



Dean's Day Competition 2018

Shalkar Adambekov

EPIDEM

Central Asian Journal of Global Health: Mentored Journal Model to End Scientific Isolation

Objective. Scientists in Central Asia, Africa, and in developing world in general have difficulty publishing in the international peer-reviewed biomedical journals due to many reasons, including scientific isolation, language barriers, high publication fees, and lack of formal training in research methods. To improve access to scientific publishing in Central Asia, we at the University of Pittsburgh, established a Central Asian Journal of Global Health or CAJGH (cajgh.pitt.edu), with the key aim to assist researchers from Central Asia and other parts of developing world to improve the visibility of their research.

Methods. As a part of CAJGH, a mentored model has been created where authors whose writing, methods, or statistics are not perfect, have a chance to work with the editorial board appointed volunteers to improve their article and make it publishable. In this observational study, we analyzed publication and rejection trends at the CAJGH with the goal of identifying key publication trends and rejection reasons. **Results.** Since July 2012, over 250 articles have been submitted to CAJGH, mostly in research and short report categories. Corresponding authors of these articles were mostly from the developing countries, including Central Asian region, Afghanistan, Mongolia, India, Bangladesh, Mexico, Ukraine, and many others. Due to the introduction of mentorship model, no article has been rejected on the basis of language insufficiency. Small proportion of articles (~5%) has been rejected on the basis of inability to adhere to IMRAD format. Methodological problems are still responsible for large number of rejections (~80%), followed by inability to perform adequate literature review (~15%). Research is on the way to describe region-specific patterns of publication trends, where article submission and download data are collected and analyzed for each submitting country. **Conclusions.** In December 2016, CAJGH has been accepted to PubMed, giving researchers in Central Asia and other countries an opportunity to make their work visible. Our ultimate goal is to become the leading biomedical journal in Central Asia, and to contribute to improvement of scientific visibility of research produced in the developing world, especially Central Asia, over the next decade.



Dean's Day Competition 2018

Rahul Amruthapuri

BCHS

Distance from bus stops as a determinant of change in population, housing, and business characteristics between 2000-15 in Allegheny County, Pennsylvania

Evidence on bus-transit induced displacement is equivocal. Key Corridor bus routes of the Port Authority of Allegheny County could be associated with displacement of low-income families. This study in partnership with an advocacy group, Pittsburghers for Public Transit, determines the role of distance from bus stops on Key Corridor routes on population, housing, and business characteristics. We mapped changes in selected indicators for Census Tracts less than .5 miles away (<0.5CT) and for Census Tracts more than 0.5 but less than 2 miles away (0.5-2CT) from bus stops for two-time periods (2000-10 and 2010-15). We then determined the pattern of change in indicators in relation to distance. We subsequently identified spatial clustering of these indicators over time using bi-variate local Moran's I. We conducted additional analysis for a bus rapid transit route. Workers above 16 years using public transportation decreased further in 0.5-2CT during 2000-10 and in <0.5CT during 2010-15. Households with no vehicle decreased more in <0.5CT during 2000-10 and in 0.5-2CT during 2010-15. Poverty and renter-occupied housing units increased more in 0.5-2CT during 2000-10 and in <0.5CT for during 2010-15. Median value of owner-occupied housing units and median gross rent increased more in <.05CT for both time periods. Clusters identified for these indicators point to differences in hot and cold spots based on distance from bus stops. Businesses clustered close to bus stops on the East Busway. Changes in indicators and clustering point to need for affordable housing in proximity to bus stops on the Key Corridor routes.



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Regina Brecker	BCHS
India Hunter	BCHS
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Elizabeth Schwartz	NURS
Audrey Semel	BCHS
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Pitt Moves - A physical activity breaks project for graduate students

Introduction: Short physical activity breaks (PAB), especially peer-led ones, enhance cognition, improve mood and decrease boredom, leading to better academic achievement and satisfaction. We are currently implementing a student-led PAB project, Pitt Moves, at the University of Pittsburgh. We aim to determine the feasibility of implementing PAB for graduate students and to develop evaluation methodology to inform future initiatives.

Methodology: We piloted PAB in a single class in Fall 2017. Based on this experience and student feedback, we developed Pitt Moves for scaled-up implementation during Spring 2018. We identified interested instructors and student facilitators in three schools at Pitt. Facilitators underwent a three-hour training to lead PAB. We are collecting baseline, midpoint, and endpoint data on students' feelings during classes using a four-point scale for evaluation using Qualtrics. A logic framework guides the project implementation.

Results: Baseline survey (n=45) reveals that a higher proportion of students report better focus, mood, interest, and energy during the second hour of a class following a break when compared to the end of first hour. Around half of the students (n=22) reported being very motivated to take part in peer-led PAB. Eight facilitators are leading PAB in ten courses. Close to 130 students are taking part in Pitt Moves, some of them in more than one class. Facilitators expressed positive feedback on training received.

Conclusion: The outputs of our project, including a training module, protocol outline, mixed-methods evaluation plan, and lessons learned, will help improve and expand the implementation of PAB for graduate students at the University of Pittsburgh.



Dean's Day Competition 2018

Renee Anderko

IDM

Optimizing Antigen Presenting Dendritic Cells for an International HIV Immunotherapy

The 'kick and kill' strategy to control HIV infection proposes the unmasking of latently infected cells for immune exposure, followed by their elimination through the induction of potent anti-HIV-1 CD8+ cytotoxic T lymphocyte (CTL) responses. Major impediments to CTL control of HIV-1 infection include immune exhaustion events associated with chronic infection and the remarkable ability of HIV-1 to establish CTL epitope escape variants. Importantly, HIV-1 antigenic diversity is less within those who start antiretroviral therapy (ART) during early HIV-1 infection. In collaboration with the US Military HIV Research Program (MHRP) and the Thai Red Cross (TRC) in Bangkok, we are researching the unique R254 cohort of study participants who initiated ART during the earliest stages (Fiebig I/II) of acute HIV-1 infection (AHI). We hypothesize that control of HIV-1 can be achieved in these individuals using an optimized type-1 polarized dendritic cell (DC1)-based therapeutic designed to induce strong CTL responses against highly conserved regions of HIV-1. Preclinical studies are being performed to test the feasibility of generating largescale DC1 preparations in Pittsburgh for shipment back to Thailand for therapeutic use. The DC1 are loaded with peptide antigens derived from highly conserved regions of the HIV proteome and tested for their capacity to induce antigen-specific CTL responses in vitro. We found the major logistical issue related to DC1 production to be poor yields achieved under serum-free conditions due to strong cell adherence to the tissue culture plastic. Therefore, we tested various culture conditions to optimize recovery and viability of the DC1, which included the use of ultra-low protein binding tissue culture surfaces. The use of the ultra-low binding surface significantly improved the yield of viable DC1 and did not affect their surface expression of CD83, CD86, CCR7, or Siglec-1. These DC1 also maintained their ability to produce IL-12p70 and to induce antigen-specific CTL responses. The finding that ultra-low attachment plates improve DC1 yield and recovery without sacrificing function is significant because it highlights the feasibility of successful and consistent DC1 preparations, an essential component in the collaboration with Thailand for developing an effective HIV-1 immunotherapy.



Dean's Day Competition 2018

Teresa Anguiano

EOH

Arsenic disrupts muscle stem cell determination through fibroblast mitochondrial maladaptation that directs a dysfunctional extracellular matrix memory

Chronic arsenic (As(III)) exposure increases risk of a number of cancers and non-cancer diseases, as well as adverse health outcomes that include skeletal muscle dysfunction and mobility decline. We reported that As(III) impairs muscle maintenance and regeneration by inducing maladaptive mitochondrial phenotypes in muscle stem cells (MuSC), connective tissue fibroblasts (CTF), and fibers. We also found that As(III) imparts a dysfunctional memory in the extracellular matrix (ECM) that disrupts the MuSC niche and is sufficient to misdirect differentiation of muscle progenitor cells from myogenesis to fibrogenesis. Therefore, we asked whether dysfunctional mitochondria in As(III)-exposed CTF directed ECM alteration and whether restoring CTF mitochondrial function reverts the ECM memory. CTF were isolated from hind limb muscles of mice exposed to 0 or 100 µ/L As(III) in drinking water for 5 weeks. The CTF were cultured on collagen and elaborated ECM for 2 days before gentle decellularization. Human muscle progenitor cells (HMPC) were seeded onto the elaborated ECM and stimulated to differentiate for 2-3 days. There were fewer properly formed multinucleated myotubes from HMPC seeded on ECM derived from As(III)-exposed CTF, relative to control. In addition, MyoD and desmin, indicators of myogenic differentiation, were downregulated in the cells derived from HMPC plated on As(III)-CTF ECM at the same time cells expressing PDGFR α and CD34, indicators of fibroblast/adipocyte progenitors, were increased. To demonstrate that As(III)-impaired mitochondrial function is responsible for CTF elaborating a pathogenic ECM, we treated mice with SS-31, a peptide that repairs inner mitochondrial matrix architecture, for 1 week after the 5 week As(III) exposure period. Selective injury to the tibialis anterior (TA) muscle with BaCl₂ followed by 2 week recovery examined the restorative effects of SS-31 on muscle regeneration. SS-31 restored arsenic-impaired TA regeneration and HMPC seeded onto ECM elaborated by CTFs isolated from As(III)-exposed/SS-31-treated mice had normal myotube differentiation and MyoD expression, as well as increased desmin expression, compared to ECM of CTF from control or arsenic-exposed mice. These data indicate that As(III) impairs muscle maintenance and regenerative capacity by targeting CTF mitochondria and that therapies restoring muscle mitochondria may effectively treat skeletal muscle dysfunction and mobility decline in As(III)-exposed individuals. Supported by NIEHS grants R01ES023696, R01ES023696.S1, and R01ES025529.



Dean's Day Competition 2018

Sara Baumann

BCHS

Exploring menstrual practices and accompanying motivations among adolescent girls in far-west Nepal using collaborative filmmaking

In this study we develop and pilot a novel, qualitative participatory arts-based research method called collaborative filmmaking to explore menstrual practices and accompanying motivations in far-west Nepal. Throughout Nepal, women and girls face numerous restrictions during menstruation, which leave them vulnerable to poisonous snake bites, hypothermia, dehydration, pneumonia, asphyxiation, rape, and even death. This study aims to use collaborative filmmaking, where participants are trained as Community Producers to create films related to the research question, to understand nuances in menstrual practices and accompanying motivations. This feasibility pilot was conducted with seven girls aged 16-18 from one village in far-west Nepal. Participants were recruited for maximum diversity from four caste groups and two religious backgrounds. The films and associated interviews highlighted an array of menstrual practices such as keeping distance, ritual cleansing, and restrictions in touching, washing, cooking, among others. Though there are many commonalities, the study revealed a number of dissimilarities in menstrual practices. The accompanying motivations for practicing these menstrual traditions included religious and spiritual beliefs, family tradition, negative consequences, social pressure, and guilt. These results illustrate that in one village alone, menstrual practices and restrictions vary widely, and are motivated by a number of social and religious factors. In designing menstrual health interventions and policies, a range of menstrual practices and motivations must be considered to ensure context-specificity, particularly in the ethnically and religiously diverse Nepal.



Dean's Day Competition 2018

Joanne Beer

BIOST

Predicting Social Responsiveness Scale scores from fMRI data using structured sparse penalized regression

Penalized regression estimators, such as lasso, ridge regression, or elastic net, yield unique solutions when data is high dimensional (i.e. when there are more predictors than subjects) by imposing optimization constraints that result in global sparsity or shrinkage of estimated coefficients. However, often more is known about the relationships between predictors. For example, when neuroimage voxels are used as predictors, we might expect the estimated coefficients of neighboring voxels to exhibit some degree of spatial smoothness. Additionally, we might expect voxels residing in the same functional networks or anatomical regions to be selected or shrunk to zero as a group. We propose incorporating information about voxel spatial and functional relationships into the optimization constraints by using a fused sparse group lasso estimator. We apply the estimator to resting state fMRI data from the Autism Brain Imaging Data Exchange (ABIDE) Preprocessed dataset in order to pinpoint the cortical regions whose functional connectivity with a subcortical seed region best predicts Social Responsiveness Score, a continuous measure of autistic social impairment.



Dean's Day Competition 2018

Candice Biernesser

BCHS

Suicidal Adolescent and Parent Perspectives of Automated Methods of Social Media Monitoring

Suicide has recently risen to the 2nd leading cause of death among youth ages 10-24. This upward trend in adolescent suicide has occurred with the mass use of smartphones. This is concerning to adolescent's suicide risk, because heavy use of social networking sites places youth at 6 times great risk of suicidal thought. Due to this heightened risk, there is a growing demand to begin collection of a "digital phenotype," which would add to routine information collected at health care visits to include personal data received from adolescent's smartphones, e.g. social media and text message content. This poster will provide the preliminary results of a qualitative study aimed to inform the development of an automated social media monitoring intervention, which will detect and communicate risk from suicidal adolescent's digital media to their mental health providers. Suicidal adolescents from the Services for Teens At-Risk Center and their parents participated in focus groups and brief surveys investigating social media use, interactions, and monitoring practices and perceptions. Adolescents in the study were frequent social media users, two-thirds of whom used social media for over 2 hours per day. All adolescent participants indicated that social media impacted their suicidal thoughts, but none had ever discussed this with their clinicians. Adolescents were strongly resistant to the notion of social media monitoring, preferring the freedom and autonomy they derive from unsupervised personal expression. Methods of monitoring that would be acceptable to youth and parents are discussed and summarized.



Dean's Day Competition 2018

Shivkuma Biradar

IDM

Utilization of oligo-mannose targeted Chimeric Antigen Receptor (CAR)-expressing T-cell to control HIV.

Anti-retroviral therapy (ART) has improved the quality of life for HIV infected individuals, but it fails to eliminate the virus from the body. Naturally occurring HIV-specific T cells can control HIV initially, but this response is not sustained in the majority of people living with HIV due to issues related to viral evolution and immune escape. Use of genetically modified cytotoxic T cells to specifically target conserved aspects the HIV reservoir offers therapeutic approach to this problem (1). We hypothesize that autologous peripheral blood derived CD8+ cytotoxic T cells genetically engineered to express a chimeric-antigen receptor (CAR) capable of targeting high mannose moieties (Man9) present on the surface glycoproteins of the HIV envelope protein gp120 can be effective as an immunotherapeutic tool to control HIV infection. The anti-Man9 monoclonal antibody 2G12, which has been shown to effectively target the HIV envelope with broadly neutralizing capability (2), is the antigen specific component of the CAR-T cell construct we are exploring. In this study, we propose to optimize the engineering of Man9 specific CAR-T cells and characterize their function by testing their capacity to target and kill autologous naturally infected HIV reservoir associated CD4+ T cells in vitro, and in vivo using a humanized mouse model. Our preliminary results addressing the optimization of the T cell transfection protocol using a nucleofection-based approach to deliver a GFP indicator construct indicate that we can achieve a 65% transfection efficiency of activated T cells. However, when using this same strategy to transfet T cells with the 2G12 antigen receptor plasmid, we were unable to achieve efficient transfection. We hypothesized that the larger plasmid size of the 2G12 construct was the problematic issue. To test this, we compared the transfection efficiency using GFP plasmids of different sizes, including a size comparable to the 2G12 plasmid we used earlier. In doing so, we found that the transfection efficiency using our nucleofection-based system is indeed dependent on the size of the plasmid. Currently, we are continuing to optimize the transfection protocol using the bigger GFP plasmid and testing different transfection reagents. As an alternative, we plan to explore a more stable lentivirus-based approach to transfet T cells with the 2G12 construct.



Dean's Day Competition 2018

Rahel Birru

EOH

Phloretin, an apple polyphenol, reduces chronic obstructive pulmonary disease (COPD) pathogen-induced mucus overproduction.

Pathogen-induced mucus overproduction is associated with exacerbations in COPD. A diet enriched in hard fruits protects against declining lung function in persons with COPD. We assessed whether the apple polyphenol phloretin could reduce bacterial-induced mucus production in vitro and in mice. We examined phloretin activity against Nontypeable Haemophilus influenzae (NTHi), a common bacteria isolated from COPD patients experiencing exacerbations. Mice were given a phloretin-supplemented diet (100 mg/kg body weight) and challenged intratracheally with NTHi (105 CFU). Lungs were harvested after 24 hours and analyzed for mucin 5AC (MUC5AC), a major component of mucus, mRNA. The human lung mucoepidermoid cell line (NCI-H292) was pretreated with 100 μ M phloretin and exposed to NTHi (multiplicity of infection 7.5). Cells and supernatant were analyzed for MUC5AC by qPCR and ELISA. The involvement of the epidermal-growth factor (EGFR) and mitogen-activated protein kinase (MAPK) pathway was determined by western blot. Proteinase levels were measured by luminex and immunostaining. Phloretin inhibited NTHi-induced MUC5AC in mouse lungs (mRNA) and NCI-H292 cells (mRNA and protein). Inhibition was accomplished by reducing EGFR phosphorylation and accompanying decreased MAPK 3/1 (aka ERK 1/2) and MAPK8 (aka JNK) activation. Phloretin also inhibited NTHi-induced matrix metalloproteinase-13, which cleaves ligands of EGFR that subsequently activates this pathway. Phloretin inhibits NTHi-induced MUC5AC induction by reducing ligand-dependent activation of EGFR, resulting in the inhibition of the EGFR-MAPK cascade. Overproduction of mucus in COPD can lead to exacerbations, and consequently hospitalization, reducing the overall quality of life for patients. Phloretin is a promising candidate for relieving and preventing the development of bacterial-induced COPD exacerbations.



Dean's Day Competition 2018

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EPIDEM

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EPIDEM

The Effect of Estradiol (E2) and Follicle-Stimulating Hormone (FSH) Changes on the Incidence of Type 2 Diabetes in Women Transitioning through Menopause: A Longitudinal Analysis based on the SWAN Study

Objective: In the United States, the incidence of type 2 diabetes (DM2) is highest among people who aged between 45 and 64 years old compared to other age groups among both genders. The reason for this age pattern of DM2 incidence is still unclear. The sex hormones changes in the middle of life may explain the high risk of diabetes among this age group, especially for females transitioning through menopause. There were supporting and contrasting findings for the association between sex hormones levels and DM2 incidence from previous studies. We aim to assess whether 1) the risk of developing diabetes is increasing over 10 years in the SWAN women transitioning through menopause and 2) the incidence of diabetes and fasting glucose levels over time are associated with time-varying estrogen estradiol (E2) and follicle-stimulating hormone (FSH) levels.

Methods: The Study of Women Across the Nation (SWAN) is a historical longitudinal population-based study that aimed to explore changes in women's health during their middle ages since 1994. The eligible criteria were SWAN participants with E2 and FSH data, fasting glucose levels less than 126 mg/d and menses within past 3 months, and without pregnant at baseline visit. There were 2032 participants eligible for this analysis. There were 7-10 follow-up visits which collected E2 and FSH levels, fasting glucose levels, diabetes status information and other covariates, including BMI, smoking status and lipids. E2 and FSH were measured within the first five days of the menstrual cycle. The primary outcome was the incidence of DM2 occurring after baseline visit and the secondary outcome is the fasting glucose levels in each follow-up visit. A generalized mixed linear model was used to assess the association between change in E2 and FSH levels and incidence of diabetes after adjusting for BMI, smoking, and lipids.

Results: Over 10 years of follow-up, 101 women had DM2 (Pending).

Conclusion: Our study can help identify high risk women of diabetes based on their E2 and FSH changes during menopause transition to implement timely preventive interventions, which have great public health significance considering the large disease burden of diabetes in the United States (Pending).



Dean's Day Competition 2018

Hannah Bitzer

BCHS

The Relationship Between the Vestibular Ocular Motor Screening (VOMS) and Length of Recovery After Concussion

INTRODUCTION: Comprehensive assessment of concussion should evaluate multiple domains including symptoms, cognitive, vestibular, oculomotor, and psychological functioning¹, to allow for more targeted and effective treatment. The VOMS is one such tool that identifies individuals who have vestibular/oculomotor impairment and may require formal treatment². VOMS is a brief assessment including seven components: 1) smooth pursuits, 2) horizontal saccades, 3) vertical saccades, 4) near point of convergence (NPC), 5) horizontal vestibular ocular reflex (VOR), 6) vertical VOR, and 7) visual motion sensitivity (VMS). This tool assesses self-reported symptoms, as well as average NPC distance.

METHODS: A sample of 83 participants (48 males, 35 females) between the ages of 15-50 years (16.08, +/- 2.914) were included in this study. Patients were diagnosed with a concussion within 10 days of injury ($M = 7.11$, +/- 2.279), and the number of days participants took to recover from the concussion ($M = 29.11$, +/- 16.451) were recorded. VOMS data were collected at initial and clearance visits.

Symptoms for each domain were compared to baseline measurements to measure provocation.

Participants were classified as having a vestibular profile if their VOMS symptom score increased by at least 2 from baseline on either VOR measurement or VMS, to represent vestibular impairment.

Symptoms on VOMS at the initial visit was split into two groups: 0-20 (low symptom burden) and >21 (high symptom burden). A chi-square test was performed to examine the relationship between the days to recovery and total VOMS scores at their initial visit. A chi-square test was also performed to examine the relationship between days to recovery and number of participants with a positive vestibular profile.

RESULTS: Days to recovery was categorized into 5 ranges: 0-7, 8-14, 15-21, 22-30, and 31+. In this population 47% recovered in 21 days or less, with 38% recovering in greater than 31 days. A high symptom burden on VOMS was present for 62% of the population. A chi-square test showed a significant relationship between the days to recovery and a positive vestibular profile at their initial visit ($\chi^2 = 10.133$, $.001$, $OR=4.485$; Figure 2).

DISCUSSION: Findings suggest that the VOMS is useful for identifying patients at risk for protracted recovery following concussion. Participants with a total VOMS score >21 at their initial clinical visit were more likely to have a longer recovery period. Similarly, individuals with a vestibular profile took longer to recover. Further research should examine the role of VOMS scores in identifying chronic patients and the relationship of VOMS scores to other clinical profiles such as anxiety/mood.

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Dean's Day Competition 2018

Brandon Blobner

HUGEN

The burden of rare ENAC variants associated with increases or decreases in blood pressure

Proper maintenance of extracellular fluid volume and extracellular [Na⁺] is critical for controlling blood pressure. The kidney has a major role in regulating extracellular [Na⁺] and extracellular fluid volume through the reabsorption and excretion of Na⁺ and water. The epithelial Na⁺ channel (ENaC) is part of the mechanism for fine-tuning Na⁺ reabsorption in the distal nephron. Gain-of-function or loss-of-function ENaC mutations have profound effects on renal Na⁺ reabsorption and blood pressure. While a several ENaC single nucleotide variants (SNVs) with large effect sizes on blood pressure have been identified, the impact of rare ENaC SNVs on blood pressure has not be assessed. With the recent availability of a large genomic sequencing database, TOPMed, we are able to explore the functional effects of human ENaC variants, many of which are rare (MAF < 0.01), sequenced from 62,784 individuals. By prioritizing ENaC SNVs based on proximity to key functional domains, conservation across species and among ENaC subunits, and online resources for predicting SNV deleteriousness, we have identified a subset of 33 ENaC SNVs that affect ENaC expression or function. Using burden tests and sequence kernel association tests (SKAT), as well as single variant analyses, we have analyzed the burden of rare ENaC variants associated with blood pressure phenotypes from a subset of studies in TOPMed.



Dean's Day Competition 2018

Kristina Boyd

BIOST

Years of life lost in Allegheny County due to drug-related overdose: an exploration using Poisson regression and grouping analysis

Objectives: To descriptively explore the relationship between years of life lost due to drug-related overdose deaths in Allegheny County by municipality, age, sex, and race using Poisson regression and grouping analysis.

Methods: Drug-related overdose death data were collected from medical examiner reports in an online database. Years of life lost will be calculated from standard population tables using 2010 US Census population counts to form rates. Poisson regression will be carried out using Stata SE 15th edition. Grouping analysis will be carried out using ArcGIS Pro.



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Noel Britton	EPIDEM
Amanda Delligatti	EPIDEM
Curtis Tilves	EPIDEM

Trends and Correlates of Suicidality in Youth from Trinidad and Tobago

This is an analysis of data collected as a part of the Global School-based Student Health survey completed as a group as a part of our coursework for EPIDEM 2230.



Dean's Day Competition 2018

Noel Britton

EPIDEM

The Composition of the Lung Mycobiome in Adult Critically Ill Patients With or At Risk For The Acute Respiratory Distress Syndrome

Background: Microbiome research has primarily focused on the bacteriome although there is increasing awareness of the importance of the mycobiome. Microbiome perturbations (dysbiosis) have been observed to occur rapidly in patients with critical illness and the Acute Respiratory Distress Syndrome (ARDS). In the setting of heavy antibiotic treatment potentially altering the bacterial community in the lung, the lung mycobiome may play an important role in the progression of ARDS. However, the lung mycobiome in ARDS remains unexplored and understanding of the potential impact of mycobiome dysbiosis on ARDS progression and outcomes remains limited.

Objective: To describe the composition of the lung mycobiome in patients with ARDS versus critically-ill controls and examine for discriminating features of the mycobiome in association with clinical outcomes.

Methods: We prospectively recruited mechanically ventilated patients within the Pittsburgh Acute Lung Injury Registry and Biospecimen Repository. Patients were classified into ARDS according to the Berlin Criteria, patients at-risk for ARDS (i.e. patients with risk factors for ARDS who did not meet radiographic or hypoxemia criteria) and patients not-at-risk for ARDS (i.e. without risk factors and intubated for airway protection). We collected endotracheal aspirates at enrollment. Fungal rRNA gene sequencing (internal transcribed spacer (ITS) region 1 to 2) was performed on clinical samples and reagent controls. Taxonomic analyses were performed using Dada2 and Phyloseq.

Results: 92 patients (30 with ARDS, 42 controls at-risk and 20 controls not at-risk for ARDS; mean age 54.9 years; 58% males) were included. 47 (51%) patients had a positive blood or sputum culture. Beta diversity analyses showed significant differences between groups (permutational analysis of variance, $p=0.001$). At the species level, taxonomic differences were observed between patients with ARDS and at-risk and not at-risk controls with ARDS patients having a more diverse taxonomic composition than at-risk and not at-risk controls (Figure).

Conclusion: Next-generation sequencing analysis identifies taxonomic differences in the mycobiome of patients with ARDS compared to both at-risk and not at-risk controls. Further study including functional network interactions between bacterial and fungal communities as well as correlation with clinical outcomes are needed to determine the role of mycobiome in ARDS.



Dean's Day Competition 2018

Jennifer Burwinkel

IDM

Using Tissue Culture to Model Early Events in *Francisella tularensis* Pathogenesis

Description of The Problem: *Francisella tularensis* is a gram negative facultative intracellular bacterium that causes tularemia (a.k.a. rabbit fever). Tularemia causes severe morbidity and mortality in humans with a 30% fatality rate if untreated. Infection can occur by a number of routes but the most severe disease results from inhalation of *F. tularensis*. Inhalation of as few as 15 cfu can cause disease in humans. Attenuated strains can also infect and replicate inside host cells. *F. tularensis* produces no known toxins and the pathogenic mechanisms behind the disease are not clear.

Objectives/Aims: While macrophages are an important target for *F. tularensis*, initial interactions in the lung would most likely be with epithelial cells. The goal of this study was to evaluate the interaction between *F. tularensis* and the lung epithelium. We have compared infection and replication rates with different *F. tularensis* strains in a human alveolar epithelial cell line (A549 cells) and a murine macrophage cell line (J774 cells). We have also evaluated the ability of *F. tularensis* to infect and replicate in lung epithelium using a 3-D air-liquid interface culture model with primary human bronchial epithelial (HBE) cells.

Method(s) Used/Approach Taken: The Live Vaccine Strain (LVS) and SCHU S4 strains of *F. tularensis* were previously obtained and frozen stocks made for use in experiments. A549 and J774 cells were obtained from the ATCC. HBE cells were obtained from Dr. Mike Myerburg's lab. *F. tularensis* was grown for two days on cysteine heart agar (CHA) prior to infection. Mammalian cells were infected with *F. tularensis* and then lysed at 0, 24, 48, and 72 hours post-infection. Dilutions were made of the lysate and plated on CHA to determine bacterial concentration. The colony forming units were determined one to two days later.

Results: Although *F. tularensis* could more readily infect J774 cells than A549 cells, once inside the cell the replication rate of *F. tularensis* was the same in both J774 and A549 cells. The number of infected cells typically peaked between 24 and 48 hours then decreased at 72 hours. Initial results suggest that *F. tularensis* can infect HBE cells.

Discussion/Implications/Conclusions: The higher rate of infection in macrophages compared to epithelial cells is likely a result of the bacteria subverting the natural phagocytic properties of macrophages. Replication rates are the same in both cells, suggesting that entry is the major difference between the two mammalian cell types. Infection of primary HBE in a 3-D culture model is more physiologically relevant to in vivo infection than infection of cells in liquid culture. This model could provide valuable information on the early events of *F. tularensis* infection in the host.



Dean's Day Competition 2018

Rachel Butler

HPM

Utilization of palliative care among individuals with Alzheimer's disease and related dementias in their last 12 months of life: an exploratory analysis of Pennsylvania dual-eligible beneficiaries

RATIONALE: Palliative care has been shown to relieve physical, psychological, emotional, and spiritual distress for individuals with serious illnesses, improving their quality of life and their quality of dying. Research in palliative care has largely focused on cancer diagnoses, leading providers and scholars to call for research on the impact of palliative care in the face of other illnesses. Alzheimer's disease and related dementias (ADRD) are characterized by rapid, progressive functional deterioration, yet little is known about the use of palliative care among individuals with ADRD, including if, when, where, and by whom palliative care is delivered. The cognitive impairment and total dependency that is characteristic of the ADRD trajectory makes it difficult, and sometimes impossible, for individuals with ADRD to express their unrelieved pain and other distressing symptoms, placing additional pressure on strained caregivers to identify appropriate care needs near the end-of-life. Understanding the mechanisms by which individuals with ADRD and their families access timely and appropriate palliative care is paramount to informing evidence-based policy and practice.

OBJECTIVES: To understand the rate of consultation and predictors of palliative care use among individuals with an ADRD diagnosis in their last 12 months of life.

METHODS: We utilized a nonrandomized, retrospective design. Using Pennsylvania Medicaid claims for dual-eligible beneficiaries from 2013-2015 merged with Medicare enrollment data and restricted to beneficiaries who were dually-eligible for the full benefit year, we identified individuals who: 1) died in 2014 or 2015, 2) were diagnosed with ADRD at least 12 months prior to death, and 3) were seen by a board certified palliative care physician during their last 12 months of life. We used multivariate logistic regression, with an ADRD diagnosis as the main independent variable and a dichotomous dependent variable indicating a consultation to a multidisciplinary palliative care team with a board certified palliative care provider. Covariates included age, gender, race, living arrangement (i.e. nursing home or home), geographic location (i.e. county), and comorbidities.

HYPOTHESIS: We hypothesize the rate of palliative care use will be lower for individuals with ADRD but higher in urban areas where there is access to an academic medical center with an established inpatient palliative care service. We expect to see differences in palliative care use across gender, race, and living arrangement.



Dean's Day Competition 2018

Teresa Capasso

HUGEN

Bmp10 is necessary for Alk1 activation in skin and liver vasculature throughout life

Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant vascular dysplasia characterized by development of high-flow arteriovenous malformations (AVMs) that can lead to stroke or high-output heart failure (HOHF). HHT2 is caused by heterozygous mutations in ALK1, which encodes an endothelial cell bone morphogenetic protein (BMP) receptor. Because HHT2 is likely caused by ALK1 haploinsufficiency, ligand-based therapies that enhance flux through remaining wild type receptors may ameliorate disease. To define spatiotemporal ALK1 ligand requirements, we generated zebrafish mutants in bmp9, bmp10, and bmp10-like, which encode putative Alk1 ligands expressed in liver, endocardium, and myocardium, respectively. Homozygous loss of each of these genes individually has no effect on the embryonic vasculature, whereas simultaneous loss of bmp10 and bmp10-like causes cranial AVMs indistinguishable from alk1 mutants, confirming functional redundancy during embryonic vascular development. In contrast, Bmp10 is the only Alk1 ligand required non-redundantly in the juvenile-to-adult period, with mutants displaying enlarged vessels, hemorrhage, edema, and heart dysmorphology as early as six weeks of age. Heart defects in bmp10 mutants do not stem from embryonic defects in trabeculation or cardiomyocyte number, size, or sarcomeric structure. Instead, our results suggest that Bmp10 is required for development of anterior cutaneous and liver vessels, and that heart defects in bmp10 mutants are secondary to vascular defects, with dilated vessels and hemorrhage leading to low systemic vascular resistance and HOHF. HOHF is an increasingly recognized complication of severe liver involvement in HHT. We postulate that BMP10 treatment may be effective in stemming progression to HOHF in HHT patients.



Dean's Day Competition 2018

Abigail Cartus

EPIDEM

Phthalate exposure and first trimester human chorionic gonadotropin (hCG) in women with low vs. high stress

Background: Phthalate compounds, plasticizers used in a variety of applications, are ubiquitous in the environment and in human bodies in the industrialized world. Studies conducted in The Infant Development and Environment Study (TIDES) cohort suggest that placental production of human chorionic gonadotropin (hCG) may be a mechanism by which exposure to phthalate compounds disrupts genital development. Analyses from this cohort also indicate that the association between phthalate exposure and disruption of genital development is stronger in women reporting fewer stressful life events. In this analysis, we attempt to unify these findings by examining maternal stress and phthalate effects on placental hCG.

Methods: We analyzed a subset of TIDES subjects (N = 340), who were recruited at 4 US centers (NY, MN, CA, WA) in the first trimester of pregnancy, at which time phthalate concentrations and placental hormone levels were measured (in maternal urine and blood, respectively). Our primary outcome, first trimester hCG, is modeled as a z-score, to address differences in hCG distribution between clinical labs. Stressful life events (SLE) were collapsed to 3 categories. We used generalized linear models adjusted for confounders and stratified by fetal sex to estimate whether maternal stress modifies the associations between urinary phthalates and hCG. Associations were assessed in both fetal sexes for a wide range of phthalates and phthalate metabolites; here, we report specifically on associations between two metabolites of di-2-ethylhexyl phthalate (DEHP): 1) mono-2-ethylhexyl phthalate (MEHP, a monoester metabolite of DEHP), and 2) the molar sum of DEHP oxidative metabolites (DEHP-Oxo, consisting of MEHHP, MEOHP, MECPP). MEHP is a biomarker of DEHP exposure, and DEHP-Oxo is a biomarker of DEHP metabolism. MEHP and DEHP-Oxo were collinear ($VIF > 5$) and not included in the same models.

Results: In all pregnancies, higher maternal stress was associated with lower first trimester hCG. We report on the associations between MEHP/DEHP-Oxo and hCG in women carrying females; findings in women carrying male fetuses were null. The interaction between MEHP and maternal stress was statistically significant with p-value for the interaction term = 0.02. Stratum-specific estimates ($\hat{\beta}^2$ [95% CI], p-value) were: 0 stressful life events: +0.05 higher hCG for a log unit in MEHP [-0.14, 0.24], 0.58; 1 stressful life event: -0.29 [-0.53, -0.04], 0.02; 2+ stressful life events: -0.31 [-0.66, 0.05], 0.09. The interaction between DEHP-Oxo and maternal stress did not reach statistical significance (p = 0.11).

Conclusions: In women carrying females, our results suggest that first trimester hCG production by the placenta may be a mechanism by which women with higher vs. lower stress in pregnancy might be more susceptible to the hormonal effects of DEHP exposure. However, as prior findings from this cohort indicate that maternal stress modifies the effect of the relationship between phthalate exposure and reproductive development in males, these results suggest that placental function (as measured by hCG) may not be the mechanism by which stress modulates phthalate effects on genital development.



Dean's Day Competition 2018

Cristian Chandler

BCHS

Towards Understanding the Impact of Syndemics on HIV Screening among Black Men who have sex with Men (BMSM) in the United States: Results from the POWER Study

Background: The theory of syndemic production, the co-occurrence of several epidemic and ecological factors to worsen health outcomes, has often been used to explore HIV transmission risk or HIV-infections, but has not been used to study HIV prevention behavior, or large samples of non-Whites. This study is the first to explore the impact of psychosocial syndemic factors on previous six-month HIV screening behavior among a large sample of BMSM. Six-month screening is the current recommendation for sexually active MSM in the United States. It was hypothesized that younger BMSM (under 30 years old) would be less likely to have been tested in the previous six months based on extant literature. Further, it was hypothesized that participants would report less frequent screening with each increasing level of syndemic variable count.

Methods: Data have been used from the Promoting Our Worth, Equality and Resilience (POWER) study of BMSM in six US cities recruited at national Black Pride events in 2014-2017. Cross sectional survey and HIV screening data were analyzed from 3,294 participants in bivariate and stepwise logistic analyses, using syndemic variable counts for additive effects. To model interactions beyond additive effects, measures of interaction/synergy were calculated according to the synergy index (S). Syndemic variables included: past three-month poly-drug use, depression, last year intimate partner violence, HIV risk (e.g. inconsistent condom use) and problematic binge drinking.

Results: In bivariate analyses, BMSM under 30 were more likely to have been screened than men aged 40 and above ($OR = 2.14$, 95% CI: 1.73,2.64). Participants lacking insurance were less likely to have been tested ($OR = 0.73$, 95%CI: 0.61,0.88) and men with HIV transmission risk were more likely to have been tested ($OR = 1.20$, 95%CI: 1.01,1.41). In multivariable analyses, BMSM with two syndemic conditions were more likely to report screening ($AOR = 1.37$, 95%CI: 1.04,1.80) with no significant associations for three or more conditions. Synergy index values revealed that when men reported poly-drug use and depression ($S=1.02$), depression and problematic drinking ($S=3.70$) or poly-drug use and problematic drinking ($S=3.70$) they were less likely to report having been screened for HIV in the previous six months. **Conclusion:** Results of this study suggest that individual factors cannot entirely explain the lack of testing and excess disease burden among BMSM compared to White and other MSM. Findings indicate the need for a more complex method of theorizing and modeling BMSM syndemics focused on the contextual and structural factors impacting HIV behavior to include such exposures as discrimination and incarceration, which may be of greater impact.



Dean's Day Competition 2018

Jonathan Chernus

HUGEN

Finding genes for Down syndrome: GWAS of maternal nondisjunction of chromosome 21

Nondisjunction (the failure of chromosomes to separate properly during cell division) is the leading cause of intellectual disabilities, birth defects, and pregnancy loss in humans. To identify genetic variants and genes affecting the likelihood of nondisjunction, we performed a genome-wide association and candidate gene study for Down syndrome (trisomy 21, most often caused by maternal nondisjunction during meiosis). Our study group ($n = 2,186$) consisted of 749 children with Down syndrome and their parents, who were assayed for several million common genetic variants (SNPs) via an Illumina genotyping platform and subsequent imputation of unobserved variants. By comparing the genotypes of parents and children, we confirmed maternal origin of the nondisjunction in each family; similarly, we determined whether each nondisjunction occurred in the first or second stage of meiosis (MI vs MII). To explore the hypothesis that MI and MII nondisjunctions may have both shared and unique genetic architecture, we contrasted three subgroups in our analyses: mothers with MI nondisjunctions, mothers with MII nondisjunctions, and fathers (a convenient control group). We also performed analyses powered to identify variants affecting survival to term of a fetus with Down syndrome. Although no association reached genome-wide significance ($p < 5E-8$), we observed suggestive associations ($p < 1E-5$) near genes with known or plausible roles in meiosis. At the gene level, several significant associations were found in candidate genes involved in disjunction and meiotic recombination.



Dean's Day Competition 2018

Damian Da Costa

HPM

Functional Status and Cognitive Impairment on Admission to Nursing Homes in Pennsylvania, 2013-2015

In the last several years, states have shifted the balance of long-term-care delivery from institutional settings toward home-and-community-based services (HCBS). Prior research indicates that greater utilization of HCBS may reduce nursing home utilization as intended, however it may also have the effect of increasing the acuity of nursing home case mix. Using Minimum Data Set assessment data from 2013-2015, we provide descriptive analysis of trends in the level of functional status and cognitive impairment among new admissions across three policy-relevant regions of Pennsylvania. Results are stratified by age, gender, race, and insurance status. We observe significant differences in functional and cognitive impairment at admission among regions and strata that provide strong motivation for future investigation into the differential impacts of HCBS utilization on acuity of nursing home case mix across regions.



Dean's Day Competition 2018

Olivia D'Annibale

HUGEN

Breast Cancer Screening in a Pennsylvania Managed Care Organization

Background: Breast cancer is the most common cancer among women in the US: annually more than 230,000 women are diagnosed and more than 40,000 die. Although breast cancer screening (BCS) is a covered benefit and associated with reduced risk of developing breast cancer, a large percentage of the population are not screened. We examined possible predictors of BCS among women enrolled in a Managed Care Organization (MCO).

Methods: Women 52-74 years old enrolled continuously in the MCO between October 1, 2014-December 31, 2016 were included in the analysis: 3,624 were BCS utilizers and 3,298 were non-utilizers. We used the Behavioral Model of Health Care Utilization framework to identify predictors of BCS utilization, including predisposing (e.g., age group), enabling (e.g., area of residence), and need-related (e.g., smoking) factors. Differences between BCS utilizers and non-utilizers were assessed using chi-square and logistic regression analyses conducted in SAS Enterprise 6.1.

Results: Overall, mean age of the women was 59 (± 4) years, 20% were African American, 2% were Asians or Pacific Islanders, and 12% were Hispanic. Approximately 5% had family history of breast cancer, 23% were from rural areas, 39% had 3-5 chronic health conditions, 10% were obese, 15% were smokers, and 48% were non-BCS utilizers. Results showed utilizers were more likely to be African American (OR: 1.28; 95%CI: 1.12-1.47), Hispanic (OR: 1.88; 95%CI: 1.51-2.35), have a family history (OR: 6.95; 95%CI: 4.94-9.83), smoke (OR: 1.20; 95%CI: 1.04-1.39), and had more PCP visits (OR: 1.02; 95%CI: 1.00-1.03). Women residing in rural areas (OR: 0.77; 95%CI: 0.68-0.88), Southwest PA (OR: 0.73; 95%CI: 0.61-0.87), and with no chronic health conditions (OR: 0.30; 95%CI: 0.21-0.42) were less likely to be utilizers.

Conclusion: Despite evidence that regular screening improves diagnosis and treatment of breast cancer, screening rates were low. We observed reverse health disparities with regards to race and ethnicity. Women with higher numbers of PCP visits and/or family history of breast cancer were more likely to be screened. Geographical disparities were also observed. These results indicate the MCO should target specific interventions to educate, inform availability of breast screening services, and remind beneficiaries about their annual screening. Increasing the rate of screening would decrease the rate of breast cancer (or some such words) regarding public health significance.



Dean's Day Competition 2018

Susan Devaraj
Andrea Stewardt

EPIDEM
EPIDEM

Trends in Disparities in Health Behaviors and Outcomes by Race in Allegheny County: 2009 to 2015

Introduction: Health disparities persist in the United States despite national initiatives to monitor and eliminate them. According to the Healthy People 2020 definition, health disparities are health differences among groups of people who systematically face greater obstacles based on social, economic or environmental disadvantages. Historically, Allegheny County has documented disparities by race from 2002 to 2009 with Black residents demonstrating less favorable rates in indicators such as self-reported general health, diabetes, hypertension and smoking. The purpose of this analysis is to describe more recent trends in health behaviors and outcomes by race using Allegheny County Health Survey (ACHS) data from 2009 and 2015.

Methods: Surveys were administered by telephone using random digit dialing of Allegheny County residents 18 and older with oversampling from communities with larger proportions of Black and low-income individuals. Analyses were limited to health behavior and outcome data available at and consistently collected across both survey time points. Health behaviors studied include smoking and alcohol use and health outcomes studied include general health, heart attack, stroke, cholesterol, diabetes, hypertension, and asthma. Prevalence of health behaviors and outcomes by race were compared using 95% confidence interval overlap to indicate disparity at each time point. Additional analysis included change in prevalence using logistic regression models with an interaction term for year and race and adjusted for education, income, gender, age and marital status.

Results: The 2009 ACHS survey included responses from 3,592 households and the 2015 survey included responses from 6,395 households. 19% of respondents in 2009 and 12.9% of respondents in 2015 identified as Black. Preliminary results demonstrate that disparities in some health behaviors and outcomes of interest were present in 2009 and remained present in 2015, including asthma and smoking. For health behaviors, there was a disparity in smoking status with Blacks having higher rates than Whites in 2009 and 2015 - based on no confidence interval overlap in both 2009 and 2015. For outcomes, there was a racial disparity in diabetes prevalence in 2009 with Blacks having slightly higher rates than whites, however in 2015 the disparity was no longer present. Similar trends were seen with high cholesterol, blood pressure and stroke. Change in overall health was different by race ($p=0.02$), with fewer non-Hispanic black respondents reporting "Fair or Poor" health over time compared to non-Hispanic white respondents.

Discussion: In Allegheny County, some disparities in health behaviors and outcomes persisted and some were no longer present between 2009 and 2015. Indicators vary in the trend shown, with some indicators demonstrating a reduction in disparity over time, some showing an increase in disparity over time and some showing no difference over time. Future analyses will focus on comparing rate of change for each outcome by race to further inform these trends and on exploring disparities by socio-economic status.



Dean's Day Competition 2018

Erika Dreikorn

HUGEN

Cutis Laxa Mutations in Fibulin-5 Cause Decreased TGF β Signaling

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. To further understand the molecular mechanisms of 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). When analyzed by western blotting, intracellular FBLN5 amounts normalized to actin were 2.796 ± 1.088 in controls and 4.678 ± 0.9681 in mutants, however this difference did not reach statistical significance, possibly due to small sample size ($p= 0.3189$, t-test). Extracellular FBLN5 levels normalized to FBLN4 were 0.7757 ± 0.3674 in controls and 0.03772 ± 0.0214 in mutants. These results were also not statistically significant ($p= 0.2178$, t-test) and did not include all patient samples; further westerns are to be done which will include all patient samples. In addition to these two extracellular matrix assembly proteins, proteins in signaling pathways were also studied via western blotting. The amount of pSMAD3 protein was significantly decreased ($p= <0.0001$) in patient cells. This indicated that there was less transforming growth factor beta (TGFB) signaling in patient cells compared to control cells, which has downstream transcriptional regulation implications. Immunostaining revealed that mutant cells deposited reduced amounts of mature elastin, while tropoelastin and other extracellular matrix proteins, such as fibronectin and fibrillin-1, remained unaffected. Preliminary colorimetric elastin assays indicated that mutant cells assembled decreased amounts of elastin. Future studies will determine if the observed signaling alterations are caused by defective elastic fiber formation or represent independent functions of FBLN5. CL syndromes are orphan diseases with no viable treatment options. The observed TGFB signaling alterations are potential therapeutic targets that are easier to alter pharmacologically than structural proteins such as elastin.



Dean's Day Competition 2018

Kirsten Eom

HPM

Gender Differences in the Impact of Medicaid Expansion on Guideline-Recommended Colorectal Cancer Screening Rates: Evidence from the Patient Protection and Affordable Care Act

Background: Colorectal cancer (CRC) is the third most common cancer among adults and the second leading cause of cancer deaths in the U.S. Despite increased CRC screening rates over time, disparities in screening by insurance status and other socioeconomic factors persist. However, the evidence of gender differences in CRC screening is equivocal. Using the natural experiment of the Medicaid Expansion under the Patient Protection and Affordable Care Act (ACA) in 2014, this study examined overall and gender-specific effect of health insurance expansion on guideline-recommended CRC screening rates.

Methods: We used data from the Behavioral Risk Factor Surveillance System (2008-2016) for adults aged from 50 to 64 years in 39 states. We measured self-reported ever use of guideline-recommended CRC screening and whether the time since their most recent screening was concordant with guidelines. We employed difference-in-difference models comparing changes in CRC screening rates in 20 Medicaid expansion states before and after the ACA to changes in 19 states which did not adopt the ACA.

Results: We found that the proportion of adults who received any CRC screening increased by 1.44 percentage points in the states with Medicaid expansion after the ACA. While no significant changes in CRC screening were observed among males, the proportion of females who underwent colonoscopy increased by 2.18 percentage points in Medicaid expansion states. Among adults whose household income was <133% federal poverty level, the proportion of females who had any CRC screening increased by 15.5 percentage points whereas no significant effect was reported among males.

Conclusion: Our findings showed that health insurance expansion had a significant effect on CRC screening in Medicaid expansion states. A significant increase in CRC screening among females provided more evidence that barriers to CRC screening differ by gender, and clinical practice to increase CRC screening need to be tailored by gender.



Dean's Day Competition 2018

Zeynep Erdogan-Yildirim

HUGEN

ESR1-fusions - A recurrent mechanism of endocrine treatment resistance in metastatic ER+ breast cancer

Endocrine therapy is the mainstay treatment for estrogen receptor positive (ER+) breast cancer (BrCa) and reduces the 10-year disease recurrence risk by 50%. Despite initial response to endocrine therapy, many patients ultimately relapse with lethal endocrine resistant recurrent or metastatic disease. Mutations in the ligand-binding domain (LBD) of ER had been reported as a mechanism of endocrine resistance. Recently, fusions involving LBD of ESR1 has been proposed as an alternative mechanism, which leads to ligand independent activation of ER and insensitivity to endocrine therapy. We are investigating the biological significance of four distinct ESR1-fusions detected in metastatic BrCa patient samples which disrupt the LBD; ESR1-DAB2, ESR1-GYG, ESR1-LATS1 and ESR1-SOX9. Fusion driver algorithms classified these fusions as significant drivers in the tumors. Following confirmation of the expression of ESR1-DAB2 and ESR1-GYG1 at the mRNA and protein level in patient samples we employed pcDNA3.1(+) to express the fusion constructs and transiently transfected these into the HEK293T ,MCF7 and T47D cell lines. In vitro ERE-Tk-luciferase assays revealed constitutive activity in all ESR1 fusions that was hormone independent and insensitive to endocrine therapy. The DAB2 and SOX9 fusions also demonstrated hyperactivation of ER signaling, the extent to which was cell line dependent. Additionally, we monitored the localization of the exogenously expressed ER fusions using immunofluorescence and determined largely nuclear localization. Currently, we are establishing stably expressing cell lines containing ESR1-fusions in order to assess the biological consequences of the fusions and determine their effects on cell proliferation and other key phenotypes as well as to assess their effects on gene regulation (ChIP-seq) and expression (RNA-seq).



Dean's Day Competition 2018

Bethany Flage

IDM

Heme induced acute lung injury by inflammasome activation in vascular endothelial cells

Acute lung injury (ALI) is a form of acute respiratory failure having an estimated annual incidence of 200,000 with a 40% mortality rate in the United States alone. Patients suffering from malaria, sickle cell disease, and sepsis are placed at an increased risk of developing ALI due to intravascular hemolysis, which is the lysing of red blood cells. Large amounts of hemolysis leads to the release of heme, the oxygen binding portion of the hemoglobin molecule. When free from the hemoglobin molecule, heme is toxic. We have previously shown that excess free heme can disrupt the lung vascular endothelial cell layer resulting in lethal ALI in transgenic sickle cell mice, suggesting that heme is particularly toxic to those cells. However, the cellular mechanisms of heme-induced endothelial cell damage remain largely unknown. Studies of inflammation have demonstrated that heme is able to induce inflammasomes within monocytes to stimulate the production and release of pro-inflammatory molecules leading to cell death. However, the potential of heme to induce inflammasomes in endothelial cells has not been reported. We therefore hypothesize that heme induces inflammasome activation within the lung vascular endothelial cells causing cell death and ultimately leading to ALI. To test this hypothesis, we challenged human lung vascular endothelial cells with heme and assessed cell death, cell-to-cell barrier integrity, and potential inflammasome activation. In cells treated with heme, we found an increase in cell death which corresponded to large gap formation throughout the cell layer as compared to vehicle. We were able to quantify this barrier disruption through electric cell-substrate impedance sensing (ECIS) and found a forty-fold decrease in cell-to-cell barrier resistance. These heme-mediated changes were concomitant with a significant two-fold increase in pro-inflammatory proteins Interleukin-18 and Interleukin-1 ($p<0.005$). These results demonstrate that heme is able to induce cell death and cause barrier disruption in endothelial cells. Furthermore, these heme-mediated changes are associated with an inflammatory response known to be initiated by inflammasome activation. Future studies are warranted to identify mechanisms of heme mediated inflammasome formation and activation. Finding ways to selectively inhibit inflammasome pathways may reduce damage caused by heme and could lead to novel treatments for ALI to decrease morbidity and improve patient survival.



Dean's Day Competition 2018

Lily Francis

HUGEN

Neuropathology of POLG-related mitochondrial diseases in patient iPSC- derived neurons

Lily Francis, Jason Callio, Noelle Toong, Simon Watkins, Brett Kaufman, Leonardo D'Aiuto, Donna Stolz, Vishwajit L. Nimgaonkar, Alejandro Soto-Gutierrez, Amy Goldstein and Charleen T. Chu

DNA polymerase gamma (Polg) is responsible for mitochondrial DNA (mtDNA) replication and repair. Mutations in POLG, the gene encoding the catalytic subunit of Polg, result in a set of clinical syndromes characterized by mtDNA depletion in affected tissues, with variable organ involvement and severity. The brain and neuromuscular system are the most commonly affected organs, with intractable seizures, developmental delay, dementia, ataxia, liver failure, axonopathies, myopathy and ophthalmoplegia comprising major symptoms. Treatment for POLG-related disorders remains mostly supportive, with the majority of patients progressing to severe disability and death within a few years of diagnosis.

Therefore, a better understanding of disease mechanisms in the affected cell types is needed to illuminate new therapeutic options for these devastating diseases that typically affect children and teenagers. Most patients with POLG mutations are compound heterozygotes bearing a different mutation in each allele. Here we describe our work studying cortical neurons differentiated from two new patient-derived models of POLG-related mitochondrial diseases: PgATWS and PgATLX. Fibroblasts from diagnostic skin biopsies were reprogrammed into induced pluripotent stem cells (iPSCs), and mutation status confirmed by DNA sequencing. While the patient-derived iPSCs did not show mtDNA depletion relative to control iPSCs, both PgATWS and PgATLX failed to undergo the dramatic increase in mtDNA content observed in control lines upon differentiation to cortical neurons. Neurons differentiated from patient iPSCs exhibited simplification and shortening of the neuritic arbor, with multiple abnormal neuritic swellings. Both mutant lines also exhibited abnormal mitochondrial ultrastructure by electron microscopy, with accumulation of autophagic vacuoles, and altered neuritic trafficking of lysosomes. The majority of mitochondria in PgATWS and PgATLX neurons exhibited decreased mitochondrial membrane potential accompanied by decreased expression of proteins involved in the electron transport chain. Ongoing studies are aimed at developing strategies to reverse these pathological neuronal phenotypes.



Dean's Day Competition 2018

Fiona Gao

BCHS

Forecasting Morning Surface Temperature Inversion (MSTI) in Allegheny County

A morning surface temperature inversion (MSTI) is a meteorological phenomenon. As we learned in high school, during "normal" conditions, air temperature decreases with increasing altitude. This is because warm ground keeps low lying air warmer than air higher up. The warm air can then rise, causing the atmosphere to mix. At the same time, air pollutants in the atmosphere can mix, generally reducing their concentration. A temperature inversion is the opposite situation that frequently happens overnight. During a temperature inversion, air temperature increases with increasing altitude. This is because the air next to the ground cools faster than air higher up. So, warmer, lighter air is found above cooler, heavier air. In such a situation, air is stable and there is little or no mixing. Air pollution can be trapped and concentrated. Temperature Inversions usually form during the night, are strongest before dawn, and "burn off" after sunrise. They are usually broken before noon. Air pollution is a major environmental risk to health. By reducing air pollution levels, the burden of disease from stroke, heart disease, lung cancer, and both chronic and acute respiratory diseases, including asthma, can be reduced. MSTIs can lead to poor air quality which harms public health, but it can be forecasted using meteorological parameters. If poor air quality is expected, actions such as source control can be implemented to protect public health. Synoptic (weather map) situations can be used to forecast MSTIs. The following parameters are normally considered. Surface Wind Speed and Direction, Pressure, Relative Humidity, Upper-air Observations, Sun Angle. MSTI forecasts can be used to predict air quality, and, if the air quality is forecasted to be bad, to help protect public health, an Air Quality Action Day can be declared. Such a declaration requires air pollution emission curtailment from certain industrial sources and other effective actions. Furthermore, the forecast can be used in other ways, such as to direct agricultural activities like the application of pesticide spray. Usually, a morning with a strong temperature inversion coupled with light wind would be ideal for spraying pesticides, because the chemicals would stay near the ground and would be less likely to travel far beyond the targeted crop field.



Dean's Day Competition 2018

Christian Garcia

EPIDEM

Influenza and pneumonia death rate in elders is related to poverty levels in municipalities from Chile, 2001-2014.

Chile is facing an advanced demographic transition where the proportion of elders of 65 years and over is 10.3% and is expected to increase in the next decades. Pneumonia and Influenza is the 5th cause of death among elders after cardiovascular diseases and dementia. The goal of this study is to determine the spatial association of Influenza and Pneumonia death rate and poverty in 343 mainland municipalities in the period 2001-2014. Death rates were calculated based on the Ministry of health death certificates database with ICD-10 code J09 to J18 and census data. Municipal variables were obtained from the national system of municipal information. The proportion of elders had an average of 10% ($SD=2.8\%$), Poverty level of 18% ($SD=8\%$) and Death Rate of 2.3 per 1000 population ($SD=0.9$). There were two high mortality rate “belts” in the center and in the south of the country. A positive and significant linear association was found between death rates and poverty ($R^2=0.05$, $p=0.000$). The spatial analysis showed a significant global Moran’s I for death rate (0.314 ; $p=0.001$) and for poverty (0.63 ; $p=0.001$). Also, the local G* showed overlapping clusters of high death rates ($n=50$) and high poverty ($n=65$). A multivariate linear regression and a spatial error model regression were fitted. Both models found a significant association of death rates and poverty after adjusting for Poverty among elders, Population density, physicians per 1000 population and per 1000 elders. The spatial error model showed an increased fit compared to the multivariate model ($R^2 0.217$ vs 0.85) and found a significant spatial relation ($\Lambda=0.4$; $p=0.000$). The increasing elderly population is a challenge for the Chilean health system. Poverty levels in municipalities are associated to influenza and pneumonia mortality among elders. Future studies are needed to understand this relation and help to make decisions at the local level rather than one size fits all interventions from central institutions.



Dean's Day Competition 2018

Jerome Givi

HUGEN

Automated Histochemical Image Capture and Analysis to Quantify Dermal Elastin in Cutis Laxa

Cutis laxa (CL) is a connective tissue disorder that results in loose, wrinkled skin, caused by elastic fiber dysfunction. Reduced abundance and abnormal morphology of dermal elastic fibers has been used qualitatively as a diagnostic sign of CL, but quantitative data has not been reported yet. The purpose of this project is to quantify and compare the amount of elastin protein in skin tissue samples of CL patients to those of unaffected family members. We have collected a series of skin biopsy samples from 85 individuals, including 64 affected and 21 unaffected family members. The biopsies were fixed in formalin, embedded in paraffin and 3 consecutive $5\text{-}\frac{1}{4}\text{m}$ sections for each biopsy were stained for elastin using a modified Hart's elastin staining protocol to optimize the spectral contrast of elastic fibers. Images of the sections were captured using the TissueFAXS Histo upright brightfield microscope. The TissueFAXS automated imaging and analysis software were used to quantify the percentage of tissue area occupied by elastic fibers. The data collected showed a reduction in elastin content in the skin of individuals with ATP6V0A2-related cutis laxa and arterial tortuosity syndrome but not for other types of cutis laxa. Cross sectional analysis of ELN-related cutis laxa showed interesting age dependence of elastin content with high values early in life, low values in young adults and high values in older adults, suggesting previously unappreciated dynamic changes in elastin content that will be studied moving forward with more young control samples. These studies can be expanded in the future for more sophisticated analysis of the shape and distribution of elastic fibers and other relevant components of the skin (fibroblasts, blood vessels, melanocytes, etc.) to completely characterize the skin pathologies associated with CL.



Dean's Day Competition 2018

Matthew Good

IDM

Impact of Zika Virus On Myeloid Derived Antigen Presenting Cell Survival and Function

Zika virus, a mosquito-borne flavivirus, typically causing mild clinical symptoms, has been linked to a range of adverse complications including microcephaly in fetuses and Guillain-Barré syndrome in adults. Zika virus's recent emergence, combined with a limited understanding of the role of Zika in the development of these adverse pathologies, requires the attention of researchers and the public health community alike. The dendritic cell - a key immune responder in early viral infections - has known interactions with Zika, but their interplay must be further explored. Here we hypothesize that dendritic cell interaction with Zika is most likely critical, and the infection of these cells will impact their survival and function, contributing to disease outcome. These findings will contribute a better understanding of Zika pathogenesis and may provide pertinent knowledge towards developing an effective vaccine against Zika.



Dean's Day Competition 2018

Emma Gossard

BCHS

"They're Messing Up Our Future Because We Need To Learn These Things": A Qualitative Exploration of Sexual Health Education Experiences of Allegheny County Adolescents

Introduction: Comprehensive Sex Education contributes to positive sexual and reproductive health outcomes among adolescents. Pennsylvania schools are not required to provide students with any sex education, though they must provide information about HIV and STDs and are required to stress abstinence. As a formative element of a larger needs assessment, the purpose of this work is to understand the sexual health education experiences and needs of adolescents in Allegheny County, as well as their recommendations for improving sexual health education and services.

Methodology: In this qualitative study, semi-structured focus groups were conducted with eighteen adolescents recruited through community organizations. Focus groups were recorded and transcribed, and data were analyzed for key themes using initial and focused coding methods.

Results: Most participants reported that their sex education was lacking, and believed that subpar sex education impacts health outcomes. However, differences were noted when stratifying participant feedback by the schools they attended. Participants recommended that school-based sex education be improved by covering more topics, such as gender and sexuality, contraception, and relationships; using a student-centered framework; and facilitating a school culture of openness. Participants also suggested that schools provide them with condoms and that community organizations increase advertising and outreach to their demographic. Additionally, participants indicated that stigma associated with sexual health impacts the flow of information in schools.

Conclusions: Findings suggest that both school and community organizations can improve the sexual health education and services that they provide to adolescents. Community organizations in particular will use these results to build upon their existing sexual health education programming and services and better serve adolescents in Allegheny County and to advocate for improved state and local sex education policy and implementation.



Dean's Day Competition 2018

Megan Hager

HUGEN

Assessing Perinatal Palliative Care Education within Genetic Counseling Training Programs

Perinatal palliative care (PPC) is a specialized clinical program that provides holistic care to critically ill fetuses and infants, and psychosocial support to their family members. Genetic counselors are often consulted to explain prenatal or infantile conditions that are life-limiting or life-threatening. The function of the genetic counselor is to provide both education about a condition and supportive resources for those they work with. Referral to a PPC program is one support a counselor may offer to a family experiencing perinatal loss. Therefore, being knowledgeable about the medical and psychosocial services offered by PPC programs within a patient's community is important. A recent survey found that 11.4% of genetic counselors feel uncomfortable referring to these programs due to a lack of familiarity with PPC. This study proposes to increase awareness of PPC services amongst genetic counselors by creating educational resource materials for use by Genetic Counseling Training Programs accredited by the Accreditation Council for Genetic Counseling (ACGC). In order to generate educational materials, a Qualtrics survey was developed and administered to ACGC accredited program leadership to assess what is currently taught about PPC within training programs, what knowledge gaps may exist, and if programs would benefit from creation of educational material. Data from the administered survey shows 85% of responding programs currently provide education about PPC, and 88.9% of respondents would benefit from the creation of resource material. There were nine possible options for resource materials presented to leadership via the survey. This study will create the top three selections. Respondents indicated they would like clinical case examples that may provide insight into the benefits of PPC (17.7%), a list of current documentaries, books, popular movies, etc. that illustrate the need for PPC (15.3%), a list of websites that could provide valuable resources for faculty and staff (14.1%), and packets of peer reviewed articles that can be used to generate a discussion about PPC (14.1%). This study impacts public health by strengthening the educational experiences of genetic counseling students, who will in turn adequately refer a greater proportion of the public to PPC services.



Dean's Day Competition 2018

Emmett Henderson

BCHS

A Comparison of Health-Related Quality of Life Among Transgender Individuals: Behavioral Risk Factor Surveillance System, 2014-2016

Background: Most studies have relied on convenience samples to study transgender individuals, or have combined transgender men and women into a single group for analysis. To date, there are no studies that have used a nationally-representative, probability-based sample to investigate differences between transgender men, women, and gender nonconforming individuals.

Objectives: This study builds upon prior work by Meyer et al. and Streed et al. that used data from the Behavioral Risk Factor Surveillance System (BRFSS) to compare health-related quality of life (HRQoL) between cisgender individuals and a composite group of transgender individuals. We aim to assess differences in sociodemographic characteristics and HRQoL among transgender men, transgender women, and gender nonconforming individuals. Additionally, this study aims to identify differences in predictors of HRQoL among these groups.

Methods: Data from the 2014-2016 BFRSS were analyzed on 2,229 respondents age > 18 years. In the Gender Identity Module, participants were asked “Do you consider yourself to be transgender?” In the survey, 701 identified as female-to-male transgender (transgender men), 1,078 identified as male-to-female transgender (transgender women), and 450 identified as gender nonconforming. Weighted multivariable logistic regression analyses compared differences in HRQoL among transgender individuals. This analysis controlled for sociodemographic and health-related characteristics. Lastly, separate weighted multivariable logistic regression analyses compared predictors of HRQoL by gender identity.

Results: Compared to transgender women, transgender men were more likely to report frequent mental distress (aOR: 1.99, 95% CI: 1.19-3.33). There were no significant differences in odds of frequent physical distress. In transgender women, being younger, unemployed, reporting a financial barrier to healthcare, tobacco use, and alcohol use were significantly associated with frequent mental distress. In transgender men, being a race other than white, being unemployed, reporting a financial barrier to healthcare, and having an annual household income \$25,000-\$49,999 were significantly associated with frequent mental distress. In gender nonconforming individuals, being younger, unemployed, having health insurance, reporting a financial barrier to healthcare, and being obese were significantly associated with frequent mental distress.

Conclusion: Transgender individuals differed significantly in risk factors for poor mental and physical health. These groups should continue to be studied separately and interventions should be targeted towards the unique needs of each subgroup.



Dean's Day Competition 2018

Emmett Henderson

BCHS

Rural/Urban Differences in HIV testing among US Adults: Findings from the Behavioral Risk Factor Surveillance System

Background: Individuals in rural areas face barriers to HIV-related healthcare. Recently there have been no nationally-representative studies evaluating the frequency of HIV testing in rural versus urban areas.

Objectives: To assess differences in frequency of lifetime and past-year HIV testing between rural and urban residents of the United States. Additionally, this paper aims to assess differences in HIV testing site location between rural and urban residents of the United States.

Methods: Data from the Behavioral Risk Factor Surveillance System (BRFSS) 2015 were analyzed on 441,456 respondents age >18 years. Weighted multivariable logistic regression analyses compared rural/urban differences in lifetime and past-year HIV testing. Weighted multinomial logistic regression compared urban/rural differences in HIV testing site. In the regression analyses we controlled for sex, age, race and ethnicity, marital status, education, income, census region, health insurance, and sexual or gender minority status.

Results: Overall, 26.9% and 24.5% of urban residents received lifetime and past-year HIV testing, respectively, compared to only 21.5% and 20.2% of rural residents. Compared to urban residents, rural residents were less likely to receive lifetime ($aOR: 0.84, 95\% CI: 0.77-0.91$) and past-year ($aOR: 0.81, 95\% CI: 0.67-0.99$) HIV testing. Rural residents were more likely to receive an HIV test at the hospital or emergency room ($aOR: 1.24, 95\% CI: 1.01-1.53$) than at a doctor's office.

Conclusion: This study highlights significant rural health disparities in rates of lifetime and past-year HIV testing. Targeted interventions are needed to address the unique needs of rural communities including wider use of rapid oral testing, and reduction of stigma and other barriers to care.



Dean's Day Competition 2018

Mara Hollander

HPM

Financial Relationships with Pharmaceutical Companies are Related to Increased Opioid Prescribing

Research Objective: In 2013, providers wrote enough opioid prescriptions for every American adult to have their own bottle of pills, and by 2014, nearly two million Americans abused or were dependent on prescription opioids. Regional variation in opioid prescribing cannot be explained by population health status alone. Self-report data suggests that physicians who have financial relationships with pharmaceutical companies are more likely to prescribe the drugs promoted within those relationships. This study explores whether or not there is a relationship between regional prescribing of opioids and financial contributions from pharmaceutical companies related to opioid medications.

Study Design: CMS 2014 Open Payments data were scanned for payments related to opioid medications from pharmaceutical companies to clinicians in Pennsylvania and condensed to hospital referral region (HRR). Publicly-available 2014 Medicare Part D summary data was also condensed to Pennsylvania HRR; HRRs with ten or fewer prescribing clinicians were removed, leaving 18 HRRs with a total of 37,616 providers. A stepwise ordinary linear regression was conducted to ascertain the predictive value for the percent of filled prescriptions written for opioids using the follow covariates: the proportion of different specialties of providers within an HRR, the proportion of female providers, the mean risk of patients of Part D clinicians with an HRR, the total number of records of financial contributions in that HRR, and the proportion of records related to opioids.

Population Studied: Pennsylvania clinicians whose patients filled prescriptions through Medicare Part D in 2014.

Principal Findings: On average, 5.64% of Part D prescriptions in each HRR are filled for opioids. A total of 583,036 financial contributions were made by the industry to Pennsylvania Part D providers; 10,758 of these are related to opioid medications for an average of 2.68 percent per HRR. A stepwise linear regression identified several factors related to the percentage of filled prescriptions written for opioids in an HRR, including the percentage of industry contributions related to opioids – every contribution is related to a relative increase in opioid prescriptions of approximately 1.9 percentage points (coefficient .53, 95% confidence interval .37-.69, p=.000). A higher percentage of Part D clinicians per HRR working in psychiatry (coefficient .25, 95% confidence interval .09-.41, p=.005) and in emergency medicine (coefficient .15, 95% confidence interval .02-.27, p=.023) was also related to a relative increase in prescriptions filled for opioids.

Conclusions: There is a significant relationship between opioid prescribing and financial contributions from pharmaceutical companies related to opioids within hospital referral regions. The kinds of clinicians within a hospital referral region, specifically those working in emergency medicine and psychiatry, are also predictive of relative opioid prescribing.

Implications for Policy or Practice: States regulatory agencies and health systems may consider limiting interaction between pharmaceutical companies and clinicians, particularly with regard to opioids.



Dean's Day Competition 2018

Mara Hollander

HPM

Emergency Department and Outpatient Utilization Among the Medicaid Expansion Population in Pennsylvania

Research Objective: Under the Patient Protection and Affordable Care Act, 31 states expanded Medicaid eligibility to individuals under 138% of the federal poverty level. Limited access to primary care services prior to Medicaid enrollment may have resulted in complex, unmet health needs, and along with the reduction in out-of-pocket-costs associated with Medicaid coverage, expansion enrollees may have high rates of emergency department (ED) visits, some of which may be avoidable. Expansion enrollees may also reduce ED use as they gain access to primary care and experience navigating the health care system. Evidence of the impact of Medicaid expansion on ED use is mixed and draws largely on cross-sectional hospital discharge data. Little is known about the extent to which ED use changed over time post-expansion or the relationship to other ambulatory care use. We therefore studied Medicaid expansion enrollees to determine patterns of ED visits not resulting in hospital admissions and outpatient ambulatory care visits.

Study Design: We conducted a longitudinal analysis of Pennsylvania expansion enrollees using enrollment and claims data for 2015-2016. We identified ED visits not resulting in a hospital admission as well as outpatient visits in non-emergency settings after the 2015 Medicaid expansion. We categorized enrollees by utilization in the 24 months after enrollment (ED only, non-emergent outpatient only, both, and neither) and compared demographic groups. We measured the sequence of, and changes in the frequency of, ED visits relative to other outpatient visits.

Population Studied: 778,645 Medicaid expansion enrollees, continuously enrolled in Pennsylvania Medicaid for at least 6 months between January 2015-December 2016.

Principal Findings: 7.1 % of Pennsylvania's expansion enrollees had ED visits and no non-emergent outpatient visits, 37.6% had outpatient visits and no ED visits, 34.2% had both visit types, and 21% used neither service. 40.4% of expansion enrollees with both visit types visited the ED first. The mix of services varied by demographic group: enrollees ages 19-34 made up 65.2% of those with ED visits only vs. 50.4% of those with both ED and other outpatient visits ($p<0.0001$). Male enrollees made up 61.8% of the group with ED visits only vs. 41.6% of those with ED and other outpatient visits ($p<0.0001$). White enrollees made up 61.4% of the those with only outpatient visits versus 47.3% of those with only ED visits. ($p<.0001$). ED visits among expansion enrollees dropped significantly in the first 6 months of Medicaid enrollment, from an average of 9.4 to 7.7 per thousand member-months ($p<0.0001$), while non-emergent outpatient visits increased from 370 to 605 per thousand member-months ($p<0.0001$).

Conclusions: Under 10 percent of Medicaid expansion enrollees used the ED as their sole source of care in the 2 years after expansion in Pennsylvania. A decrease in ED use and an increase in visits with non-emergency ambulatory care providers in the six months after enrollees gained coverage point to early engagement in outpatient care.

Implications for Policy or Practice: Emergency departments have an opportunity to facilitate referrals to outpatient providers, particularly for young, male, and white Medicaid expansion enrollees. Health systems can target outreach to these enrollees to encourage them to engage with outpatient providers.



Dean's Day Competition 2018

Michaela Holliday

HUGEN

The Prevalence of Inflammatory Disorders in Huntington's Disease

Background: Huntington's Disease (HD) is a neurological, genetic disease that can be characterized by the degradation of neural cells over time. Similarly, inflammatory disorders, such as Multiple Sclerosis (MS) and arthritis, are described as an overactive immune system. The relationship between inflammation and neurodegenerative diseases is poorly understood, but a few studies indicate that alleles associated with immune response and neuroinflammation are enriched in HD patients. Using data from an established, multinational, observational HD study (Enroll-HD), I assessed whether the presence of inflammatory disorders was higher among individual with manifest HD symptoms versus pre-symptomatic HD patients and individuals who did not carry the HD genotype (genotype-negative).

Methods: Data were available on 4752 individuals with manifest symptoms, 1862 pre-symptomatic individuals, and 1089 genotype-negative individuals with mean age 32 ± 14 years, who joined between 2013 and 2016. Analyses were done using Stata SE version 14.0. **Results:** Overall, 55% of participants were from Europe and 40% were from Northern America, 4% had arthritis, 0.25% had MS, 46% drank alcohol, and 25% smoked. Individuals with manifest symptoms were less likely to drink compared to pre-symptomatic and genotype-negative individuals (0.38, 0.60 and 0.53, respectively, $p<0.001$) and more likely to smoke (0.27, 0.25 and 0.21, respectively, $p<0.001$). The frequency of MS was lower among individuals with manifest HD than among pre-symptomatic and genotype-negative individuals (0.002, 0.004 and 0.005), but non-significant. The prevalence of arthritis was similar among these three groups.

Conclusion: The observation that individuals with manifest HD are less likely to drink alcohol and more likely to smoke than individuals in the other two groups is consistent with results from other studies. However, the prevalence of MS was not higher among individuals with manifest HD, as initially hypothesized. Thus, neuroinflammation may not contribute to a worse prognosis of HD. This study has several limitations, including: MS is a poor proxy for neuroinflammation, the prevalence of MS is low and the analyses were not done using longitudinal data. Additional studies with better measures of neuroinflammation need to be performed to assess the potential effects of neuroinflammation on HD prognosis.



Dean's Day Competition 2018

Franya Hutchins

EPIDEM

Mwanatumu Mbwana

EPIDEM

Loren Schleiden

PHARM

Management of high cholesterol among the MIDUS Refresher cohort: a cross-sectional analysis of prescription use and participant characteristics

Background: Cardiovascular disease (CVD) is the leading cause of death in the United States. Elevated low-density lipoprotein cholesterol (LDL-C) is a major risk factor for CVD and is associated with the progression of atherosclerosis. Cholesterol-lowering medications, primarily statins, are a key component of clinical CVD prevention. Despite this, over 40% of the 78 million American adults who meet the American College of Cardiology and the American Heart Association (ACC/AHA) eligibility guidelines for cholesterol treatment are not currently taking a cholesterol-lowering medication. The objective of this study was to identify factors that may be associated with underprescribing among individuals for whom cholesterol treatment is indicated.

Methods: This study is a secondary analysis of biomarker and questionnaire data collected from the Midlife in the United States (MIDUS) Refresher cohort. The Refresher cohort consists of 863 adults (ages 25-80) with biomarker data. Survey respondents were deemed eligible for the present analysis if they met any of the ACC/AHA criteria for lipid lowering therapy. Specifically, respondents who: 1) had CVD; 2) had LDL-C levels of ≥ 190 mg/dL; 3) were ages 40-75, had diabetes mellitus, and had LDL-C levels of 70-189; or 4) were ages 40-75, did not have diabetes mellitus, and had a 10-year ASCVD risk $\geq 7.5\%$. The main outcome measure was underprescribing of cholesterol-lowering medications, defined as having no prescription for any medication indicated for lowering cholesterol levels. Multivariate logistic regression analysis was used to identify predictors of undertreatment. Potential predictors considered included factors related to demographics (age, sex, race/ethnicity), socioeconomic status (education, household income, health insurance status), health behaviors (smoking, alcohol use), and health status (comorbidities, number of prescription medications, BMI).

Results and Conclusions: (pending)

Public Health Significance: Improving prescribing of cholesterol-lowering medications among those indicated for such treatment could help to reduce the incidence and burden of CVD events. Results from this study will help to elucidate factors associated with the absence of such treatment in order to identify potential actionable targets for health policy interventions.



Dean's Day Competition 2018

Tumader Khouja

HPM

Opioid Prescriptions by Dentists in PA Medicaid 2007-2016

Background: Opioid abuse, misuse and mortality is a significant public health problem in the U.S. Dentists and oral surgeons are among the top opioid prescribers, 31% of adolescents receive their first opioid from a dentist. However, evidence shows that Non Steroidal Anti Inflammatory Drugs are sufficient to manage dental pain and have less adverse side effects than opioids with little or no concerns of misuse, abuse or diversion. **Objective:** to describe opioid prescribing by dentists among PA Medicaid beneficiaries from 2007-2016

Methods: PA Medicaid dental claims, pharmacy claims and enrollment files were used to identify beneficiaries who have filled an opioid prescription written by a dentist. Descriptive statistics were used to describe the rate at which beneficiaries received an opioid prescription from a dentist, opioid prescriptions rate per 1000 beneficiaries and number of dentists prescribing opioids per 10,000 beneficiaries.

Results: there were 7,504,029 unique dental visits between 2007-2016. Depending on the year 8.9-12.3 % of beneficiaries who visited a dentist received an opioid prescription. Opioid prescriptions decreased from 51.62 per 1000 beneficiaries in 2007 to 39.48 per 1000 beneficiaries in 2016. Prescriptions filled by beneficiaries under the age of 21 decreased from around 22% to 15.12% and increased among the age group 21-64 from around 77% to 83.9%. The number of dentists who prescribed opioids decreased from 10.24 per 10,000 beneficiaries to 5.16 per 10,000 beneficiaries during the same time period. General dentists were the most common prescribers followed by oral surgeons. The three most commonly prescribed opioids were Hydrocodone-acetaminophen, Acetaminophen-codeine and oxycodone-acetaminophen.

Conclusion: between 2007-2016, opioid prescribing has been decreasing among dentists in PA Medicaid, following the national trend. However, opioids are still prescribed at high rates for dental procedures.

Public Health significance: Dentists are in the primary prevention position, especially when addressing young patients and acute pain prescribing. Dentists have a relatively high prescribing rate in this population, and primary prevention strategies such as patient/parent counseling are important strategies that can help keeping opioids from harming patients and their families.



Dean's Day Competition 2018

Tumader Khouja

HPM

The extent of severe periodontal disease as a predictor of cardiovascular complications and mortality in type 1 diabetes (T1D)

Periodontal disease (PD) has been linked to systemic diseases such as diabetes and cardiovascular disease. Our aim was to assess the role of PD as a predictor of cardiovascular complications and mortality in a cohort of T1D. This analysis was based on 320 participants (mean age=32.1 years and duration=23.7 years) of the Pittsburgh Epidemiology of Diabetes Complications study of childhood-onset (<17 years) T1D, who during 1992-94 received a comprehensive oral health exam including periodontal assessment of 3 facial sites (mesial, mid-cervical and distal) of the right maxillary/left mandibular or left maxillary/right mandibular quadrants and were subsequently followed for up to 19 years to ascertain complication incidence. PD was defined as clinical attachment loss of ≥ 4 mm for at least 10% of the examined sites. Predictors of all-cause mortality; Hard Coronary Artery Disease (HCAD; CAD death, myocardial infarction or revascularization); and Coronary Artery Disease (CAD; HCAD but also including angina and ischemic ECG) were assessed using Cox models. In multivariable models, PD was not significantly associated with all-cause mortality (HR=1.07, 95% CI=0.48-2.37) although it was a significant predictor of both HCAD (HR=1.27, 95% CI=1.09-1.48) and CAD (HR=1.07, 95% CI=1.02-1.14). As smoking status was identified as a significant effect modifier of the PD-CAD and PD-HCAD associations, thus analyses were also conducted stratifying by smoking status. PD was associated with an increased risk of HCAD (HR=2.13, 95% CI= 1.26-3.61) and CAD (HR=1.27, 95% CI 1.05-1.53) only among smokers, whereas no relationship was observed among non-smokers (CAD HR=1.08, 95% CI=0.83-1.40; HCAD HR=1.18, 95% CI=0.83-1.69). PD was a significant predictor of HCAD and CAD among smokers with T1D.



Dean's Day Competition 2018

Li An Lai

EPIDEM

Plastics in pregnancy, reproductive hormones, and genitalia at birth: physiologic insight into fetal endocrine disruption

The phthalate exposure and reproductive hormone concentration are two important factors associated with anogenital distance (AGD). Previous studies evaluated the role of testosterone, estradiol, and HCG in explaining the association between phthalate exposure and anogenital distance. Other hormones that are associated with the growth of the fetus during the pregnancy have not been studied in relation to phthalates and AGD, namely pregnancy associated plasma protein (PAPP-A), Estriol, Inhibin-A, and alphafetoprotein (AFP). The goal of the current analysis is to explore the association between phthalate levels, these four hormones, and neonatal AGD.

Method: The Infant Development and Environment Study (TIDES) is a prospective birth cohort study. The study recruited pregnant women from 2010 to 2012 in 4 sites in the US: San Francisco, CA, Rochester, NY, Minneapolis, MN, and Seattle, WA. The phthalate analysis was based on the maternal urine sample collected from the first trimester and analyzed by HPLC-tandem mass spectrometry in the National Center for Environmental Health, Center for Disease Control and Prevention (CDC). The hormone concentration was analyzed as part of prenatal serum screening in the first (PAPP-A) and second trimesters (Estriol, Inhibin-A, and AFP). AGD was measured at birth by trained nurses with standard method. The subset of TIDES participants that had phthalate, hormone and AGD measures is 326 (30% of the full cohort).

Result: Among women carrying females, log MnBP concentrations were positively associated with PAPP-A ($\beta=0.28$, 95% CI 0.01, 0.55) and Inhibin-A ($\beta=0.61$, 95% CI 0.09, 1.12), adjusted for TIDES Center, Maternal race, household income, time for day of urine collection, gestational age at time of blood draw, maternal weight, and phthalate concentrations in the same urine sample (MnBP, MBzP, MEHP, and MEP). Log MEHP concentrations were inversely associated with inhibin-A ($\beta=-0.46$, 95% CI -0.84, -0.09 p<0.05). No significant associations were observed among women carrying males. Estriol ($\beta =-0.34$, 95% CI -0.65, -0.04) was negatively associated with the short form of AGD (anus-scrotum) among male infants. Inhibin-A was positively associated ($\beta=0.23$ 95% CI, adjusted for 0.04, 0.43) . The long-form of AGD (anus-penis) was also related to the Inhibin-A concentration in boys ($\beta=0.28$ 95% CI 0.07, 0.49). No significant relationship was observed in female infants.

Conclusion: The study provided additional insight into placental-fetal hormones that may be operating in a sex-specific manner as intermediaries between maternal exposures to plastics, and reproductive health of the future child. There is evidence that the plastics are modulating placental-fetal hormones in female but not male fetuses. Conversely, the hormones were associated with male but not female genital development. The next level of analysis will integrate and reconcile these two sets of findings to assess environmental risks in the first and second trimesters of pregnancy.



Dean's Day Competition 2018

Kelsea LaSorda

EPIDEM

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

The new construct of fatigability - fatigue in relation to a defined activity of a specific intensity and duration - constitutes an objective metric by which to assess the degree to which someone is physically limited due to fatigue. Measuring fatigability accounts for self-pacing bias and thus provides greater capacity to assess fatigue's role in the disablement pathway. Fatigability may also be more sensitive to interventions, particularly those targeting increased physical activity. Fatigability is an important early predictor in the disablement pathway, having been associated with poorer physical function, yet little is known about its genetic basis or association with age and sex. We examined prevalence and heritability of perceived physical fatigability using the Pittsburgh Fatigability Scale (PFS, 0-50, higher score=higher fatigability) in the Long Life Family Study, a cohort of two generations of older adults enriched for familial exceptional survival. PFS scores (mean \pm SD) and proportion with higher fatigability (% PFS \geq 15) increased across age strata: 60-69 (N=1009, 11.0 \pm 7.6, 28%), 70-79 (N=847, 12.5 \pm 8.1, 37%), 80-89 (N=253, 19.3 \pm 9.9, 65.2%), and \geq 90 (N=266, 28.6 \pm 9.8, 89.5%), p<0.0001, adjusted for sex, field center, and family structure. Females reported higher perceived physical fatigability than males, with the largest difference in the 80-89 age strata, 74.8% vs. 53.5%, respectively, p<0.0001. After adjustment for age, sex, and field center, the residual heritability of fatigability was 0.263 (p=6.6*10 $^{-9}$). Future research should target interventions aimed at those most at-risk for higher perceived physical fatigability early in the aging process.



Dean's Day Competition 2018

Cassandra Leighton

HPM

Home- and Community-Based Provider Preparation for Pennsylvania Managed Long-term Services and Supports

Objective: The CHC program in Pennsylvania has been structured to coordinate and provide managed LTSS through three selected Medicaid managed care organizations (MCOs). CHC began in Southwestern Pennsylvania in January 2018, and implementation will be phased in over the next two years. The use of Medicaid MCOs to coordinate and pay for providers for rendered services is a large shift from current reimbursement system. To explore organizational structure, culture, and services associated with HCBS provider activities and anticipated impacts of CHC implementation, we surveyed HCBS providers across the Commonwealth.

Design: A survey was conducted during October to December 2017, prior to program initiation (final 1% of surveys were completed in January 2018), to collect data on HCBS providers' perception and preparation for CHC across Pennsylvania. We generated a sample frame of 1003 HCBS providers from 2015 Medicaid administrative data by identifying the billing provider on claims with select HCBS procedure codes.

Principal Findings: We received a response rate of 35.79% (n=359), with 84.64% of respondents indicating that they were prepared to continue delivering services in the MLTSS model. Overall, many HCBS providers did not provide a definitive opinion on CHC's program and its impact, with only 37.46% believing that CHC will be successful in achieving program goals (48.3% undecided) and only 36.23% agreeing that CHC will improve beneficiary access to HCBS (49.54% undecided). We also conducted some between group comparisons based upon CHC phase in which the majority of the HCBS provider's services are delivered and type of service delivered. When comparing between groups, we again did not see large differences.

Conclusions: Many of the HCBS providers are still uncertain about the impact of CHC on the delivery of care and organizational performance. However, over 84% indicate that CHC participation is integral to future organizational sustainability and solvency. MCOs have covered more topics in conversations with those in the Phase 1 part of the Commonwealth. This indicates MCOs and providers are having more in-depth, strategic, and operational discussions during the contracting process. As the roll-out continues, we anticipate that the nature and topics of those interactions will become more operational- and quality-focused. Additionally, we anticipate stronger opinions about program impact and success as providers operate in the new system.



Dean's Day Competition 2018

Cassandra Leighton

HPM

Market Power and Supply of Home- and Community-Based Providers in Pennsylvania

Research Objective: Access to home- and community-based services (HCBS) has traditionally been measured through length of wait lists and wait time for services. However, another dimension of access is the availability and choice of HCBS providers within one's community. To understand the HCBS provider market in Pennsylvania, we measure provider market concentration for ten HCBS service categories delivered to Medicaid 1915(c) waiver beneficiaries from 2013 to 2015. We also evaluate the supply of providers, volume of services, and number of beneficiaries served over the same time period.

Study Design: Using 2013 Pennsylvania Medicaid administrative data, we identified claims with the procedural codes for the 10 selected HCBS categories. We used the Herfindahl-Hirschman Index (HHI) to generate measures of market concentration for each county.

Principal Findings: During the three year period, over half of all counties had highly concentrated markets for home health, service coordination, meals, home modification, and transportation. In many counties, there is only one available provider. There are another 27 counties with no adult day care providers at all. The count of providers operating within each county remained stable over from 2013 to 2015 for all categories except respite, which experienced a 13.42% increase in counties without a provider. Contrastingly, a 148 new providers entered into the market for personal assistance services, causing market concentration to decrease and expanding capacity to serve over 12,000 new beneficiaries.

Conclusions: Over the three year period, there were many counties which did not have any providers or had a limited number of providers billing for select HCBS categories. This could indicate a lack of availability and access to services, which is instrumental to nursing facility clinically eligible Medicaid beneficiaries' ability to remain in the home and community.



Dean's Day Competition 2018

Bijun Li

HUGEN

Zebrafish bmp10 mutants recapitulate hereditary hemorrhagic telangiectasia-associated high output heart failure.

Hereditary hemorrhagic telangiectasia (HHT) is an inherited disease caused by impaired signaling through the bone morphogenetic protein (BMP) receptor, ALK1, and is characterized by fragile, direct connections between arteries and veins, called arteriovenous malformation (AVMs). AVMs can form in skin, mucous membranes, brain, lung, and liver and can be life-threatening if severe shunting or rupture occurs. For example, severe liver AVMs result in low systemic vascular resistance, which can lead to a transient, compensatory high-output cardiac state followed by decompensation and heart failure. The only treatment for HHT-associated high-output heart failure (HOHF) is liver transplant. No existing animal models recapitulate HHT-associated HOHF, and little is known about the pathological progression of this phenotype. Here, we describe zebrafish bmp10 mutants as the first animal model of HHT-associated, age-dependent HOHF. Bmp10 is one of three Alk1 ligands in zebrafish, and homozygous bmp10 mutants develop dilated and hemorrhagic skin vessels, edema, and enlarged hearts as early as six weeks of age. bmp10 mutants with severe early-onset vascular phenotype exhibit cardiac myofiber disorganization and early death, whereas later-onset or milder vascular phenotype is associated with compensatory changes in the heart, with increased stroke volume and increased thickness of compact myocardium suggestive of adaptive remodeling toward a high-output state. Our long-term goal is to use this zebrafish model to understand the mechanisms involved in cardiac compensation and in the pathological progression to heart failure, which may aid in design of medical therapies to prevent HOHF in HHT patients.



Dean's Day Competition 2018

Xingyuan Li

BIOST

Modeling exposure-time-response association in the presence of competing risks

In studies with long-term follow-up, exposures are often measured overtime and have a protracted effect on the outcome. Also, the intensity, duration, and timing of the exposure may vary among subjects, which create challenges in modeling the exposure-time-response association. Meanwhile, an increasing number of clinical studies involve data with competing risks, where subjects may fail from one of multiple events that failure from one precludes the risk of experiencing others. In this study, we proposed a survival regression model that can be used to quantify the exposure-time-response association in which the intensity, duration, and timing of an exposure are taken into consideration while the event of interest is subject to competing risks. The proposed model is able to differentiate the effects of different time-dependent exposure patterns even though these patterns have the same overall intensities. Performance of the proposed model was evaluated through a simulation study. We applied this model to investigate the effect of different opioid use patterns on the risk of overdose among Medicare beneficiaries, while death was treated as a competing risk.



Dean's Day Competition 2018

Jonathan Lin

EPIDEM

Exploring Potential Risk Factors Associated with Interval Colorectal Cancer

Background: Colorectal cancer (CRC), as the third most commonly diagnosed cancer and the second leading cause of cancer mortality in the United States, is a major public health issue. While screening with colonoscopy will decrease CRC incidence and mortality, CRC may still develop within the recommended time interval between colonoscopy examinations. These cancers, referred to as "interval cancers," make up a small (5-7%) but significant portion of CRCs. Identification of risk factors associated with interval CRCs may be useful for the creation of modified CRC screening strategies for patients at higher risk for interval CRC.

Methods: We reviewed approximately 64,000 colonoscopy records of patients (>40 years of age) seen in the UPMC health system from 2013-2015, and identified 327 patients who were diagnosed with invasive CRC at the time of their colonoscopy. We subsequently reviewed their medical records for evidence of a previous colonoscopy in the system going back to 1990. Demographic (age, sex, race, etc.) and clinical characteristics were abstracted from colonoscopy and pathology reports. Interval CRC was defined as cancers diagnosed after a screening examination in which no cancer was detected, and before the date of the next recommended examination. To identify risk factors associated with developing interval cancer, differences between patients diagnosed with versus without interval cancer were assessed using t-tests for continuous variables and Chi-square or Fisher's exact tests for categorical variables. Odds ratios (OR) and corresponding 95% confidence intervals (95% CI) were calculated using logistic regression models.

Results: The association between interval CRC and patients' demographic and clinical characteristics will be presented.

Conclusions: The identification of risk factors associated with interval CRC for the creation of modified CRC screening strategies has important implications for public health.



Dean's Day Competition 2018

Peng Liu

BIOST

MethylSeqDesign: A framework for Methyl-Seq genome-wide power calculation and study design issues

Bisulfite DNA methylation sequencing (Methyl-Seq) is an important technology to study disease-related methylation alterations at a genome-wide scale. To our knowledge, no power calculation and study design method is available for Methyl-Seq data so far. Here, we propose a "MethylSeqDesign" framework for power calculation and study design of Methyl-Seq by utilizing information from pilot data. Differential methylation analysis is based on beta-binomial model. Power calculation is achieved using mixture model fitting of p-value distribution from pilot data and a parametric bootstrap procedure. To circumvent the issue of existing tens of millions of methylation sites, we focus on inference of pre-specified targeted regions. The performance of the method was first evaluated with simulations and real examples of Katz's data and chronic lymphocytic leukemia data were used to demonstrate our method. An R package "MethylSeqDesign" is publicly available.



Dean's Day Competition 2018

Chia-Hsin Liu

EOH

Chronic inflammation promotes cigarette carcinogen NNK-induced lung tumorigenesis through Th1- and Th17-modulated tumor microenvironment

Clinical and epidemiological evidence suggest that chronic infection and inflammation increase 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, resulting in acute exacerbations. Additionally, COPD is characterized by chronic airway inflammation and associated with an increased risk of lung cancer independent of cigarette smoking. However, the mechanism by which chronic bacterial infection-induced lung inflammation promotes lung tumorigenesis remains unknown. We have established a mouse lung cancer model to elucidate this mechanism 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, LPS/NNK treatment significantly increased lung tumor incidence, tumor number, and tumor area compared to NNK treatment alone. Microarray mRNA analysis of mouse lung tissue showed that genes related to inflammation, including Ifng, Il17a, Pdcd1, and Pdcd1lg1, were significantly upregulated in the LPS/NNK treatment group. Ingenuity pathway analysis showed upregulated Th1 and IL-17A signaling in LPS/NNK treatment. In addition, the inflammatory cell counts in the bronchoalveolar lavage (BAL), especially those of the lymphocytes and neutrophils, were significantly increased in the LPS/NNK treatment group. Flow cytometry analysis of the mouse lung tissue revealed significantly increased CD4+Th1, Th17, Treg, M-MDSC, and G-MDSC expression in LPS/NNK treatment compared to that of the NNK alone group. The BAL fluid of chemokines/cytokines, as analyzed by luminex assays, revealed higher levels of GM-CSF, G-CSF, MIP-1 α , IL1 β , IL-6, CXCL10, IL-17A, and KC in LPS/NNK than in NNK treatment. Our results suggest that chronic LPS-induced inflammation promotes NNK-induced lung tumorigenesis through Th1- and Th17-mediated inflammation with immune suppression in the tumor microenvironment.



Dean's Day Competition 2018

William Louth-Márquez

BCHS

Spatial correlation between poverty, educational attainment and the incidence rates of sexually transmitted infections (STIs) in Pennsylvania and Erie County.

Background: The incidence of STIs in the United States (US) has increased in the past few years, affecting all the sexually active population, but particularly women, men who have sex with men and young people¹. Evidence suggests a spatial correlation between the incidence of STIs, crime rates and poverty^{2,3}.

Methods: Data about STI average rates from 2005-2008 and population (poverty, educational attainment, population) from Pennsylvania were obtained from factfinder.census.gov and the Erie County Department of Health. The data was used to build different maps to show STI rates vs. poverty in the State of Pennsylvania, at the county level, and at the census tract level in Erie County. The same data was utilized to create two cartograms and a conditional plot map with the percentage of poverty and percentage of population with less than high-school education as variables, using the STI rates per census tract as theme. The statistical analysis for clustering of STIs consisted of a global autocorrelation analysis (Moran's I) and a Local Indicators of Spatial Association (LISA) test.

Results: In Pennsylvania, the highest average rates of STIs have reoccurred within the same counties from 2005-2015. The current analysis suggests that at the county level, there is not a spatial association between poverty, low educational attainment and the incidence rates of STIs. However, in Erie county, at the census tract level it was observed that between 2005 and 2008 there was a statistically significant clustering of census tracts with high STI rates, high poverty levels and low educational attainment. Thus, there seems to be spatial correlation between poverty level and the incidence of sexually transmitted infections in Erie County.

Conclusions: The incidence of STIs has been consistently increasing in the past few years in the US. The implementation of interventions need to take place to revert this trend, particularly to address disproportionately affected populations, such as women, young people and men who have sex with men. More data is needed at the census tract level to better understand the dynamics of STI transmission in every county. Future research opportunities include incorporating crime rates in the analysis and developing interventions that address these issues at different levels of the Social Ecological Model.

Dean's Day Competition

2018

Kathleen Maksimowicz-McKinnon

EPIDEM

From a myth to a menace: ANCA-associated vasculitis in African-American patients

Background: Antineutrophil antibody-associated vasculitis (AAV) is a systemic inflammatory disorder frequently associated with significant disability and morbidity, which may lead to end-stage renal disease or death. AAV has been primarily described and studied in non-African-American populations, as it occurs less commonly in African-Americans, whose susceptibility to this condition is often underappreciated. The purpose of our study was to examine disease characteristics and outcomes in our African-American AAV population and to compare them with those of our Caucasian AAV population.

Methods: A detailed chart review of patients with positive anti-neutrophil cytoplasmic antibody testing was performed to identify patients with AAV using the 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. African-American AAV patients were matched 1:2 to Caucasian AAV patients by gender and age within 5 years.

Results: 21 African-American patients with AAV were identified, of which fourteen (66.7%) were female, with a mean age at diagnosis of 61 years. Microscopic polyangiitis occurred more commonly in African American patients than Caucasian patients (38% vs. 14%), while granulomatosis with polyangiitis was more common in Caucasian patients (76% vs. 47%), $p=0.026$. African-American patients had more severe disease at the time of diagnosis, as demonstrated by the increased need on admission for ICU care (50% vs. 30%, $p=0.038$), mechanical ventilation (67% vs. 11%, $p=0.007$), hemodialysis (52% vs. 19% $p=0.007$), with lower hemoglobin (mean 7.0 vs. 10.0, $p=0.001$), and higher serum creatinine (mean 6.1 vs. 2.7, $p=0.001$). Although the likelihood of receiving high dose pulse steroid therapy at diagnosis was not significantly different between groups, the mean dose of prednisone initiated at disease diagnosis in African American patients was significantly lower (mean 143 mg vs. 455 mg, $p=0.004$), while the concomitant use of steroid-sparing immunosuppressive agents for induction therapy did not differ significantly between groups. There was a striking increase in the incidence of end-stage renal disease in African American patients when compared to Caucasian patients (62% vs. 17%, $p=0.001$) without significant differences in the prevalence or severity of hypertension and diabetes at the time of diagnosis between groups. Death occurred in 50% of the African-American patients and 21% of Caucasian patients during follow up.

Discussion: In our urban cohort, African-American patients with AAV were more likely to present with severe disease requiring ICU care, mechanical ventilation, and hemodialysis in comparison to our Caucasian patients. Despite similar rates and severity of diabetes and hypertension in these populations, African-American patients were significantly more likely to develop end-stage renal disease. There are many factors that could influence these outcomes, including other comorbid conditions, genetics, differences in treatment and response to immunosuppressive therapies, environmental factors, and limited access to care because of socioeconomic factors. Further study is needed to better understand factors that influence AAV severity and morbidity in African-American patients in order to improve long-term outcomes and survival.



Dean's Day Competition 2018

Jenna Malinauskas

IDM

Using NGS platforms for SNP characterization of the palladin gene from AIDS progressors and non-progressors

Human immunodeficiency virus (HIV) is one of the most significant public health issues globally, however; little is known about the factors contributing to the rate of AIDS progression. Prior studies have demonstrated that host genetic factors, as opposed to differences in viral pathogenicity, play a role in susceptibility and disease progression. Recent HT12 microarray, and qPCR data demonstrates that few genes including Palladin are differentially expressed in dendritic cells from individuals identified as progressors (PR) and non-progressors (NP). This data suggests that Palladin, a highly uncharacterized gene involved in cytoskeleton rearrangements, may be playing a role in AIDS disease progression. Using two next generation sequencing platforms, the Palladin gene will be characterized for biallelic SNPs at 3 major exons between PRs and NPs in hopes of identifying a promoter variant that contributes to differential gene expression. Initial analyses with the Oxford Nanopore Technologies MinION indicate its utility in sequencing PCR amplicons for this purpose. Future studies will evaluate the functional contribution of differential Palladin gene expression in progressors and non-progressors. Broadly, this study will further develop our understanding of how host genetics contribute to AIDS disease progression and may be used to inform future treatment options.



Dean's Day Competition 2018

Megan Marron

EPIDEM

Metabolomics of frailty severity among black men in the Health ABC study

Frailty is an important public health issue at both the individual- and societal-level. It is more prevalent with older age and associated with a higher risk of multiple adverse health outcomes, such as falls, hospitalization, and mortality. Currently, the understanding of the pathophysiology of frailty is incomplete. Metabolomics is a promising tool to further our understanding of the biology of frailty, to discern how to prevent or slow the progression of frailty during late-life. We sought to identify metabolites that correlate with frailty severity among older black men from the Health, Aging, and Body Composition (Health ABC) study and determine significant biological pathways that contribute to frailty. The Health ABC study was a prospective cohort of N=3075 ambulatory older black and white men and women from Pittsburgh, PA and Memphis, TN. Metabolomics (350 metabolites) was performed by the Broad Institute using fasting plasma samples drawn at the second visit (1998-1999) from a random subset of n=319 Health ABC black men aged 70-81. Frailty severity was measured using the modified Fried Frailty Phenotype, based on unintentional weight loss, weakness, low energy, slowness, and low levels of physical activity. Thirty-seven metabolites were correlated with frailty severity ($p\text{-value}<0.05$), while adjusting for age and study site, of which 14 remained significant after adjusting for multiple comparisons using a 0.30 false discovery rate. Among the 14 metabolites, 6 were negatively correlated (tryptophan, methionine, tyrosine, C14:0 sphingomyelin, 1-methylnicotinamide, and asparagine) and 8 were positively correlated (glucoronate, N-carbamoyl-beta-alanine, isocitrate, creatinine, C4-OH carnitine, cystathione, hydroxyphenylacetate, and putrescine). Applying a pathway analysis using MetaboAnalyst, we found significantly more metabolites were involved in nitrogen metabolism and aminoacyl-transfer RNA biosynthesis than what you would expect by chance among the 14 metabolites that were correlated with frailty severity. The pathway analysis was repeated using all 37 metabolites that were correlated with frailty at a 0.05 significance level, which supported our evidence for the nitrogen metabolism and aminoacyl-transfer RNA biosynthesis pathways, as well as for the citrate cycle. Nitrogen metabolism, aminoacyl-transfer RNA biosynthesis, and the citrate cycle may be involved in the pathophysiology of frailty in late-life.



Dean's Day Competition 2018

Kelsey Messerschmidt

IDM

A logistical review of points-of-dispensing sites in Allegheny County

Introduction: In the event of a public health emergency, the Allegheny County Health Department (ACHD) may have to open Points-of-Dispensing sites (PODs) to distribute medical countermeasures, such as vaccine or antibiotics, to the public. Federal guidelines require ACHD to demonstrate that their ability to dispense countermeasures to their entire jurisdiction within 48 hours. ACHD has designated 46 public high schools to be used as PODs throughout Allegheny County. From September 2017 to December 2017, ACHD conducted a survey of all POD sites to update information for the department's All-Hazards emergency response plan.

Methods: ACHD identified key personnel from all school districts in Allegheny County. 41 site visits were conducted to administer the survey, brief key personnel on POD operations, and observe the available space that would be used for the POD. Survey responses are under analysis.

Results: ACHD updated information on 41 number of POD sites. Information was collected about: 24-hour contact information; parking availability; internet and cold-storage capacity for vaccine; and the number of security staff, nurses, and potential volunteers from the school district. Preliminary results indicate that 100% of sites have adequate ability to store vaccines and at least one emergency generator, 51% of which operate with natural gas. 30 sites identified having overflow parking availability, and only 63% of sites reported having more than 200 total parking spaces. 57% of sites reported having hardwire internet availability near the areas within in the school best identified for a POD. On average, designated POD sites have 3 security staff and 1 nurse. A total of 1699 staff willing to volunteer from 38 of the sites were reported, an average of 45 per site. 56% of sites were identified by ACHD staff as suburban, and over 29% as rural.

Discussion: School district personnel are important partners in ACHD's POD planning and volunteer capacity. Logistical considerations play a role in the Allegheny County's ability to respond effectively to public health emergencies. ACHD can use the survey results to determine which POD sites to activate in order to maximize public turn out and success. 5 schools designated as POD sites within the Pittsburgh Public School district were unable to complete the survey, limiting the data generated and Allegheny County's overall preparedness. Another limitation exists in that the survey questions are self-reported and may not accurately reflect the situation at each site. Based on the results from the survey, parking seems to be the most variable and influential consideration in success of a POD.



Dean's Day Competition 2018

Roberta Mettus

IDM

Role of pmrCAB expression in colistin resistance of *Acinetobacter baumannii*

Background: *Acinetobacter baumannii* is a nosocomial pathogen that causes a variety of infections and has a remarkable ability to acquire resistance to powerful drugs such as colistin. Several mechanisms are implicated in *A. baumannii* colistin-resistance, including mutations in the pmrAB two component regulatory system, encoded by the pmrCAB operon. This system adds a phosphoethanolamine by way of PmrC, a phosphoethanolamine transferase, to the lipid A component of LPS, decreasing the affinity for interaction between the cell surface and colistin. In this study, we examined the effects of non-synonymous mutations in the pmrA and pmrB gene to understand the genetic components behind colistin resistance. **Methods:** Colistin-resistant *A. baumannii* isolates were collected from hospital patients after colistin therapy. pmrAB alleles containing various mutations from resistant clinical strains were clones into a pmrB mutant in the *A. baumannii* ATCC 17978 background. Minimum inhibitory concentrations of these isolates were determined and correlated with expression of pmrCAB by qRT-PCR and lipid A profiles determined by MALDI-TOF analysis. **Results:** Preliminary data suggests that there is a correlation between increased transcription of pmrC and increased MIC in the complemented clones. These increases can be traced back to specific mutations located in either pmrA or pmrB. We are awaiting results of the lipid A analysis to examine the specific pmrA and pmrB mutations' effect on spectra peaks.



Dean's Day Competition 2018

Sarah Minion

EPIDEM

Gestational weight gain patterns and the prediction of small-for-gestational age and growth discordant twin infants

Introduction: Certain trajectories of gestational weight gain in twin pregnancies may increase the risk of adverse birth outcomes; however, no studies have examined serial weight gain patterns in twin pregnancies. Inadequate total gestational weight gain has been associated with small-for-gestational age and growth discordance in twins, but the pattern of weight gain accumulation throughout pregnancy may provide more information on the relationship.

Objective: To determine whether distinct trajectories of gestational weight gain exist in twin pregnancies and, if so, whether they predict SGA and growth discordant twins.

Methods: Repeated gestational weight gain measurements were abstracted from the medical records of women pregnant with twins who delivered at Magee Women's Hospital in Pittsburgh, PA from 1998-2014. We used group-based trajectory modeling (GBTM) to categorize up to four patterns of gestational weight gain, and we used Bayesian information criterion to determine the best model. The resulting gestational weight gain class membership was used in pregnancy-specific, Poisson models.

Results: 2,033 women pregnant with twins were included in the analysis. GBTM identified four distinct patterns of gestational weight gain classified as very low throughout, low to normal, referent, and consistently high. The consistently high pattern has a steep slope throughout pregnancy, while the very low and low patterns have a period of little weight gain or loss prior to substantial gain. In multivariable analyses, the very low weight gain trajectory was associated with a 1.5 (1.1, 1.9) increased risk of SGA and the low with a 1.3 (1.1, 1.6) increased risk of SGA compared to the referent group. No trajectories significantly predicted growth discordance.

Conclusion: Low patterns of weight gain across pregnancy increased the risk of SGA in twins.



Dean's Day Competition 2018

Ian Murphy

BCHS

Novel Adaptation of Video-Scoring System to Longitudinally Assess Social-Emotional Development in 3 to 5-Year-Olds Through Behavioral Observation

Simple Interactions is a strengths-based education tool for child care professionals. Currently, there is a lack of methodology for assessing children's social-emotional development over time. Based on the domains of parent-child interactions outlined in Simple Interactions, we developed a series of flowchart-style diagrams to code parent-child interactions on the basis of key behavior domains. The result is a reliable scoring system that can be used by individuals without expertise in the field of child development.



Dean's Day Competition 2018

Sushma Narra

HPM

The Impact of State Family Planning Policies on Women's and Children's Health and Social Outcomes

Background: Contraception access is strongly connected to women's greater educational and professional opportunities, increased lifetime earnings, and improved reproductive health outcomes. The objective of my research is to compare the correlation between state family planning policies in the United States in relation to state-level health and social outcomes.

Methods: I conducted a policy scan to analyze 5 policies (Medicaid family planning program, state decision on ACA Medicaid expansion, insurance coverage of prescription methods, prohibits cost sharing of contraceptives, refusal provisions of insurance coverage of contraceptives) in each state for the most recent year of data available. I next collected state-level data on 6 relevant outcomes (median earnings among women, reproductive females in poverty, rate of unintended pregnancies (per 1000), maternal mortality rate (per 100,000 births), children (aged 2-12) in poverty (%), infant mortality (per 1000 live births)) in the same time period. I investigated whether any relationship exists between state family planning policies and relevant outcomes among women and children. I conducted a bivariate correlation analysis using the Pearson's Correlation Coefficient (PCC) to determine the direction and magnitude of the correlation between the number of state policies and each outcome.

Results: There was a moderate positive correlation between the number of state family planning policies and median earnings of women ($p=.015$). There was a small negative correlation between the number of policies and percentage of women and child in poverty ($p=-0.03$ and $p=-0.01$) and maternal mortality rates ($p=-0.04$). There was a moderate negative correlation between the number of state family planning policies and infant mortality rates ($p=0.11$)

Conclusions: The moderate correlations observed between the number of family policies and health and social outcomes justifies the need for future causal research. This analysis begins to draw conclusions about specific health and social outcomes in order to drive policy decisions to reduce barriers to access to contraception for women.



Dean's Day Competition 2018

Ekaterina Orlova

HUGEN

GWAS of Early Childhood Caries in an Appalachian Population

Early childhood caries (ECC) is a complex, multifactorial disease with multiple environmental and genetic etiological factors and serious consequences for the child's subsequent oral health and quality of life. It is the most common chronic disease of childhood, affecting almost one in four children nationwide, and disproportionately impacts vulnerable populations including ethnic/racial minorities and low SES groups. Although ECC is known to be heritable in part, few associated genetic loci have been identified. Here, we report a GWAS of ECC in 447 Caucasian, non-Hispanic children of up to six years of age, recruited through the Center for Oral Health Research in Appalachia study (COHRA-1). ECC was assessed by intraoral examination by a dentist or research dental hygienist. DNA from saliva samples was genotyped on the Illumina Human610 Quadv1 B array and imputed to the 1000 Genomes Project phase 1 (June 2011) reference. Logistic regression while adjusting for age, sex, and the first principal component of ancestry was used to test association under the additive genetic model for 3.37 million common (MAF > 5%) SNPs passing quality filters. No significant associations (*p*-value <5x10⁻⁸) were found, but 11 loci were associated at a suggestive level (*p*-value <10⁻⁵). The top result of the ECC GWAS was rs1582413 (*p*-value 1.48x10⁻⁷; OR 2.76; 95% CI 1.89-4.04), within an intron of the gene MYT1L, which encodes a neuronal transcription factor. Identifying genetic variants predisposing to caries in primary dentition may ultimately inform downstream caries treatment and prevention efforts, and help alleviate disparities in disease burden currently impacting disadvantaged groups.



**Dean's Day
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Yuae Park

BCHS

Learning what works: Listening to WISEWOMAN participants

Twenty-eight Pennsylvania WISEWOMAN (WW) clients participated in phone interviews about their experiences over 2016 and 2017. WW provides low income, uninsured and under-insured women aged 40-65 with free health screening and free access to community-based lifestyle programs (LSPs) in order to reduce cardiovascular disease. Interviews were conducted by the University of Pittsburgh Evaluation Institute for Public Health in order to explore participants' experiences with the WW Program in general, and with LSPs promoted through WW specifically. Participants indicated a wide range of invaluable supports, including access to LSPs which they had not been able to afford before, and information gained through their participation in WW to promote behavior change. In particular, participants indicated the importance of having tailored information, individualized attention and social support through twice-monthly health coaching and in the clinic settings. Participants also identified key social supports they found through group participation in some LSP options, helping to maintain their motivation in a community setting. Participants cited the welcoming climate of WW clinics, staff time and attention, and the non-judgmental approach of clinic staff and health coaches in helping them change their health behaviors. Staff shared health information and resources, supported participants through making health changes in diet and exercise and quitting smoking. Researchers coded participant interviews, identified emerging themes and share representative quotes throughout this presentation to illustrate participant perspectives and lessons learned.



Dean's Day Competition 2018

Joya Petersen

HUGEN

Magee-Womens Hospital of UPMC's clinical experience with Non-invasive prenatal testing

Fetal aneuploidy is the leading cause of miscarriage and congenital birth defects in the United States. It is estimated that fetal chromosome abnormalities account for 10-30% of annual pregnancy losses and 0.65% of live born infants. As a result, pregnancy screening for fetal aneuploidy is offered as the standard of prenatal care to all pregnant women throughout the United States. In 2011, the clinical introduction of Non-invasive Prenatal Testing (NIPT) significantly impacted the field of pregnancy screening for fetal aneuploidy. NIPT offers higher detection rates and a broader array of conditions screened for than prior prenatal screening options at no additional risk to the fetus. Multiple professional organizations have recommended that NIPT should be offered to all pregnant women in addition to other prenatal screening options. However, since its integration into clinical care, studies on the clinical application of non-invasive prenatal testing have been primarily limited to research published by commercial laboratories and clinical centers outside of the United States. The purpose of this study is to quantitatively and qualitatively characterize the clinical experience of Magee-Womens Hospital of UPMC with NIPT. A prospective chart review was conducted for patients who had non-invasive prenatal testing at Magee-Womens Hospital of UPMC from 2014-2016 and received positive or failed NIPT results. The positive predictive values, false positive and test failure rates were calculated in addition to association studies of maternal demographics and fetal/neonatal characteristics. Determination of these statistical measures and clinical findings regarding the utilization of NIPT is essential for the facilitation of informed reproductive decision making, and provision of accurate and timely diagnoses. Moreover, the results of this study elucidate important concerns to consider in further universal screening policy decisions in order to reduce maternal and neonatal morbidity and mortality due to fetal aneuploidy.



Dean's Day Competition 2018

Landis Powell

EOH

Spatial Modeling of the Social and Environmental Factors Associated with the Pittsburgh Mosquito Population

Mosquito-vectored pathogens are responsible for devastating human diseases, such as Zika virus, West Nile Virus (WNV) and dengue fever. Zika has gained national attention in recent years because it can lead to birth defects if a woman is infected during her pregnancy. Because no vaccine exists to prevent or treat Zika, mosquito control is the most effective way to prevent this virus. Expectedly, concern for such diseases and their ability to spread within the United States has increased as mosquito habitats expand towards the East Coast due to climate change and increased temperatures. Baltimore, MD and Washington, DC have conducted studies in order to compare the density of mosquito habitat and pupae production across neighborhoods with varying poverty levels. No such research has examined mosquito prevalence in Pittsburgh, PA in relation to the population's demographics or the physical environment. Improved knowledge of the social factors contributing to mosquito prevalence, such as poverty level and race and ethnicity, has public health relevance for effective mosquito control in urban environments. Pittsburgh-specific spatial data analysis and mapping will provide a better understanding of where mosquitoes lay their eggs, which will be helpful to the city when deciding how and where to concentrate their efforts. The number of mosquito eggs laid (2016-2017) were mapped against several factors, including: percent poverty and different ethnicities and races, as well as public pools, highways, playgrounds, and other factors thought to be correlated with mosquito prevalence. Clustering of mosquito eggs and statistical relationships were determined using the mapping program Geoda. Pittsburgh's lower income residents were found to be at greater risk of exposure to mosquito-disease vectors; census tracts with a higher percent of black people and other minorities tended to host mosquito traps with a higher number of eggs. From these results, we infer that Pittsburgh's lower income residents may be at greater risk for mosquito-vectored diseases. Public health officials should focus their efforts on spraying these identified areas and educating these community members on different ways to reduce the mosquito population and protect themselves.



Dean's Day Competition 2018

Nandini Ramesh

HUGEN

Pathogenic mutations in Matrin 3 perturb nuclear morphology and induce neurodegeneration *in vivo*

Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disorder that is characterized by loss of upper and lower motor neurons. Pathogenic mutations in Matrin 3 (MATR3), a nuclear matrix protein, have been linked to familial ALS and distal myopathy. In addition, cytoplasmic inclusions containing MATR3 have been identified in a subset of sporadic ALS cases. However, the underlying molecular mechanism of neurodegeneration caused by MATR3 mutations remains poorly understood. To elucidate the mechanism of MATR3-mediated ALS, we generated Drosophila and mammalian cellular models. Targeted expression of wildtype and mutant MATR3 to Drosophila muscles and motor neurons leads to reduced lifespan and locomotion defects. Furthermore, ubiquitous expression of MATR3 causes prepupal lethality, suggesting that transgenic expression of MATR3 is toxic in flies. Interestingly, unlike other ALS-associated proteins, MATR3 mutations do not affect its subcellular localization or induce formation of cytoplasmic aggregates. However, overexpression of wildtype or mutant MATR3 in mammalian cells results in perturbed nuclear morphology characterized by nuclear membrane invaginations. Interestingly, these nuclear defects were also found in motor neurons from MATR3 patient-derived induced pluripotent stem cells (iPSCs). Taken together, our data suggest that MATR3 mutations mediate neurodegeneration through disruption of nuclear morphology that could directly impact key mechanisms including nucleocytoplasmic transport and gene regulation.



Dean's Day Competition 2018

Vatsala Rangachar Srinivasa

IDM

Clostridium difficile spread within the hospital environment

Authors: Rangachar Srinivasa V (1), Hariri R (2), Pokrywka M (2), Magee E (2), Kingsley L (1), Frank L (1) and Yassin M (1)

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Background: Clostridium difficile Infection (CDI) is one of the leading causes of hospital-associated infections (HAIs) accounting for nearly half a million infections in the United States (2015). It was associated with approximately 29,000 deaths nationwide in 2011. This study focusses on the role of the environment in the spread of CDI within the hospital environment in a non-outbreak setting.

Method: The study was conducted at a 495- bed academic University-affiliated single center. The first step was to identify and collect data on all positive CD cases in 2016. Bed tracing was performed for all the in-patients who tested positive for CD in 2016 using Electronic Medical Records. Their movement within the hospital was traced from Jan 1, 2016 through Jun 15, 2017. The second step was to perform room cultures of the immediate patient environment to identify lapses in environmental cleaning.

Results: Bed tracing was performed for 115 HA- and 96 CA- CDI (community associated) patients. Initial analysis between HAI and CAI revealed that the length of stay was significantly longer in HAIs. However, readmission and recurrence were significantly higher in CAIs. Bed-tracing showed specific medical and intensive care unit rooms to be associated with CDI patients and CD patient-days. However, environmental culturing using a selective CD medium failed to show an association with CD positive cultures.

Conclusion: Environmental culturing shows that manual disinfection and additional ultraviolet use were effective in reducing CD spores. However, it is possible that the culture method was not as sensitive as previously reported. It is also possible that the bulk of these hospital-associated CDIs are endogenous and manifest in patients who receive antimicrobial therapy for an unrelated condition.



Dean's Day Competition 2018

Sharon Renner

EPIDEM

Physical Fatigability Increases Prospective Fall Risk in Older Men: The Osteoporotic Fractures in Men Study (MrOS)

Fall-related injuries are increasingly common among older adults, highlighting the need to identify modifiable risk factors to address this public health problem. Previous analyses have found that fatigued men had a higher fall risk than non-fatigued men; however, the measurement of fatigue was a crude, single item question that may be subject to bias. Fatigability provides a more standardized method that classifies whole-body fatigue in relation to a defined activity of specific intensity and duration. We examined the role of physical and mental fatigability on prospective fall risk in 2,113 men aged 77-101 years (mean 84.6 ± 4.3) in MrOS at Year 14. Fatigability was measured using the Pittsburgh Fatigability Scale (PFS, 0-50 score), using established cut points for the physical (physical PFS ≥ 15 , 57%) and mental (mental PFS ≥ 13 , 26.1%) components. Prospective falls were assessed by triannual questionnaire. After 12 months, 25.3% with higher vs. 16.7% with lower physical fatigability and 29.1% with higher vs. 19% with lower mental fatigability fell. Using GEE, higher physical fatigability increased the risk of prospective falls by 20% (RR: 1.20, 95%CI: 1.01, 1.44) independent of mental fatigability, and also adjusted for demographics, medical history, medications, depression, and function. Physical fatigability provides a promising target for intervention on fall risk. Physical activity is one potential promising intervention, as physical activity interventions have improved fatigue in subpopulations with high rates of fatigue. Reducing physical fatigability would have numerous public health benefits, including lowering fall risk, in this vulnerable population.



Dean's Day Competition 2018

Emily Russell

HUGEN

The relationship between a genetic variant in CREBRF, body mass index, and type 2 diabetes in Sāmoans.

Background: The prevalence of obesity among Polynesians is among the highest in the world, and obesity-related disorders like type 2 diabetes (T2D) are a growing public health problem in Polynesia and among Polynesians living in the USA, Australia, and New Zealand. In our cross-sectional study of 2,861 individuals from the Independent State of Sāmoa, obesity and T2D are highly prevalent: 42% of men and 65% of women are obese, and 16% of men and 17% of women are diabetic. There are many factors which could underlie these high prevalences. Here we delved into the effects of one factor in particular, the effect of a genetic variant, rs373863828, known to be associated with both obesity and T2D in Sāmoans. The A allele of a genetic variant in CREBRF, rs373863828, which causes an arginine-to-glutamine amino acid change in the CREBRF protein is associated with increased body mass index (BMI) in Sāmoans, Tongans, and Māori. This variant is common in Sāmoans (minor allele frequency [MAF] = 0.26), Tongans (MAF = 0.15), and Māori (MAF = 0.09), but is rare in non-Polynesian populations (MAF < 0.0001). This genetic variant has the largest genetic effect on BMI of any genetic variant observed at a high frequency in any population, associated with a 25% increase in obesity risk per copy of the A allele. While higher BMI is a risk factor for T2D, the A allele is associated with lower-than-expected odds of T2D in Sāmoans.

Research Question: How can the relationship between the A allele of a genetic variant in CREBRF, BMI, and T2D be modeled in Sāmoans?

Methods and Results: We hypothesized that, in addition to main effects, there is a statistical interaction between the CREBRF variant and BMI that affects risk of T2D. We used logistic regression and path analysis to test this hypothesis. Our study participants were 2,861 adults (ages 24–64) recruited in 2010 in Sāmoa. In a logistic model, the interaction between the CREBRF variant and BMI was not significantly associated with T2D ($p = 0.830$). However, both BMI and the CREBRF variant were significantly associated with T2D as main effects in an analysis that did not include an interaction term ($p = 8.31 \times 10^{-9}$ and $p = 1.97 \times 10^{-8}$, respectively). We do not see evidence of a statistical interaction in this analysis. However, large sample sizes are required to detect statistical interaction, so a full exploration of the relationship would require a much larger study with greater statistical power. Next, we used path analysis to model the relationship between age, sex, the CREBRF variant, and BMI. Our model indicates that the CREBRF variant has a small direct negative effect on T2D risk ($p < 0.001$, path coefficient $(PT2D \leftarrow CREBRF) = -0.102$) as well as a small indirect positive effect on T2D risk through its positive effect on BMI ($p < 0.001$, $PBMI \leftarrow CREBRF \times PT2D \leftarrow BMI = 0.014$).

Conclusion: These analyses suggest that the A allele of the CREBRF variant, rs373863828, has both a direct negative main effect on T2D and an indirect positive effect on T2D as mediated by BMI. While the A allele is associated with a decreased risk of T2D it is also associated with increased BMI, a risk factor for T2D. The complex relationship between genetics, BMI, and T2D in Sāmoans and in other Polynesian populations merits additional research to understand why such disparate effects on BMI and T2D exist.



Dean's Day Competition 2018

Amrita Sahu

EOH

Role of α -Klotho in muscle progenitor function and skeletal muscle regeneration

Aging is associated with an impaired capacity of skeletal muscle regeneration after an acute injury which results in decline in functional mobility and is associated with an increased morbidity in the elderly population. While young muscle can restore the original architecture of damaged muscle fibers, aged muscle displays a markedly reduced regenerative capacity. Such impairment is attributed to muscle stem cell (MuSC) dysfunction, which are major players in muscle regeneration. Studies have shown that an enhanced micro-environment of the muscle can revitalize the MuSCs and hence the regenerative capacity of skeletal muscle. We show that expression of an “anti-aging” protein, Klotho, is upregulated within young injured muscle, however, this response is attenuated with aging. Genetic silencing of Klotho in young muscle progenitor cells (MPCs) drives mitochondrial DNA (mtDNA) damage, senescence and decreased cellular bioenergetics. Conversely, Klotho supplementation to aged MPCs restores mtDNA integrity and oxygen consumption to youthful levels. Consistent with in vitro findings, decreased Klotho gene expression in young muscle results in impaired myogenesis after injury, whereas systemic supplementation with Klotho enhances regeneration of aged muscle. These studies identify a novel role for Klotho in the regulation of MPC mitochondrial integrity and senescence, and implicate Klotho declines, as a driver of impaired muscle regeneration with age.



Dean's Day Competition 2018

Samantha Sanford

IDM

Determining the impact of oxidized dNTPs and nucleoside reverse transcriptase inhibitors (NRTIs) on telomerase activity

An increasing number of HIV-1 patients have received decade-long Highly Active Antiretroviral Therapy (HAART), but long-term side effects are poorly understood. Long term HAART is associated with chronic inflammation, mitochondrial dysfunction, oxidative stress, and telomere shortening, all of which have been implicated in age related diseases such as neurocognitive disorders and cancer. One class of drugs used in the HAART regimen includes nucleoside reverse transcriptase inhibitors (NRTIs). NRTIs not only act as chain terminators to HIV reverse transcriptase (RT), but also inhibit human telomerase (hTERT), a structurally similar RT in human cells. Telomerase enzyme performs de novo synthesis of telomeric TTAGGG repeats at the ends of linear chromosomes. Telomeric repeats are highly susceptible to damage from oxidative stress, which results from excessive reactive oxygen species (ROS) and leads to accelerated telomere shortening. NRTI treatment of human cells induces oxidative stress by inhibiting mitochondrial DNA polymerase γ , thereby disrupting mitochondrial function. Defective mitochondria elevate ROS, which damage cellular components including DNA and free nucleotide pools, thereby amplifying NRTI toxicity. The Opresco lab recently found that one of the most common DNA lesions resulting from oxidative stress, 8-oxoguanine (8oxoG), regulates telomere elongation by telomerase. Telomerase can incorporate 8oxoG during telomere extension, however, addition of the oxidized dNTP is mutagenic and terminates further elongation. Thus, evidence indicates that oxidative damage to telomeric DNA and free dNTP pools can induce telomere dysfunction and shortening, exacerbating the direct effect of NRTIs on telomerase. Here, we investigate the impact of NRTIs (including Didanosine and Tenofovir) and naturally occurring oxidized dNTPs (including 8-oxodATP, 2-OH-dATP, and 6-ThioDG) on telomerase activity and fidelity. Using biochemical assays, we found telomerase extension was aborted after the addition of one telomeric repeat in reactions containing both NRTIs or 8-oxodATP and 6-ThioDG. We observed moderate telomeric synthesis in the presence of 2-OH-dATP, but processivity (i.e. the number of repeats added per binding cycle) was 3-fold lower than the control containing the unmodified dATP. The aborted extension products suggest that the NRTIs, 8oxodATP, 8oxodGTP, and 6-ThioDG are strong chain terminators of telomerase whereas 2-OH-dATP was less inhibitory. Further studies will determine the errors caused by oxidized dNTPs during telomere elongation by telomerase. Telomere maintenance is important for cell survival, genome stability, and healthy aging. These studies will fill a significant void in our understanding of how NRTIs and naturally occurring oxidized dNTPs contribute to inhibition of telomere maintenance.



Dean's Day Competition 2018

Jordan Sang

BCHS

Assessing HIV stigma among Black Men who have Sex with Men in the United States—Strategies for Prevention

Background: Black Men who have sex with men (BMSM) are disproportionately burdened by the HIV epidemic, with BMSM accounting for the largest proportion of new diagnoses in the US. The deleterious effects of HIV stigma on HIV+ BMSM and care continuum outcomes have been well-documented. How HIV stigma shapes HIV prevention for HIV- persons in these communities is poorly understood. The present study addresses current gaps in the literature by focusing on the impact of HIV stigma among HIV-negative BMSM for HIV prevention outcomes: HIV testing, PrEP awareness, and PrEP use.

Methods: Data comes from the Promoting Our Worth Equality and Resilience (POWER) study in 2016 and 2017. Cross-sectional time-location sampling was used to recruit participants at Black Pride events across five U.S. cities. Participants completed anonymous questionnaires and were offered free, confidential HIV testing. Multivariable logistic regression models assessed the association of HIV stigma on prevention outcomes adjusting for sociodemographic variables. All analyses were weighted according to POWER's time-location sampling; we report unadjusted frequencies and weighted percentages.

Results: Our analytic sample included 1,009 BMSM who identified as HIV-negative. Among participants, 69% had received an HIV test in the past six months, 71% had heard of PrEP, and 18% reported having ever used PrEP. HIV stigma was negatively associated with HIV testing in the past six months (AOR=0.85; CI=0.72, 0.99), positively associated with PrEP awareness (AOR=1.35, CI=1.14, 1.61), and not associated with PrEP use. Among PrEP awareness, being in a relationship and internalized homophobia were negatively associated with awareness (AOR=0.64; CI=0.42, 0.95) and (AOR=0.67; CI=0.56, 0.79), respectively.

Conclusion: Our results indicate the importance of public health leaders to adopt HIV stigma in prevention research. The capacity to curb HIV incidence in disproportionately burdened communities like Black MSM is challenged by perceptions of community HIV stigma. Results from the study adds new knowledge around PrEP awareness and utilization among BMSM and adds to research on racial/ethnic sexual minorities. We support community-based anti-HIV stigma efforts as a necessary complement to HIV prevention service provision.



Dean's Day Competition 2018

Emily Schmitz

IDM

Multidrug-resistant organisms (MDRO): cost-effective analysis of horizontal vs. vertical surveillance

Introduction: Multidrug-resistant organisms (MDRO) are still a serious public health problem in healthcare facilities and are a major cause for morbidity and mortality in hospitalized patients. There is currently no consensus for the most effective surveillance approach for MDRO management. The objective of this study is to compare focused enhanced surveillance for populations at high-risk for MDRO colonization to the current vertically oriented (organism focused) surveillance strategy. A cost-effective analysis will be performed to determine which approach is more economical.

Methods: Electronic medical record surveillance was performed to randomly identify 100 high-risk patients. Nursing staff in the UPMC-Mercy ICUs and infection control department gathered samples from patients for the following MDRO: Methicillin-resistant Staph aureus (MRSA), Vancomycin resistant Enterococci (VRE), Carbapenem resistant enterobacteriae (CRE) and extended spectrum Beta lactamase producing organisms (ESBL). Specimens were analyzed, and the results were recorded. Chart abstraction collected patient characteristics, severity index and comorbidity index. StataSE 15.1 was used for data analysis to compare the current surveillance method to the horizontal approach. TreeAge software was used to conduct a cost-effective analysis to compare the two approaches.

Results: From Oct 1st, 2017 through Nov. 30th, 2017 there were total of 155 eligible patients identified through EMR surveillance. We screened 74 patients who met our clinical criteria and 26 patients who met our 7-day length of stay criterion. There were 52% men in our cohort, with an average age of 60.1 years. The mean severity index was 38.8 and the mean comorbidity index was 4.4. There was evidence of MDRO (CRE, ESBL, VRE & MRSA) in 30% of patients with high-risk clinical criteria and 27% in 7-day LOS patients, as compared to 10% MRSA captured using the current screening strategy.

Discussion: Clinical-based horizontal surveillance is a more effective way of identifying MDRO colonization and infection. The next step in our research is to include a larger patient sample to verify these data results.



Dean's Day Competition 2018

JoAnna Shaw

IDM

Identification of Novel Bacterial MurA Inhibitors

Antibiotic resistance is a persistent and serious public health issue which causes many illnesses and deaths per year. In contrast to the rapid increase and spread of drug-resistant bacteria, antibiotic development has slowed, and there is a clear need to identify and develop antibiotics with new scaffolds and mechanisms of action. In particular, there is a specific need for novel antimicrobial agents which are active against both gram negative and gram positive pathogens. The bacterial enzyme MurA catalyzes the transfer of enolpyruvate from phosphoenolpyruvate (PEP) to uridine diphospho-N-acetylglucosamine (UNAG), which is the first committed step of bacterial cell wall biosynthesis. Currently, the only antibiotic targeted toward MurA is fosfomycin, which inhibits MurA by forming a covalent bond with MurA's active site residue, Cys115. However, MurA variants which lack the cysteine residue in the active site (e.g. *M. tuberculosis* MurA and some vancomycin resistant Enterococcus (VRE) strains) are resistant to fosfomycin. The goal of this study was to identify novel MurA inhibitors with a different mechanism of action than fosfomycin, and which are active against a range of gram negative and gram positive bacteria. To this end, we have developed and optimized an *in vivo* high-throughput screening assay to test recombinant MurA enzyme against the TimTec ApexScreen library, a drug library with 5,040 structurally diverse compounds. The hits identified from this screen were further validated using different assays, including bacterial growth curves. The mechanism(s) of action of the most promising hits were also characterized.



Dean's Day Competition 2018

Celeste Shelton

HUGEN

Classification of Pancreatitis Subtypes Using RNA-SEQ from Human Pancreatic Tissue

Background: Pancreatitis is a complex acute and chronic inflammatory disorder in which different genetic and environmental factors produce a similar clinical phenotype and for which no effective preventive or therapeutic agents exist. The etiology of inflammation, how it becomes continuous and irreversible, and why there is variability in pain and loss of function remains obscure, in part because human tissue has been largely unavailable for study. For some patients, the pain, disability and potential outcomes are so severe, progressive, or unpredictable that they opt for total pancreatectomy with islet autotransplantation (TPIAT). Leftover tissue from TPIAT is collected at the optimal time to evaluate the underlying pathogenesis after a pathogenic, progressive natural history is predicted, but before the insulin-producing islets are lost. This tissue represents a rich resource to study biological drivers of chronic pancreatitis (CP) progression in humans.

Methods: Two separate studies were used to evaluate underlying gene expression. First, RNA was extracted from 18 pancreata (6 control, 3 CP, 6 pancreatic adenocarcinoma, 3 neuroendocrine tumors) and used for mRNA-Sequencing to demonstrate feasibility. Second, RNA was extracted from TPIAT RNA later samples (1 PRSS1 CP; 2 idiopathic CP; 1 alcoholic recurrent acute pancreatitis (RAP)) and histologically normal tissue from pancreatic cancer. RNA integrity was consistent among samples, and total RNA-sequencing was used for optimal coverage.

Results: On principal component analysis (PCA), clear separation was seen between normal tissue, pancreatic cancer, neuroendocrine tumors and CP. Further analysis of phase 2 data demonstrated clear separation between TPIAT tissue by stage and etiology. Tissue expression profiles provided functional insights into disease mechanisms and drivers of CP progression. Pathway-dependent differences in gene expression enabled subclassification of pancreatitis tissue by stage and underlying molecular pathogenesis, such as activation of the humoral immune response.

Conclusion: We demonstrate that RNA-Seq can be used to effectively classify human pancreatic tissue by diagnosis (normal, cancer, CP, neuroendocrine tumor). Clustering of pancreatitis subtypes (e.g. RAP, CP) from TPIAT tissue provides a framework to predict disease stage and etiology, as well as possible therapeutic targets from underlying expression pathways. Differences in expression profiles reveal divergent disease mechanisms and provide functional clues into etiopathogenesis.



Dean's Day Competition 2018

Emily Spoth

HUGEN

Biomechanical Properties of the Skin in Arterial Tortuosity Syndrome

Arterial tortuosity syndrome (ATS) is a rare autosomal recessive connective tissue disorder caused by loss of function mutations in SLC2A10, encoding for a class III facilitative glucose transporter. ATS is characterized by a lengthening of systemic medium and large arteries and subsequent tortuosity, which significantly increases affected individual's risk of aortic dilation and dissection. While most individuals with ATS possess cutaneous findings characteristic of connective tissue disorders, ranging from soft, hyperextensible skin to lax skin in redundant folds, no study has quantified differences in the biomechanical properties of the skin between individuals with ATS and healthy controls. In this study, rapid, non-invasive, *in vivo* cutaneous measurements were performed using the DermaLab® Combo SkinLab on a total of 8 affected individuals, 15 heterozygous carriers, and 6 individuals with no mutations in SLC2A10 to determine differences in elasticity, hydration, and dermal thickness between groups. Preliminary data shows significant difference in skin elasticity between affected and unaffected individuals. However, correction for age remains to be completed for our dataset. This research significantly impacts public health by contributing to rare disease research, specifically by further characterizing the natural history of ATS and aiding diagnosis in the general population.



Dean's Day Competition 2018

Julia Stone

HUGEN

Caregiver Perceptions of Quality of Life in Adolescents with Duchenne Muscular Dystrophy

Duchenne Muscular Dystrophy (DMD) is a rare neuromuscular disorder characterized by early-onset muscle weakness and progressive loss of muscle ability that primarily affects males. Although there is currently no cure for the disease, there is ongoing research into methods to slow the disease progression which could impact overall quality of life (QoL) for boys with DMD. Many early studies on QoL in DMD were conducted using parent-proxy reports, but more recent research has suggested that boys with DMD might perceive their QoL differently than their caregivers do. This study aims to determine if parents of boys with DMD perceive their child's QoL the same as the children perceive their own QoL and to determine if specific aspects of DMD (glucocorticoid use, loss of ambulation, noninvasive respiratory support, and inability to self-feed) affect these perceptions. We are analyzing data from PedsQL 4.0 surveys administered to participants ages 11-17 years old and their caregivers through the Cooperative International Neuromuscular Research Group (CINRG) Duchenne Natural History Study (DNHS). Data analysis is still ongoing, but preliminary results suggest no difference between caregiver and child perceptions of the overall QoL for boys with DMD. However, there are significant differences between participant and parent-proxy reports regarding subscales of QoL, with caregivers reporting lower physical QoL scores ($p<0.002$) and higher social ($p<0.001$), and school-functioning ($p<0.02$) QoL scores compared to their children. These results indicate that adolescents with DMD have more positive perceptions regarding their physical QoL and more negative perceptions regarding their psychosocial QoL than their parents perceive, suggesting a disconnect between child experiences and parent perceptions.



Dean's Day Competition 2018

Priyanka Talukdar

IDM

Expression of Type III Interferons in Tuberculosis Granuloma

The recently classified type III interferon group consists of four isoforms of interferon lambda, IFNL (IFNL1 or IL-29, IFNL2 or IL-28A, IFNL3 or IL-28B and IFNL4). This interferon group is related to IL-10 and might have important anti-viral response that might be different from that of type I and type II interferon. High levels of IFNLs, but not IFN- α , have been found to be present in virus infected liver and lung tissues [1]. Much of the early research on Type III Interferons have been done to find its role in anti-viral response. No as such work has been done regarding the role of Type III Interferons in TB infection. Hence to characterize the expression of Type III Interferons in macaque lung and granuloma, we started with the developing of PCR primers for IFNL1, IFNL3 and IFNL4 to compare their expression in normal macaque lung and macaque lung granulomas, U937 cell lines and PBMCs. IFNL4 appeared to be constitutively expressed in U937 cells. In PBMCs IFNL4 was found to be absent. We identified antibodies for the three Type III Interferons and did Immunohistochemistry staining on macaque lung and granulomas to find their localization. Lastly, a qPCR analysis was done on macaque lung and granuloma mRNA to find differences in the expression levels of the three IFNL3 genes. Currently, we are testing the influence of IFNL4 on macaque macrophages to determine how this cytokine influences anti-microbial response. Our data suggest that type 3 interferons are a component of the antimycobacterial response in TB that may have implications for protection and disease pathogenesis.

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Dean's Day Competition 2018

Jessica Thompson

BCHS

Spatial Relationships between Cardiovascular Disease Mortality for Women and Medical Resource Distribution in Appalachian Pennsylvania

In Appalachia, a largely rural and low socioeconomic status region, premature mortality rates are 25 percent higher than all US counties. Appalachian populations have significantly higher rates of heart disease mortality than national averages, including high rates for women. This study explores how medical resource distribution (e.g., density of hospitals, rural health clinics, FQHCs) relates to cardiovascular disease (CVD) mortality for women in the 52 counties of Appalachian Pennsylvania (PA). Using QGIS and GeoDa, I conducted Exploratory Spatial Data Analysis (ESDA) to display: 1) CVD mortality rates among women and 2) medical resource density. I generated a spatially lagged variable for medical resource density, as resource utilization does not adhere to county boundaries. I assessed global spatial autocorrelation for CVD mortality ($I = 0.331, p = 0.001$) and spatially lagged resource density ($I = 0.419, p = 0.001$) and the local clustering of significantly high and low values for each variable. I also conducted an OLS regression and spatial lag model to assess the relationship between CVD mortality rates for women, lagged resource density, physician density, population density, and socioeconomic predictors. These findings establish evidence for additional spatial exploration of the role of medical resources in CVD health outcomes for women in Appalachian PA; they show clusters for CVD mortality and resource density, provide evidence for socioeconomic factors within this relationship, and suggest more accurate ways are needed to capture resource availability, including number of physicians each site and other indicators such as type and quality of services available.



Dean's Day Competition 2018

Curtis Tilves

EPIDEM

Trends and Correlates of Suicidality in Youth from Trinidad and Tobago

Background: Suicide is the third leading cause of death among adolescents worldwide. According to the WHO, rates of suicide in adolescents in the Republic of Trinidad and Tobago are among the highest worldwide, and are the second highest among countries in the West Indies. The Global School-based Student Health Survey (GSHS) reported in 2007 that 17.9% of adolescents in Trinidad and Tobago had seriously considered attempting suicide in the past year. Public health interventions designed to target adolescents at high risk for suicidal ideation are necessary to prevent adolescent deaths. In order to identify at-risk adolescents, we will identify behaviors associated with suicidal ideation and attempts in Trinidad and Tobago adolescents.

Aims: We aim to assess population trends related to suicidal ideation in the Republic of Trinidad and Tobago using cross-sectional data from the 2007 and 2011 GSHS. We will also examine potential risk factors associated with increased suicidal ideation in adolescents ages 13-15 from this region.

Methods: The Global School-based Student Health Survey (GSHS) is a global surveillance project designed in collaboration by WHO, UN, and CDC to assess behavioral risk and protective factors among students. All assessments for this study will be assessed at the full country level (both Trinidad and Tobago) and stratified by island (Trinidad vs. Tobago), using serial cross-sectional survey data from the 2007 and 2011 time points. The primary outcome measure is suicidal ideation. Changes in the prevalence of suicidal ideation over time will be assessed using Chi-square analysis that accounts for the complex survey design. Associations of multiple risk factors (age, gender, loneliness (yes/no), anxiety (yes/no), depression (yes/no), having no close friends (yes/no), alcohol and drug use, having been bullied, and exposure to physical violence) for suicidal ideation will be assessed using Chi-square analysis with the Rao-Scott F adjusted Chi-square statistic and logistic regression, accounting for the complex sampling design.

Results: (Pending)

Discussion/Significance: This study will improve upon the current literature on risk factors associated with youth suicidal ideation in the Republic of Trinidad and Tobago through use of a large dataset at two time-points and investigating differences between both islands. The public health importance of understanding the correlates of suicide in this population could lead to the development of improved prevention or intervention strategies.



Dean's Day Competition 2018

Lycia Tramujas Vasconcellos Neumann

BCHS

The profile and unmet needs of cancer patients' family caregivers in Brazil

In Brazil, where about 600,000 new cases of cancer are diagnosed every year, families are the main source of support for cancer patients offering emotional and instrumental assistance throughout treatment. Without proper guidance and support to perform this role, burdens of caregiving can deeply affect family caregivers' lives and undermine their health. Understanding who these informal caregivers are, what kind of support and unmet needs they have is essential to inform programs and policies that will help decrease their burden and increase their self-efficacy. This was the goal of this exploratory research, conducted in partnership with two Brazilian organizations: Instituto Oncoguia and Hospital Israelita Albert Einstein.

Methods: This observational cross-sectional study used qualitative methods to explore the perceptions of family caregivers and health professionals about the impact of cancer on the lives of family members. Three focus groups were held in the city of São Paulo, with a total of 25 participants: six family caregivers and 19 health professionals (physicians, nurses, social workers, psychologists, and physical therapists).

Findings: Participants underscored the fact that cancer is a "family illness" and its diagnosis triggers a series of emotions, doubts, and challenges not only to patients but also to those who assume the role of supporting them throughout treatment and recovery. Often one person is self-selected or chosen as the main caregiver based on their relationship with the patient, their role in the family, and their availability. Especially for low-income families, this choice also takes into consideration the impact of working fewer hours or losing their jobs. Most family caregivers do not receive any training or professional support and assume this new role on top of other responsibilities, leading to great impact on their emotional and physical health, as well as on their social and professional lives. Family cancer caregivers' have unmet needs regarding information about the disease's process, caregiving training, psychological support, greater family and societal understanding, and instrumental tools to help them better manage their daily lives.

Implications for practice and further research: This study's findings will inform the adaptation of a scale to measure cancer caregiver burden in Brazil, which will be implemented as part of a national survey with family caregivers of cancer patients. In addition, these findings are already informing the development of a training and support program for family caregivers by Instituto Oncoguia.



Dean's Day Competition 2018

Raymond Van Cleve

HPM

Home and Community Based Service Use among Aging Pennsylvania Medicaid Recipients

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 however is not a program with one standard form that can applied to all beneficiaries. To effectively serve seniors with physical and cognitive limitations, HCBS must be tailored to meet the specific health and environmental needs of each individual to whom it serves. HCBS programs meet the unique individual needs of their clients by addressing physical environmental needs, supporting the person's health, and assisting with basic and instrumental activities of daily living. There is little known about the type and amount of specific HCBS that is administered through Medicaid. This study seeks to identify the type and amount of HCBS services used by aged Pennsylvania Medicaid aging waiver beneficiaries. This is a descriptive study that will examine the distribution of each major service type used between 2013 - 2015. I use a generalized estimating equation to identify if people with certain demographic characteristics are more likely to use certain services and to identify if certain services are used as complements or substitutes for each other. The data will come from Pennsylvania Medicaid and Medicare claims from people enrolled in the aging waiver for at least one month between 2013-2015.



Dean's Day Competition 2018

Julia Verbiar

HUGEN

Genetics of the Relationship Between Periodontitis and Cardiovascular Disease

Oral health can have an impact on many aspects of systemic health. One example of this is the connection proposed between periodontitis and cardiovascular disease. Periodontitis involves chronic inflammation of the gingiva and deterioration of connective structures in the oral cavity. Research has suggested that periodontitis and cardiovascular disease may share an underlying inflammation pathway that in periodontitis exacerbates gingival irritation and in cardiovascular disease promotes atherosclerotic plaque formation. It has been proposed that this link extends to the molecular level and that there is overlap in some of the genes significant for these two conditions related to inflammation and immune system function. In 2017, Aarabi et al conducted an assessment of the field and found three single nucleotide polymorphisms (SNPs) to be significantly associated with both periodontitis and heart disease, in regions associated with noncoding RNAs, kinases, bacterial binding, and phagocytosis. Further literature review identified another SNP, in the pro-inflammatory gene interleukin 6, that has been associated with both diseases individually. This study is intended to test the significance of these four SNPs in relation to periodontitis and cardiovascular disease both independently and jointly using data from the Center for Oral Health Research in Appalachia. Both conservative and non-conservative estimates of periodontitis were developed, as was a composite heart disease score based on patient-reported personal and family medical history. Using linear and logistic regression models, the significance of periodontitis and heart disease as predictors of each other and the impact of the SNPs on the relationship between the two was analyzed. Although the majority of the models showed otherwise, there were multiple instances in which there was a statistically significant relationship between the two health outcomes including and independent from the SNPs of interest. There is still more work to be done to solidify the findings, but with the results of this study, there is additional support for the relationship between periodontitis and cardiovascular disease.



Dean's Day Competition 2018

Gretchen White

EPIDEM

Do Associations Between Alcohol Use and Alcohol Use Disorder Vary by Weight Status? National Epidemiological Survey on Alcohol and Related Conditions-III Results

Purpose: To determine if associations between alcohol use and alcohol use disorder (AUD) differ by weight status.

Data: 24,869 NESARC-III non-pregnant participants with a body mass index (BMI) $\geq 18.5 \text{ kg/m}^2$ who reported past-year alcohol consumption were included. Methods: Self-reported BMI was categorized into healthy weight ($18.5 < 25 \text{ kg/m}^2$), overweight ($25 < 30 \text{ kg/m}^2$), and class 1 ($30 < 35 \text{ kg/m}^2$), class 2 ($35 < 40 \text{ kg/m}^2$), and class 3 ($\geq 40.0 \text{ kg/m}^2$) obesity. The NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule-5 was administered to identify past-year AUD. Logistic regression was used to test associations between levels and patterns of alcohol use (i.e., past-year frequency of days with any drinking, average quantity of alcohol per drinking day, and frequency of heavy drinking days) and AUD. Logistic regression models adjusted for age, race/ethnicity, education, employment status, income, marital status, physical activity, smoking status, past-year major depressive disorder, and family history of alcohol problems. Interactions between weight status and alcohol use variables in relation to AUD were examined. Analyses were stratified by gender.

Results: For men and women, the odds of AUD were higher with more days with any drinking and heavy drinking, and greater quantities of alcohol. Among men, there were significant interactions between weight status and quantity of drinks per drinking day ($p < .001$) and frequency of heavy drinking ($p < .001$), but not frequency of any drinking ($p = .36$): At the same quantity of alcohol or frequency of heavy drinking, men with class 3 obesity had higher odds of AUD than men with healthy weight to class 2 obesity. Conversely, among women, there was a significant interaction between weight status and frequency of any drinking only ($p < .001$): At the same frequency level, women with class 3 obesity had lower odds of AUD than women with healthy weight to class 2 obesity.

Conclusions: Associations between some, but not all, measures of alcohol use and AUD differed for men and women with class 3 obesity versus lower weight status. Further AUD screening may be needed at lower levels of alcohol use among males with class 3 obesity and females of healthy weight.



Dean's Day Competition 2018

Elizabeth Winter

BCHS

The Role Of Mentorship: Developing Advocacy Skills Among Adolescents with Disabilities and Chronic Illness

A novel mentorship program will pair adult mentors with adolescent mentees and focus on increasing advocacy skills in the participating mentees. The adult mentors are members of a highly active local advocacy group and are all individuals who live with disabilities and/or chronic illness. They will be matched to adolescents and young adults living with disabilities and/or chronic illness who are existing members of the CHANGE program—a Children’s Hospital youth-led initiative that focuses on medical transition. This pilot mentorship program will be evaluated in several ways. Free listing and pile sorting (FLPS) methodology will be used to develop an understanding, both qualitatively and quantitatively, of how this population thinks about the concept of advocacy. A FLPS session will be conducted with mentees before they engage in the mentorship program and then again after they have been involved for several months. Additionally, previously validated survey metrics will be used to measure self esteem and future orientation of the participating mentees, conducted at the same time as the FLPS sessions. A separate FLPS session will be conducted with the mentors. This research will allow for defining this population’s understanding of advocacy, creating a new framework for the development and implementation of a mentor-mentee program and evaluating the development of advocacy skills in this population. Finally, the FLPS methodology is highly adaptable and accommodations will be made for it to be accessible to any willing participant, regardless of their level of ability. This broadens the application of this mixed method approach and allows for more diverse voices to be included.



Dean's Day Competition 2018

Fan Wu

EOH

Assessing the Cancer Incidence in the Transgender Population in Pennsylvania, 1992-2015, Using State Cancer Registry Data

Cancer risk in the transgender population is an emerging area of public health research. The WHO reported that transgender communities were facing high risks for several cancers, including ovarian, uterine, and cervical cancer [1]. The goal of the present analysis was to determine the utility of using state cancer registry data in studies of cancer incidence among transgender patients. We used Stata to obtain descriptive statistics for the subset of transgender patients in the Pennsylvania Cancer Registry (PCR) and ArcMap to examine the geographic pattern of cases at the county level. In the PCR, there are 45 recorded transgender patients diagnosed from 1992 to 2015, aged from 23 to 90 years old. These cases are mainly concentrated in more urban areas of the state. Thirty-six percent of the cases were diagnosed between 2010 and 2015. More patients were diagnosed at younger ages (<30 years old) starting in 2010 compared to earlier years. The most frequent primary cancer sites were digestive organs (29%), which was also the top site in white transgender cases (33%). However, the two top sites among blacks were respiratory system and intrathoracic organs (27%), and lymph node (27%). A complex set of issues may limit transgender people's access to care or dissuade them from seeking care, which seems to be reflected in the small number of cases captured in the registry dataset. Though the small sample size offers limited information on cancer risks among the transgender population in Pennsylvania, this dataset enables us to have a preliminary understanding of the spatial and temporal distribution of the cancer cases of different primary sites and possible risk factors, which could be helpful for further studies.



Dean's Day Competition 2018

Li-Yun Wu

HPM

Hospitalist Implementation in Ismett: Surgical Comanagement

In order to achieve a better quality of life, we must recognize that the collaboration between public health agencies and hospital sectors are inseparable and strongly associated with each other. For example, lower readmission rates not only mean less cost for the health care organizations, it also represents better quality of care, which can not only prolong the length of life but also provide the better quality of it. Even the way health care organizations deliver care can affect the outcome of public health. As more and more hospitals are emphasizing patient-centered care, it also means that patients' self-awareness is rising. In other words, if patients are more aware of their choice of care and health care professionals are more able to provide relevant education to patients, then the population will be more aware of their own health overall. Consequently, this concept will eventually combine with disease prevention and education. The hospitalist is a type of care model that redistributes human resources within the health care organizations to provide more efficient and quality care, at the same time reducing unnecessary waste. It also alleviates the work load for particular health care professionals and therefore achieves a more balanced work flow. This essay is a retrospective study showing the implementation of the hospitalist model in a surgery unit and analyzing its outcome to demonstrate the performance of the model, ultimately showing positive results. The essay also conducts an introduction of the hospitalist development in the United States and a literature review regarding the surgical co-management model.



Dean's Day Competition 2018

Nina Yacovoni

HPM

Patient Outcomes in the Populations of the Outpatient Clinic (OPC) and the Pregnancy Recovery Center (PRC) at Magee-Womens Hospital of UPMC

This study examines patient outcomes for one unit within the outpatient center (OPC) and the Pregnancy Recovery Center (PRC) at Magee-Womens Hospital of UPMC. Outcomes are analyzed in terms of no-show rates, number of patients in each unit, and types of appointments attended. This study then examines the population of the PRC regarding if patients receive a long-acting reversible contraceptive (LARC) after birth, and if they attend their post-partum appointments. Maps were created using QGIS and GeoDa software to analyze the patients and their home locations in relation to where the PRC and OPC are. The locations where patients come from in terms of zip codes were looked at and compared to the number of visits to both the selected unit within the OPC and the PRC to examine if home location had effects on no-show rates. Maps were also made showing poverty and households without a vehicle in Allegheny County to see if these also had any effects on no-show rates. Another map was made that showed the locations of all six of Magee's current PRCs in the region and five-mile buffers around each location along with the zip codes where patients come from to get to the PRC. Limitations to this study were recognized and recommendations were made both to Magee-Womens Hospital of UPMC and policymakers. Overall, the public health relevance of this study is that for treatment of pregnant women with substance use disorder (SUD), there are many barriers to receiving care including fear of a stigma of being labeled as a "bad mother". However, in order to receive care and start the road to recovery for both them and their families, it is essential that these women receive care especially since they are a population that is only growing in need and numbers.



Dean's Day Competition 2018

Lei Zhu

EPIDEM

Using electronic medical record data to study social determinants of Rheumatoid Arthritis

Background: There is growing evidence that racial and SES disparities affect both the risk and clinical course of individuals with RA, a debilitating illness affect up to 1% of all adults. The National Health and Nutrition Examination Survey-III and other investigations in the US and Europe reported associations between lower education level and increased risk of RA. The results indicate that many social and health disparities influence both the risk as well as the clinical course of the disease. We have a unique opportunity using our Pittsburgh RA cohort to study this further. Our objectives are to utilize this valuable cohort to: 1) evaluate whether there are differences in RA disease activity at baseline for different social economic factor (SEF) groups, including different race group (white vs. black), education (\geq college vs. high school education), and income (high vs. low income); and 2) assess whether there are differences in RA disease activity over 5-year for different SEF groups.

Methods: Data was drawn from the University of Pittsburgh RA Comparative Effectiveness Research observational registry (2010-2015) on visits where patients had rheumatoid factor (RF) data available, which allows us to evaluate associations for overall RA and the 2 subgroups of RA: RF+ and RF-. The potential confounding variables for assessing SEF and RA risk association, including demographic data, disease duration and morbidity are included for model building. The study outcome is Disease Activity Score-28 joint (DAS28), which were collected at baseline and time of patients' each appointment.

Results: To evaluate the impact of SEF on RA, we analyzed the RA registry data including approximately 1100 RA patients seen by rheumatologists from University of Pittsburgh Medical Center in 2010-2015. We will test the differences by SEF groups (race, education, and income) on RA using DAS28 mean scores at baseline. Unadjusted and adjusted multivariable model will be created for assessing association between DAS28 and SEF. Multilevel models will be used to evaluate association between the changes in DAS28 repeated measurements per patient over 5-year and their SEF. Interaction term of SEF by time will be tested to determine if the SEF variances explain differences in DAS28 over 5-year.

Conclusion: We hypothesize that the lower SEF (only for race, black; and low education) is associated with higher DAS28 at baseline, but not with the DAS28 longitudinal changes. These findings will provide us guidance for future model building regarding whether to include SEF as confounders, in cross-sectional and longitudinal analyses.