem-solving approaches and created a new position on the executive board: public health lead. In January of 2018, several graduate students from Pitt Public Health joined EWB-Pitt and filled leadership positions on the international team and executive board, completely integrating public health and engineering. Attitudes and opinions regarding the partnership were assessed using survey methods. Survey responses showed strength in the group's differences: public health was highly valued by members (regardless of field of study), positive attitudes about the collaboration, and an interest in further opportunities for interdisciplinary work. By combining public health and engineering, EWB-Pitt is not only tackling technical issues (i.e., water insecurity), but doing so more effectively by utilizing community-engaged strategies, as well as social and behavioral theories and research methods to assess our communities at the individual, organizational, and community levels.



Maura Elizabeth Jacob

BCHS

V

The Live Well Allegheny Conversation Project: Increasing Social and Civic Engagement in Order to Address Health Disparities in the Mon Valley

The Mon Valley region currently experiences a disproportionate burden of chronic disease when compared to county and national standards. Live Well Allegheny (LWA) Mon Valley, a program of the Allegheny County Health Department, works to combat regional disparities by partnering with area municipal councils and others to draft and implement health policies that combat chronic disease behaviors and promote healthy community environments. The effectiveness of the LWA program is hindered by a lack of community buy-in and direct resident engagement. The purpose of this thesis is to produce a program plan for a LWA community-engagement initiative, called the LWA Conversation Project, which will host resident-led discussions and create action plans inspired by resident input. The program plan is drafted using the PRECEDE-PROCEED model and includes community health assessments, implementation and evaluation frameworks, and a facilitator's guide. The intervention incorporates community organizing principles and draws from established community engagement models. The creation of a resident-driven complement to the current Live Well Allegheny program serves the dual purpose of empowering residents to take an active role in health promotion in their region and of providing LWA and its partners with first-hand information about the needs of the communities they serve. By increasing the social and civic engagement of the region's residents, the program will increase the social capital and overall health of the Mon Valley region through the empowerment of individuals to become active participants in shaping their community.



Zachary Koenig

IDM

V-4

Rift Valley Fever Virus Sensitivity to Type III Interferons at Epithelial Cell Barriers

Rift Valley fever (RVF) is a zoonotic mosquito-borne emerging infectious disease. RVF virus (RVFV) causes highly lethal disease primarily in domesticated livestock with various clinical manifestations. One of the most devastating characteristics seen in previous outbreaks are among pregnant livestock which experience "abortion storms" wherein the virus induces abortogenic rates of 90-100%. Type III interferons, the IFN- λ family of proteins, are a recently characterized group of innate antiviral molecules that function in modulating host immune responses to viral infection at epithelial barriers, including at the placenta. Primary human trophoblasts, the barrier cells of the placenta, constitutively release IFN- λ 1 which has been shown to protect trophoblast and non-trophoblast cells from Zika virus infection. These studies have been designed to examine the possible modulatory effects of type III IFNs on RVFV. Because of the ability of RVFV to bypass the placental barrier in a number of animal species, we hypothesized that RVFV may be insensitive to some of the antiviral effects of type III IFNs. We further hypothesized that, a viral nonstructural protein, NSs, which is known to inhibit other interferon type pathways, would similarly inhibit IFN- λ 1 antiviral responses in these experiments. Our initial results indicate that exogenous IFN- λ 1 treatment of HepG2 cells immediately following infection was able to reduce viral titers 24 and 48 hours after infection. Future work will focus on elucidating the function of RVFV NSs protein in modulating the type III IFN immune response as well as contrasting RVFV with Zika virus infection with exogenous IFN treatment.



Joseph Krajcsik

HPM

V-14

Transferring Psychiatric Patients under EMTALA

The current method of transfer used for incoming psychiatric patients is often inefficient, leaving many psych patients waiting in a holding room for hours before they are transported to a more appropriate facility with the necessary capabilities to properly treat them. For hospitals participating in Medicare, these transfers are governed by the Emergency Medical Treatment and Labor Act (EMTALA), which among other things, requires an “unstabilized” patient to be transferred via an “appropriate transfer” using qualified personnel and equipment. Ambulances are commonly used, but can be expensive and stigmatizing, and because they are incredibly busy, they often place these transfers low on their priority list, which can result in elongated waiting times. This frustrates hospitals, the patient, and their family members, who often request to drive their loved one to the nearby facility themselves. EMTALA is not explicitly clear on many specifics regarding what constitutes an “appropriate transfer,” or “qualified personnel,” particularly when it comes to transferring psychiatric patients, whose condition may not be as tangible or easily manageable as a physical injury. A dive into Interpretive Guidelines, promulgated by the Centers for Medicare and Medicaid Services (CMS), as well as relevant case law, offers a little direction, but ultimately shows that the transfer of an unstabilized psychiatric patient in a private vehicle by a family member, likely would result in a violation of EMTALA’s “appropriate transfer” requirements. If they are unstabilized, by definition, they are considered a threat to themselves or others, and it would be a legal risk to allow them to be transferred to a more appropriate facility without some sort of medical supervision and equipment, or security. However, if they are deemed stable, their transfer is no longer regulated by EMTALA, so they would be allowed to be privately transferred by a family member. For psychiatric patients, the line between stabilized and unstabilized is extremely fine, and great care must be exercised before labeling someone as stable for discharge or transfer.

Association of FTO-rs9939609 with body mass index in a fixed-effect meta-analysis in people of Polynesian ancestry living in Aotearoa/New Zealand and other Pacific nations

The fat mass and obesity associated (FTO) locus consistently associates with obesity and increased body mass index (BMI) in most ancestral groups with rs9939609 being the most commonly described variant associated with anthropometric measures of adiposity. Yet, previous small studies have failed to replicate the association of FTO with obesity among people of Polynesian ancestry. In this study, we tested for association of rs9939609 with BMI in (1) 1,239 people of East Polynesian ancestry (indigenous NZ Māori, Cook Island Māori and Tahitian) living in Aotearoa/New Zealand and (2) 771 people of West Polynesian ancestry (Sāmoan, Tongan, Niuean, Pukapukan, Tokelauan and Tuvaluan) living in Aotearoa/New Zealand, and in (3) 3,072 indigenous Sāmoans living in the Independent State of Sāmoa. Published statistics of three small sample sets of Polynesian (Tongan, n=116), Melanesian (Solomon Islander n=129) and Micronesian (Kiribatian living in the Solomon Islands n=75) peoples were meta-analysed with the three study groups for association of rs9939609 with BMI. The minor allele frequencies (MAF) for the East Polynesians, West Polynesians and Sāmoans were 0.25, 0.19 and 0.20 respectively. Significant evidence of association was not found ($P > 0.05$) between rs9939609 and BMI in the East (n=1,239, 0.55kg/m²), West (n=711, 0.51kg/m²), or in the Sāmoan group (n=3,072, 0.35kg/m²). Meta-analysis of these groups along with the small Tongan group, did show association of the rs9939609 minor (A) allele with higher BMI in Polynesian peoples (0.38kg/m², $P = 0.023$ n=5198,) but not with the wider Oceanic (0.28 kg/m², $P = 0.064$, n = 5,402) samples using a Bonferroni adjusted P-value of 0.025. These data demonstrate that rs9939609 is associated with BMI in Polynesian peoples. Previous studies investigating the association of FTO with BMI among people of Polynesian ancestry may have been limited by low statistical power.



Florence Kwok

EPIDEM

II-4

Understanding How Patient Perceptions of Clinic Contribute to Non-Urgent Emergency Department Visits

Authors: Florence Kwok, Marnie Bertolet, Alicia Colvin, Katherine Gitz, Noelle Marousis, Maria Marcos, Kristin Ray. Research Objective: On average, 37% of all emergency department (ED) visits are judged to be non-urgent. Use of the ED for non-urgent conditions may lead to excessive healthcare spending, unnecessary testing and treatment, and weaker patient-primary care provider relationships. To inform quality improvement interventions to reduce ED use, we examined parent perceptions of access at UPMC Children's Hospital Primary Care Center (PCC) of Oakland among families who presented to the ED versus the PCC with acute respiratory infections. We hypothesized that caregivers with ED visits would perceive decreased access at the PCC compared to caregivers with PCC visits. Study Design: From December 2017 to July 2018, we identified children aged 1-5 years who are primary care patients at the PCC who received care for an acute respiratory infection (viral upper respiratory infection (URI), conjunctivitis, pharyngitis, otitis, and sinusitis) at either the PCC (controls) or the ED (cases). Caregivers were called 1-4 weeks after their visit and invited to participate in a phone survey to assess their perceptions of access at the PCC. We compared the percentages of caregivers with ED versus PCC visits for each response. Population Studied: Seventy-six caregivers of pediatric patients of an urban, academic primary care practice in southwestern Pennsylvania, including caregivers from 36 PCC and 40 ED visits. Principal Findings: Caregivers who presented at the ED were more likely to identify as African American, have only one child at home, and be younger. No differences were found in the distributions of insurance types, caregiver education, and child age. While all caregivers identified the PCC as their usual practice, only 65% of caregivers with ED visits reported having a usual doctor compared to 80% of those with PCC visits. Additionally, 25% of those with ED visits reported never calling the PCC for advice, compared to only 6% of those with PCC visits. Caregivers who presented at the ED reported better perceived access in terms of availability, affordability, geographic accessibility, and accommodation of care at the PCC. However, they reported poorer perceived access for specific acceptability domains, including trust and communication. Conclusions: Among PCC patients, caregivers using the ED for acute respiratory infections appeared less connected to the PCC as they did not identify a specific primary care pediatrician, had never called for advice, reported lower trust in PCC providers, and had lower perception of the quality of communication with doctors at the PCC. To reduce ED use, focusing on increasing connection through improved telephone access, effective communication, and bolstering parent-pediatrician relationships were identified as potential interventions for ongoing quality improvement work.



Huang Lin

BIOST

I-15

Analysis of Composition of Microbiomes with Bias Correction(ANCOM-BC)

Increasingly, researchers are finding associations between human diseases and human microbiome. Therefore, determination of differentially abundant taxa across groups, while controlling false discovery rate, is an important problem. Unlike commonly seen genomic data, the microbiome data are compositional data with excess zeros. Consequently, it is not appropriate to apply standard methods when identifying differentially abundant taxa. Recently a method called "Analysis of Composition of Microbiomes (ANCOM)"² was proposed by Mandal et al. (2015) to address this problem which can be computationally intensive. In this paper, we introduce a bias-correction methodology, referred to as "Analysis of Composition of Microbiomes with Bias Correction (ANCOM-BC)", that is computationally more efficient than ANCOM while retaining all its important features. Thus, similar to ANCOM, it controls the FDR and maintains a high power. However, unlike ANCOM, ANCOM-BC also provides p-value associated with each individual taxon and can be applied to multi-group comparisons.



Qiao Lin

EOH

II-18

Rapidly accumulated tobramycin resistance by *Pseudomonas aeruginosa* in CF-like acidic pH environment

Background: Cystic fibrosis (CF) is a genetic disease with a loss of cystic fibrosis transmembrane conductance regulator (CFTR) function that leads to impaired airway host defense. Chronic infection and colonization by gram-negative *Pseudomonas aeruginosa* (*P. aeruginosa*), an opportunistic pathogen, contribute to high mortality rates in CF. While the airway surface liquid of CF patients becoming more acidic with aging, the prevalence of *P. aeruginosa* lung infection also gradually increases over time in CF patients from age 2 to 45 and *P. aeruginosa* eventually becomes the dominant bacterial strain colonized in the lungs of CF suffers. We previously demonstrated that the acidic CF lung microenvironment promotes *P. aeruginosa* biofilm formation and multi-drug resistance. But the effects of acidic CF lung microenvironment on tobramycin treatment-associated antibiotic resistance (AR) remains unknown. In this study, we hypothesize that the acidic microenvironment promotes faster and stronger tobramycin resistance compared to physiologically neutral pH non-CF lung microenvironment. Methods: Planktonic and bead-transfer biofilm models were used for *P. aeruginosa* PA14 evolution study in pH 6.5 and 7.5 with or without tobramycin treatment. Bacterial whole genome sequence data were acquired by Next-Generation Sequencing (NGS) technology. Results: Our results indicated that PA14 exhibited a rapid morphological change under acidic pH conditions. Acidic environment also stimulated faster and stronger PA14 tobramycin resistance compared to neutral pH conditions. NGS results showed that acidic environments elicited several DNA mutations that were likely pH-dependent. Conclusions: Our results indicated that PA14 generated AR quickly under tobramycin treatment and the acidic lung microenvironment promoted even faster tobramycin resistance in the biofilm mold of growth. The pH-dependent DNA mutations are potential targets for future treatment in CF patients to effectively eliminate *P. aeruginosa* infection.



Chia-Hsin Liu

EOH

III-10

Lipopolysaccharide-mediated chronic inflammation promotes tobacco carcinogen-induced lung tumorigenesis in the context of an immunosuppressive microenvironment

Clinical and epidemiological evidence suggest that chronic infection and inflammation increase the risk of lung cancer. *Pseudomonas aeruginosa* infection is frequently found in patients with chronic obstructive pulmonary disease (COPD) and is associated with increased lung inflammation and acute exacerbations. However, the mechanism of chronic bacterial infection-induced lung inflammation in promoting lung tumorigenesis remains unclear. To elucidate this mechanism, we established a murine lung cancer model by treating mice with or without recurrent lipopolysaccharides (LPS) from *Pseudomonas aeruginosa* in combination with nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK). Interestingly, combined LPS and NNK exposure significantly increased tumor number, tumor incidence, and tumor area compared to NNK treatment alone. In addition, the inflammatory cell counts in the bronchoalveolar lavage (BAL) including macrophages, neutrophils, and lymphocytes were significantly increased in the LPS/NNK treatment group. The BAL fluid of chemokines/cytokines, as analyzed by luminex assays, revealed higher levels of IL-17, CXCL10, GM-CSF, G-CSF, MIP-1a, and KC in LPS/NNK than in NNK treatment group. Flow cytometry analysis of the mouse lung tissue revealed that combined LPS and NNK exposure significantly increased CD4⁺ T cells including Th1, Th17, and Tregs and myeloid-derived suppressor cells recruitment in the lung. Real-time polymerase chain reaction of mouse lung tissue showed T cell exhaustion related genes, including *Pdcd1*, *Ctla-4*, *Tim-3*, *Lag-3*, and *Foxp3*, were significantly upregulated in the LPS/NNK treatment than NNK treatment. Moreover, immunohistochemical staining of LPS/NNK-exposed lung tumors showed higher PD-L1 expression than NNK-exposed lung tumors. Our data suggest that chronic LPS exposure-promoted and NNK-induced lung tumorigenesis is associated with immunosuppressive tumor microenvironment. The changes include recruitment of Tregs and MDSCs, increased T cell exhaustion, and upregulated PD-1/PD-L1 pathway, which may be used as the therapeutic target for chronic inflammation-associated lung cancer treatment.



Dongjing Liu

HUGEN

IV-18

Low-frequency genetic variants contribute to human facial morphology

The genetic basis of normal variation in human craniofacial traits is still poorly understood. Several GWAS and candidate genes studies have focused on identifying associations with common genetic variants, with moderate success to date. The influence of low-frequency variants has not been evaluated, and their contribution to facial morphology remains elusive. In order to better understand the genomic architecture of normal-range facial traits, we used burden-style tests to evaluate the role of low-frequency variants against 24 quantitative facial measurements derived from the 3D surface images. A cohort of 2447 healthy individuals of European ancestry were genotyped on Illumina OmniExpress+Exome v1.2 array. Two complementary statistical tests, Sequence Kernel Association Test (SKAT) and Combined Multivariate and Collapsing (CMC) method were performed using two ranges of minor allele frequency cutoffs (1% and 5%). A total of ~92,000 variants grouped into ~12,950 genes were included, and significance threshold was defined by Bonferroni method taking into account the number of phenotypes and the number of genes tested. We observed associations involving two genes. GRAMD1B was associated with the morphology of the lower lip (SKAT p-value = 6.34×10^{-12} , CMC p-value = 1.64×10^{-7}). There were 3 variants with MAF<1% in this gene and single variant linear regression showed a significant effect for a missense variant (rs191981781; p-value = 2.83×10^{-11} ; MAF=0.0008). OR2C1 was associated with the height of the entire face (CMC p-value = 3.05×10^{-8} , SKAT p-value = 3.86×10^{-6}). There were 7 variants with MAF<5% and single variant analysis showed suggestive significance for one variant (rs62000975; p-value = 1.90×10^{-5}). GRAMD1B and OR2C1 have not previously been implicated in human facial traits, and we consider them as potential candidate genes worthy of follow up in future studies. Our findings demonstrate that low-frequency variants contribute to normal-range human facial morphology.



Xinyan Lu

Post Doc

I-11

Uncovering access points for development of targeted therapeutics for hereditary hemorrhagic telangiectasia

Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant vascular disorder that affects at least 1 in 5000 people worldwide. HHT patients develop arteriovenous malformations (AVMs), or direct connections between arteries and veins, that can lead to stroke or heart failure. Heterozygous mutations in *ACVRL1*, which encodes ALK1, a bone morphogenetic protein (BMP) type I receptor serine/threonine kinase, and endoglin (*ENG*), which encodes a BMP accessory receptor that facilitates ligand binding, are responsible for up to 85% of HHT. However, despite our clear understanding of the genes responsible for HHT, there are no targeted medical therapies for this disease. Because HHT is thought to be caused by gene haploinsufficiency, enhancing *ACVRL1* gene expression or ALK1 signaling are logical approaches to development of HHT therapeutics. Using zebrafish as a model organism, we discovered that blood flow tightly regulates *acvrl1* expression at the level of transcription and identified an *acvrl1* intronic element that drives arterial-specific, flow-regulated gene expression. Ongoing studies are focusing on isolating the cis elements that control this pattern of *acvrl1* expression and defining the gene expression profile in *acvrl1*-positive versus *acvrl1*-negative arterial endothelial cells expression. Together, these studies will provide a clearer picture of how *ACVRL1* expression is regulated and how ALK1 activity affects arterial endothelial cell gene expression, thereby revealing access points for development of novel drug therapies for HHT.



Lingyun Lyu and Marcy Lee Nilson

BIOST

II-12

Neck Disability and Health-Related Quality of Life among Head and Neck Cancer Survivors Following Surgical and Non-surgical Treatment

Abstract Background: While neck morbidity has been described following neck dissection or surgical resection with and without radiation therapy (RT), limited studies have investigated the association between non-surgical treatment and neck dysfunction. Objective: The aims of this study were to 1) explore the association between neck disability and head and neck cancer (HNC) treatment modalities (surgery alone, non-surgical, and surgery plus adjuvant therapy) and 2) investigate the impact of neck disability and treatment modalities on Health-Related Quality of Life (QOL). Methods: Data were collected on 222 survivors after HNC treatment. Neck impairment was evaluated with the Neck Disability Index. Health-related QOL was measured using University of Washington QOL questionnaire. Logistic regression was performed to analyze the association between neck disability and HNC treatment groups. Furthermore, using constrained inference methods, trend tests were performed to test the hypothesis that the probability of neck disability is ordered among treatment groups. Multiple linear regression was conducted to explore the impact of neck disability and treatment modality on QOL. Trend tests were also performed to test the hypothesis that QOL (neck disability absence), QOL (neck disability presence), QOL (surgery alone), QOL (non-surgical), QOL (surgery and adjuvant treatment), with at least one strict inequality. Results: Over half of survivors (n=122, 55.2%) reported neck disability, with the majority (n=111, 91.0%) describing mild-moderate disability. The odds of neck disability for survivors receiving non-surgical therapy and those receiving surgery plus adjuvant treatment, compared to surgery alone, were 2.52 (95% CI, 0.84-7.59) and 4.16 (95% CI, 1.50-11.58) times higher, respectively. We discovered a statistically significant increasing trend, at 5% level of significance with $P < 0.001$, in the probability of neck disability with the lowest probability for surgery alone group and the highest probability for surgery and adjuvant treatment, the non-surgical group being in the middle. Survivors with neck disability had significantly lower QOL scores, at 5% level of significance, with $P < 0.001$. As for the influence of treatment type on QOL, the trend test revealed that the physical QOL are ordered among three treatment types ($P < 0.001$) in the following sequence: Physical (surgery alone), Physical (non-surgical), Physical (surgery and adjuvant treatment). however, there was no significant association between social QOL and treatment types at 5% level of significance ($P = 0.091$). Conclusion: While surgical treatment has been attributed to neck disability, this study suggests that non-surgical treatment may also play a significant role in the development of neck dysfunction. We also found that treatment types and neck disability



can significantly affect QOL beyond physical impairment. Thus, early identification and intervention are crucial to prevent progression of neck disability.

Henry Ma

IDM

V-15

Increased Intracranial Pressure and Electroencephalographic Abnormalities Follow Viremia in Venezuelan Equine Encephalitis

Venezuelan equine encephalitis (VEE) virus causes incapacitating febrile encephalitis in humans, and neither licensed treatments nor vaccines against VEE exist. We have developed a telemetered cynomolgus macaque model of as a model of human VEE infection to evaluate potential medical countermeasures. Fever remains the gold standard biomarker of encephalitis in macaques but is nonspecific to VEE infection. Intracranial pressure (ICP) and electroencephalography (EEG) offer additional modes of identifying encephalitis. We aimed to investigate the relationship between continuously-monitored EEG/ICP and VEE fever/viremia.

Metabolic adaptation in macrophages as a mechanism of defense against crystalline silica dust

Inhalation of respirable silica leads to silicosis, progressive pneumoconiosis associated with autoimmune diseases, tuberculosis, and lung cancer. About 2 million workers are at risk in the United States, but no specific therapy is available. Here, we hypothesize that macrophages exposed to silica undergo metabolic reprogramming, characterized by an impaired Krebs cycle, suppressed mitochondrial oxidative phosphorylation, and increased glycolysis, which leads to a pro-inflammatory phenotype. To test this hypothesis, murine macrophages RAW264.7 were exposed to silica (50 $\mu\text{g}/\text{cm}^2$) with or without priming, with lipopolysaccharide (LPS, 1 ng/ml) and metabolic parameters were assessed after silica exposure up to 24 hours. To assess the effect of silica with and without LPS on mitochondrial respiration and changes in central carbon metabolism we utilized state of the art instrumentation including the Oroboros O2k high-resolution respirometer and liquid chromatography-high resolution mass spectrometry (LC-HRMS). Lactate and lactate dehydrogenase (LDH) released in the supernatant was also measured with lactate and LDH assay. Pro-inflammatory cytokines, such as interleukin (IL)-1 β and tumor necrosis factor (TNF)- α , were quantified by ELISA and the expression of hypoxia-inducible factor (HIF)-1 and Caspase 1 was assessed using Western-Blot. Exposure of cells to a non-toxic concentration of silica augmented the activation of complex II of the electron transport chain, independently from the complex I activity, to a greater extent than LPS-primed cells. In fact, stimulation of silica-exposed cells with succinate (CII activator), with or without pre-stimulation with rotenone (CI inhibitor), increased respiration and oxygen consumption more than LPS-exposed cells. As a result, HIF-1 stabilization, caspase-1 activation, and IL-1 release were significantly elevated in silica-exposed cells. Secreted lactate was similar in silica- and LPS-exposed cells; however, the co-exposure increased lactate secretion, LDH, and cell death. In conclusion, unlike the current opinion, silica alone can induce metabolic changes in RAW macrophages that eventually determines chronic inflammation and silicosis.



Megan Marron

EPIDEM

IV-11

Metabolites associated with high versus low walking ability among community-dwelling older adults

Low walking ability is highly prevalent with advanced age and associated with a higher risk of major adverse health outcomes. Metabolomics provides the potential to better characterize molecular differences among older adults with vastly different walking abilities to provide insight into altered age-related metabolic processes contributing to the decline in physical functioning. Here, we sought to identify metabolites associated with high versus low walking ability using a nested case-control study of 120 community-dwelling adults ages 79-95 (40% men, 10% black) from the Cardiovascular Health Study (CHS) All Stars study, matched on age, gender, race, and fasting time. Using liquid chromatography-mass spectrometry, 569 metabolites were identified in overnight-fasting plasma. High versus low walking ability was defined as gait speed and Walking Ability Index scores in the best versus worst tertiles (>0.9 versus <0.7 meters/second and 7-9 versus 0-1, respectively). Ninety-six metabolites were associated with walking ability extremes ($p < 0.05$, $q < 0.30$), where 24% were triacylglycerols. Triacylglycerols containing mostly polyunsaturated fatty acids (e.g., omega-3) were higher, whereas triacylglycerols containing mostly saturated or monounsaturated fatty acids were lower among those with high versus low walking ability. Arginine and proline metabolism was a top pathway identified. Body mass index partly explained the association between a subset of metabolites and walking ability extremes. These findings may partly reflect pathways of modifiable risk factors of excess dietary lipids and lack of physical activity contributing to obesity, which then causes further alterations in metabolites and metabolic pathways, leading to decline in walking ability in this cohort of older adults.



Heritability and Prevalence of Perceived Mental Fatigability in the Long Life Family Study

Fatigability is a multi-dimensional trait with physical (whole-body tiredness) and mental (cognitive tiredness) constructs. Perceived physical fatigability is greater with age and is modestly heritable, but little is known about the epidemiology and heritability of perceived mental fatigability. We examined heritability and prevalence of perceived mental fatigability across age and sex among older adults enrolled in the Long Life Family Study, a unique family cohort enriched for exceptional longevity. Participants (N=2342; 55% female) self-administered the Pittsburgh Fatigability Scale (PFS; scores range 0-50; higher score=higher fatigability). Analyses include a generalized linear model to examine differences across age strata (adjusted for family structure and field center) and sex, and Sequential Oligogenic Linkage Analysis Routines (SOLAR) to determine genetic heritability (adjusted for age, sex, and field center). Mean \pm SD and percent higher mental fatigability (PFS score >13) was greater across age strata: 60-69 (N=996, 5.9 \pm 6.5, 14.5%), 70-79 (N=830, 6.8 \pm 7.6, 18.7%), 80-89 (N=251, 11.7 \pm 10.8, 41.8%), and >90 (N=265, 20.2 \pm 13.6, 67.2%), $p < 0.0001$ after adjustment. Mental fatigability did not differ by sex, except in the >90 age strata: females, 21.7 \pm 13.5 vs. males, 18.0 \pm 13.5 ($p = 0.03$). Residual heritability of mental fatigability was 0.167 ($p < 0.0001$) after adjustment. Perceived mental fatigability is highly prevalent in older adults, is greater with age, and has a genetic heritability component of approximately 17%. Future work will evaluate potential risk factors of mental fatigability to identify avenues for intervention to reduce fatigability in older adults.



Olivia Messina

EPIDEM

II-11

Identifying Communities at High Risk of Tobacco Exposure in Allegheny County

Background: The tobacco retail environment, known as the point of sale (POS), is the primary channel tobacco companies use to advertise their products. Exposure to tobacco in the retail environment is associated with encouraging smoking initiation and decreasing cessation, particularly for youth. This project intended to determine characteristics of tobacco retailers in Allegheny County, associated demographic factors, and high-risk geographic areas using a community survey. **Methods:** A customized version of the Standardized Tobacco Assessment for Retail Settings (STARS) surveillance tool was embedded into the Survey123 ArcGIS mobile application for data collection. Surveys were completed for a total of 572 tobacco retailers in Allegheny County between June and August 2018. Survey results were reviewed in ArcGIS to determine store characteristics, including products, prices, and promotions. Additional analyses will be performed to determine associations between store characteristics, store density, and community demographics. These analyses will be used to identify communities at high risk of tobacco exposure in Allegheny County. **Results:** Community risk factors and associations between store characteristics, store density, and demographics will be presented. **Conclusions:** Identifying communities at high risk of tobacco exposure will help develop targeted tobacco interventions and policies in Allegheny County.



Sarah Minion

EPIDEM

IV-14

Geospatial analyses of maternal, infant, and child health people 2020 indicators in Butler County, PA

Background: Butler County, PA has a history of inadequate accessibility to maternity care, especially for low-income, uninsured mothers. Recently, the county statistics are meeting most Maternal and Child Healthy People 2020 (HP2020) goals; however, it is unknown whether pockets of disparities still exist. Our objective was to identify spatial autocorrelation of HP2020 Indicators and to analyze the association between spatial clustering and demographic and socioeconomic characteristics in Butler County.

Methods: We merged 8,950 geocoded Pennsylvania birth records (2011-2015) with 2013 census data at the block group level. Univariate Moran's I analyses were used to assess global and local spatial autocorrelation. Multivariate spatial relationships between indicators related to c-section delivery, smoking, breastfeeding, preterm birth, low birth weight, prenatal care, and adolescent pregnancy rates with important demographic and socioeconomic covariates were assessed using spatial dependence testing in individual OLS and spatial lag regression models.

Results: All 11 indicators analyzed had significant univariate local clustering; however, in multivariate global spatial analyses, only one indicator had significant global spatial clustering: percent of women initiating prenatal care in the first trimester. We identified significantly different high rate clusters of early prenatal care in the south-west corner of the county and low rate clusters in the north-east corner. High rates of college graduates, married mothers, low rates of Medicaid usage, less than or equal to high school education, and self-pay insurance best predicted spatially-distributed high rates of 1st trimester prenatal care.

Conclusions: Within Butler County, maternal and child health spatial analyses identified regions for targeted intervention. Our findings suggest that within these high-risk areas, select demographic and socioeconomic characteristics identify women most likely to not be meeting all HP2020 goals.



David Moffa

HPM

VI-12

Developing the public health workforce: Results from a core competency assessment at a local health department

Introduction: Maintaining a competent and qualified workforce is crucial to delivering the ten essential services of public health. The Core Competencies for Public Health Professionals reflect foundation skills applicable to the research and practice of public health. Core Competencies are a piece in the accreditation process but serve as the starting point for local state and tribal agencies. The competencies represent core skills applicable to the dynamic and broad practice of public health. Through assessment of these competencies, agencies can identify training needs and create a workforce development plan. The Allegheny County Health Department (ACHD) first assessed and adapted version of the training competencies in 2014 which served as the baseline for training and workforce developmental during their initial accreditation process. Recently, the same assessment tool was administered in 2018 to measure the impact of training, workforce development, and prepare ACHD for their upcoming re-accreditation application. Methods: ACHD adapted an assessment tool developed by the Public Health Foundation. The tool provided a baseline and comparative assessment in 2014, and 2018 respectively, to assess workforce competency and identify training needs. The tool in both assessment years was delivered through a web-based platform system. Respondents were able to self-rate their perceived skill on each identified core competency. Information was de-identified and collected electronically for further analysis. From September 4th-24th all active ACHD employees were able to participate and complete the survey tool. Results: In 2018, all active employees at ACHD completed the assessment. The results were analyzed by several variables such as, ACHD overall, job title, years of experience, bureau and/or program. Overall, in 2018, the Allegheny County Health Department observed a increase in average response across all domains (D1-D8). ACHD was strongest in Policy Development/Program Planning Skills (D2, avg. 2.895), Communication Skills (D3, avg. 2.983), and Cultural Competency Skills (D4, avg. 2.971). In 2018, ACHD was found with the greatest improvement in Communication Skills (D3, delta: 0.268). Limitations: Limitations of self-assessment data must be considered when using these results for workforce development planning. Self-assessment bias and workforce changes such as educational background, retirement and internal job restructuring. The increase in competencies across all domains suggests that workforce development at ACHD has been successful and should be continued.



Jenna Napoleone, Alexandra Miragaia and Mary Schiff EPIDEM III-19

Socioeconomic and geographic disparities in unmet mental health care needs among US adults 18+, National Survey on Drug Use and Health (2002-2016)

Background Mental health (MH) disorders are a leading causes of disability in the US. Many adults lack access to MH services and fail to receive treatment despite need. Disparities in health care utilization and access have been shown regarding socioeconomic factors (income level) and urbanicity; however, more research is needed to understand how income affects utilization of MH services, as well as the joint impact of financial and geographic factors on MH services. To identify US subpopulations who experience the greatest disparities related to MH treatment, we describe the relationship between income and prevalence of unmet MH care need and characterize the role of urbanicity in this association. Methods All data were obtained through National Survey on Drug Use and Health (NSDUH) for years 2002-2016. Unmet need was the main outcome and is defined as a self-reported perceived need for MH treatment/counseling that was not received in the last year. We estimated the prevalence of unmet need, the association between unmet need and income level, and report results stratified by urbanicity (Large, Small, and Non-metro) based on a priori consideration of this variables influence as an effect modifier. We present both crude and adjusted logistic regression models and stratum-specific odds ratios and 95% confidence limits. We used sampling weights, clustering, and stratification factors to generalize our findings nationally and account for complex survey design. Results Our sample consisted of 576,710 adults above the age of 18 (unweighted), 5% (n=39,171) of whom reported having needed MH treatment or counseling but had not received within the last year. The odds of unmet need were 1.79 (1.70, 1.89), 1.31 (1.24, 1.38), and 1.14 (1.08, 1.21) times higher in those making less than \$20,000, between \$20,000 - \$49,999, and between \$50,000 - \$74,999 (versus those reporting an annual household income of \$75,000 or greater) respectively, after adjusting for age, race/ethnicity, insurance status, gender, and survey year. Results were then stratified by urbanicity (a priori), with the interaction also remaining empirically significant in our final model ($p=0.045$). Consistent and significant gradient trends were observed across the strata, with the poorest individuals boasting the highest odds of unmet need across the Large, Small, and Non-metro strata. In particular, odds of unmet need were 2.02 (1.79, 2.28) times higher among non-metro residents with annual incomes below \$20,000 (relative to those making \$75,000+) after adjustment. Conclusions US adults with the lowest incomes remain most likely to report an unmet need of MH services within the past year. Access to MH services should be considered in



future research, since the poorest individuals living in non-metro areas were the most likely to report an unmet MH need.

Abisola Olaniyan, Eli Andrade and Chinwoke Isiguzo

BCHS

III-7

Facilitators and barriers to seeking and accessing childhood immunization services in Lagos state, Nigeria: Perspective of caregivers, community leaders, and health personnel

Introduction: Immunization is one of the most significant public health interventions and a cost-effective method of reducing morbidity and mortality resulting from vaccine-preventable diseases. Despite the efficacy of immunization, 1300 - 1700 children lose their lives daily in Nigeria as a result of vaccine-preventable diseases. In 2018, out of the 36 Nigerian states, Lagos state alone accounted for 8% of unvaccinated children in the country. State government and immunization partners have implemented various programs and policies to improve immunization coverage; however, the state has not yet met immunization targets in keeping with the country and World Health Organization goals. This study aimed to (a) understand the barriers and facilitators to seeking and accessing childhood immunization services and (b) explore potential interventions to improve immunization coverage from the perspective of caregivers, community leaders, and health care workers that provide immunization services in Lagos state. Method: We conducted 10 focus groups (6 to 10 caregivers and community leaders per group) from the 20 Local Government Areas across the state, and nine semi-structured interviews with healthcare workers providing immunization services. Semi-structured interview guides were developed based on extant literature and translated to the local language (Yoruba). We conducted focus groups and interviews in English and Yoruba. Preliminary findings: Both caregiver and provider groups identified individual, community, contextual, and vaccine-specific factors that act as barriers and facilitators to immunization seeking behavior. Identified facilitators include the provision of free immunization services, availability of immunization commodities, provision of incentives during special programs or campaigns, and use of community members to create awareness. Barriers highlighted include lack of knowledge of the benefit of immunization, the occurrence of adverse events following vaccination, traditional/cultural beliefs, geographical access to immunization services, poor condition of the health centers, negative healthcare worker attitude, the timing of immunization sessions, caregiver wait time and lack of regular incentives. Discussion: Stakeholders including government officials, immunization partners, and community leaders have made efforts to increase childhood immunization uptake. Our findings may inform potential interventions to improve caregiver's immunization seeking behavior and reduce childhood mortality as a result of vaccine-preventable diseases. Even though state policy ensures the availability of immunization commodities in the state, further research is needed to



investigate barriers to immunization including vaccine-hesitant behaviors among caregivers. This should be explored by geographical location (urban and rural areas) as a wide disparity occurs in immunization coverage across these regions in that state.

Teagen O'Malley

BCHS

V-10

Intimate partner violence, PrEP acceptability, and barriers to use: Guidance for PrEP use among women

Pre-exposure prophylaxis (PrEP) is a valued component of HIV prevention and has the potential to expand options for women in abusive relationships. This study assesses HIV risk, intimate partner violence (IPV), PrEP acceptability and barriers to uses. A cross-sectional survey among women (N=145) seeking health care at an urban family planning clinic in Pittsburgh, Pennsylvania from September 2018 to January 2019. The self-administered survey addressed HIV risk perception, IPV experience, and PrEP acceptability and barriers to use. Open-ended questions examined additional context about barriers to PrEP use and acceptability. Logistic regression assessed the impact of barriers on willingness to use PrEP, and whether results varied by IPV experience. Over 40% of women reported IPV experience within the past year, and 71% disclosed lifetime IPV. 45% of the participants reported being worried about HIV risk. Approximately 70% reported willingness to take PrEP. Among women reporting past-year IPV, a majority identified PrEP barriers of drug effects (96%), access/affordability (76%), and adherence (74%). Over 50% reported issues associated with intimate partner reaction as a barrier to use. Mistrust was associated with reduced willingness to use PrEP among women with past-year IPV. Findings illustrate that IPV is important to consider when examining women's PrEP interest and use. Underestimated need for HIV prevention may be present among women with IPV experience, despite short-term HIV worry. Further conversation around expanding PrEP screening to include IPV and perceived HIV worry and risk is needed. A high percentage of women were willing to use PrEP, yet a number of potential barriers were identified. Concerns around drug effects, access/affordability, and adherence may have implications on women's PrEP decision-making. Results contribute to our understanding of PrEP acceptability and use barriers among women in violent relationships. Additional research should explore intervention development that appropriately assesses PrEP interest and need, and implements care that ensures women's safety.



Teresa Pacella

BCHS

VI-3

Interprofessional Education for Health Professionals: Utilizing the power of communication and collaboration to improve patient outcomes

PURPOSE Medical errors are a major public health problem. Many errors are the result of poor communication between professional healthcare staff and are avoidable. The need exists to educate hospital staff and health profession students on how to effectively communicate and collaborate in an interprofessional setting. We designed an interprofessional education intervention for health care professionals working in the hospital setting, with a goal of improving communication and collaboration. We hypothesize the intervention will: 1) improve knowledge and attitudes related to interprofessional practice (IPP), 2) increase use of interprofessional practice skills, 3) have a positive impact on unit culture, 4) reduce adverse patient events, and 5) have a positive or neutral impact on patient outcomes.

METHODS I conducted a baseline program evaluation of this intervention. To measure baseline staff behavior, knowledge and attitudes regarding IPP as well as unit culture, I conducted pre- and mid-intervention unit observations and pre-intervention semi-structured staff interviews. I thematically coded and analyzed the qualitative data through NVivo. Quantitative data medical errors and patient outcomes (including length-of-stay and hospital-acquired conditions such as infections and falls) will be assessed using patient data through The Wolff Center. Pre- and post-intervention quantitative results will be compared to see if changes have occurred potentially as a result of the intervention.

IMPLICATIONS If the intervention is successful at changing health professionals' attitudes and behavior, and there is a corresponding reduction in adverse patient events and improvement in patient outcomes, this would support expansion of the model to other hospital units and other health care systems, which may have major implications for population health.

POTENTIAL USES FOR FINDINGS Once results are analyzed and disseminated, the IPP intervention will be implemented in other UPMC-Presbyterian units, and eventually all UPMC hospitals. Ultimately, we want IPP to become part of required hospital and healthcare accreditation standards such as The Joint Commission and also be incorporated into CMS. For this to occur, the need for further research is necessary, and further funding will be pursued for program evaluation and continuation of the intervention. Ongoing program evaluation will be necessary to implement changes in the education, implementation and hospital policy. The continued success of the program will require methodologies to be developed to identify and integrate changes in medical knowledge and clinical practice.



Yuae Park

BCHS

IV-7

Addressing in food insecurity and diabetes prevention in a predominantly Hispanic population in Oakland, CA

In 2017, an estimated 1 in 8 Americans were food insecure. The rates of food insecurity were disproportionately higher in Black (21.8%) and Hispanic households (18%) than the national average (11.8%). Food banks are a well-known critical access point for addressing food insecurity, but evidence on chronic disease prevention in these settings is limited. As a pilot project, Alameda County Community Food Bank implemented a year-long intervention, administered by bilingual (English and Spanish) staff, provided participants with monthly food packages, text-based health education, referrals to healthcare, and referral to community-based Diabetes Prevention Program across 11 food distribution sites. Of the 248 participants at baseline, 192 completed the six month assessment (77.6% Hispanic; 22.4% Non-Hispanic including Black, Asian, some of White and other ethnicities). Hispanics were less likely than other ethnicities to have completed high school or high school equivalent (32.2% vs 83.1% for others; $p < .001$). Nevertheless, while Non-Hispanics did not have significant improvements in key outcomes except for general health status, Hispanics had improvements in food insecurity scores (-.46, $p < .001$), food consumption (whole grain score +.25, $p < .001$; fruits and vegetable score +.36, $p < .01$), minutes of physical activity per week (+51, $p < .01$), and depression screening score (PHQ-2, -.44, $p < .01$). Self-reported health was significantly improved between baseline and 6 months in both Hispanic and Non-Hispanic groups ($p < .001$). These results suggest that the Food bank's intervention was successful at improving food insecurity, diet, and physical activity and engaging Hispanics in the project.



Lizz Piccoli

IDM

V-20

Disruption of HIV care services following natural disasters in the Deep South

Objective: To investigate the impact of natural disasters on the HIV-positive population in the US Deep South by identifying the individual, interpersonal, community & policy barriers to accessing care. **Background:** Every year the United States is faced with the task of responding to a myriad of natural disasters that often have dire consequences on the populations within the affected areas. Southern states have the highest prevalence of HIV in the country as well as the highest frequency of natural disasters. These events have been associated with negative changes in risk behaviour, medication adherence, socio-economic status and treatment in the HIV-positive population in the Deep South. **Methods:** A narrative review of the literature synthesizing the findings from Medline, CDSR, PubMed, hand searches and reference lists of primary articles was conducted to retrospectively investigate the short- and long-term consequences of natural disasters on populations at risk for becoming infected with HIV and those already HIV-positive. **Discussion:** Barriers to health and access to care were organized within the social ecological model. HIV prevalence data and natural disaster incidents by county were compared to identify geographic areas with the highest overlapping burden of HIV and natural disasters. This data was used to consider the potential impacts of natural disasters on both high-risk communities and individual disease status. **Conclusion:** This narrative review highlights possible areas for improvement in current disaster preparation practices. Two possible public health initiatives that could improve health outcomes of PLWH are to increase healthcare responder training on HIV and to target emergency preparation programs towards at-risk populations. It is hoped that this article will encourage future research into both the short and longitudinal impacts of natural disasters on PLWH.



Michaela Quinlan

HPM

V-13

Smoking in Allegheny County: The Local Bar Point of View

This research project was developed by University of Pittsburgh graduate student Michaela Quinlan in completion of her practicum with the Allegheny County Health Department (ACHD) to address indoor tobacco use in Allegheny County. The purpose of this report is to answer the following questions: 1) Why have smoking bars in Allegheny County chosen to remain smoking bars? 2) Are non-smoking bars and restaurants in Allegheny County aware of the vaping ordinance, Article 22 Use of Electronic Cigarette Devices in Public Places? A total of 10 bars were interviewed in the Pittsburgh-Metro area. Bars were categorized by their status of an exception in accordance with the Pennsylvania Clear Indoor Air Act (PA CIAA). Smoking bar interviews addressed Question 1, while non-smoking bar interviews addressed Question 2. The following findings are based on conducted interviews. Smoking bars can be divided into two classes: those that have interest in transitioning to non-smoking, and those that are open to transitioning to non-smoking. Bar owners who never intend to transition to non-smoking will only do so if a smoking ban is enacted. Bar owners who show interest in transitioning to non-smoking fear that doing so will lose business. Bars that have transitioned from smoking to non-smoking state they did not experience a loss in profit or a decline in business. There is little to no awareness of vaping ordinance Article 22. Service industry employees are not necessarily choosing workplaces according to their own personal smoking habits. The following recommendations for ACHD are based on interview findings. If the Pennsylvania General Assembly introduced a new bill to repeal the Section 11. Preemption Clause from the PA CIAA, Allegheny County would have the authority to pass a county-wide smoking ordinance without exceptions. ACHD should petition for the Pennsylvania General Assembly to repeal the Section 11. Preemption Clause of the PA CIAA. Opportunities exist to align efforts with other local health departments to jointly address this issue. According to smoking bar owner sentiment, an overall smoking ban is the only circumstance in which some smoking bars will transition to a non-smoking establishment. A county-wide smoking ban would also address tobacco-related health concerns for bar staff and customers, and notably decrease the risk of adverse tobacco-related health risks. ACHD should also conduct community outreach to smoking and non-smoking bars. Community outreach to smoking bars should focus on the profitability and benefits of transitioning to non-smoking, rather than negative themes such as adverse health effects. Further, the message should focus on long-term gain and identify short-term loss as a



necessary but temporary state. Focusing the outreach message on the positives of transitioning to non-smoking could mitigate reluctant behaviors. Community outreach to non-smoking bars should highlight how staff can enforce a non-smoking/vaping policy. ACHD should also distribute non-smoking signage to businesses including images of e-cigarettes and vapes.

Xinhui Ran

BIOST

II-9

Association of objective sleep apnea severity with mortality in chronic and end stage kidney disease patients

Abstract Introduction There is limited and conflicting evidence on the association of objective sleep measures with mortality in patients with kidney disease. The aim of our study was to examine the association of sleep apnea severity with mortality in patients with advanced non-dialysis dependent chronic kidney disease (CKD) and end stage kidney disease (ESKD). **Methods** In this prospective cohort study, sleep apnea severity, as measured by apnea hypopnea index (AHI) and oxygen desaturation index (ODI), was obtained using polysomnography (PSG) from patients with advanced CKD stage 4-5 or ESKD in Western Pennsylvania. Based on clinical cut points, the primary analyses categorized AHI into 4 groups (≤ 5 , 5 to ≤ 15 , 15 to ≤ 30 , >30), and ODI into 2 groups (<5 , ≥ 5). Mortality data until Dec 31, 2016 was obtained from the National Death Index. Time from PSG measurement to mortality was the primary outcome of interest. To determine if sleep apnea severity affects mortality, Cox proportional hazard models were fitted with either AHI or ODI as the primary predictor, adjusting for patient characteristics with kidney transplant as a time-varying covariate. In sensitivity analyses, AHI and ODI were also examined as continuous variables that allowed for nonlinear associations with the log-hazards. **Results** Among the 180 patients (mean age 54 ± 14 years, 37% females, 66% Whites, 39% diabetics, 49% CKD with mean eGFR (estimated Glomerular Filtration Rate) 18 ± 7 ml/min/1.73m², 51% ESKD, 71% had sleep apnea (AHI >5) and 23% had severe sleep apnea (AHI >30). Median AHI was 13 (range 4, 29). There was no significant difference in AHI in patients with advanced CKD or ESKD, but there was significant difference in ODI in patients with advanced CKD or ESKD ($p=0.046$). Over a median follow up of 9.1 [3.9; 11.1] years, there were a total of 84 (46%) deaths and 85 (47%) kidney transplants. Among transplant recipients, 20 died. Unadjusted survival analysis (Kaplan-Meier) showed there was significant difference in mortality either between AHI groups ($p<0.001$) or ODI groups ($p<0.001$). AHI was not significantly associated with increased mortality after adjusting for age, sex, race, diabetic status, CKD/ESKD status and kidney transplant (AHI >5 to ≤ 15 vs ≤ 5 hazards ratio (HR) [95% confidence interval]: 2.14 [0.96, 4.78]; AHI >15 to ≤ 30 vs ≤ 5 : 2.18[0.94, 5.01]; AHI >30 vs ≤ 5 : 1.38[0.59, 3.25]). Using AHI as continuous covariate yielded similar results. There was no overall association between ODI and mortality ($p=0.17$), but ODI had a significant interaction with age ($p=0.04$). Higher ODI is associated with increased mortality among 60 years old patients or younger (HR [95%CI] ODI <5 vs ≥ 5 : 2.48[1.26, 4.87]), but not among those above 60 years old (0.83 [0.39, 1.79]). Using ODI as a continuous covariate also did not show significant association with mortality ($p=0.72$). **Conclusion** Overall, AHI was not associated with mortality. However, higher ODI increases the hazards of mortality among younger patients.



Roberta Reis and Mark Wagner

IDM

IV-1

Regulation of Synaptic Protein Neurogranin in HIV-1 Associated Neurocognitive Disorders (HAND): Role of Noncoding RNAs

More than half of individuals infected with HIV-1 receiving combined antiretroviral therapy (cART) exhibit some degree of cognitive impairment, referred to as HIV-1-associated neurocognitive disorders (HAND). Histopathological evaluation of the frontal cortex of HIV-1 patients with and without HAND, revealed Neurogranin (Nrgn), a post-synaptic protein, is dysregulated in brain tissues from HIV-1-positive patients with HAND. However, the mechanism(s) involved in Nrgn dysregulation remains to be determined. To investigate Nrgn dysregulation, mRNA levels were assessed in post-mortem brain tissues from control and HIV-1 infected subjects with and without HAND. Our results indicate that relative Nrgn mRNA level is reduced (5.5 average fold-change, $p < 0.001$) in HIV-1 subjects ($n=49$) when compared to control subjects ($n=21$). We further used bioinformatic approaches to delineate the transcriptional regulation of Nrgn expression and identified a lncRNA transcript (RP11-677M14.2) from the antisense strand that could potentially modulate Nrgn expression. qRT-PCR analysis of HIV-1 patients brain tissue revealed that this lncRNA is aberrantly upregulated ($>12,000$ average fold-change, $p=0.0337$) in HIV-1 subjects compared to control. To identify the viral and cellular factors responsible for the dysregulation of Nrgn in neurons, we exposed differentiated neuroblastoma cells (dSH-SY5Y) to supernatant of infected human monocyte-derived macrophages (MDM) and measured Nrgn and lncRNA levels. We observed that exposure of neurons to supernatant of HIV-1 infected MDM cells resulted in 1.8-fold decrease in Nrgn mRNA and a 6.8-fold increase of RP11-677M14.2 transcript level compared to control supernatant exposed dSH-SY5Y cells. Our data suggest that both viral and inflammatory factors released by infected macrophages could affect Nrgn and the antisense transcript levels through mechanisms yet to be elucidated. Finally, to test the prediction of a discordant regulation of RP11-677M14.2 and Nrgn mRNA, we overexpressed full-length lncRNA in 293T. Our data shows that Nrgn expression was knocked down by 8.3-fold ($p=0.007$) in the cells overexpressing RP11-677M14.2. Loss of Nrgn in the brain due to HIV-1 infection is thought to contribute to synaptic dysfunction, synaptic plasticity impairment, and consequently cognitive impairment observed in HAND. Thus, our results suggest a plausible role for RP11-677M14.2 in modulating Nrgn expression, and the dysregulation of this lncRNA by HIV-1 may be one of the mechanistic links between HIV-1 and HAND.



Rachael Richter

BCHS

VI-11

The "Fuzzy" Factors of Consent and Healthy Relationships: A Qualitative Study with College Students with Disabilities

Background: Rates of sexual violence (SV) and intimate partner violence (IPV) remain high among young people in the United States and are even higher among college students with disabilities. A first step in tailoring interventions related to consent and healthy relationships for vulnerable populations is developing a nuanced understanding of how these individuals experience SV/IV.

Methods: This qualitative study focused on participants who reported a disability or health condition while in college (n=49) and an experience with SV/IPV and used thematic analysis to examine their definitions of consent and healthy relationships within a semi-structured interview.

Results: Six themes were produced from the data: 1) Healthy relationships require both mutual care for one another through trust, respect, support, and communication, as well as care for one's self as an individual through independence, self-confidence, and finding support outside the relationship; 2) Those experiencing unhealthy treatment by a partner may normalize the behaviors due to manipulation, denial, and their love for that person; 3) Dichotomous definitions of consent lead to misunderstandings and confusion about how to apply consent to real life experiences; 4) Within the context of a relationship, active consent can be facilitated through comfort and open communication but hindered by implied or assumed expectations as well as difficulty balancing one's own discomfort with the possibility of their partner feeling rejected; 5) Students assume that when healthcare providers are asking about relationship health they are trying to elicit disclosure of abuse rather than facilitating a discussion of relationship health; and 6) Students are less likely to disclose abuse when they believe health care providers are fulfilling routine screening requirements rather than asking about their safety due to genuine concern, or, when they fear that disclosure will result in a loss of control over what happens next.

Conclusion: Interventions that aim to reduce rates of SV/IPV students should take into account the lived experiences of those with an elevated risk. College students with disabilities need



interventions that address the complex nature of their sexual and romantic relationships and healthcare providers who can address relationship health in a confidential, open, and non-judgmental manner.

Natasha Robin Berman

HUGEN

I-8

Telegenetic Education in Genetic Counseling Graduate Programs

Telemedicine has made strides in acceptance and is being utilized more as a way to connect specialists with patients who otherwise would not be able to receive specialized medical services. There are currently not enough genetic counselors to meet the needs of the population and genetic counselors tend to be more concentrated in cities. There have been studies showing the efficacy of telegenetics an alternative service delivery model and studies about how providers feel about telgenetics. There has yet to be a study that looks at how graduate programs include telegenetics education in their program or how graduates of these programs feel their education has prepared them to engage in telegenetics. As the demand for genetic counselors grows, it is important that students are prepared for the type of work they will be doing once they graduate. Therefore, it is imperative to better understand if genetic counseling programs are preparing their students to feel confident in using telegenetics. A Qualtrics survey was developed by the primary investigator with assistance from the members of the thesis committee and was distributed through the Association of Genetic Counseling Program Directors as well as the National Society of Genetic Counselor email blast to general membership. Only those who graduated from a genetic counseling program in 2016, 2017 and 2018 were included in the analysis. The data was analyzed using STATA, which included the use of chi-squared tests for association. The preliminary analysis utilized chi-square testing to determine if there was an association between if students' graduate education had included exposure to telegenetics and if that had an impact on confidence. There was a statistical significance for some of the associations of inclusion of education about telegenetics in terms of confidence in providing genetic counseling using telegenetics right after graduation. There was also association found with education about telegenetics and feeling prepared to engage in telegenetics and education and feeling confident in the ability to provide psychosocial support using telegenetics. The goal of graduate level education is to prepare students to provide service based on the needs of the population, it is important to include education so that graduates are able to advocate for service delivery models when needed, but also comfortable providing these services themselves. The association between having education included and the confidence in providing the type of service, it is something that should be included in graduate education.



Caitlin Russell

HUGEN

III-13

Assessment of Hemoglobin Trait Notification in Western Pennsylvania Newborn Screening

Background: Newborn Screening (NBS) is a state-run public health program, which screens infants at birth for congenital conditions that may cause significant disability or death without prompt intervention. Carriers for sickle cell disease (SCD) are identified incidentally in the screening process, yet they are generally considered to be healthy. States' policies regarding the incidental finding vary. Programs that do disclose the results use a variety of means to notify stakeholders. The information is primarily shared for its reproductive implications. However, this is outside the traditional scope of NBS, and the history of sickle cell screening in the United States cautions against the program's potential harms. This study sought to evaluate the effects of sickle cell trait (SCT) notification on families in Pennsylvania, who are informed via a mailed letter. **Methods:** Parents in western Pennsylvania who received the SCT notification letter within the past year were surveyed regarding their understanding of SCD, anxiety related to the NBS results, and anticipated sharing of the health information. **Results:** Ninety-four families completed the survey by mail or telephone. Over 36% of respondents were unclear regarding the inheritance pattern of SCD, and 29% answered that SCT could develop into SCD. The greatest misunderstanding was found regarding Hemoglobin C trait and specific reproductive risks. The letter elicited anxiety in about one-third of parents. Over 90% of respondents planned to discuss the letter with their partner, their infant's primary care provider, and their infant at an appropriate age. **Conclusions:** The current notification letter inadequately conveys the health and reproductive implications of SCT and may contribute to anxiety in a meaningful proportion of parents. These findings support the utility of follow-up services to promote understanding and minimize stress related to carrier identification through NBS. Parents appear to appreciate the relevance of the information, based on their stated intent to share it with appropriate family and healthcare providers. Further research is needed to clarify additional effects of the program, in particular for the infant, who should be a primary beneficiary of NBS. **Public Health Significance:** This study may inform policies regarding disclosure of SCT status in NBS programs.



Emily Russell

HUGEN

IV-13

Genome-wide association study of type 2 diabetes in Samoans

Type 2 diabetes (T2D) is prevalent in the Independent State of Samoa in Polynesia with an age-standardized prevalence of 22.7% for men and 26.6% for women. Unique genetic factors may exist that contribute to this high prevalence. In addition, the effect of genes on susceptibility to T2D can differ between obese and lean cases. The Samoan population is genetically isolated, making it a prime candidate for genetic studies. We used whole-genome sequence data generated through NHLBI's TOPMed Program for 1,195 Samoans to create a Samoan-specific reference panel to impute genotypes for an additional 1,897 Samoans. To identify genes and variants associated with T2D phenotypes, we completed genome-wide association studies (GWAS) of (1) T2D, (2) T2D in obese (Polynesian cutoff of BMI >32 kg/m²) and (3) T2D in non-obese with 9,609,170 sequenced and imputed variants, adjusting for age, sex, principal components of ancestry and empirical kinship (model 1). We also adjusted for BMI in model 2. In the T2D GWAS (n=478 cases, n=2,389 controls), a variant in a known T2D gene, PPARGC1A, was genome-wide significant in both models 1 and 2 ($p=1.30 \times 10^{-8}$ and $p=8.32 \times 10^{-9}$, respectively). This variant is common both in other TOPMed populations (minor allele frequency (MAF)=0.376) and in Samoans (MAF=0.250). In the non-obese T2D GWAS (n=148 cases, n=1,119 controls), variants in or near three BMI-associated genes were significantly associated with T2D in models 1 and 2 (in ADAM23, $p=6.67 \times 10^{-11}$ and $p=2.08 \times 10^{-11}$, respectively; near SATB2, $p=1.37 \times 10^{-10}$ and $p=6.68 \times 10^{-10}$; and near CREB1, $p=1.17 \times 10^{-9}$ and $p=7.02 \times 10^{-10}$), and a variant in MAP2, which has not been previously associated with T2D or related traits, was genome-wide significant in models 1 and 2 ($p=4.80 \times 10^{-10}$ and $p=5.22 \times 10^{-11}$, respectively). These four variants are common in other TOPMed populations (MAF:0.094 - 0.179), but rare in Samoans (MAF<0.009). In the obese T2D GWAS (n=330 cases, n=1,270 controls), no variants were genome-wide significant. However, a suggestive (model 1: $p=5.38 \times 10^{-8}$) variant near known BMI gene TMEM182 is notable because this variant is rare in other TOPMed populations (MAF=0.0003), but common in Samoans (MAF=0.151). Additional exploration is necessary to further replicate these novel associations and characterize these variants. This highlights the importance of including diverse populations in genetics research to further characterize a map of disease-associated variation.



Dan Rzewnicki

BCHS

III-8

Computer-Mediated Communication and Social Provisions in the Multicenter AIDS Cohort Study

Background: Social support is a critical component of healthy living, affecting, among other things, mental health, chronic disease outcomes, and immune function. Social support is an area of concern for older adults, especially older gay and bisexual men (MSM); this group of adults is much more likely to live alone and also bears a disproportionate percentage of the HIV disease burden. Some studies have evaluated the use of computer-mediated communication (CMC) to provide support to older adults, but research about the utilization and effectiveness of computer-mediated social support for older MSM remains limited. **Methods:** 1066 MACS participants completed a survey of healthy aging, which included the Social Provisions Scale, a validated survey used in many studies of social support. Following this scale, we asked participants how they primarily communicated with the people they received the most support from, with possible responses in person, via Skype or other video chat, over the phone, via text or messenger, email, or over a gaming platform. Any medium other than in person was considered CMC for the purposes of analysis. Participants also reported their degree of satisfaction with the support they received. We utilized logistic regression analysis for binary outcomes, linear regression for continuous variables and multinomial logistic regression for outcomes with more than two response categories. **Results:** Of the 912 participants in the analytic sample, 224 (24.6%) reported computer-mediated social provisions (CMSP). Preliminary logistic regression analysis suggests no relationship between age and CMSP (Odds ratio (OR) = 0.99, 95% confidence interval (CI) = 0.97-1.01), but found that HIV+ participants had higher odds of reporting CMSP (OR = 1.9, CI = 1.38-2.56). Linear regression analysis found that participants reporting CMSP were more likely to report lower social provisions scores ($\hat{\beta}_1 = -2.38$, CI = -3.29 - -1.47). Multinomial regression analysis found that participants reporting CMSP were more likely to report feeling either neutral (relative risk ratio (RRR) = 2.25, CI = 1.52-3.35) or dissatisfied (RRR = 1.75, CI = 1.16-2.62) with the support they received (compared to satisfied). **Discussion:** Preliminary results of this study suggest that a significant proportion of older MSM are primarily obtaining their social support via CMC, and that these people are more likely to be HIV+. However, the results also suggest that CMC may not be as effective an avenue for obtaining social support as in-person communication. More research is needed to examine the social-support seeking behavior of older MSM and to examine mechanisms to improve the social support of those reporting CMSP.



Amrita Sahu

EOH

III-17

Exosomes carrying Klotho: a potential biomarker for developing customized rehabilitation protocols for aging population

Physical activity is a long-term predictor of mortality rate and lack thereof can have profound detrimental effects on overall organismal health. Muscle contractile activity is critical for secretion of myokines into the circulation that subsequently work in a hormone-like fashion to influence health and function of distal organs such as the brain and heart. Epidemiological studies in aging individuals have shown a strong association of high levels of a circulating anti-aging protein, Klotho, with higher physical activity levels. Similarly, interventional studies in rodents have also shown that an acute bout of exercise upregulates circulating and hippocampal levels of Klotho protein and gene expression, respectively. These findings have raised the intriguing hypothesis that exercise-induced increases in circulating Klotho may contribute to enhanced cognitive function. However, the underlying mechanisms for such cross-talk between muscle activity and brain health, are still unknown. Extracellular vesicles, including exosomes, that are released into the circulation may serve as communication vehicles between distal organs. Exosomes are tissue and cell secreted membrane-enclosed, nano-sized vesicles that contain a broad cargo range, including cellular and membrane proteins, lipids, mRNAs, noncoding RNAs, and DNA. Here, we tested the hypothesis that exosomes may carry Klotho cargo, and that the cargo is altered in response to muscle contractile activity via neuromuscular electrical stimulation (NMES).



Saad Samargandy

EPIDEM

IV-12

Increase in Abdominal Visceral Adipose Tissue Accelerates Two Years Prior to Menopause: the Study of Women's Health Across the Nation (SWAN) Heart

Introduction: Abdominal visceral adipose tissue (VAT) contributes to pathogenesis of cardiometabolic disease through endocrine and paracrine secretion of adipocytokines. Midlife women experience adipose tissue redistribution towards increasing central adiposity. A few studies suggested a contribution of the menopausal transition, but evidence is lacking to characterize the change in VAT relative to time of the final menstrual period (FMP). We hypothesized that VAT would change non-linearly relative to FMP with a significant rise close to FMP. **Methods:** We evaluated participants with no self-reported CVD from the SWAN Heart Ancillary study. Women had up to two computed tomographic planimetric measurements of VAT over a median of 2.2 years of follow-up and known dates of FMP. LOESS splines were used to determine potential inflection points of VAT change relative to FMP. Piecewise linear mixed-effects models were used to estimate and compare yearly % changes in VAT at LOESS spline-identified time segments. Model adjusted for race, study site, income, physical activity, alcohol consumption, and hormone therapy use. **Results:** The study included 321 women (at baseline: mean age (SD) of 51.0 (2.8) years; 60% White, 40% Black; 9% premenopausal, 51% early/ 13% late perimenopausal, and 27% postmenopausal). LOESS splines suggested a non-linear association between VAT change and time of FMP with two inflection points demarcating 3 segments: segment 1: > 2 years before FMP, segment 2: 2 years before FMP to the FMP, and segment 3: after FMP. After adjusting for study covariates, VAT increased significantly by 10.5% (95% CI: 5.9, 15.3) per year in segment 2, and this increase was greater than changes in segments 1 [1.3% (-2.0, 4.7)] and 3 [3.1% (0.8, 5.4)], both $P=0.01$. Additional adjustment for concurrent body mass index attenuated difference only between segments 2 and 3 ($P=0.07$). **Conclusions:** Women show significantly faster increase in VAT two years prior to menopause, which may place them at greater risk of cardiometabolic outcomes later in life. These results encourage lifestyle modifications early in menopausal transition.



Sarah Sanders

BCHS

III-4

Does Individual-level Social Capital mediate the relationship between Adverse Childhood Events and Adult Health Outcomes?

Background: There is an established relationship between exposure to childhood adversity and adult physical, mental, and social health outcomes, but the pathway is not well understood. Individual-level social capital, which measures access to resources via the diversity and quality of one's social connections, may help to explain how childhood adversity impacts health through a reduced social network. **Objectives:** To understand the role that social capital plays in mitigating the negative impacts of child adversity on adult health outcomes, above and beyond known social determinants. **Methods:** Using a population survey of 29 counties in Western Pennsylvania, we conducted secondary analysis of 983 adult residents' responses to survey items regarding health, experience of Adverse Childhood Events (ACEs), and social capital via a social position generator tool. While controlling for demographic and socioeconomic factors known to influence health, we conducted multivariate logistic regression to assess the impact of ACEs on adult health outcomes, as mediated by social capital. **Results:** In this sample, initial analyses show that exposure to ACEs was associated with self-reported health, the Kessler-6 Scale (a measure of serious mental illness), and other chronic illnesses. Additional analyses will investigate whether including social capital in the logistic model attenuates the main effect between ACEs and adult health. **Conclusions:** Understanding the pathway between childhood adversity and its effect on adult health can better inform prevention and mitigation strategies for at-risk youth. This study represents the first examination of individual-level social capital's role in this pathway.



Laura Savariau

HUGEN

III-9

Understanding the loss E-cadherin in invasive lobular carcinoma

Breast cancer is the most common cancer in women with about 1 in 8 women in the US developing invasive breast carcinoma over the course of their lifetime. Invasive carcinomas are classified as either ductal (IDC) or lobular (ILC), with the latter representing 15% of all invasive carcinomas. The hallmark of ILC is the genetic loss of E-cadherin (CDH1), which leads to the disruption of adherens junctions and is thought to be responsible for the discohesive, linear growth of ILC cells in tissues. Beyond its effects on this unique histology, there is limited data on the molecular consequences of E-cadherin loss in ILC. To this end, we re-expressed E-cadherin upstream of an IRES-GFP reporter in the human ILC cell lines MDA-MB-134, SUM44PE and BCK4, which harbor inherent CDH1 deletion and truncating mutations. We confirmed E-cadherin overexpression by immunoblotting, which also revealed significant induction of the other adherens junction proteins Alpha-catenin, Beta-catenin and p120-catenin. Microscopic evaluation indicated that E-cadherin overexpression led to a shift from the normally discohesive morphology to a more cohesive growth pattern. Immunofluorescence and confocal microscopy showed an incomplete restoration of adherens junction on the membrane with substantial E-cadherin localized to the cytoplasm. Interestingly, we noted punctate staining in ILC cells with loss of E-cadherin, which we are currently further investigating by co-staining with endosomal and lysosomal markers. Preliminary growth assays revealed that re-introduction of E-cadherin had no major impact on the proliferation of ILC cells. Ongoing work is aimed at assessing the localization of the other adherens junction members by immunofluorescence, as well as generating a dox-inducible overexpression system to assess the acute effects of E-cadherin restoration. In addition, we will monitor the effect of E-cadherin over-expression on additional phenotypes such as 3D growth in ultra-low attachment plates, soft agar and ECM gels, as well as migration, and invasion. Furthermore, we will utilize RNA-sequencing to delineate the transcriptional programs downstream of E-cadherin restoration and compare these results to IDC cell lines with E-cadherin ablation to uncover ILC-specific mechanisms. Finally, we will evaluate the effects of E-cadherin restoration on the growth and metastatic spread of ILC cell line xenografts in mice. Collectively, the results will lead to a better understanding of the hallmark loss of E-cadherin and disease mechanisms in ILC, which will ultimately help the development of more effective therapies and improve the outcome of patients with this understudied subtype of breast cancer.



Alexandra Schmidt

HUGEN

IV-6

Determining the Role of Sirt2 in Hepatocellular Carcinoma

Liver cancer is the sixth most common cancer in the world, with an estimated 850,000 new diagnoses each year, and is the fourth leading cause of cancer deaths globally. The most common form of liver cancer is Hepatocellular Carcinoma (HCC), which accounts for approximately 75% of all liver cancer cases. Before new drugs can be developed to treat HCC, a definitive disease mechanism needs further elucidation. There is convincing evidence that a key component of HCC etiology is in the metabolic reprogramming of hepatocytes. All tumorigenic tissues, including HCC, rely almost entirely on aerobic glycolysis for energy production by suppressing mitochondrial function, giving rise to the rewired metabolic phenotype known as the Warburg Effect. SIRT2, which expresses a cytosolic lysine deacylase, is downregulated in humans with HCC. It has been shown that *Sirt2*^{-/-} mice develop spontaneous HCC with aging. I hypothesize that SIRT2 is an HCC suppressor in hepatocytes. This hypothesis is being tested in vitro with a human HCC cell line and in vivo with a novel mouse model in which *Sirt2*^{-/-} mice express a doxycycline-suppressible transgene bearing the oncogene *c-Myc*. This reflects the molecular dysregulation of MYC seen in patients with HCC. Although the survival curves for mice with initiation of MYC expression at age P21 are similar between WT and *Sirt2*^{-/-} mice, my preliminary data suggest that the loss of Sirt2 alters the regulation and/or activation of key glycolytic enzymes during tumor growth, resulting in significantly smaller tumors in *Sirt2*^{-/-} mice. Leveraging this Sirt2 mechanism to modulate the Warburg effect may be a promising therapeutic strategy for HCC.



Georgie Scott

IDM

II-16

Mosquito-Borne Disease Control in Allegheny County

West Nile Virus (WNV) is classified as a Flavivirus along with Dengue and Zika Viruses. It first entered Allegheny County by way of migrating avian species in 2002 and has been considered endemic ever since. The mosquito species that transmit WNV in Allegheny County, *Culex pipiens* and *Culex restuans*, are trapped and tested for the virus from May to September each year. This is done in order to monitor current levels and determine the risk of human disease based on Vector Index (VI) values. Allegheny County Health Department's Mosquito-Borne Disease Control Program uses a large array of surveillance and control methods as a long-standing effort to reduce the risk of WNV to those who reside in the county. This program, as part of a larger statewide effort, utilizes Vector Index comparisons to aid in predicting neighborhoods of high risk along with making control decisions such as using a truck-mounted sprayer to decrease the adult mosquito population. Programs such as this are vital in order to protect the population from WNV as it wildly fluctuates year to year.



Rehab Sherlala

HUGEN

V-10

Assessing the age-dependent association between IGF1 and adiposity in the Long-Life Family Study

Serum levels of insulin-like growth factor 1 (IGF-1) and measures of adiposity, such as body mass index (BMI), are associated with susceptibility to age-related diseases. Previous reports of the relationship between IGF-1 and BMI ranged from positive to negative to no relationship, perhaps because previous reports studied different age cohorts. Using data on 4270 participants (aged 24-110 years) from the Long Life Family Study, we investigated the relationship between IGF-1 and BMI overall and by age groups. IGF-1 and BMI were positively correlated in the total sample ($\beta=0.161$, $r^2=0.0038$, $p<0.0001$). However, further analyses revealed that the relationship between IGF-1 and BMI varied by age quartile: in the 1st quartile (24-58yo) the relationship was negative ($\beta=-0.204$, $r^2=0.011$, $p=0.0008$); in the 2nd quartile (59-66yo) the relationship was negative but non-significant ($\beta=-0.069$, $r^2=0.0012$, $p=0.28$); in the 3rd quartile (67-86yo) the relationship was positive but non-significant ($\beta=0.106$, $r^2=0.002$, $p=0.13$); and in the 4th quartile (87-110yo) the relationship was positive ($\beta=0.388$, $r^2=0.019$, $p<0.0001$). This pattern did not differ by sex. We also detected a similar age-related pattern between IGF-1 and BMI using an independent dataset (NHANES III), comprising 2550 men and women aged 20-90 years. Our results may clarify some of the inconsistency in previous literature about the relationship between IGF-1 and BMI. Additional studies of IGF-1 and adiposity measures are needed to better understand the underlying mechanisms involved.



Molly Shiflet and Yei Gbaintor

HPM

I-10

An Evaluation of Overdose Prevention Policies at Colleges and Universities in Allegheny County, PA

Background: The current opioid crisis plaguing the U.S. is the worst addiction crisis in American history. The extremely high number of overdose deaths makes this drug crisis deadlier than gun violence, car crashes, and AIDS, none of which have killed as many individuals in a single year. Over 70,000 people in the U.S. died from drug overdose in 2017, and the majority of those deaths, approximately 68%, involved an opioid. In 2017, Pennsylvania had the third highest death rate (44.3 per 100,000) due to opioid overdose. The opioid crisis impacts people of all races, age, and socioeconomic status, which means college students are not immune to its devastating effects. Thus, it is imperative that colleges and universities have comprehensive and effective policies pertaining to opioid overdose prevention. **Methods:** A literature review of the best opioid-related policies on college campuses throughout the country was conducted in order to form the basis for the development of policy recommendations. These policy recommendations were then utilized to create a gradebook in which colleges and universities in Allegheny County were graded according to the comprehensiveness of their opioid overdose prevention policies. All four-year colleges and universities in Allegheny County were included in the gradebook evaluation, as well as the largest two-year community college in the county. The four major policy areas in which the colleges and universities were assessed are: medical amnesty, drug education, naloxone accessibility/training, and treatment/recovery resources. **Results/Conclusion:** The results of our research reveal the specific policy strengths, weaknesses, and potential areas for improvement for each of the colleges and universities included in the gradebook evaluation. The administration at these institutions should be encouraged to utilize the gradebook in order to help drive future policy decisions aimed at reducing non-medical opioid use and, subsequently, deaths due to opioid overdose.



Kevin Stoner

HPM

V-7

Barriers to Dental Care for Children with Medical Assistance

Recently it has become more widely accepted that oral health is a corner stone of overall health. Studies indicate when someone has poor oral health there is a higher likelihood that they will develop coronary artery disease, rheumatoid arthritis, and some cancers. There has long been a disparity in access to care between the middle and upper classes and those of the lowest socioeconomic class. This is particularly true in access to dental care for children with Medical Assistance (MA). A secret shopper survey of dental practices in Allegheny County was conducted to determine how many hours of dental care are available to children that utilize MA. There were 98 practices identified as accepting MA, information about these practices was used to conduct a geospatial analysis to determine what true access looks like in the county based on distance, drive time, or transit time between where children with MA live within the county and the hours available at dental practices that accept MA. A what-if analysis was then performed to determine how dental practices would need to be redistributed throughout the county if children with MA would be afforded equal access. These analyses showed that if a child with MA lives in one part of the county, they may have relatively easy access to dental care compared to a child that lives in another area. There are 26 zip codes where children with MA live without easy access to public transit, and five dentists that are not located near public transit. There would need to be a median of 11 dentists and 372 hours redistributed across each zip code to provide each child in the county with MA access to the same number of dentists and hours of availability. This work has demonstrated that even though MA plans are required to provide dental insurance to children, that does not mean that they will have access to care. More efforts need to be made to ensure that all dental practices accept MA so those most in need can have access to care.

Cognitive Functioning and Alzheimer's Disease Pathology in Community-Based Older Adults Without Dementia: The MYHAT Neuroimaging Study

Alzheimer's disease (AD) is neuropathologically defined by two hallmark brain biomarkers: amyloid beta ($A\beta$) and hyperphosphorylated tau protein, both of which can be assessed in vivo using positron emission tomography (PET). Higher burden of $A\beta$ and tau has been associated with preclinical or mildly symptomatic stages of AD and predict progressively worsening cognitive and functional ability, but most biomarker studies have been conducted in relatively homogenous clinic-based samples of older adults who are typically selected for few comorbidities, and may not generalize to broader populations. It is less understood what the association between cognitive function and $A\beta$ and tau is in more representative community-dwelling older adults who have not progressed to dementia. In the present study, a subsample of older adults was recruited from a well-characterized population-based cohort study: The Monongahela-Youghiogheny Healthy Aging Team (MYHAT). The present sample includes 77 older adults (mean age=79.1, 53.2% female) who underwent PET scanning using tracers Pittsburgh compound B (PiB) to assess $A\beta$ and AV-1451 to assess tau. A full neuropsychological assessment and Clinical Dementia Rating interview was included in the primary MYHAT study visit. All analyses were adjusted for age, sex, and education. In comparison to $A\beta$ -negative participants ($n=46$), $A\beta$ -positive participants ($n=31$; determined by PiB regional status), performed worse on the Boston Naming Test (BNT; $\beta=-2.57$, $p=.064$), the Token Test assessing language comprehension ($\beta=-.854$, $p=.013$), and the Fuld Object Memory Evaluation (OME; $\beta=-1.402$, $p=.059$). Higher tau burden in Braak areas 3 and 4 was also associated with worse performance on the BNT ($\beta=-13.52$, $p=.061$) and Fuld OME ($\beta=-10.20$, $p=.007$). Higher tau burden in Braak areas 5 and 6 was similarly associated with worse performance on the BNT ($\beta=-13.74$, $p=.033$) and Fuld OME ($\beta=-10.36$, $p=.002$). We observed no associations between any other cognitive assessments with $A\beta$ or tau burden. Our findings suggest that both $A\beta$ and tau brain pathology affect language and memory in community-dwelling older adults who are mostly cognitively intact.



Lindsay Summers

IDM

III-14

Building Skills at the Local Level: A Competency Based Approach to Public Health Workforce Development

Description of The Problem: Maintaining a skilled and qualified workforce is vital to the delivery of the Ten Essential Services of Public Health. Recognizing this relationship, the Public Health Accreditation Board (PHAB) has incorporated workforce development and training into its national accreditation standards for State, Local, and Tribal Health Departments. Workforce development at local health departments can be a challenge for many reasons, including time and funding constraints, workforce diversity, and changing public health priorities. The Allegheny County Health Department (ACHD) maintains an annual workforce development plan that covers training across all programs and services. **Objectives/Aims:** The objective of this project is to identify training needs for the 2019 ACHD workforce development plan. **Method(s) Used/Approach Taken:** Three main sources of data contribute to the 2019 workforce development plan: ACHD's core competency assessment, prior training evaluations, results from qualitative interviews with deputy directors, program managers, and key informants throughout the department. Trainings required by both Allegheny County and ACHD's All-Hazards preparedness plan will also be incorporated into the overall 2019 training plan. **Results:** Qualitative interviews conducted over the summer provide essential data for the 2019 workforce development plan. The majority of trainings requested by infectious disease departments were to improve core competency skills within the Communication and Cultural Competency domains. Departments that rely heavily on technology, such as the Bureau of Assessment, Statistics, and Epidemiology and Chronic Disease, require continuous training in the Analytical/Assessment and Public Health Sciences domains. Every department within ACHD requested training for supervisors and managers to improve skills within the Financial Planning and Management and Leadership and Systems Thinking domains. Results from evaluations of previous trainings and qualitative interviews show a need for expanded sexual orientation, gender expression and gender identity training as well as cultural competency training. **Discussion/Implications/Conclusions:** Developing a training plan that supports the diversity of programs at ACHD is a challenge; however, utilizing this type of evidence-based approach will best prepare its workforce to address current and future public health issues. Trainings are necessary for a competent workforce to be able to deliver the 10 Essential Services of Public Health and they improve skills that directly tie into the Public Health



Core Competencies. Results from qualitative interviews show a variety of trainings that can be integrated among several departments. A strong focus can be put on improving interpersonal, management, and technology-based skills moving forward.

Tao Sun

BIOST

V-12

Deep learning with GWAS to predict AMD progression

Recent advances in deep learning techniques have made extraordinary achievements in establishing flexible and powerful prediction models. However, the application of deep learning in biomedical research is limited. The genome-wide association studies (GWAS) of Age-related Macular Degeneration (AMD), a progressive eye disease, is the first and most successful GWAS research, where the massive GWAS data provide unprecedented opportunities to study disease risk and progression. Motivated by the need to establish a flexible and reliable prediction model for AMD progression, we develop a novel framework, which builds deep neural networks on time-to-event outcomes to effectively extract features from the wealthy GWAS data. Specifically, we employ the Tensorflow and Keras frameworks to obtain high computational efficiency. Finally, using data from a large randomized clinical trial on AMD progression, Age-Related Eye Disease Study (AREDS), we apply our method to develop, evaluate and validate a novel prediction model to predict the risk of progression to late-AMD given the patient's age and genetic profile. The result provides valuable insights to patients and clinicians for early prevention and tailored intervention.



Gretchen Swabe

EPIDEM

II-6

The contribution of estradiol and HDL-C to subclinical cardiovascular disease in SWAN Heart women at midlife

Introduction: It is recognized that HDL-C is cardio protective, but recent studies suggest there is a reversal in the association of HDL-C and cardiovascular disease (CVD) in women transitioning through menopause. Some research suggests that estrogen has anti-inflammatory properties, which may be associated with a protective effect with respect to CVD. Decreasing estrogen levels during the transition may explain this reversal, altering the HDL particles to render them dysfunctional and increasing the risk of CVD. C-reactive protein (CRP) may also contribute to this risk.

Objective: To determine whether either estradiol concentration or hs-CRP concentration modifies the association between HDL-C and aortic calcification presence (AC), a proxy measure of CVD risk.

Methods: Participants from the Study of Women's Health Across the Nation (SWAN) Heart ancillary study who had AC, estradiol and hs-CRP measures available were evaluated. AC presence was defined as AC Agatston score >100. Logistic regression was used to assess the effect modification of estradiol level on the relationship between HDL-C and AC presence, controlling for age, study site, race, hs-CRP, waist circumference, triglycerides, and smoking.

Results: Of the 358 included women, 211 (59%) were pre/early perimenopausal and 147 (41%) were post/late perimenopausal. The average age of women in the study was 51.2 (SD=2.8) years, and the sample was 38% black and 62% white. AC was present in 82 women (23%). In the unadjusted model, HDL-C was associated with a 3% lower risk for AC presence. Hs-CRP was associated with a 1.56 times higher risk of AC presence, controlling for HDL-C, estradiol, and cycle day ($p=0.00$). This association was not observed when controlling for confounders. In the final model, the interaction between hs-CRP and HDL-C showed no significant effect, but the interaction between estradiol and HDL-C showed decreased odds of high AC ($p=0.03$). For each one-unit increase in the log of estradiol concentration, the estimated OR between HDL-C and AC presence is 3% lower (OR: 0.968, 95% CI: 0.940, 0.996).

Conclusions: The protective cardiovascular association for higher levels of HDL-C was stronger at higher levels of estradiol, adjusting for confounders, which may explain the reversal in CVD risk. However, additional research is needed to determine whether these findings hold with larger sample sizes and in other populations.



Claire Thomas

EPIDEM

III-15

Urinary cotinine is as good a biomarker as serum cotinine for cigarette smoking exposure and lung cancer risk prediction

Introduction: Cotinine is a metabolite of nicotine. Serum and urinary cotinine are validated biomarkers for exposure to cigarette smoke. However, their performance for lung cancer risk prediction have not been examined in epidemiological studies. **Methods:** A nested case-control study including 452 incident lung cancer cases and an equal number of smoking-matched controls in the Shanghai Cohort Study was conducted. The mass spectrometry methods were used to quantify the concentrations of cotinine in serum and urine samples collected from current smokers at baseline, on average 10 years prior to cancer diagnosis of cases. Logistic regression method was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) as well as area under the receiver-operating characteristics curve (AUC) for lung cancer associated with higher levels of cotinine. **Results:** Serum and urinary cotinine levels were significantly higher in lung cancer cases than controls. Compared with the lowest quartile, ORs (95% CIs) for lung cancer in the highest quartiles of serum and urinary cotinine were 5.46 (3.38-8.81) and 5.49 (3.39-8.87), respectively. A risk prediction model yielded an AUC of 0.72 (95% CI 0.69-0.75) for serum cotinine and 0.72 (95% CI 0.69-0.75) for urinary cotinine combined with smoking history. **Conclusions:** Urinary and serum cotinine had the same performance in prediction of lung cancer risk for current smokers. **Implications:** Urinary cotinine is a noninvasive biomarker that can replace serum cotinine in risk prediction of future lung cancer risk for current smokers.



Jessica Thompson

BCHS

IV-3

Community-level Environmental and Social Determinants of Health: Food Deserts and Heart Failure Incidence in SWPA

Living in a food desert, defined as a low-income area with low access to healthful foods, is associated with increased risk of heart failure hospitalization. Access to healthy foods and socioeconomic factors may play a significant role in this association, as previous studies indicate a relationship between environmental and social determinants of health (e.g., neighborhood deprivation and poverty) and cardiovascular health outcomes. To date, few analyses have attempted to spatially assess patterns of food environment, socioeconomic factors, and heart failure incidence. As food desert determinations are different between urban and rural areas, exploring the variation of these associations across urban and rural low-income populations in the SWPA region will provide novel understanding of differences in these health disparate populations. Using electronic health records, we identified 21,195 patients with incident heart failure hospitalizations in 2015-2017. Using GIS and GeoDa, we conducted Exploratory Spatial Data Analysis (ESDA) to visualize relationships between heart failure incidence and identified environmental and social determinants by identifying patterns, clusters, and hotspots. We assessed global spatial autocorrelation for heart failure incidence ($I = 0.291$, $p = 0.001$) as well as various food environment and socioeconomic factors, and we analyzed the local clustering of significantly high and low values for each variable. These findings establish evidence for additional spatial exploration of the role of food environment and known socioeconomic factors in heart failure incidence among various health disparate populations in urban and rural areas. These results provide an important framework for developing preventive or early intervention activities and a more comprehensive understanding of factors affecting heart failure throughout the SWPA region. Next steps include utilizing these results for building regression models, including those accounting for spatial patterning as well as multilevel factors.



Rebecca Thompson

EPIDEM

VI-2

Hepatitis C Prevalence in Allegheny County

Background/Objective: Hepatitis C is the leading cause of liver transplantation in the United States. In the last few years, hepatitis C treatments have improved drastically. Cure rates have gone up and costs have gone down. In January 2018, Pennsylvania began covering treatment of hepatitis C for all Medicaid patients regardless of liver fibrosis score. In response to these changes, Allegheny County is launching Hep C Free Allegheny, an initiative to expand treatment, testing, and education for hepatitis C. To assist with program planning and evaluation, we estimated the prevalence of hepatitis C in the county using several methods. **Methods:** Data from National Health and Nutrition Examination Survey (NHANES) in 2003-2010 indicated that 1.3% of the general US population had antibodies to hepatitis C. However, institutionalized populations, including prisoners, nursing home residents, hospitalized individuals, and homeless individuals, which have higher prevalence of Hepatitis C than the general population, are not included in the NHANES estimate. We applied the NHANES estimate to the noninstitutionalized Allegheny County population and then accounted for these institutionalized groups. We then adjusted the estimate for underrepresentation of active drug users in the NHANES data. We also did similar calculations using state-wide prevalence estimate from HepVu, a CDC-funded project at Emory University. **Results:** The point estimate for the number of noninstitutionalized persons in Allegheny County who were hepatitis C antibody positive is 14,900 using the NHANES prevalence estimate. After adjusting for institutionalized populations, we obtained a value of 16,200 individuals, which is a 9% increase from the original NHANES estimate. After further adjusting for active injection drug users, we obtained an estimate of 17,600 antibody positive individuals, an 18% increase from the original NHANES estimate. **Conclusion:** Estimating the number of Allegheny County residents who have Hepatitis C is an important part of developing an intervention plan. Our estimates indicate that Hepatitis C is an important public health problem in Allegheny County, and they will serve as a baseline as the HepC Free Allegheny initiative moves forward.



Curtis Tilves

EPIDEM

IV-16

Intermuscular Fat Density: Novel Risk Factor for Cardiometabolic Risk Factors in African-Ancestry Men

Background: While overall obesity remains a major risk factor for cardiometabolic diseases, the location of stored fat is also thought to play a role. In addition to fat storage in ectopic sites, the density of fat, a marker of fat quality, is emerging as a novel risk factor for cardiometabolic diseases. Previous studies have focused primarily on visceral (VAT) and abdominal subcutaneous (SAT) adipose tissue density and in predominantly white cohorts; however, studies in populations of African ancestry who are at higher risk of cardiometabolic diseases are lacking. Additionally, information is lacking on associations of density of other relevant ectopic fat depots, such as thigh intermuscular adipose tissue (IMAT), with cardiometabolic risk factors.

Methods: We investigated whether VAT, SAT, or thigh IMAT densities were associated with cardiometabolic measures in 706 men aged 50-91 years (median age 62.0 years, median BMI 27.2 kg/m²). Adipose tissue volume (cm³) and density (Hounsfield units, HU, with adipose tissue ranging -190 to -30 HU) was measured in the abdomen (between L4 and L5) and mid-thigh from computed tomography scans. Cardiometabolic measures, including blood pressure, fasting serum glucose and insulin homeostasis, and serum lipids (N=516), were transformed as needed and used as outcomes in multiple linear regression models adjusting for age, lifestyle factors, medication use (antihypertensive, antidiabetic, or lipid-lowering), and corresponding fat depot volume.

Results: After adjustment, VAT, SAT, and IMAT densities were significantly associated with greater fasting insulin and insulin resistance, and with worse lipid profiles. Results remain similar in our sensitivity analysis after excluding those taking relevant medications.

Conclusion: As reported in other studies, in our study among African ancestry individuals VAT and SAT densities were associated with several cardio-metabolic risk factors. Importantly, our findings suggest that thigh IMAT density may be a novel predictor of cardiometabolic risk in African ancestry men.



Erin Tomaszewski

EPIDEM

V-8

Skin intrinsic fluorescence (SIF) scores and mortality risk in type 1 diabetes (T1D)

Advanced glycation end products (AGE) are biomarkers for metabolic stress and can be detected in skin collagen non-invasively via skin intrinsic fluorescence techniques (SIF). AGE have been linked to complications in T1D and to mortality in both hemodialysis and type 2 diabetes patients. However, the relationship of SIF scores and mortality in T1D is unknown. This study examined the association of SIF scores to all-cause mortality in T1D. Participants were identified from the Pittsburgh Epidemiology of Diabetes and Complications study, a cohort of individuals diagnosed with childhood-onset T1D between 1950 and 1980. SIF score was measured with the SCOUT DS^Â® device in the year 2003-04 (baseline analytic year) in a convenience sample of 112 participants [mean +/-SD or median (25th-75th percentile) for SIF score=5.5 +/-4.6; years of age 48.92 (43.07-53.69); HbA1c=7.25% (6.51-8.36); cumulative excess glycemic exposure over lifetime, or, A1c months=1053.80 (707.07-1436.20); and diabetes duration in years=37.46 (32.57-43.11)]. In this sample, mean SIF scores ranged from -3.5 to 17.8 AU. Vital status was assessed as of 12/10/2018, as of when 18 mortality events occurred. Univariately, compared to those who survived, the deceased had longer diabetes duration (45.4 vs. 36.9 years), higher median (25th-75th percentile) A1c months [1459.45 (1171.11-1817.29) vs. 985.86 (665.65-1378.43)], higher mean (+/- SD) SIF scores (8.87 +/-5.21 vs. 4.8 +/-4.25 AU), and were older [54.65 (49.79-59.75) vs. 47.62 (41.88-52.78)], all $p < 0.001$. SIF score was adjusted for age in years and gender. SIF score was significantly associated with mortality after adjusting for baseline diabetes duration: for each one-unit increase in SIF score the odds of death increased by 18% (OR=1.18, 95% CI 1.03-1.34). A significant association persisted after adjustment for both baseline diabetes duration and A1c months (OR=1.17, 95% CI 1.02-1.34). These findings support the hypothesis that SIF scores provide additional predictive power for mortality in T1D beyond duration, age, gender, and cumulative A1c. The study sample is limited by sampling method, size, lack of diversity, and possible survivor bias. Given these limitations, further studies are required to confirm these findings.



Samantha Ttoni

EOH

II-5

The Dieldrin Dilemma

Dieldrin is a banned pesticide that biomagnifies in food chains, and has been detected in the blood of people who eat self-caught fish. Studies have also confirmed dieldrin in fat-rich sites such as human brains and breast milk, as well as placentas, umbilical cords, and in the blood of infants. Information from the Food and Drug Administration, the Environmental Protection Agency, state agencies, and scientific studies reveals that some states still rely on an antiquated FDA standard for dieldrin that allows for people to be exposed to hundreds of times more dieldrin in fish than the EPA recommends. Other state agencies rely on EPA science that's half a century old from a time when scientists were still in the dark about all of dieldrin's health effects. In the decades since then, studies uncovered dieldrin's toxicity to the brain, including links between dieldrin and Parkinson's Disease. But just how much dieldrin may be "too much" for the brain remained unknown until a study in 2018 used cell cultures from newborn rats to determine the amount of dieldrin that permanently changed developing brain networks. This new information may be the key to finally incorporating dieldrin's effects on the brain into fish consumption advice. But will state agencies be able to use it?



Samantha Toton

EOH

VI-18

Under the Radar: Lead exposure in the hunting community

Primary prevention is a crucial aspect of addressing lead exposure, for which there is no safe threshold. Most deer hunters in the United States use lead-based ammunition. An association between consumption of lead-shot meat and increased blood lead levels has been well documented. However, this topic is often excluded from lead exposure prevention information provided by public health agencies across the United States, including in states with the greatest number of deer hunters. This omission ignores a potential source of lead exposure for the families of the 11 million deer hunters in the U.S., as well as low-income recipients of donated venison. Consumption of lead-shot meat is also a matter of environmental reproductive justice for women in the hunting community who may regularly and unknowingly ingest this contaminant, which could impact their future or current pregnancies. We highlight gaps between scientific findings and lead exposure prevention information at the national and state level, including questionnaires for the identification and management of lead exposure in pregnant and lactating women. We also discuss plans to collect, analyze, and summarize focus group data on hunters' knowledge, attitudes, and beliefs regarding lead in deer meat and explore their communication preferences for sources of lead-related information. Findings from the focus group data with recent scientific findings about lead-shot meat to develop and inform health communication efforts in the hunting community about lead exposure.



Khouja Tumader

HPM

V-3

Does Providing Medicaid Adult Dental Benefits Effect Children's Receipt of Preventive Dental Services?

Research Objective: There is substantial variation in adult dental benefits across state Medicaid programs. Providing dental coverage for adults can improve access to oral health services and could impact their dependent children's use of preventive dental services. Prior studies found spillover effects in medical coverage between parents and children insured by Medicaid. We sought to examine whether there was a similar spillover effect for dental coverage among low-income families. The objective of this study was to evaluate the impact of state Medicaid dental coverage for parents and children's use of preventive dental services. **Study Design:** We used two quasi-experimental study designs to evaluate the relationship between state Medicaid policies and children's use of preventive dental services. First, using state fixed effects models, we assessed the association between changes in the coverage of dental services for adults with a child's probability of receiving preventive dental services. Second, we harnessed variation in states' implementation of the Affordable Care Act's Medicaid expansion, and differences in Medicaid's coverage of dental services for adults, to examine whether Medicaid expansions in states with adult dental coverage were associated with a greater likelihood that low-income children received preventive dental services. We defined preventive dental services as dental prophylaxis, fluoride treatment or sealant application. **Population Studied:** We examined parent-child dyads in families with incomes less than 200% of the Federal Poverty Level (FPL) who were surveyed in the Medical Expenditure Panel Survey between 2003-2016. **Principal Findings:** Our analytic sample consisted of 27,851 parent-child dyads representing 151,889,212 weighted pairs through the study period. Overall, 36% of the children received preventive dental services, which included prophylaxis (35%), fluoride (12%) and sealants (3%). We did not find an association between state Medicaid coverage of adult dental benefits and the probability that children received at least one annual preventive dental service ($\hat{\tau}^2=-0.003$; 95% CI, -0.037 to 0.032). Compared with changes in adult Medicaid dental services in states that did not expand Medicaid coverage after the ACA, we found no significant change in the probability that children received any preventive dental service in states that covered adult Medicaid dental services before and after ACA Medicaid expansion ($\hat{\tau}^2=-0.010$; 95% CI, -0.066 to 0.045). **Conclusions:** The receipt of preventive dental services for children in families with incomes less than 200% FPL was low in states that did and did not provide Medicaid dental coverage for adults. We did not find evidence of an association between states' provision of Medicaid dental benefits for adults and children's use of preventive dental services. **Implications for Policy or Practice:** Although prior research found that changes in Medicaid coverage for parents have spillover effects on children's use of medical services, we did not find evidence of a similar relationship for children's use of preventive



dental services. This finding implies that factors other than the policy changes in adult Medicaid benefits may be more salient determinants of children's preventive dental care use in this low-income population

Raymond Van Cleve

HPM

VI-19

Risk of Hospital Admission and Home and Community Based Service Use

Home and community based services (HCBS) are a growing form of long-term care and account for over half of the Medicaid spending on long-term care. HCBS is a preferred form of long term care when compared to institutional nursing facilities (i.e. nursing homes) because HCBS allows a person to age in their preferred setting. To effectively meet the needs of aged and disabled people living in the community, most HCBS programs offer a number of different services that address the unique individual environmental and health needs of their clients. Many people who use HCBS use constellations of care; HCBS users will use two or more types of in-home services to meet their needs and age in their preferred setting. Previous research has identified that specific HCBS programs (i.e. one service within a constellation of service) are associated with a lower risk of experiencing a hospital admission, but no analysis has examined if specific constellations of service are associated with a higher or lower risk of experiencing a hospitalization. This study addresses that gap. This is an analytic study that compares the risk of experiencing a hospitalization associated with the use of different constellations of HCBS. The data for this study will come from Pennsylvania Medicaid claims from 2014-2016. The claims data used contain enrollment information, HCBS service use, and assessment data for Pennsylvania Medicaid 1915(c) waiver clients living in Pennsylvania. I used the service use data to identify different constellations of service. I performed a logistic regression to compare each group of people using a specific constellation of service to aged and disabled Pennsylvanians who applied for the 1915(c) waiver but did not qualify for the program. This analysis found that people with eight or more hours of PAS per day and any other services did not have a statistically different risk of hospitalization than people who applied for HCBS services but were deemed ineligible. People who received 4-8 hours of PAS per day with adult day care and people who received 4-8 hours of PAS per day with adult day care and home-delivered meals were 18 and 4% respectively more likely to experience a hospitalization. People who received 4-8 hours of PAS per day with home-delivered meals and people who received 0-4 hours of PAS with adult day care and meals did not have a statistically different risk of experiencing a hospitalization. People who received home-delivered meals and 0-4 hours of PAS were 21% less likely to experience a hospitalization while people with just 0-4 hours of PAS per day and people



with 0-4 hours of PAS per day and adult day care were 40 and 53% more likely to experience a hospitalization, respectively.

Raymond Van Cleve

HPM

II-14

Risk of Hospitalization Associated with Agency vs Community Based In Home Care

Home and community based services (HCBS) are a growing form of long-term care and are an important piece of supporting a person's ability to age in their preferred setting. While HCBS regimens frequently incorporate many different programs, HCBS in many instances is designed around attendant care, also known as personal attendant services (PAS). PAS is when an in-home aid supports a person in completing activities of daily living (bathing, dressing, toileting, transferring, feeding, and managing continence) and instrumental activities of daily living (preparing meals, walking outside, transferring throughout a community, shopping, managing money, and communicating). PAS offered through Pennsylvania Medicaid can be administered by an agency or by the consumer. A person who receives agency directed PAS is allotted a specific number of hours per month where the state Medicaid program will pay a home health care agency to send an aide to the home of a Medicaid recipient. A person who receives consumer directed PAS is allotted a specific amount of money every month and the Medicaid recipient is charged with hiring, training, managing, and possibly firing his or her personal care aid. Consumer directed care is a relatively new form of in-home care and there has not been a study yet comparing outcomes associated with each form of PAS within one population. This is an analytic study that examines the risk of experiencing a hospitalization for people who receive consumer directed PAS, agency directed PAS, and both forms of PAS to people receiving no PAS who applied for the Pennsylvania aging waiver but were deemed ineligible. The data for this study will come from Pennsylvania Medicaid claims from 2014-2016. The claims data used will contain enrollment information, HCBS service use, and assessment data for Pennsylvania Medicaid 1915(c) waiver clients living in Pennsylvania. I used the service claims data to identify the type and amount of PAS a person had used. I used logistic regression to compare the risk of experiencing a hospitalization associated with each PAS regimen (only consumer PAS, only agency PAS, both forms of PAS, no PAS because the person was ineligible for waiver services). When comparing the risk hospitalization associated with the different types of PAS, people who received consumer PAS were 15% less likely to experience a hospitalization than people who received agency directed PAS.



Patel Varun

EOH

III-5

Environmental Health Disparities Associated to Air Stressors in Allegheny County, Pennsylvania

Allegheny County, located in southwestern Pennsylvania, has a rich history of industry that includes glass making, steel production, coal fired power plants, and mining activities such as coke processing. Facilities related to these industries contribute significantly to air pollution, releasing toxics such as, butadiene, formaldehyde, and acetaldehyde into the air. Coke oven emissions are major air stressors in southeast regions of the county. Coke oven emissions predominantly release from large ovens used in heating coal to produce coke in steel and iron manufacturing facilities. The emissions are complex mixtures of dust, vapors, and gases that typically include carcinogens such as cadmium and arsenic. In addition, traffic-related pollutants including diesel particulate matter also contribute to poor air quality. Spatial associations between cancer incidence and mortality with air pollution is well studied in several cities in the United States and around the world. However, this study is an attempt to examine the association at a smaller scale i.e., census tract level of Allegheny County. For this study, we used United States Census data, the Pennsylvania Cancer Registry, and the Environmental Protection Agency's (EPA) National Air Toxic Release Assessment (NATA) data for geospatial analysis at the census tract level for Allegheny County. Spatial analysis was used to investigate the association between ambient concentrations of air toxics, cancer incidence (lung [N = 6,435], thyroid [N = 1,882], and prostate [N = 4,617]), and socioeconomic status (SES) (race/ethnicity and income) in the county from 2010-2015. ArcGIS and QGIS were used to create interactive maps, and GeoDa was used to examine spatial and statistical relationships. We used global and local measures of spatial autocorrelation (Moran's I) to identify clusters of tracts where cancer incidence was significantly higher. We identified a few local hotspots of higher cancer incidence. In our current hypothesis we are expecting to find SES positively related to cancer incidence and mortality as well as ambient levels of certain air toxics. This study revealed associations between cancer risk and environmental exposures and identified vulnerable communities where future resources could be allocated to help reduce the disproportionate health burden.



Nefertiti Wade

IDM

I-1

STIs in the US Military: Policy & Prevention Program Analysis

Problem: Serving in the United States armed forces can often expose individuals to high stress situations, which has been shown to negatively impact decision making. Increased high risk sexual behaviors is one of the manifestations reported possibly resulting in the acquisition of a sexually transmitted infections (STIs). Undetected STIs within a highly mobile military population poses a threat to military readiness. **Methods:** The United States Department of Defense, Air Force, Army, Marine Corps and Navy's STI screening policies were examined. STI incidence rates within all branches were identified and compared with rates in the general population. Past through modern day preventative approaches, incidence rates and limitations of screening policies were analyzed, and guided the development of screening recommendations. **Methods** included review of relevant literature, obtained using PubMed, Medical Surveillance Monthly Report and Military Medicine (Oxford's International Journal of AMSUS). Articles were analyzed for applicable content and appropriate time periods. Key informant interviews with military personnel were conducted to obtain information regarding screening policy and past practice. **Results:** In alignment with medical advances and the simplification of STI treatment, the US military has significantly reduced transmission of STIs within its enlisted. Nevertheless, STIs continue to be the among the highest reported communicable diseases within the Armed Forces. High risk behaviors reported in this group include: binge drinking, multiple partners, sex with a new partner without using a condom and co-occurring substance use. **Conclusions:** Routinized STI screening and annual health education training of the enlisted could serve to reduce stigma, detect asymptomatic STI infections and prevent further spread of STIs within the military population.



Junyao Wang

BIOST

IV-17

Response-Adaptive Randomization in a Two-stage Sequential Multiple Assignment Randomized Trial

Sequential multiple assignment randomized trials (SMARTs) are systematic and efficient media for comparing dynamic treatment regimes (DTRs), where each patient is involved in multiple stages of treatment, and the treatment randomization at each stage could depend on that patient's previous treatment history and interim outcomes. However, the different benefits of treatments observed during the previous stages are neglected while assigning treatment at the current stage. In this paper, we propose a response-adaptive SMART (RA-SMART) design that incorporates a technique of unbalancing the allocation probabilities at the current stage based on the accumulated information on treatment efficacy from previous stages. A simulation study is conducted to assess the operating characteristics of RA-SMART design, including the consistency and efficiency of response rate estimates for each DTR, and the power of identifying the optimal DTR. Practical suggestions on design parameters are discussed.



Xianling Wang

BIOST

IV-2

Improving inference on discrete diagnostic tests without a gold standard

Discrete diagnostic tests such as tumor grade in cancer are usually important prognostic factors but often suffer from intra-rater and inter-rater errors. With at least three independent readings, the prevalence and classification rates of independent raters are estimable up to a permutation of labels for the unknown truth under a latent class model (Kruskal, 1977; Dawid, 1979). Violation of the conditional independence assumption on the independent raters leads to biased estimates (Vacek, 1985). Although the raters may rate the study subjects independently, dependence can be induced when a group of subjects has distinct features such that all raters have consensus on the classification of them. Here a new latent class method is proposed to deal with such induced dependence and the likelihood ratio test is used to check the violation of conditional independence. With an available auxiliary variable, the model is further extended to provide global identification of model parameters. These methods are illustrated by an analysis of tumor grade reading data from a joint study of the National Surgical Adjuvant Breast and Bowel Project (NSABP) and the Genomic Health Inc.



Xinjun Wang

BIOST

VI-9

A comparison and assessment of tree-based methods for subgroup identification with time-to-event data

With rapid advances in understanding of the human diseases, the paradigm of the medicine shifts from one-fits-all to targeted therapies. Subgroup analysis and identification becomes a critical topic in clinical researches. The existence of treatment effect heterogeneity makes it important to identify subgroup of patients with enhanced efficacy for the treatment to target, or to decide the optimal treatment rule for any future patients based on their characteristics and treatment response histories. Many data-driven methods for subgroup analysis have been developed, most of which utilize machine learning techniques such as lasso and decision trees. Since decision trees are known to have advantages such as performing variable selection and providing easy interpretation, several tree-based methods, such as Virtual Twins, Interaction Trees and SIDES, are available for identification of subgroups with differential treatment effect. Although several comparative studies have been conducted to assess the performance among those methods, few considers a time-to-event data setting. In this work, we assess the availability of available tree-based methods for subgroup identification with survival outcome, and we compare their performances with a real survival data application.



Alix Ware

HPM

VI-17

Street Medicine Providers as Good Samaritans: A Legal Epidemiological Survey of Good Samaritan and Charitable Immunity Laws in the United States and Territories

Although homelessness rates have decreased over the last decade, rates of unsheltered homeless, or rough sleepers, have become a greater portion of those experiencing homelessness. These individuals can be geographically so close to the rest of society but can be miles away from accessing the same resources and services. With a significant number of individuals experiencing homelessness due to mental health issues or other comorbidities, health care providers must be creative in reaching this population to provide the care they need, want, and deserve. To address the disconnect between this population and the health care system, physicians have taken to the street to provide care. When providing care outside of their usual work setting, additional concerns arise, specifically, are these providers legally responsible for any sustained injuries or other issues that arise while providing care in unconventional environments? Are the providers covered under Good Samaritan or charitable immunity statutes? Is there a variance between protections provided by each jurisdiction? Through a survey of Good Samaritan and charitable immunity laws in 50 states, 6 U.S. territories, the District of Columbia, and the Federal government, an analysis determined how these laws protect and fail to protect providers practicing street medicine. Despite the intention of Good Samaritan and charitable immunity laws to increase physician involvement in providing care in unconventional situations for vulnerable populations, these laws overwhelmingly do not provide liability protection for Street Medicine providers. Model statutory language has been written to provide this necessary liability protection for Street Medicine providers.



Kortni Watkins

BCHS

V-19

Characterization of Maternal Perspectives Toward Parent-Child Communication on Healthy Relationships, Sex, and Dating Violence

Intimate partner violence (IPV) is a major source of numerous poor health outcomes in the US. One method of IPV prevention is encouraging parent-adolescent conversations about healthy relationships and IPV. Mothers are more likely than fathers to discuss dating and sex with their children. Our study objective, then, was to survey women about their communication with their children about healthy relationships and dating violence (DV). We developed questionnaires asking mothers to describe their conversations with their children about sex, healthy relationships and DV/IPV. We are distributing surveys to mothers of children (ages 10-18) at UPMC's Adolescent Medicine Clinic and Magee-Womens Hospital. Women indicating interest are filling out questionnaire forms voluntarily and anonymously. Responses are being compiled for statistical univariate analysis or bivariate comparison. Qualitative responses are being studied using descriptive analysis. Data is still being collected, and the following findings are preliminary. Currently, we have 133 completed surveys; 53 available for analysis. Mothers believed the age for children to begin dating should be ~15 years (range 13-18) and that healthy relationship discussions should begin around age 12 years (range 2-16). 97.7% of mothers described having talked to their children about healthy relationships; 84.6% described having talked about dating violence. 10 mothers indicated having talked with their parents about DV/IPV when they were children. 16 (31.4%) mothers reported experiencing IPV themselves. Our preliminary data suggest that mothers are more likely to discuss healthy relationships than DV/IPV with their children and are more likely to discuss DV/IPV than parents had with them.



Lauren Winter

HUGEN

V-2

Addressing barriers to recruitment in All of Us Pennsylvania

The goal of precision medicine is to identify the right intervention for the right patient at the right time. To meet this goal, health care providers need to know how an individual's genetic variants, environmental influences, and behavior may affect their response to different therapies. Thus, information is needed on all subgroups within the U.S. population. Historically, however, human studies have not expanded beyond the Caucasian population. The All of Us Research Program's goal is to include more people of various backgrounds into biomedical research in order to develop a large database that reflects the variety of individuals in the U.S. Studies using information from this inclusive database will enable development of treatments that are more precise and appropriate for a wider variety of individuals. To increase representation in this biomedical research database, All of Us strives to break down barriers imposed by a variety of factors, such as age, sex, ethnicity, and ancestry. I assessed the effectiveness of All of Us Pennsylvania's recruiting strategies in achieving the diversity that is critical to the initiative. Data were entered into the participant management database, JoinLite, with the goal of contacting individuals interested in participating in All of Us Pennsylvania. For individuals who completed the initial study visit, demographic data and timeline to competition were obtained. From this data, factors that affected completion rates are assessed. Monthly enrollment rates were analyzed from July through October 2018. Initial analyses indicate that completion rates (among initial respondents) were similar throughout the first four months of implementing the Join Lite system (approximately 75% each month). Because many factors likely affect participation, I will also investigate distance to study site and proximity and availability of clinic as factors in appointment completion. To facilitate participation in research by members of many population subgroups, assessment of these quality assurance measurements is required. Identifying and removing barriers to participation should improve recruitment efforts of underrepresented groups into future studies in biomedical and genetic research, thus enabling all individuals in the U.S. to benefit from results of biomedical research.



Lingshu Xue

EPIDEM

V-1

Cardiovascular disease risk and the time to insulin initiation for Medicaid enrollees with type 2 diabetes

Background: Early insulin initiation at the diagnosis of type 2 diabetes (T2DM) was associated with a reduced risk of microvascular complications and non-fatal myocardial infarction (MI) in clinical trials. However, the relationship of the time to insulin initiation after first-line glucose-lowering agents (GLAs) and cardiovascular disease (CVD) risk in young and middle-aged adults in real-world settings is poorly understood. **Objectives:** To evaluate the relationship between the time from first-line GLAs to insulin initiation and CVD risk in Pennsylvania (PA) Medicaid enrollees with T2DM. **Methods:** This study included 17,873 Medicaid enrollees (age 47.4 ± 10.3 years) initially treated with non-insulin GLAs from 2008 through 2016. Based on American Diabetes Association (ADA) guidelines, four groups were identified: early (N=1,158; insulin initiation 6 months after first line GLAs), in-time (N=569; within 6-12 months), delayed (N=2,761; >12 months), and non-insulin users (N=13,385; no insulin during the study period). Prentice, Williams, and Peterson (PWP) models with time to insulin initiation as a time-independent/dependent predictors were used to compare risk of incident and recurrent CVD (i.e. stroke and acute MI) in the cohort with inverse probability treatment weighting (IPTW) based on demographic characteristics, healthcare utilization, medications use, and comorbidities at baseline. As the predictor was time-dependent, individuals were considered as non-insulin users before insulin initiation, and as early, in-time or delayed insulin users after insulin initiation until the end of study period. **Results:** In our cohort, 18% had CVD events before first-line GLAs. Regardless of time to insulin initiation, insulin users had an increased CVD risk after first line GLAs compared to non-insulin users (HR: 2.0 [1.5-2.5] for early, 1.8 [1.2-2.6] for in-time, 1.9 [1.6-2.3] for delayed insulin users). A higher CVD risk after insulin initiation was found in early (HR: 1.4[1.1-1.8]) and delayed insulin users (HR: 1.3[1.0-1.7]) vs. those without insulin initiation by the same time. **Conclusions:** Even with insulin initiation in the early stage of pharmacotherapy of T2DM, young and middle-aged PA Medicaid enrollees may not be protected from future CVD risk. Potential explanations include advanced disease progression of T2DM at young/middle age or that CVD was pre-existing or concurrent to the diagnosis of T2DM and/or insulin initiation. Screening and treatments for other CVD risk factors such as



blood pressure and blood lipid levels may be important to reduce incident CVD in this young and middle-aged Medicaid population with T2DM.

Xiaoshuang Xun

EPIDEM

IV-9

The role of placental human chorionic gonadotropin in the relationship between maternal first trimester body mass index and birthweight

Birthweight (BW) is a crucial indicator of fetal development, yet the early pregnancy determinants of BW are not well understood. The first trimester is critical for placental and fetal growth. First trimester body mass index (T1-BMI) has a positive relationship with BW. The placental hormone human chorionic gonadotropin (hCG) is also associated with BW. The aim of this study was to examine the role of hCG in the relationship between T1-BMI and BW. Study subjects were 525 women recruited into The Infant Development and Environment Study (TIDES) in 4 U.S. cities. Subjects' information was collected using T1 questionnaires and birth records. T1-serum hCG levels were obtained from clinical laboratories and z-score transformed to normalize across sites. BW was modeled as a z-score to normalize for gestational age at delivery and fetal sex. Multivariate linear regression models were used to estimate associations between all key variables. A four-way decomposition of the total effect (TE) was used to compare the TE and the controlled direct effect (CDE), and to identify mediation and/or interaction effects. Maternal T1-BMI was positively associated with BW. This association was stronger in women carrying males. The data suggested that the association between T1-hCG and BW varied by fetal sex, being negative for women carrying males ($\hat{\tau}^2 = -0.20$, 95% CI: -0.39, -0.01) and positive for women carrying females ($\hat{\tau}^2 = 0.08$, 95% CI: -0.06, 0.22). In women carrying males, there was no difference between the TE and CDE. However, in women carrying females, the TE ($\hat{\tau}^2 = 0.09$, 95% CI: -0.13, 0.31) was smaller than the CDE ($\hat{\tau}^2 = 0.15$, 95% CI: -0.07, 0.38). Most of this difference was due to the indirect effect of hCG ($\hat{\tau}^2 = -0.09$, 95% CI: -0.18, -0.01). The association between T1-BMI and BW was partially mediated by the T1-hCG only in women carrying females. This finding provides evidence for a sex-specific placental mechanism in the pathway between maternal BMI and BW.



Xiaoshuang Xun

EPIDEMVI-14

The Association between Cardiovascular Health Metrics and Sex Steroid Hormones in Women in the 2015-2016 National Health and Nutrition Examination Survey(NHANES)

Background: Cardiovascular disease remains the leading cause of death among women in the United States. Sex hormones play a role in determining cardiovascular disease risk. The American Heart Association (AHA) has created a composite of modifiable metrics to define cardiovascular health in an effort to promote prevention. The association between sex hormones, sex-hormone binding globulin (SHBG) and cardiovascular health (CVH) metrics is less established. The aim of this study is to determine whether CVH metrics are associated with serum testosterone, estradiol, and SHBG levels in adult women.

Methods: Women with no missing data for CVH metrics and hormone level-related variables were included in the analyses. According to the AHA, CVH is quantified by seven metrics (diet, physical activity, smoking status, BMI, fasting blood glucose, total cholesterol, and blood pressure) that are categorized as ideal, intermediate and poor. The associations between hormone levels and CVH metric score were evaluated using both linear regression, using the total number of metrics within the ideal range, and multinomial regression, looking at categories of low, moderate and high levels of ideal metrics. Potential confounders (age, sex, race/ethnicity, education level, marital status, and/or menopausal status, and hormones therapy) were adjusted in the model. Stratified analyses by menopausal status were conducted to test effect modification. Statistical computing was conducted by SAS version 9.4 (Cary, NC). Statistical significance was defined as 2-sided p-value <0.05.

Results: There were 1231 women included in the analysis. The average age of the entire sample was 50 years old, and 54% of them were post-menopausal women. The average total ideal CVH metric score was 3, and it was most likely that women were in the ideal range for smoking status and blood pressure. There were significant differences between estradiol, SHBG and testosterone among pre- and post-menopausal women. Physical activity, BMI, total cholesterol, blood pressure and fasting blood glucose were significantly different by menopause status. From the bivariate analyses, higher levels of estradiol and SHBG were associated greater number of CVH metric scores. Higher levels of log₁₀ transformed SHBG were positively associated with high ideal CVH metric score vs. low ideal metric score in overall women (OR=31.44, 95%CI: 9.82 – 100.63). The association became much stronger among postmenopausal women (OR = 511.15, 95% CI: 46.44-999.99) vs. premenopausal women (OR = 6.00, 95% CI: 1.26-28.50). There was no significant association between ideal CVH metrics score and estradiol or testosterone in either linear or multinomial logistic regression model.



Conclusion: Higher level of SHBG was associated with higher ideal CVH metrics score in adult women in NHANES 2015-2016, especially among postmenopausal women versus premenopausal women.

Coursework of Epi 2230: Advanced Topics in Epidemiological Methods

Qing Yin

BIOST

V-16

Prenatal phthalate concentrations and placental hormones: comparing two multivariable models

Linear models (LM) are often used to model the relationship between prenatal exposures, such as phthalate metabolites and endogenous biomarkers, such as placental hormones. However, there is no evidence to justify the use of LM in all cases. Analyzing data from The Infant Development and Environment Study (TIDES), we discovered that LMs are appropriate in some cases but not in all. Since a priori one does not know the choice of the model, we explored the Generalized Additive Model (GAM), a flexible nonparametric alternative. TIDES data included 1st trimester pregnant women (N=525) enrolled at prenatal clinics in four U.S. cities. We considered the phthalate metabolites, MnBP, MiBP, MBzP, MEHP and MEP, and placental hormones, hCG, PAPPa, estriol, Inhibin-A and AFP to compare LM and GAM. All analyses were adjusted for specific gravity, stressful life events, study center, gestational age at blood draw, maternal age, race, education, BMI, income and marital status. Residual analysis using LM suggested some nonlinear relationships. In all such instances, GAM had better adjusted R² than LM. Visually and quantitatively, GAM fitted the data better than LM to model the relationship between phthalates and hormones. For example, for MEP and estriol in females, the adjusted R² and p-value from LM were 0.47 and 0.31, respectively. Whereas, the adjusted R² and p-value from GAM were 0.59 and < 0.01, respectively. For MiBP and Inhibin-A in males, the adjusted R² and p-value from LM were 0.07 and 0.77, respectively. Whereas, the adjusted R² and p-value from GAM were 0.25 and 0.047, respectively. In all instances where LM fitted the data well, so did GAM. However, whenever the data exhibited nonlinear patterns, the GAM was a better choice. In summary, we show that GAM is a flexible nonparametric model to describe associations between a prenatal exposure and a placental response, both measured as biomarkers.



Jerry Zhang

BIOST

IV-4

Multivariate Bayesian Genetic Association Analysis of CREBRF

Previous studies have shown that a minor allele of CREBRF (encoding CREB3 regulatory factor) rs373863828 (p.Arg457Gln) is strongly associated with BMI and reduced risk of type 2 diabetes in Polynesians. While this variant is exceedingly rare in non-Samoan populations, it is common in the Samoan population (MAF = 0.259)¹. The aim of this study to investigate the association between CREBRF and an array of anthropometric and lipid profile measurements under the conditions of the correlation between phenotypes. In addition to testing for association, the analysis attempts to decipher the association pathways through a multivariate Bayesian framework.

The effect of high-dose omega-3 fatty acids on atherosclerosis: a systematic review and meta-analysis of randomized clinical trials

Background Two recent randomized clinical trials (RCTs) of high-dose omega-3 fatty acids (ω -3 FAs), REDUCE-IT in Western countries (4 g/day) and JELIS in Japan (1.8 g/day, equivalent to 4 g/day in Western countries due to remarkably higher dietary intake in Japan), showed significant reduction in cardiovascular disease (CVD). Contrarily, many RCTs of <1 g/day of ω -3 FAs all failed to show any beneficial effect, indicating that high rather than low-dose ω -3 FAs is cardioprotective. However, the mechanism underlying the relationship between high-dose ω -3 FAs and CVDs is not understood. **Hypothesis** High-dose ω -3 FAs alleviate the progression of atherosclerosis. **Methods** A systematic review was performed according to the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines. A search of databases was undertaken from January 1, 1960, to March 1, 2019, including PubMed, Embase, Cochrane library and ClinicalTrials.gov. RCTs that were lasted at least 6 months duration, with high-dose ω -3 FAs (3 g/day or 1.8 g/day in Japan) and atherosclerotic outcomes measured by imaging-based techniques were included. Random effects models were used to estimate the standardized mean differences (SMDs), pooling the changes compared to baseline in the measures of diverse atherosclerotic outcomes. Subgroup analyses were conducted by region of the study, characteristics of the participants, study design and imaging-based techniques. **Results** Seven RCTs (752 participants) were retained from 483 studies retrieved. Participants were from Europe, the U.S., and Japan, with either CVD or high risk of CVD. The primary outcomes were either the characteristics of coronary plaque (fibrous-ap thickness, lipid, and non-calcified volume), coronary artery minimal diameter or carotid intima-media thickness by a variety of imaging-based tools. High-dose ω -3 FAs significantly ameliorated the atherosclerosis progression (SMD: -1.32, 95%CI: -2.03 to -0.61, $p=0.0002$, $I^2=96\%$). **Conclusions** High-dose ω -3 FAs significantly slowed the progression of atherosclerosis. The anti-atherosclerotic effect of high-dose ω -3 FAs is one of the potential mechanisms in preventing CVD.



Yuqiao Zhou

Post Doc

VI-5

Genetic variants in ER stress signaling molecules IRE1 and XBP1 are associated with human bone and tooth phenotypes

Introduction: Our preliminary work in knockout mice suggests that the endoplasmic reticulum (ER) stress IRE1/Xbp1s signaling axis is important for mineralized tissues, with roles in bone formation and tooth eruption. Specifically, mice with ERN1, the gene encoding IRE1, knocked out in Osterix-positive cells showed delayed tooth eruption, skeletal and dental morphological differences, and low bone mineral density (BMD). Whether human genetic variants in these two genes influence bone and dental phenotypes remains unknown. Therefore, we employed an in silico candidate gene approach testing the genetic association of common variants in ERN1 and XBP1, with BMD, tooth eruption, and dental caries phenotypes. **Methods** Participants were Caucasian, Non-Hispanic children from: the Center for Oral Health Research in Appalachia (COHRA, N=506; ages 0-6), Iowa Fluoride Study (IFS, N=410; ages 3-6) and Iowa Head Start Study (IHS, N=266; ages 0-6). The three cohorts were genotyped together using an Illumina SNP chip. Common SNPs in the candidate genes plus 500kB up- and downstream flanking regions were tested for genetic association with timing of primary tooth eruption and caries, DXA-derived spine and hip BMD and BMC while adjusting for ancestry and pertinent covariates. A total of 1363 and 1395 SNPs were tested for the ERN1 and XBP1 loci, respectively. The locus-wise threshold for significance given the effective number of independent tests was $P < 0.0002$. **Results:** We observed significant associations for variants in both ERN1 and XBP1 loci with bone phenotypes. For the XBP1 region, we detected association of rs5752758 with spine BMC ($P = 2 \times 10^{-6}$). This SNP also showed suggestive evidence of association for all other bone phenotypes (hip BMD $P = 0.0007$, hip BMC $P = 0.0009$, spine BMD $P = 0.0007$). For the ERN1 region, SNP rs71376922 ($P = 2.5 \times 10^{-5}$) was associated with hip BMD. This SNP is in strong LD with a variant in known promoter and enhancer regions in osteoblasts. A different SNP in the 5 regulatory region of ERN1 locus, rs75160892, was associated with dental caries ($P = 0.0001$); this SNP is in LD with several SNPs showing enhancer chromatin marks in multiple cell types. Furthermore, one SNP in high LD with rs75160892 is a known eQTL for ERN1. **Conclusion:** Our findings revealed that common genetic variants at the ERN1 and XBP1 loci are associated with both bone and dental phenotypes in humans. These data, coupling with deregulated bone and tooth development in mice model, highlight a role of the IRE1/XBP1s axis in regulating these biological processes.