

## **Inhibition of CaMKK2 Decreases Osteophyte Volume in Rabbit Models of PTOA**

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**Background:** Post-traumatic osteoarthritis (PTOA) is a debilitating, multifactorial degenerative disease of the joint occurring in 20-50% of all joint injuries, with a total annual cost of \$15 billion. Currently there exists no disease-modifying therapies for PTOA. The initial impact or injury, along with a cascade of downstream pathobiological and pathomechanical changes illicit further inflammatory mediators, leading to osteophyte formation in the joint—a highly painful marker for PTOA. We hypothesize that inhibition of Ca<sup>2+</sup>/CaM dependent protein kinase kinase 2 (CaMKK2), a kinase associated with the inflammatory effects in PTOA, will mitigate the disease-propagating mechanisms and decrease subsequent osteophyte formation.

**Methods:** We utilized a rabbit model of PTOA and two distinct approaches: a surgical transection of the anterior cruciate ligament (ACL) to generate joint instability, as well as a drop-tower, impact model to induce direct cartilage damage to the medial femoral condyle. Rabbits were then treated tri-weekly with either STO-609 (CaMKK2 inhibitor, 0.033 mg/kg) or saline (control) for 16 weeks from the time of surgery or on a delayed timeline (2 weeks post-surgery). Amobarbital (ROS inhibitor, 0.62mg/ml), a one-time intra-articular injection, was utilized as a positive control in some rabbits. Rabbits were sacrificed at 16 weeks post-surgery.

**Results:** Osteophyte volume was increased in saline controls compared to Amobarbital and STO-609-treated rabbits in both modalities. This was consistent with gross morphological damage and histological analysis, that was also performed. Early vs. delayed treatment varied in efficacy between the modalities.

**Conclusions:** This study addresses the unmet clinical need for novel disease-modifying therapeutics for PTOA. Preliminary results show that inhibition of CaMKK2 has the potential to decrease cartilage degradation and osteophyte formation after joint injuries, even if treatment is delayed.

## **Intermediate-Term Outcome of Goniotomy in Primary Open Angle Glaucoma**

**Aarthi Chockalingam**, Massood Mohammadi

**Background:** Goniotomy procedures, such as bent ab interno goniectomy (BANG) and Kahook dual blade (KDB) goniotomy, are considered minimally invasive glaucoma surgeries (MIGS) when combined with cataract extraction (phacoemulsion). These MIGS have seen a surge in popu-

larity among patients for the treatment of adult open-angle glaucoma in recent years. Though MIGS limit risks associated with traditional glaucoma surgeries, few evaluations of longer-term outcomes exist. We performed this study to assess the reduction in intraocular pressure (IOP), visual acuity (VA), and IOP-lowering medication use, up to 3 years after phaco-goniotomy.

**Methods:** We performed a retrospective chart review of 89 eyes of 62 patients who underwent phaco-goniotomy. IOP, VA, and medication data were collected for up to 3 years. Results were analyzed using linear mixed-effect model statistics.

**Results:** The average patient age was 71 years, with 41 male and 48 female eyes in the dataset. There were 80 BANG and 9 KDB goniotomies. We included glaucomatous patients of all stages, and 79 eyes were diagnosed with primary open-angle glaucoma (POAG). At 3 years post-op, the average IOP reduction was found to be 7.3%. However, when patients were split into two groups based on pre-op IOP (Group 1: IOP≤15, Group 2: IOP>15), Group 1 saw an 8.4% increase in IOP (p=0.999) and Group 2 saw a 19.5% decrease in IOP (p=0.001). VA also saw an improvement overall.

**Conclusions:** There was a statistically significant reduction of IOP in Group 2, but the IOP changes in Group 1 were clinically small and insignificant. Therefore, those who have a pre-op IOP of greater than 15 will likely have greater benefit from the studied goniotomy procedures. Further analysis of more diverse patient demographics should be conducted to solidify these results.

## **Analysis of Amyloid Beta Plasma Biomarkers in Intensive Care Unit Delirium Survivors**

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**Background:** Intensive care unit (ICU) delirium occurs in up to 70% of patients with 20-40% later developing dementia post-discharge. Plasma amyloid-beta (Aβ) levels have been associated with Alzheimer's Disease. Whether ICU delirium compared to subsyndromal delirium (SSD), a less severe form of delirium, is associated with higher plasma Aβ levels at hospital discharge is not well described.

**Methods:** This is a secondary analysis of the IMPROVE randomized controlled trial. Subjects were ICU delirium survivors aged 50 years or older who provided venous blood samples at discharge. Delirium was assessed twice daily until discharge using Confusion Assessment Measurement in the ICU (CAM-ICU). Samples were analyzed using a Multiplex Luminex Assay (ThermoFisher); values were reported in pg/mL and compared using the Wilcoxon Rank Sum Test using SAS.

**Results:** In total, 68 subjects were included, 45% experienced SSD, and 54% had delirium. The mean age in the SSD group was 63.7 years [SD 7.3] vs. 64.4 years [SD 7.1] in the delirium group ( $p=0.667$ ). The SSD group had a mean education of 13.6 years [SD 2.6] vs. 13.1 years [SD 2.3] ( $p=0.441$ ) in the delirium group. Median plasma A $\beta$ 1-40 levels were 200.55 pg/mL (IQR 137.76, 286.57) in the SSD group, and 189.35 (IQR 150.38, 283.00) in the delirium group. The median plasma values of A $\beta$ 1-42 were 0.02 (IQR 0.02, 0.72) for the SSD group and 0.67 (IQR 0.02, 1.85) for the delirium group. There were no significant differences in plasma levels between the two groups (A $\beta$ 1-40:  $p=0.936$ ; A $\beta$ 1-42:  $p=0.178$ ).

**Conclusions:** There were no significant differences in plasma A $\beta$  levels between ICU delirium and SSD. Further studies are needed to explore the relationship between delirium and plasma A $\beta$  levels.

### Decreased Risk of Cardiac and Vascular Complications in Patients with Alpha-1-Antitrypsin Deficiency

Adele Hemmerlein, Michael Roscoe

**Background:** Alpha-1-antitrypsin deficiency (AATD) is a genetic disorder characterized by low levels of the anti-protease Alpha-1-antitrypsin protein (AAT) within blood. In AATD, research has shown misfolded AAT accumulates within the liver and poorly controls protease activity in the lungs, resulting in liver and lung sequela. AATD's impact on cardiac and vascular health is far less researched and conflicting data has emerged. This study aims to determine if AATD's possible protective role against cardiac and vascular complications is consistent between the COSY-CONET and RWEdataLab's databases.

**Methods:** The IU School of Medicine-Evansville RWEdataLab (CRC/Sidus Insights) psychiatric and cardiac databases were used to select two groups for comparison: patients with AATD and patients without AATD with a diagnosis of COPD, emphysema, or chronic bronchitis, all without a history of lobectomy or lung or liver transplant or malignancy. Differences in diagnosis history were compared using odds ratios.

**Results:** Comparing 879 AATD patient's diagnoses against 3489 non-AATD patients with lung condition's diagnoses within the psychiatric database shows a protective role in both vascular and cardiac health with the following odds ratios and respective 95% CIs: 0.501 (0.325-0.771) for cerebrovascular accident, 0.499 (0.430-0.579) for hypertension, 0.377 (0.289-0.494) for chronic heart failure, 0.442 (0.273-0.714) for myocardial infarction, 0.490 (0.398-0.605) for coronary artery disease, and 0.742 (0.589-0.935) for peripheral artery disease. Similar searches were performed

in the cardiac database, but too few AATD patients were found to perform calculations with statistical significance.

**Conclusion and Implications:** These findings suggest that AATD may have a protective role in cardiac and vascular health. The mechanism behind these findings is unknown and may highlight an area of potential future study. Additionally, further research is needed to determine if AAT augmentation therapy is affecting this protective aspect.

### 6-Month Retrospective Review of Level I Trauma Center Referrals within a Regional Healthcare System

Adhitya Balaji, Thomas Lardaro

**Background:** It is often difficult for EMS providers to determine when patients should bypass a lower level of care to proceed to a higher level of care, such as a Level I trauma center (TC). This poses challenges for emergency medical services (EMS) system oversight in determining the most appropriate destination for the transport of injured trauma patients when trauma centers are in close geographic proximity. This study aims to understand trauma referral patterns within a regional healthcare system to better inform EMS resource deployment of both 9-1-1 and interfacility (IFT) assets in the care of trauma patients.

**Methods:** This retrospective case-series focused on a 6-month review from May 2022 through November 2022 of trauma patients brought to a Level III TC with a subsequent transfer to a Level I TC. Length of stay, patient diagnoses, interventions, and dispositions were gathered from the patient records at both TCs for further assessment. Data, including interventions and vital signs, from the 9-1-1 and interfacility EMS records were also utilized when patient care was performed by the hospital-based EMS agency.

**Results:** This review found that the primary reason for transferring to the Level I TC was due to the need for specialty services, such as neurosurgery and pediatrics, which are not readily available at the Level III TC. 9-1-1 patient encounters for patients transferred to the Level I TC from the Level III TC tended to have declining blood pressure and Glasgow Coma Scale over their continuum of care. One patient required CPR during interfacility transport and eventually died at the Level I TC emergency department.

**Conclusion:** Understanding trauma center referrals within a regional healthcare system can help inform resource deployment for both the 9-1-1 operations and interfacility transfer of trauma patients, potentially identify prehospital indicators for eventual transfer to a Level I trauma center, and subsequently advise expedited transfer to definitive

care.

### **FNA diagnosis of secondary malignancies in the parotid gland: over 20 years of experience from a single institute**

**Aditya M Bhatt**, Hector Mesa, Shaoxiong Chen, Brent Molden, Tieying Hou

**Background:** Metastatic solid tumors account for a significant portion of malignancies in the parotid gland. Fine-needle aspiration (FNA) is a primary tool to diagnose these tumors.

**Methods:** We retrospectively reviewed 134 FNA cases of metastatic solid tumors affecting the parotid gland, spanning from 2000 to 2023 at our institute. We summarized the medical histories, cytology diagnoses, correlations with surgical resections, clinical treatments, and follow-up outcomes.

**Results:** The patient cohort included 107 male and 27 female patients, with a median age of 71 years (range: 4-96 years). Eighty-five percent of metastases (113 of 134) originated from head and neck (H&N) malignancies, comprising 66% from cutaneous sources and 19% from mucosal sites. The most frequent primary sites outside the H&N were lung (4%), kidney (2%), and non-H&N skin (2%). Sixty-eight percent of metastases (92 of 134) were squamous cell carcinoma (SqCC) including 61% conventional type and 7% human papillomavirus-related SqCC. Melanoma is the second most common metastatic malignancy (28 of 134, 21%). The median time from primary diagnosis to metastasis was 10 months (range: 0 to 132 months). During clinical follow-up, 59 (44%) patients died from the disease in a median follow-up of 10 months (range: 2 to 56 months).

**Conclusions:** This study represents one of the largest series of secondary malignancies in the parotid gland collected from a single institution. Most of these tumors are metastases from H&N malignancies, with cutaneous SqCC being the most prevalent primary site and histology. Accurate diagnosis relies heavily on clinical history, morphologic evaluation, and ancillary studies.

### **Reducing Death Anxiety: The Impact of Advanced Care Planning**

**Adrienne Ceruti**, Kendra Hollenbeck, Brian Henriksen

**Background:** Advanced care plans (ACP; e.g. living wills, DNR, post forms) enable patients to outline their wishes for medical care in the event they are unable to make medical decisions for themselves. Little research has been done on how completion of these forms or how conversations surrounding end-of-life (EOL) care impact on a patient's feelings about anxiety and death. We hypothesized that

patients with ACPs would have significantly lower anxiety about death.

**Methods:** We performed an IRB approved cross-sectional study of 101 patients 40 years of age and older utilizing a 17 question survey called the Scale of Death Anxiety (SDA). The survey was graded on a 5-point Likert scale. Patients were stratified into two cohorts (Cohort 1 included 40-64 y/o and cohort 2 included 65 y/o and older). We used Mann-Whitney U to compare responses between patients with ACPs and those without, as well as patients who have had EOL conversations and those who have not. Chi-squared tests to compare ACP status and EOL conversation status between cohorts. An alpha of 0.05 was used for significance.

**Results:** Intra-cohort comparisons of SDA responses based on ACP completion status showed no significant difference in anxiety levels for both cohorts. Comparison of ACP status stratified by cohort showed no significant difference in anxiety levels.

**Conclusion:** Although our current findings do not support that ACP completion directly reduces death anxiety, it remains imperative to have EOL conversations with patients. This allows them the opportunity to outline their wishes for EOL care and ultimately reduces hospitalizations and burdens on the patient's family support system.

### **A Systematic Review of Therapeutic Interventions for Atopic Dermatitis Affecting the Lips (Atopic Cheilitis) in Adults: Efficacy, Safety, and Emerging Paradigms**

**Albab Uddin**, Faseeh Khan

**Background:** Atopic dermatitis (AD) affecting the lips, or atopic cheilitis, is a localized manifestation of AD that significantly impacts quality of life through pain, functional impairment, and psychosocial distress. Despite its clinical importance, treatment guidelines specific to lip involvement are lacking.

**Objective:** This systematic review evaluates the efficacy, safety, and outcomes of established and emerging therapies for atopic cheilitis in adults while identifying gaps in current knowledge to inform future research.

**Methods:** A comprehensive search of MEDLINE, EMBASE, Web of Science, Scopus, and Cochrane CENTRAL was conducted through September 2024. Studies included randomized controlled trials (RCTs), cohort studies, retrospective analyses, and case series involving adults with lip-specific AD. Data on interventions, outcomes, and adverse events were synthesized narratively.

**Results:** Of 47 included studies, topical corticosteroids

(TCS) and calcineurin inhibitors (TCIs) demonstrated short-term improvements in erythema, fissures, and pruritus, though relapse was common upon discontinuation. Biologics, particularly dupilumab, showed significant and sustained symptom improvement in severe cases, with favorable safety profiles. Janus kinase (JAK) inhibitors, such as upadacitinib, were effective in reducing inflammation and pruritus, but limited data on lip-specific outcomes were available. Barrier repair strategies, including ceramide-rich emollients, provided adjunctive benefits but were insufficient as standalone treatments. Allergen avoidance and psychosocial interventions (e.g., mindfulness) were explored in small studies, with mixed outcomes. The lack of validated lip-specific severity measures hindered standardized assessments across studies.

**Conclusions:** Both conventional topicals and newer systemic agents like biologics and JAK inhibitors offer potential benefits for atopic cheilitis, particularly in refractory cases. However, the evidence base is limited by study heterogeneity and the absence of standardized lip-focused outcome tools. Future research should prioritize the development of validated severity indices, long-term safety data, and targeted trials to improve therapeutic strategies for this unique manifestation of AD.

### **Incremental Value of Left Atrial Strain in the Identification of Patients Requiring Readmission with Heart Failure**

**Alex Buchanan,** Constance Adams, Scott Mattson

**Background:** Heart failure (HF) is a leading cause of hospital readmissions, increasing adverse events and straining finances. Research claims many readmissions are preventable, yet there has been little change in readmission rates. Left atrial (LA) volume can estimate heart health and correlates with readmissions and death. However, it is a poor predictor because it is a delayed anatomic change. Left atrial reservoir strain (LARS) occurs during systole and is highly responsive. It reflects left ventricular systolic and diastolic function and correlates with adverse outcomes. However, clinical applications are poorly understood.

**Methods:** 412 IU Health patients with HF were identified between January 1st, 2023, and March 31, 2024. 271 patients were analyzed; multiple readmissions resulted in 275 admissions total. Exclusion criteria included age under 18 years, dialysis, missing echocardiogram, hospice discharge, or death during hospitalization. HF data was extracted; automated LARS calculation was performed via TomTec. Of the 271 patients, LARS data was calculated for 120; 7 patients were excluded due to poor image quality. 15 healthy patients were randomly selected as controls. A cardiologist performed manual corrections when needed.

**Results:** Age ( $p=0.002$ ) and BSA ( $p=0.048$ ) were correlated

with adverse events. LA volume index was significantly different between conditions ( $p=0.005$ ). Creatinine levels ( $p=0.002$ ) and eGFR ( $p<0.001$ ) had significant differences between groups. LARS showed a significant difference between HF groups ( $p<0.05$ ), while ejection fraction (EF) did not ( $p=0.07$ ).

**Conclusions:** Current measurements such as EF demonstrate limitations in identifying HF patients at higher risk for adverse events. LA volume was correlated with adverse events, reinforcing the relevance of the LA. LARS showed significant differences between HF groups, suggesting that it may add clinical value to patient assessments. Limitations included a broad inclusion criteria and lack of independent data verification. Future directions will be the continued analysis of LARS with readmissions.

### **Effects of Gabapentin and the $\alpha 2\delta 1$ Voltage-Sensitive Calcium Channel Subunit in Skeletal Muscle**

**Alexander Buttars,** Jung Min Hong, Meloney Gregor, Eliza Day, Julia Hum, Joshua Huot, William R. Thompson

**Background:** Gabapentin (GBP) is an approved analgesic for neuropathic pain and is prescribed to millions of Americans. GBP exerts its effects by modulating calcium influx ( $Ca^{2+}$ ) via voltage-sensitive calcium channels (VSCCs) by GBP binding to the auxiliary  $\alpha 2\delta 1$  subunit. The analgesic effects of GBP are attributed to decreased  $Ca^{2+}$  signaling in neurons; however,  $Ca^{2+}$  signaling modulates a variety of other functions, including many within skeletal muscle. While muscle dysfunction is a commonly reported side effect of GBP, the direct effects of GBP on muscle have not been reported. We hypothesized that GBP treatment and deletion of the  $\alpha 2\delta 1$  subunit impairs skeletal muscle function by disrupting transmission at the neuromuscular junction (NMJ).

**Methods:** Heterozygous breeder pairs for *Cacna2d1*, the gene encoding the  $\alpha 2\delta 1$  subunit protein, were used to generate WT and KO mice that were confirmed by genotyping. Eighteen males (9 WT, 9 KO) and 11 females (6 WT, 5 KO) were tested. The Aurora Scientific Muscle Contractility System was used to determine maximum torque, rate of contraction, rate of relaxation, and fatigue of the plantar flexors. Compound muscle action potentials (CMAPs) and single motor unit potentials (SMUPs) were recorded to obtain motor unit number estimates (MUNEs). *Ex vivo* samples were collected for qPCR analysis to assess NMJ homeostasis. In the GBP experiment, 16 male WT mice received either 150 mg/ml GBP or vehicle twice per day per os ( $n=8$  mice/drug group). All mice underwent the same procedure as previously stated at weeks 0, 2, and 4. QPCR analysis was performed on *ex vivo* samples.

**Results:** Deletion of  $\alpha 2\delta 1$  in males resulted in decreased plantarflexion torque ( $p<0.001$ ), max rate of contrac-

tion ( $p < 0.001$ ), max rate of relaxation ( $p < 0.01$ ), SMUP ( $p < 0.001$ ), and MUNE ( $p < 0.01$ ). In females, there were decreases in plantarflexion torque ( $p < 0.01$ ) and max rate of contraction ( $p < 0.05$ ). QPCR analysis of male  $\alpha 2\delta$  KO showed decreased Hspg2 ( $p < 0.01$ ) and Musk ( $p < 0.05$ ) expression. No significant results were seen in females. Treatment with GBP showed decreased max-torque ( $p < 0.01$ ), rate of contraction ( $p < 0.001$ ), rate of relaxation ( $p < 0.01$ ), and SUMP ( $p < 0.001$ ). QPCR analysis showed significant decreases in Hspg2 ( $p < 0.05$ ), Lrp4 ( $p < 0.05$ ), Agrin ( $p < 0.01$ ), and Chrnc ( $p < 0.01$ ) expression.

**Conclusions:** As GBP is a widely used neuropathic pain drug, understanding the consequences of chronic use on musculoskeletal tissues is of utmost importance. The data demonstrates that GBP treatment and KO of  $\alpha 2\delta 1$  significantly decreased muscle performance within a mouse model. This data and future research on GBP and other gabapentinoids will help clinicians carefully consider if potential side-effects outweigh analgesic benefits in their patients.

### Exploring the Impact of Plasmin Inhibitors on Clotting Characteristics as a Novel Therapeutic for Thromboembolic Events

**Alexandra Cranston**, Abigail Hall, Anushri Umesh, Nathan J. Alves

**Background:** Thromboembolisms are common, life-threatening emergencies. Systemic hemorrhaging post-thrombolytic treatment is an adverse reaction, highlighting the need for safer clot-digesting therapeutics. Our research focuses on an endogenous fibrinolytic enzyme, plasmin. We investigated how co-delivery of plasmin and pentamidine, a reversible bivalent plasmin inhibitor, impacts clotting and thrombolysis. Plasmin and pentamidine delivery were tested across ex-vivo stagnant viscoelastic assays (thromboelastography, TEG) and shear-based clot formation and digestion assays (Chandler Loop). This research aims to optimize safer clot-digesting therapeutics that minimize adverse bleeding.

**Methods:** Consenting healthy volunteers ( $n = 13$ ) donated whole blood into citrated tubes using an approved IRB protocol. Whole blood was analyzed via Chandler Loop (20 RPM at 37C for 60min) and TEG (37C for 90min). Pentamidine (0-800 $\mu$ M) and plasmin (0-0.1mg/mL) were tested independently and mixed measuring: clot mass, clot strength (MA), R-time, angle, and K.

**Results:** At increasing pentamidine concentrations, R-time and K increased while MA, angle, clot weight, and clot length decreased. At increasing plasmin concentrations, R-time, K, and angle remained unchanged while MA, clot weight, and clot length decreased. Concentrations  $> 700\mu$ M pentamidine and  $> 0.1$ mg/mL plasmin inhibited clotting. In

the presence of fixed pentamidine (50 $\mu$ M in TEG, 200 $\mu$ M in Chandler), the initial impact to clot formation resembled 50 $\mu$ M of pentamidine alone followed by limited impact at increasing plasmin concentrations with a flat decrease in clot MA (18.3%), clot length (19.5%), and clot weight (18.9%) and increase in R-time (43.4%) and K (50.6%).

**Conclusions:** Increasing plasmin concentrations results in increased clot digestion while increasing pentamidine concentrations functions more akin to an anticoagulant preventing clot formation. Co-administered plasmin with pentamidine demonstrates how an inhibitor can be used to deliver an active clot digesting enzyme. Leveraging the results presented herein, and the principles of multivalency, plasmin inhibitory molecules can be developed to create safer and more effective direct fibrinolytics for clinical use.

### Food Insecurity: An Upstream Social Determinant of 30-Day Congestive Heart Failure Readmissions

**Alison Blodgett**, Jonathan Guerrero, Baraka Muvuka

**Background:** Approximately 6.7 million Americans have congestive heart failure (CHF), costing the healthcare system over \$30 billion annually. Readmissions contribute significantly to these costs, as 20-25% of hospitalized CHF patients are readmitted within 30 days of discharge. The Hospital Readmissions Reduction Program monitors 30-day readmission rates and penalizes hospitals that do not meet targets. Previous research on factors impacting CHF readmissions has largely focused on downstream factors, such as clinical practices, patient health characteristics, income level, and insurance type, rather than upstream factors that can potentially inform high-impact interventions. This study explored downstream, midstream, and upstream factors—including demographics, social determinants of health (SDOH), and health behaviors—and their relationship with 30-day CHF readmissions in an urban healthcare system in Northwest Indiana. This project is part of an academic-health system participatory research partnership.

**Methods:** This retrospective study analyzed a limited dataset from EPIC™ with SDOH, demographic, health behavior, and health outcomes of adult inpatients between January 2021 and April 2024. Data analysis consisted of descriptive, bivariate (Chi-Square;  $p < 0.05$ ), and multivariate (Binary Logistic Regression;  $p < 0.05$ ) analyses in SPSS 29.0. This study was exempted by the Indiana University Human Research Protection Program (IRB #14040).

**Results:** The sample consisted of 5,489 patients with CHF, predominantly White (63.8%), 65+ years old (76.2%), and publicly insured (91.8%). 30-day readmissions represented 22.4% of CHF admissions. The bivariate analysis revealed significant associations between 30-day CHF readmissions and ethnicity ( $p = .003$ ), sex ( $p = .046$ ), language ( $p = .017$ ), hospital ( $p = .009$ ), insurance type ( $p = .003$ ), food

insecurity ( $p=.048$ ), and depression risk ( $p=.003$ ). Food insecurity remained significantly associated with 30-day CHF readmission ( $OR=2.128$ ;  $p=.033$ ) after adjusting for these factors in the multivariate analysis.

**Conclusion:** This study identified food insecurity as an upstream SDOH predicting 30-day CHF readmission. Future research should further explore other upstream factors contributing to 30-day CHF readmissions and evaluate evidence-based food insecurity interventions.

### **Severe Malnutrition: Is All Severe the Same?**

**Alison Hannon**, Kanika Puri, Charles Vanderpool

**Background:** The Academy of Nutrition and Dietetics and American Society for Parenteral and Enteral Nutrition have published two sets of criteria to diagnose a patient with mild, moderate, or severe malnutrition that use either single or multiple data points. Malnutrition is associated with worse clinical outcomes, and previous data showed that hospitalized children with severe malnutrition are at higher risk for mortality compared to mild and moderate malnutrition. This project aims to determine if differences in clinical outcomes exist in patients with severe malnutrition based on the cause or diagnostic criteria of severe malnutrition.

**Methods:** Analyzed patients discharged from Riley Hospital for Children within the 2023 calendar year diagnosed with severe malnutrition. Data was collected on readmission rates, mortality, length of stay (LOS), LOS index, cost, operative procedures, intensive care unit (ICU) admissions, reasoning and evidence for malnutrition, and anthropometrics.

**Results:** Data was gathered on 409 patients. 55% of patients were diagnosed with severe malnutrition based on multiple point indicators, while 31% were diagnosed with single point indicators. 14% of patients met criteria for both single and multiple point indicators. General trends seen on initial evaluation of data suggest that potential differences exist in LOS, LOS index, cost, and readmission rates based on indicator-type for severe malnutrition. Average ICU days, LOS, cost, and readmission rates were higher in patients diagnosed with only multiple point indicators. There were 8 cases of mortality seen, and 7 of these occurred in patients diagnosed with multiple-point indicators of severe malnutrition.

**Conclusion:** Further statistical analyses to determine association and clinical significance of outcomes seen based on indication of severe malnutrition will help to highlight the role of malnutrition in pediatric admissions, identify patients with severe malnutrition at a higher risk of undesired hospital outcomes, and guide outpatient follow-up for patients at highest risk of readmission.

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### **Characteristics of Hoosier Moms Cohort Participants for different Diabetes Polygenic Risk Score Quartiles**

**Allison Ellis**, Maha Aamir, Surya Bhamidipaty-Pelosi, Aric Kotarski, Rafael Guerrero, David M. Haas

**Background:** Gestational Diabetes (GDM) increases the risk of adverse perinatal outcomes. Understanding genetic-based risk for GDM is important for clinical risk prediction. The objective of this study was to examine participant characteristics in different polygenic risk score (PRS) quartiles in a study cohort of people at high risk for GDM.

**Methods:** This was a prospective observational cohort study of pregnant individuals. 411 Participants with a singleton gestation were recruited and had samples obtained for DNA analysis. PRS for diabetes was calculated for the cohort via PLINK v1.9 with 582 markers from Polfus et. Al. Continuous variables were analyzed via ANOVA, and categorical variables were analyzed via Chi-square to examine participant differences by PRS risk quartile, with quartile 1 (Q1) at lowest genetic risk and quartile 4 (Q4) at highest genetic risk.

**Results:** Compared to individuals in Q1, those in Q4 had a higher percentage of individuals who self-identified as Hispanic ethnicity ( $p=0.015$ , 9% Q1, 29.2% Q4) and self-reported minority race ( $p<0.001$ , 3% Q1, 68% Q4). Participant education attainment was lower in Q4 ( $p=0.02$ ). HbA1c was higher in Q4 ( $p=0.007$ , 5.05 Q1, 5.18 Q4). Cholesterol levels were higher in Q1 ( $p=0.025$ , 201.65 Q1, 187.88 Q4), along with LDL levels ( $p=0.037$ , 105.91 Q1, 96.46 Q4) and emotional eating ( $p=0.002$ , 25.81 Q1, 19.38 Q4).

**Conclusion:** We found that the highest PRS diabetes risk group were more likely to self-report being Hispanic or a non-White race. However, cholesterol and LDL levels were higher in Q1. These preliminary findings exploring PRS risk group characteristics, if replicated, may help clinicians understand how to stratify genetic-based GDM risk using only clinical characteristics.

### **Addition of Misoprostol to Double-Balloon Catheter for Cervical Ripening Associated with Improved Obstetric Outcomes**

**Allison Li**, Kevin Moss, Sarah Carpenter

**Background:** If induction of labor (IOL) is indicated but the cervix is deemed unfavorable, cervical ripening agents like mechanical dilators and synthetic prostaglandin E1 medications can be used. The objective of this study was to compare labor outcomes of women who underwent cervical ripening with a double-balloon catheter alone or with the addition of concurrent misoprostol. We hypothesized

that concomitant use of misoprostol and cervical ripening balloon (CRB) was associated with increased vaginal delivery rates compared to CRB use alone.

**Methods:** We conducted a retrospective cohort analysis consisting of patients who underwent IOL with CRB at Eskenazi Hospital. Comparison between the two cohorts was done using a chi-square/ Fishers' exact test for the categorical variables and t-test for the continuous variables

**Results:** A total of 134 patients were analyzed in the cohort, with 82 receiving concurrent misoprostol and 52 not receiving any additional pharmaceutical agents. Patients who received misoprostol and CRB had higher vaginal delivery rates (84.2% vs. 51.9%,  $p < 0.01$ ), decreased estimated blood loss (EBL) (388.0 vs. 592.1 mL,  $p = 0.01$ ), and were not more likely to be given terbutaline (90.2% vs. 75%,  $p = 0.02$ ) compared to patients treated with CRB alone. There were no differences in neonatal outcomes (NICU admission, birth weight, or 5-min APGAR scores) or occurrence of uterine tachysystole between the cohorts. The multivariate analyses showed similar trends, although additional medication, medication use before balloon placement, advanced maternal age, and terbutaline use were not strong independent predictors of the vaginal delivery rate.

**Conclusions:** We found that concurrent use of misoprostol and CRB during IOL was associated with increased vaginal delivery rate and decreased EBL when compared with patients who had CRB alone. Potential impacts of this study include providing evidence-based recommendations on cervical ripening practices as well as guiding future studies investigating the possible benefits with standardization of IOL practices.

### **Long Term Effects of Transient Romidepsin Exposure on Osteosarcoma Sarcospheres**

**Alyssa Walker**, Emily Seiden, Piper Wilburn, Ed Greenfield

**Background:** Osteosarcoma, the most prevalent primary bone cancer, disproportionately affects adolescents and young adults. Despite aggressive chemotherapeutics, prognosis remains poor, highlighting the need for novel therapeutics. Romidepsin, a histone deacetylase inhibitor, emerged as exceptionally potent and minimally toxic in our screen of 114 FDA-approved oncology drugs using three-dimensional osteosarcoma spheroids (sarcospheres). Due to the genetic complexity of pathogenesis, differences in sensitivity exist across cell lines and patient samples. Understanding the mechanism of romidepsin is crucial for determining predictability of treatment response, especially considering its short half-life and weekly administration regimen.

**Methods:** Sarcospheres derived from established cell lines

(LM7, MG63.3, and 143B) or patient samples (TT2) were exposed to various concentrations of romidepsin for 24 hours. Metabolic activity was measured by resazurin reduction assays at multiple timepoints following romidepsin removal.

**Results:** Effects of transient romidepsin exposure last at least 14 days. TT2 and LM7 sarcospheres do not increase in size over 48 hours of culture, and recovery is prevented at clinically achievable levels. In contrast, 143B and MG63.3 sarcospheres show growth over 48 hours and romidepsin blocks this growth. For these sarcospheres, concentrations above clinically achievable levels are required to prevent recovery.

**Conclusions:** Romidepsin is FDA-approved for weekly administration in lymphoma. Effects caused by transient exposure to romidepsin persisted for 14 days in slow growing patient-derived sarcospheres, suggesting weekly administration is likely sufficient for patients with osteosarcoma. Results of this study are consistent with our previous findings that there are two types of responses to romidepsin. Romidepsin causes a G2 cell cycle block and growth inhibition in 143B and MG63.3 sarcospheres, while it causes DNA damage and cell death in LM7 and TT2 sarcospheres. Further exploration of these mechanistic differences has the potential to personalize medicine by providing better predictability of response to treatment and insight into prognosis.

### **Difficult Cannulations in Neonatal and Pediatric ECMO: Illuminating an Obstruction to Timely Therapy**

**Amanda Wissmann Klage**, Michael Sobolic, Brian Gray

**Background:** ECMO is a vital intervention for neonatal and pediatric patients requiring cardiorespiratory support, yet unanticipated difficulties with peripheral cannulation can hinder timely therapy. Research concerning challenging cannulations is limited, and protocols guiding surgeons to consider alternative approaches in cases of potential difficulty are lacking. The purpose of this study was to identify reasons for cannulation difficulty and pinpoint predisposing diagnostic, anatomical, and operative features of this population.

**Methods:** We conducted a single-center, five-year retrospective review of neonatal and pediatric patients encountering challenging peripheral cannulations or multiple cannulations for ECMO. Variables included patient demographics, ECMO indications, prior cannulation attempts, surgical challenges encountered, alternative vascular anatomy, and outcomes from cannulation to discharge.

**Results:** An analysis of 65 cannulations (38 subjects, me-

dian cannulations per subject=1, range 1-4) revealed that venous cannulations posed challenges more often (n=28) than arterial cannulations (n=11). Intraoperative cannulation challenges were predominantly attributed to small vessel size (43.5%) and unspecified catheter advancement obstructions (23.1%). A substantial proportion of patients in this cohort exhibited congenital heart anomalies (81.6%), and 50.8% of cannulations occurred in the setting of post-procedural support, often post-cardiotomy. Alternate neck or groin vascular anatomy was identified in 19 cannulations. The rate of unsuccessful peripheral cannulation was 20.5% (n=8) and patient mortality associated with difficulty cannulating onto ECMO was 15.4% (n=6).

**Conclusions:** These findings suggest that neonatal and pediatric patients with congenital heart anomalies or a history of recent surgery may face an increased risk of challenging cannulations and poorer ECMO outcomes. Pre-operative neck and groin ultrasound could help surgeons better anticipate and address difficulties like small vessel size or obstruction. Early evaluation of risk factors for challenging cannulations will enhance surgical decision-making regarding cannulation approach and ultimately improve outcomes for children requiring ECMO.

### Investigating the Role of 11,12-DHET in Dendritic Cell Differentiation

**Amber Nelson,** Jeffrey C. Bloodworth, Joan Cook-Mills

**Background:** Dihydroxyepoxyeicosatrienoic acids (DHETs) are lipid signaling molecules that play a role in immune function. Specifically, 11,12-DHET has been linked to the regulation of dendritic cell (DC) development, a process vital for initiating immune responses. DCs are key antigen-presenting cells that activate T cells, crucial for adaptive immunity. Exploring how 11,12-DHET affects DC maturation and function is important for understanding its potential in immune regulation and therapeutic applications.

**Methods:** Bone marrow was harvested from 4-week-old mice and cultured in two groups: a control group receiving GM-CSF with ethanol (EtOH), and an experimental group receiving GM-CSF with 11,12-DHET in EtOH. After culturing, cells were stained for flow cytometry, including intracellular IRF4 staining. The DCs were analyzed for differences in generation, maturation, and MHC II expression to assess the effects of DHET on DC development.

**Results:** This project revealed intriguing findings, with the vehicle (EtOH) group demonstrating a greater presence of distinct dendritic cell (DC) subsets, such as alveolar-like cDCs, IRF4+ alveolar-like cDCs, IRF4+ resident-like cDCs, CD103+ alveolar-like DCs, and IRF4+ CD103+ alveolar-like DCs, compared to the group treated with 11,12-DHET. These outcomes indicate that the effects of

11,12-DHET on DC differentiation may be more complex and context-dependent than initially thought. This complexity suggests a nuanced role for DHET in modulating immune responses, warranting further investigation into its specific regulatory mechanisms.

**Conclusions:** The unexpected findings suggest that 11,12-DHET influences dendritic cell differentiation in a complex and context-dependent manner. Understanding these nuanced effects could offer new insights into immune regulation and potential therapeutic strategies for managing immune-related conditions. Further research is necessary to elucidate the specific mechanisms by which DHETs modulate dendritic cell function.

### Pathogenesis of White Matter Hyperintensities in Alzheimer's Disease: Evidence from Postmortem Tissue Studies

**Ammaar Basher,** Yomna Takieldeen, Yu-Chien Wu

**Background:** White matter hyperintensities (WMHs) are commonly observed in elderly brains and more pronounced in Alzheimer's disease (AD) patients. Visible on MRI scans, these lesions are linked to cognitive decline, functional impairment, and accelerated disease progression. Despite their prevalence, the pathophysiological mechanisms underlying WMHs remain poorly understood. Initially considered a byproduct of vascular risk factors, recent research indicates a complex etiology involving AD-specific pathology. This review summarizes existing research on postmortem pathology of WMH in AD.

**Methods:** A comprehensive literature review was conducted using OVID Medline with the terms "white matter hyperintensit\*", "autopsy", "postmortem changes", "white matter", and "hyperintensit\*". From 17 initial papers, 10 met the inclusion criteria after abstract screening. An additional 16 papers were identified through references, resulting in a total of 26 papers for final review and analysis.

**Results:** The review indicated that in AD, WMHs were associated with gliosis, myelin pallor, axonal loss, and macrophage infiltration. Occasional vascular pathologies such as collagenosis were noted. Concomitant cerebral amyloid angiopathy in AD was linked to higher WMH burden. WMHs were also associated with deep nuclei microinfarcts, arteriosclerosis, and amyloid- $\beta$  plaques. A strong correlation was found between WMHs and AD-related neuropathological changes, including Braak neurofibrillary tangle stages and neuritic plaques. AD cases showed higher WMH burden in parieto-occipital regions compared to frontotemporal lobar degeneration with tdp-43 (FTLD-TDP) cases. In studies which correlated MRI and histological findings, a correlation was found between diffusor imaging and histological evidence of WMH.

**Conclusion:** The pathology of WMHs in AD involves complex interactions between vascular, inflammatory, and neurodegenerative processes. Understanding WMH pathology in AD is the first step to potentially using these lesions as biomarkers for disease progression and therapeutic targets. Further research should investigate a broader range of pathologies, enhance longitudinal data collection, and correlate in vivo with postmortem imaging.

### **0.25% Bupivacaine vs 0.5% Bupivacaine: Comparisons of Local Anesthetic Regimens Used in Periacetabular Osteotomy**

**Amol Kular**, Yar Yeap

**Background:** Periacetabular osteotomy (PAO) is an incredibly painful surgical procedure to correct hip dysplasia resulting from a deformity in the acetabulum. Current protocols for controlling perioperative pain have no consensus and include the use of nerve blocks, lumbar epidural-based protocols, and local anesthetic wound infiltration. This study aims to gather information regarding the efficacy of 0.25% Bupivacaine versus 0.5% Bupivacaine in fascia iliaca nerve blocks.

**Methods:** A retrospective chart review was conducted encompassing PAO patients from June 2023 through June 2024. Patients were grouped according to concentration and volume of local anesthetic. Outcomes included pain scores in the post anesthesia care unit (PACU), 24-, 48-, and 72-hours post-operation, duration of hospital admission and use of opioid medications. The data were sorted by concentration and volume of Bupivacaine administered. Comparisons between pain scores of those receiving 0.25% and 0.5% Bupivacaine showed similar scores in the PACU and at 24 hours post-operation.

**Results:** At 48 hours post-operation, pain scores were significantly lower ( $p=0.052$ ) for the 0.5% Bupivacaine group (4.52) than the 0.25% Bupivacaine group (5.21). At 72 hours post-operation, pain scores were slightly lower ( $p=0.11$ ) for the 0.5% Bupivacaine group (3.91) than the 0.25% Bupivacaine group (4.62). The duration of hospital admission was similar. Analyzing pain scores by volume demonstrates that 40-60 mL of Bupivacaine had lower pain scores (average=4.15,  $p=0.060$ ) than those receiving 20-30 mL of Bupivacaine (average=5.22) in the PACU. Opioid usage at PACU, 24-, 48-, and 72-hour time frames showed similar milliequivalents of PO morphine needed when compared by concentration. Compared by volume, the 40-60 mL Bupivacaine group used more opioids at all time frames.

**Conclusions:** We conclude that if local anesthetic toxicity is not a problem, anesthesiologists should use 0.5% Bupivacaine 40 mL for fascia iliaca nerve blocks to provide patients with the maximum benefit from their regional

anesthesia.

### **Hammersmith Infant Neurologic Examination (HINE) in the Assessment of Infants with Dysphagia**

**Andrea Wright**, Emily Scott, Ryan Pitman

**Background:** Over the past several years, significant advancements have been made in the recognition and diagnosis of dysphagia. Intensive therapeutic interventions and diagnostic tools, such as the video fluoroscopic swallow study (VFSS), have been developed to assess and modify swallowing mechanics and ensure safe swallowing to promote growth in children diagnosed with dysphagia. Although there have been significant increases in improving dysphagia, there are minimal tools available to predict the timing of dysphagia resolution. Many children with dysphagia have impaired oromotor function and difficulty in mobilizing and clearing airway secretion. This is partly due to dyscoordination of the muscles involved in swallowing, which has been theorized to be related to reduced muscle tone. The Hammersmith Infant Neurological Examination (HINE) has been specifically designed and optimized to identify differences in motor tone and coordination in infant development. HINE is currently used in the diagnosis and prognosis of infants at risk for developing cerebral palsy (CP).

**Methods:** In this retrospective study 67 patients were examined using VFSS to assess if a lower HINE score is associated with longer resolution times for aspiration.

**Results:** Using this data, it was found that a HINE score below or above the CP cutoff score directly correlated with the recommendation of feeding (bottle modifications, thickening of liquid, or tube feeding) ( $p=0.018$ ). HINE scores were also utilized to demonstrate a linear regression model capable of predicting the approximate duration of dysphagia resolution ( $p=0.041$ ).

**Conclusion:** Future research can aim to develop a more comprehensive framework for the resolution of penetration and aspiration associated with dysphagia.

### **Towards Drug Repurposing for the Prevention of Suicidality**

**Andrew Gettelfinger**, Alexander B. Niculescu

Suicidality remains a clear and present danger in society in general, and for mental health patients in particular. Lack of widespread use of objective and/or quantitative information has hampered treatment and prevention efforts.

Suicidality is a spectrum of severity from vague thoughts that life is not worth living, to ideation, plans, attempts, and completion. Blood biomarkers that track suicidality risk provide a window into the biology of suicidality, as well as could help with assessment and treatment, and may give us greater insight of the specific physiology involved in suicide. Ongoing research in the Niculescu Alb has identified mRNA biomarkers who track and predict suicidality. Computational methods were then used to identify drugs that cause opposing gene expression, in order to find currently marketed drugs that may have promise in the treatment of suicidality.

### **MRI Prediction of Surgical Treatment for Juvenile Osteochondritis Dissecans (OCD)**

**Andrew Puthran,** Deva Chan, Christopher Newman

**Background:** Juvenile osteochondritis dissecans (OCD) is an abnormality of joint cartilage and its underlying bone. It is a leading cause of joint pain in children (affecting approximately 1 in every 1,000 children) and predisposes patients to early osteoarthritis and osteonecrosis. Its precise cause remains unknown, though repetitive trauma and multiple other factors have been implicated. Magnetic resonance imaging (MRI) aids patient management by assessing the mechanical stability of the bone and cartilage defects. Unfortunately, imaging criteria established for adults do not translate well to juvenile patients. This study aimed to determine whether quantitative analysis of standard MRI sequences of knee, elbow, and ankle joints could predict the need for surgery. The proposed hypothesis was that signal intensity could distinguish between those receiving conservative management and those requiring surgery.

**Methods:** Using pretreatment MRI sequences from the IU Health Radiology Information Systems, 41 skeletally immature patients with OCD were analyzed retrospectively to quantify the cartilage signal on standard anatomy (PD or T1) and fluid-sensitive sequences (STIR or T2 fat saturation). The entire cartilage portion of the lesion was quantified using manual segmentation (with signal intensity normalized to the opposite condyle as an internal control). Logistic regression assessed whether lesion signal intensity could discriminate surgical or non-surgical management with receiver operator characteristic (ROC) curves obtained to identify the optimal signal intensity threshold.

**Results:** Patients managed non-surgically had a mean corrected signal intensity of 1.093 on anatomy sequences and 1.303 on fluid-sensitive sequences, whereas the surgical patients had a mean corrected signal intensity of 1.148 on anatomy sequences and 1.528 on fluid-sensitive sequences.

**Conclusion:** Unfortunately, neither anatomy ( $p = 0.70$ ) nor fluid-sensitive sequences ( $p = 0.33$ ) could discriminate between surgical and non-surgical patients using logistic re-

gression. Likewise, signal intensity was not a good predictor of surgical stability in patients undergoing surgery in either anatomy sequences (ROC AUC = 0.472) or fluid-sensitive sequences (ROC AUC = 0.643). Future studies will assess signal intensity at individual joints. In addition, future studies will evaluate cartilage-specific clinical sequences to determine if quantitative cartilage analysis can improve diagnostic accuracy in these patients.

### **Exploring Health Equity Gaps in the Administration of Regional Anesthesia for Surgical Interventions: A Narrative Review**

**Angad Sidhu,** Marianne Matthias

**Background:** To identify and review relevant literature investigating racialized and ethnic disparities in the administration of regional anesthesia for patients undergoing surgical interventions. We also examined factors that may contribute to any observed differences in regional anesthesia receipt.

**Methods:** We used two main strategies to identify articles for this review. The first method was to use databases, such as PubMed, Embase, and Ovid MEDLINE, while the second method involved a manual search using reference lists of cited articles and known literature. From a total of 4,931 articles—title, abstract, and full-text review identified 26 articles that met the inclusion criteria for this review.

**Results:** Articles were identified and categorized based on related domains of surgical intervention type including breast, general, and orthopedic surgery, to identify any racialized and/or ethnic-based differences in administration of regional anesthesia. Additionally, articles examining the system- and patient-level factors associated with the receipt of regional anesthesia were identified and reviewed.

**Conclusions:** There is evidence for the presence of racialized and ethnic-based differences in the receipt of regional anesthesia for surgical interventions. Further research is required to better elucidate causes and potential avenues for intervention to address these disparities.

### **Evaluation of Murine Abdominal Aortic Aneurysms through Ultrasonography, Histology, and Scanning Electron Microscopy**

**Anish Bedi,** Cortland H. Johns, Niharika Narra, Luke E. Schepers, Claudia K. Albrecht, Craig J. Goergen

**Background:** Abdominal aortic aneurysms (AAAs) are the localized dilation and pathological weakening of the aortic wall resulting in complex flow patterns and compositional changes. In the US, the mortality rate due to ruptured AAAs is 80-90%. Moreover, rapid growth of AAAs is correlated with intraluminal thrombus (ILT) deposition,

with 75-90% of AAAs developing thrombus and increased rupture risk. There exists a need to understand the most common aortic pathology through various means. We hypothesize that different AAA imaging modalities can characterize different components of this condition using established murine models. The goals of this study were to elucidate the pathophysiological changes of AAA through novel imaging modalities and to ascertain the impact of ILT on vessel growth rates and blood flow patterns. This study aims to enhance understanding of AAA development and thrombus formation, informing improvements in diagnostic criteria and therapeutic strategies.

**Methods:** To induce aortic pathology, murine surgical intervention included topical elastase application over the infrarenal aorta with  $\beta$ -aminopropionitrile-infused drinking water to ensure sustained wall expansion. Ultrasound imaging was performed at 1- and 2-week intervals over 56 days to detect vessel expansion, thrombus deposition, and blood velocity. Ex vivo aortic samples were sliced, paraffin-embedded, and stained with Movat's pentachrome to examine thrombus composition. Scanning electron microscopy (SEM) was used to examine wall composition and RBC morphology within ILT+ samples. Statistical analysis was implemented using two-way ANOVA and Tukey's multiple comparison test.

**Results:** Ultrasound imaging revealed a significant increase in aortic diameter and rate of growth at 21 days post-surgery ( $p < 0.005$ ). Furthermore, ILT+ samples sustained significantly decreased blood velocity distal to the ILT ( $p < 0.0005$ ). Color segmentation of pentachrome staining revealed significant fibrin deposition ( $p < 0.001$ ), and SEM confirmed the organization of ILT as a multi-layer fibrin mesh.

**Conclusions:** This work established the use of ultrasound, SEM, and histology as means of evaluating the pathophysiology of AAAs. ILT deposition is correlated with the rate of AAA growth and is likely influenced by blood flow patterns. Furthermore, histology and SEM can be utilized to evaluate microscopic characteristics of ILT. Ultimately, these findings represent initial efforts to correlate thrombi formation with vessel dynamics in an experimental model of AAA.

### **Efficacy of Pharmacological Interventions to Treat and Prevent Alzheimer's Disease in Individuals with Down Syndrome**

**Anna Montelongo**, Viraj K. Patel, Emily E. Munn, Melissa M. Pangelinan

**Background:** Down syndrome (DS) is the leading genetic cause of early-onset Alzheimer's disease (AD) due to the triplication of the amyloid precursor gene on chromosome 21. In adults with DS, the symptoms of AD – rapidly

declining memory, ability to learn and communicate, and independent activities of daily living – begin in the 40s. Although many studies have evaluated the efficacy of interventions for AD in those without DS, only recently have studies investigated the efficacy of interventions to delay or prevent AD in DS.

**Methods:** This study focused on pharmacological interventions from a larger systematic review examining the efficacy of pharmacological and non-pharmacological interventions targeting AD-related cognitive symptoms in adults with DS.

**Results:** Eighteen studies were included with 1,118 participants (18-69 years). The analysis included twelve randomized controlled trials (RCTs), two non-RCTs, and four case studies. The pharmacological treatments included donepezil ( $n = 7$ ), memantine ( $n = 3$ ), epigallocatechin gallate (EGCG) ( $n = 1$ ), scyllo-inositol ( $n = 1$ ), serotonin reuptake inhibitors (SSRIs) ( $n = 1$ ), nicotine ( $n = 1$ ), acetylcarnitine ( $n = 1$ ), simvastatin ( $n = 1$ ), trazodone ( $n = 1$ ), and vitamin E ( $n = 1$ ). AD-related cognitive function was measured using cognitive test batteries that assessed several domains, including memory, executive function, and global cognition. Eight studies reported positive effects, five studies reported mixed effects, and five studies reported no effect. All donepezil trials yielded consistent positive effects, although the cognitive domains varied. There is preliminary evidence of trazodone, SSRIs, nicotine, and simvastatin efficacy. However, efficacy was not established for memantine, vitamin E, scyllo-inositol, acetyl-carnitine, and EGCG, with either mixed or no effects reported.

**Conclusions:** Donepezil is a promising pharmacological treatment for AD-related cognitive symptoms in adults with DS. Future RCTs are needed to verify efficacy and potential side effects of pharmacological interventions in the population.

### **Loss of Apolipoprotein E Results in Altered Aqueous Humor Lipidome and Reduced ERG Response in Mice**

**Anoop Magesh**, Reshma Magesh, Sutha K. John, Jungsu Kim, Padmanabhan P. Pattabiraman

**Background:** Elevated intraocular pressure (IOP) is a risk factor for primary open-angle glaucoma (POAG). Apolipoprotein E (APOE) is a cholesterol transport protein implicated with POAG risk. Preliminary data from the lab has shown that loss of APOE in-vivo has resulted in IOP elevation in mice. In this study, we aimed to elucidate APOE's role in IOP homeostasis and POAG pathology via lipid-mediated pathways and analyses.

**Methods:** Wild-type (WT) and ApoEtm1Unc knock-out homozygous (ApoE<sup>-/-</sup>) mice were used for this study. We performed: aqueous humor (AH) tap (13 mice) and shotgun lipidomics; pathway analyses using MetaboAnalyst 5.0; histology (6 mice) to validate knockout; electroretinogram (ERG) at three flicker intensities (-20, -10, 0 dB), comparing amplitudes of a and b-waves between WT and ApoE<sup>-/-</sup> mice using LKC Software EMWin 8.1 (n=4). Significance was conducted using Student's t-test for significance (p<=0.05) using GraphPad Prism 9.0.

**Results:** AH lipidomics showed significant lipid changes in ApoE<sup>-/-</sup> mice: elevated cholesteryl esters, ceramides, phosphoglycerides, and triglycerides, and decreased sphingomyelins and free fatty acids. Metabolic pathway analysis showed notable changes in mitochondrial  $\beta$ -oxidation and arachidonic acid metabolism pathways. ERG analysis showed reduced amplitude in ApoE<sup>-/-</sup> mice for both a-wave and b-waves at all intensities.

**Conclusions:** Our study indicates APOE plays a significant role in the aqueous humor lipidome in mice. Reduced ERG response patterns in ApoE<sup>-/-</sup> mice suggest a phenotypical insult to retinal subcomponents, possibly worsened by prolonged ocular hypertension. Monitoring ERG response progression with IOP changes in mice will help elucidate APOE's effects through future investigation. Additionally, the observed extracellular ceramide elevation in AH may contribute to age-related pathologies, warranting further investigation in TM outflow pathophysiology. Ongoing and future studies will aim to delineate the metabolic and physiological effects of APOE knockout in human TM tissue culture.

### **Phosphorylation-mediated Regulation of the Rubicon Interactome**

**Anslyn Freije**, Melissa Abt, Tinslee Dilday, Elizabeth Yeh

**Background:** HER2+ breast cancer uses the human epidermal growth receptor 2 (HER2) protein to grow. As an aggressive form of breast cancer, it accounts for ~20% of all breast cancer diagnoses worldwide. Previous studies show Hormonally Up-regulated Neu-associated Kinase (HUNK) is up-regulated in HER2+ breast cancer. HUNK plays an important role in the cellular process of autophagy, which recycles cellular components into new usable components. Increased autophagy, through HUNK activity, allows for improved survival and proliferation of cancer cells. Autophagy is mediated through a complex of proteins, including Beclin-1, HUNK, Rubicon, UVRAG, and Vps34. In this complex, Rubicon is responsible for the inhibition of autophagy. However, phosphorylation of Rubicon by HUNK inhibits this function, thus promoting autophagy. This phosphorylation of Rubicon is hypothesized to cause its dissociation from the autophagy proteins. To further un-

derstand this, we looked at the interaction of Rubicon with UVRAG and SQSTM1 in the presence and absence of HUNK, to validate this complex as a means for regulation of the Rubicon interactome.

**Experimental Design:** 293T cells were cultured and transfected with pcDNA, wt-Rubicon, wt-Rubicon + wt-HUNK, or wt-Rubicon + kinase-deficient HUNK-K91M plasmids. These cells were lysed to perform whole cell extraction and immunoprecipitation. The proteins of interest were visualized via Western blots.

**Results:** Autophagy proteins UVRAG and SQSTM1 could not be visualized after multiple attempts to optimize the protocol. However, results demonstrated that eliminating HUNK kinase activity in HUNK-K91M decreased HUNK interaction with Rubicon.

**Potential Impact:** Further studies should be done to assess whether HUNK kinase activity is required to stabilize binding to Rubicon. Additionally, alternative techniques, like microscopy or HER2+ cancer cells, should be used to visualize the interaction between Rubicon and autophagy proteins. Understanding the Rubicon interactome and the role of HUNK phosphorylation is imperative for better understanding of HER2+ cancer and effective treatments.

### **Association of Post-Traumatic Epilepsy on Recovery from Severe Traumatic Brain Injury: Sliding Scale Approach**

**Arlec Cabrera**, Shawn R. Eagle, David O. Okonkwo, Flora Hammond, Matthew W. Pease

**Background:** Post-Traumatic Epilepsy (PTE) affects one-third of severe traumatic brain injury (TBI) patients and is associated with poor functional outcomes. While TBI is characterized by continued recovery years after injury, the trajectory of functional recovery in PTE patients is not well understood. Using a novel sliding scale, we hypothesized that PTE acts as a 'second hit' after TBI, slowing recovery over time.

**Methods:** We performed a retrospective analysis of severe TBI patients (Glasgow Coma Scale (GCS)  $\leq$  8) treated from 2002 to 2018 at a Level 1 trauma center. We used the International Mission on Prognosis and Analysis of Clinical Trials (IMPACT) model to assign a sliding scale score. This score was based on the difference between the expected threshold for an unfavorable outcome (Glasgow Outcome Scale (GOS) = 1-3) and the actual score. Hence, a sliding score captures the magnitude of change between levels on the GOS according to each patient's baseline prognosis. Scores ranged from -3 to +2, with positive scores denoting improvement compared to baseline prognosis, as expected in most TBI patients. Thus, a sliding scale score serves as a

marker of a patient's expected recovery over time. We used the Wilcoxon Rank-Sum test to compare the change in sliding scores over time for patients with and without PTE.

**Results:** We had 392 patients with a median age of 33 (interquartile range (IQR)=23-47.5) Improvement for patients with PTE on the sliding scale was less (25.42% compared to 32.62% without PTE) over two years post-injury. PTE patients show a significant decline in functional outcomes compared to non-PTE patients during the 6 to 24-month follow-up period ( $p=0.04$ .)

**Conclusions:** Post-traumatic epilepsy is associated with delayed recovery after severe TBI. Future PTE clinical trials should consider a sliding scale approach to explore if early, aggressive treatment improves functional outcomes.

### **Metabolic recovery at 12 months postpartum among individuals with glucose intolerance in pregnancy**

**Arunabh Sinha**, Christina Lalama, Kaleab Abebe, Esa Davis, Patrick Catalano, Christina Scifres

**Background:** Glucose intolerance in pregnancy is associated with long-term risk for Type 2 Diabetes (T2D). We evaluated metabolic characteristics and  $\beta$ -cell function during pregnancy and at 12 months postpartum among varying levels of glucose intolerance in pregnancy.

**Methods:** This is a planned follow-up to the Gestational Diabetes Diagnostic Methods (GDM2) trial, which randomized pregnant individuals to either a 75-gram oral glucose tolerance test (OGTT) with GDM diagnosed using the IADPSG criteria, or a 100g OGTT with GDM diagnosed by the Carpenter-Coustan (CC) criteria. All participants with treated GDM, those with untreated mild glucose intolerance (MGI, one abnormal value on CC criteria), and half of the participants with normal glucose tolerance were invited for a 75g OGTT at 12 months postpartum. Stumvoll, Matsuda, and Disposition Indices (DI) were measured to evaluate insulin sensitivity, resistance, and  $\beta$ -cell function and other metabolic factors were assessed.

**Results:** Of the 407 individuals seen at 12 months, 49 (12%) had MGI and 53 (13%) had treated GDM (CC and IADPSG). MGI was associated with lower insulin sensitivity, lower beta cell function, dyslipidemia, and alterations in leptin and adiponectin similar to those individuals with treated GDM (Table). Measures of metabolic function, insulin sensitivity and  $\beta$ -cell function demonstrated similar rates from pregnancy to postpartum after adjusting for maternal age, BMI, and history of GDM.

**Conclusions:** Patients with MGI have impaired  $\beta$ -cell function and significant metabolic abnormalities at 12 months postpartum similar to individuals with treated

GDM and require ongoing follow-up for progression to T2D. The similar rate of change from pregnancy to postpartum in insulin sensitivity,  $\beta$ -cell function, and metabolic assessments among groups indicates that individuals were returning to their baseline levels of glucose tolerance rather than recovering from pregnancy-induced glucose intolerance.

### **Disparities in Timeliness of Care in Anal Cancer: A Retrospective Chart Review**

**Aryan Mishra**, Jacob Steffen, Emma Holler, Hannah Allison, Sanjay Mohanty

**Background and Objective:** Approximately 10,540 new cases of anal cancer (AC) will be diagnosed in the USA in 2024, but its incidence has increased two-to-four-fold in the past few decades. Areas with higher social vulnerability have decreased odds of colorectal cancer screening, resulting in delayed healthcare presentation. This project describes the elapsed time between initial symptomatic presentation and diagnosis of AC across 3 possible points of process failure and explores the impact of patient factors and social vulnerability on time to diagnostic resolution.

**Project Methods:** Patients diagnosed with AC within the Indiana University Health system from 2020-2024 were identified using the electronic health record. Cases were reviewed ( $n=478$ ); demographics and the following timepoints were noted: initial symptomatic presentation, specialist referral, diagnostic testing, and AC diagnosis. The primary outcome was time between presentation and diagnosis, with diagnostic delay classified as more than six weeks. Patient factors and clinical characteristics were compared to calculate risk ratios to explore associations between these factors and diagnostic delay.

**Results:** After exclusions, analysis of the cohort ( $n=193$ ) showed that 99 patients (51.3%) did not experience a delay, and 94 did (48.7%), with a total median SVI of 0.51 (IQR=0.29-0.75) and delay of 39d (IQR=17-90). Patients with a delay (SVI=0.53; IQR=0.30-0.76) had similar SVIs to those without a delay (SVI=0.51; IQR=0.22-0.75;  $p=0.462$ ). Older patients had a higher risk of experiencing a delay than a younger patient (RR=1.005; CI=1-1.01;  $p=0.038$ ). Patients working full-/part-time have an increased risk of delay than those retired (RR=0.832; CI=0.721-0.96;  $p=0.012$ ) or unemployed (RR=0.849; CI=0.746-0.967;  $p=0.014$ ).

**Conclusion and Potential Impact:** Older age and employment status are drivers of diagnostic delay after AC presentation. No measures of social vulnerability were associated with delayed care. Further work exploring the process failures to diagnostic resolution will inform interventions targeting barriers and facilitators. As barriers-to-care are reduced, more patients can have improved

cancer outcomes and quality of life.

### **Physical Therapy Timing: An Investigation of Physical Therapy Initiation and Case Duration, Restricted Workdays, and Imaging Utilization**

**Austin Snider**, Amelia Roebuck, Amanda Coupe, T. David Wu, Michael Knipp

**Background:** Occupational health injuries are common, and many individuals will suffer a workplace injury throughout their career. When employees cannot work for extended periods of time, companies face financial and staffing difficulties. Prior studies have suggested that early referral to physical therapy (PT) is associated with improved patient outcomes and reduced healthcare utilization. However, there has been limited investigation of this in occupational health settings and among diverse types of injuries. Our goal was to investigate how the timing of PT impacted the case duration, restricted workdays, and imaging utilization among injured workers.

**Methods:** We conducted an IRB-approved retrospective chart review of N=1191 patients who received care between 9/2017-6/2023 at Parkview Occupational Health. Timing of PT initiation was categorized as early (0-13 days), delayed (14-20 days), or late (>30 days) from date of first visit. Kruskal-Wallis tests were performed to assess differences in case duration and restricted workdays by PT timing. Chi-square tests evaluated utilization of different imaging modalities by PT timing. Bonferroni-corrected Dunn tests were performed to compare groups. Analyses were performed using Excel and Stata V.18 (alpha=0.05 for significance).

**Results:** Across PT timing groups, median case duration ranged from 44-78 days, median restricted workdays ranged from 12-28 days, and total imaging utilization ranged from 32%-48%. Early PT initiation was associated with a significant reduction in case duration (p<0.001), total imaging (p<0.01), and X-ray utilization (p<0.001) compared to delayed or late PT initiation. Early PT was associated with fewer restricted workdays compared to delayed PT (p<0.001) but not late PT (p=0.054).

**Conclusion:** These results support the benefits associated with utilizing early PT after a workplace injury with earlier initiation showing the greatest benefits.

### **Developing luciferase reporter assays to selectively assess Exenatide and Pramlintide bioactivity within an implantable $\beta$ -cell pharmacy model designed to treat obesity and type 2 diabetes**

**Ayli Anvaripour**, Rebecca Schugar, Justin Annes

**Objective:** To address the increasing burden of obesity

and type-2 diabetes through the development of an innovative implantable device capable of temporal and dose-controlled release of peptide satiety signals from implanted  $\beta$  cells.

**Design:** This study utilized a novel application of HEK-293 cells engineered to express luciferase upon stimulation by G protein-coupled receptors. Two specific cell lines, Ex-Luc and Pram-Luc, were created to selectively evaluate the bioactivity of Exenatide and Pramlintide through transient transfections and a CRE-luciferase reporter system.

**Methods:** HEK-293 cells were engineered with either glucagon-like peptide-1 receptor (GLP1R) or calcitonin receptor (CALCR) coupled with receptor activity modifying protein 3 (RAMP3). These cells were then exposed to Exenatide or Pramlintide, and luciferase activity was measured to assess drug-specific responses.

**Results:** Cells expressing GLP1R showed a concentration-dependent increase in luciferase activity upon treatment with Exenatide. Conversely, cells with CALCR/RAMP3 displayed luciferase activity upon Pramlintide exposure but did not respond to Exenatide, indicating specificity and no cross-reactivity between the pathways.

**Conclusions:** The creation of HEK-293 Ex-Luc and Pram-Luc cell lines demonstrated effective measurement of Exenatide and Pramlintide bioactivity. These cell lines provide a promising tool for further in vitro studies and the potential development of an implantable device for managing diabetes and obesity by regulating peptide release.

**Future Directions:** Future work will involve applying these assays to analyze engineered  $\beta$  cells in the context of the proposed implantable device to further assess their practical application in treatment scenarios.

### **Clinical Impact and Sustainability of a Standardized Neonatal Nephrology Consult Program**

**Benjamin Holland**, Mayra Kotlik, Kathryn Lowe, Samantha Wallace, Anna Latimer, Danielle Soranno, Cara Slagle, Michelle Starr

**Background:** Acute kidney injury (AKI) is common in high-risk neonates and is associated with increased morbidity and mortality. Standardized programs to identify AKI exist only in a few institutions. The sustainability and clinical impact of such programs have not been described. We characterized changes in AKI incidence, neonatal nephrology consultation, and outpatient neonatal nephrology visits after implementation of a Neonatal Nephrology program. We hypothesized that neonatal AKI incidence would decrease in the post-implementation era.

**Methods:** We instituted a standardized Neonatal Nephrol-

ogy program in early 2020 to identify AKI in infants admitted to the neonatal intensive care unit (NICU). Elements included (1) a shared neonatology and nephrology clinical practice guideline including creatinine monitoring, (2) electronic health record alert to identify infants with AKI, and (3) standardized nephrology consultation. All neonates with AKI were seen by nephrology, and infants with severe AKI (stage 2 or 3) were referred for outpatient follow-up.

**Results:** There was a sustained and significant decrease in AKI incidence since initiation of the program. AKI incidence decreased from 40% in 2019, before the program began, to 19% in 2023. This decrease in AKI incidence correlates temporally to increased AKI identification and inpatient Neonatal Nephrology consults. While the initial burden of neonatal nephrology consults increased, the decline in AKI incidence has led to a subsequent decrease in consultations.

**Conclusions:** We report a reduction in AKI incidence after implementation of a standardized Neonatal Nephrology program. While reasons are likely multifactorial, it is likely that increased AKI awareness and monitoring contributed to this decline. We believe our single center experience emphasizes the importance of multi-disciplinary work in neonatal nephrology. Future work will focus on risk stratification of outpatient management of high-risk infants, interventions focused on further reduction in AKI incidence, and development of standardized approaches for identification and risk-stratification of infants.

### **Orexin Blockers' Role in Glucose Homeostasis and Diabetic Retinopathy**

**Braden Baker**, Rupinder Kaur Sodhi, Neha Mahajan, Babar Khan, Ashay Dilip Bhatwadekar

**Background:** Diabetic retinopathy (DR) is the most common complication of diabetes and can lead to blindness if untreated. Orexin is a neuropeptide produced by the hypothalamus that regulates the sleep/wake cycle. Orexin-blockers are prescribed for insomnia, which recent studies have shown decrease blood glucose levels, suggesting a potential therapeutic for DR. The purpose of this study is to explore orexin-blockers' role in glucose homeostasis and diabetic retinopathy through in-vitro, in-vivo, and chart-review methods.

**Methods:** 1. In-vitro – Glucose uptake by human retinal endothelial cells (HRECs) was determined with exposure to varying levels of Suvorexant, a commonly prescribed orexin-blocker, and orexin. Additionally, Orexin expression under varying glucose concentrations was examined using fluorescent staining. 2. In-vivo – Diabetic (db/db) and non-diabetic (db/m) mice were injected with Suvorexant or DMSO daily. Mice weights and blood glucose were taken regularly to compare. 3. Chart-review – A review

that examines individuals retrospectively to determine if orexin-blockers decrease percentages of developing vision-threatening DR or macular edema compared to patients NOT taking orexin-blockers.

**Results:** 1. In-vitro – HRECs exposed to Suvorexant had increased glucose uptake while those exposed to orexin had a decreased glucose uptake. There were no significant results in orexin expression in HRECs exposed to varying glucose concentrations. 2. In-vivo – Mice treated with Suvorexant showed a downward trend in body weight, food intake, and better glucose tolerance than DMSO-injected diabetic mice. 3. Chart-review – 41 patients were identified as having non-vision threatening DR and taking orexin-blockers in 2014. MRN's for these patients are currently being retrieved by Regenstreif Institute.

**Conclusion:** The results of both the in-vitro, pre-clinical, and clinical chart review studies indicate Suvorexant has blood glucose-lowering properties. Data will continue to be collected for the clinical chart review to further determine the effects of orexin blockers on diabetic retinopathy and HbA1c.

### **Plasma Tau Biomarker Levels in ICU Delirium Survivors**

**Brendan Devine**, Anthony J. Perkins, Kyle Gannon, Abigail Olbina, Sujuan Gao, Sikandar H. Khan, Babar A. Khan

**Background:** Intensive Care Unit (ICU) delirium doubles the risk for post-ICU dementia. Plasma p-Tau181 and total Tau (t-Tau) levels have been associated with Alzheimer's Disease pathology. The association between ICU delirium and higher plasma Tau levels at discharge compared to subsyndromal delirium is not well described.

**Objective:** Identify the association between ICU delirium and plasma p-Tau181 and t-Tau biomarker levels.

**Methods:** This analysis includes patients aged 50 years or older who were enrolled in the IMPROVE randomized controlled trial and provided a blood sample at hospital discharge. The Confusion Assessment Method in ICU (CAM-ICU) was conducted twice daily until hospital discharge. Delirium was defined as any one instance of CAM-ICU+. SSD, a less severe form of delirium, was defined as at least one abnormal CAM-ICU feature. Blood samples were collected in EDTA tubes and analyzed using Multiplex Luminex assays (ThermoFisher). Values were reported in pg/mL and compared using the Wilcoxon Rank Sum Test in SAS.

**Results:** A total of 68 patients were included, 46% had subsyndromal delirium and 54% had delirium. The subsyndromal group had a mean age of 63.7 years (SD 7.3) vs.

64.4 (SD 7.1) in the delirium group ( $p=0.667$ ). Subsyndromal patients had 13.6 mean years of education (SD 2.4) vs. 13.1 (SD 2.3) in the delirium group ( $p=0.441$ ). Median levels of plasma p-Tau181 were 0.03 pg/mL (IQR 0.03, 0.62) in the SSD group vs. 0.03 pg/mL (0.03, 0.22) in those with delirium ( $p = 0.311$ ). Median levels of plasma t-Tau were 0.65 pg/mL (IQR 0.10, 4.83) in those with SSD vs. 1.53 pg/mL (IQR 0.10, 4.22) in those with delirium ( $p = 0.626$ ).

**Conclusion:** No statistically significant differences were found in plasma p-Tau181 and t-Tau levels between SSD and delirium at hospital discharge. Future studies with more sensitive assays may be needed.

### **Cardiac Trauma in the Context of Domestic Violence: Surgical Management of a Bullet Lodged in the Left Atrium of a Young Woman**

Sabin Karki, **Brooke Stephanian**, Jui Desai, Maggie Sullivan, Raed A. Abdulkareem

**Background:** Gun violence against women in the US, particularly in domestic settings, is a serious public health issue. Women are 11 times more likely to be killed with a firearm than in other high-income countries, with intimate partners as the primary perpetrators. Around 4.5 million women have been threatened with a gun, and nearly 1 million have been shot or shot at by an intimate partner. Firearm injuries are increasingly affecting younger women.

**Case Description:** A 31-year-old woman was shot in the chest by her boyfriend. Imaging revealed the bullet near the left circumflex coronary artery, raising concerns for vascular injury and requiring emergency surgery. The team prepared for a potential coronary artery bypass graft (CABG) if needed. During surgery, a no-touch technique prevented systemic embolization. After heparinization, aortic and bicaval cannulation were performed, and the patient was placed on cardiopulmonary bypass. An incision extended from the right atrium to the left atrium, where the bullet was found embedded in the posterior atrial wall. It was carefully removed, and the defect was repaired with pledgeted Prolene sutures. Both the atrial septum and right atrium were closed, and the AV groove injury was reinforced to prevent rupture. The patient was weaned off bypass without complications.

**Results:** The bullet's atypical location in the AV groove offers insights for future surgical cases. The patient's smooth recovery underscores the importance of rapid, personalized surgical intervention. This case also highlights the importance of addressing intimate partner violence to prevent life-threatening injuries.

**Conclusion:** The patient's recovery demonstrates the value of prompt surgical care. The bullet's confinement to the atrial wall, without damaging surrounding structures,

contributed to a favorable outcome. This case reinforces the need for healthcare providers to identify intimate partner violence early, potentially preventing severe injuries and invasive interventions.

### **Correlation Between Thyroid Hormone Replacement and Atrial Fibrillation Using Real World Data**

**Caleb Gosney**, Omar Elhanafy, Lawrence Judy, Gattadahalli Seetharam

**Background and Objective:** Hyperthyroidism is a known predisposing factor to atrial fibrillation (AF). Less well studied is the association, if any, between thyroid hormone replacement treatment for hypothyroidism and AF. Levothyroxine monotherapy is the first line treatment for hypothyroidism, but T3 supplementation and desiccated animal thyroid hormone are also used. Currently, levothyroxine is one of the top ten most prescribed medications in the US. We hypothesize that there is a positive correlation between a history of thyroid hormone replacement therapy and AF.

**Methods:** Using data from the CRC/Sidus Insights national Real-World cardiology and psychiatry databases containing deidentified EHR information, we searched for patients with at least one lifetime thyroid hormone replacement prescription, one lifetime AF diagnosis, or both. 73,733 patients were identified that fit both criteria in the cardiac database while 34,696 were identified in the psychiatric database. We then used odds ratios to determine the relative odds of having an AF diagnosis when also prescribed thyroid hormone replacement compared to an AF diagnosis without thyroid hormone replacement.

**Results:** The odds ratios calculated for both Indiana (5.73 95% CI (5.45-6.03)) and nationwide (3.27 95% CI (3.24-3.30)) from the cardiac database showed a significant association between thyroid hormone replacement and AF. The odds ratio from the psychiatric database (2.23 95% CI (2.20-2.26)) also showed significance.

**Conclusion and Potential Impacts:** Our findings suggest a significantly higher odds that someone prescribed thyroid hormone replacement will also have a diagnosis of AF. The observational nature of the database does not allow for causality to be determined. As such, causation was not addressed in this study. However, our findings do suggest that AF should be monitored for in those taking thyroid hormone replacement. Further works could analyze dosage of thyroid hormone replacement to observe if there is a dose-response relationship.

### **Remote Recurrence/Metastasis of Acinic Cell Carcinoma: a Case Series and Literature Review**

**Caroline Boyle**, Tieying Hou

**Background:** Acinic cell carcinoma (ACC) is a relatively indolent salivary gland tumor with recurrence usually occurring within the first five years after the primary resection. Delayed recurrence/metastasis after more than 10 years is rare and often poses diagnostic and treatment challenges.

**Methods:** The study was approved by Indiana University Institutional Review Board. Six patients with remote recurrence/metastasis were identified from January 2000 to May 2024. Clinico-radiologic presentation, pathologic findings, treatment, and follow-up were reviewed. Case reports in literature since 1960 were also summarized.

**Results:** The six patients comprised five females and one male (age range: 22 to 47 years). All tumors arose from the parotid gland. The interval between primary resection to recurrence ranged from 10 to 45 years. The most common recurrent/metastatic locations were scalp, lung, bone, and ear canal. High grade transformation was identified in one case. Two of six patients died of the disease including the case with high grade transformation, three patients were still alive at the end of the study period, and one died from unrelated condition. Another six cases identified from the literature also involved the parotid gland, including five females and one male (age range: 15 to 60 years). The interval ranged from 11 to 30 years. Bone, lung and cutaneous sites were involved. Four of six patients were still alive at the end of the study period, and follow-up was not available for two patients.

**Conclusion:** Remote recurrence/metastasis of ACC after 10 years of primary resection is very rare. This phenomenon predominantly affects females. Local recurrence usually involves structures near tumor beds. Distant metastasis affects scalp, lung, bone, or skin. Diagnosis can be challenging if patients and/or physicians are unaware of the original diagnosis. The study raises awareness of an unusual clinical and pathological characteristic of ACC. A comprehensive review of medical history is crucial for an accurate diagnosis and appropriate clinical management.

### **Associations between Primary Hyperparathyroidism and Social Determinants of Health**

**Caroline Vieira,** Meghan Lark, Nathan Lin, Kristen Kaiser, Hannah Allison, Signe Braafladt, Alexandria D. McDow

**Background:** Primary hyperparathyroidism (PHPT) is a common endocrine disorder associated with a wide range of comorbidities. The only curative treatment for PHPT is parathyroidectomy; however, many patients are undertreated. Certain factors that impact access to care, such as geographic location and socioeconomic conditions, may contribute to the undertreatment of this disease. This study aims to investigate how geographic location and socioeco-

nomie conditions impact access to parathyroidectomy.

**Methods:** A retrospective chart review was conducted for patients with PHPT who underwent parathyroidectomy by two endocrine surgeons at University or Eskenazi Hospitals from January to December 2023. Patient demographics, addresses, referring physician specialty, and course of care were collected. Area deprivation index (ADI), a marker of deprivation at the neighborhood level, was used as a surrogate for social determinants of health (SDoH). Patients were then dichotomized into high (>75 percentile) vs. low (<75 percentile) ADIs.

**Results:** Seventy-three patients underwent parathyroidectomy for PHPT, of which 75% were female, and 71% were White. Fifty-three (73%) patients underwent surgery at University Hospital. The majority of patients were referred by endocrinologists. Patients that had a high ADI were more likely to be operated on at Eskenazi (52% vs 9.3%,  $p<0.001$ ). Patients with high ADI were more likely to be Hispanic (13% vs 4.7%,  $p=0.2$ ), Black (35% vs 9.5%,  $p=0.002$ ), smokers (6.5% vs 2.3%,  $p=0.010$ ) and less likely to drink alcohol (13% vs 44%,  $p=0.004$ ). Patients with high ADI had a greater delay from referral to clinic visit (74d vs. 49d,  $p=0.2$ ), as well as clinic visit to surgery (83d vs. 73d,  $p=0.3$ ).

**Conclusions:** Patients with PHPT and high ADI are more likely to be of Black race, treated at Eskenazi hospital and use tobacco. High ADI patients waited longer for treatment for PHPT. Given the limited sample size, further data collection and investigations are needed.

### **Evaluating the Effects of Propofol on Transcytosis in a Human Stem Cell-Derived Blood Brain Barrier Model**

**Carter Shaw,** Rylee Anderson, Scott G. Canfield

**Background:** The blood-brain barrier (BBB) is a highly specialized barrier system that regulates the passage of molecules between the bloodstream and brain parenchyma. Structurally, the BBB is made up of endothelial cells, astrocytes, and pericytes that aid in its functionality. Understanding the integrity of the BBB is crucial when investigating factors such as drug delivery and various neurological pathologies. One way that the integrity of the BBB is preserved is by limiting transcytosis. This method of transport limits the ability of non-specific molecules to cross the BBB. Propofol, a short acting IV anesthetic used for the induction of anesthesia, has been implicated in modulating the integrity of the BBB. However, its specific effects on transcytosis across the BBB are poorly understood. This study hypothesizes that propofol disrupts a human-derived BBB model and alters transcellular transport, allowing more molecules to gather within cells and ultimately cross the barrier.

**Methods:** This study will be centered on utilizing three various sized dextran molecules, 3kDa, 10kDa, and 70kDa, and their accumulation post-propofol exposure. Brain microvascular endothelial cells (BMECs), neurons, and astrocytes were derived from human induced pluripotent stem cells (IPSCs). Co-culture with neurons and astrocytes were also used with the BMECs. Experimental groups were then exposed to propofol at 50  $\mu$ M for a duration of 3 hours. Transcytosis was then measured by the fluorescent intensity of dextran within the BMECs and after crossing through them with a fluorescent plate reader. These results will be compared to BMECs that did not receive the propofol treatment.

**Results:** Preliminary data provides evidence that the transcytosis of dextran is increased among all treatment groups. These findings suggest that propofol may disrupt normal BBB function by affecting mechanisms of transcytosis, potentially impacting drug delivery and CNS homeostasis.

**Conclusions:** Further elucidation of these effects could contribute to improving anesthetic practices and therapeutic strategies targeting CNS disorders.

### **UGT2B10 Variant Effects on Dexmedetomidine Metabolism Using Nicotine Studies**

**Cassidy N. Hardin**, Aislinn O’Kane, Sara Quinney

**Background:** Dexmedetomidine is a procedural sedative primarily metabolized by the UDP-glucuronosyltransferase (UGT) 2B10. UGT2B10 also contributes to nicotine metabolism. Most research on the effect of gene variants on UGT2B10’s glucuronidation efficacy has focused on nicotine. This study outlines current data on the relationship between UGT2B10 pharmacogenomics, nicotine pharmacokinetics, and race, which then extrapolates that information to dexmedetomidine.

**Methods:** A literature review was conducted on UGT2B10 variants and dexmedetomidine or nicotine in PubMed. Due to lack of studies on dexmedetomidine glucuronidation, studies using nicotine were used to classify variants as poor, intermediate, or extensive metabolizers; characterize their expression in African/African Americans (AA) and Europeans (C), and establish their respective activity based on nicotine metabolite percentages.

**Results:** UGT2B10 accounts for about 20% of nicotine metabolism. The UGT2B10 variants rs61750900 (AA=37.62%; C=0.18%) and rs2942857 (AA=4.42%; C=9.28%) are nonfunctional. Poor metabolizers (PM) are homozygous for one of these variants and see a 97% decrease in UGT2B10 metabolites. Intermediate metabolizers (IM) have one variant allele and one wild-type allele, with a 32% decrease in UGT2B10 metabolites. Extensive metabolizers (EM), have two wild-type alleles. Metabolites from other

pathways increase as UGT2B10 metabolites decrease. These results were superimposed onto dexmedetomidine metabolism to predict metabolite percentages in UGT2B10 IM and PM. In PM, only 1.02% of dexmedetomidine metabolites were predicted to be from UGT2B10.

**Conclusions:** Nicotine metabolism data suggests variants of UGT2B10 significantly impact dexmedetomidine metabolism. PMs have 97% decreased nicotine UGT2B10 metabolism and a compensatory increase in nicotine’s other metabolites. UGT2B10 accounts for the largest portion of dexmedetomidine metabolism. Thus, UGT2B10 PMs may have decreased glucuronide metabolites, with increased proportion of other pathways. Giving the same dose of dexmedetomidine to PM or ultrarapid metabolizers (UM) may result in toxicity or undersedation, respectively. More research needs to be done on UGT2B10 variants to optimize patient care.”

### **Using Artificial Intelligence to Automate the Quantification of Bacteria in Biofilms**

**Daniel Konig**, Miguel Jorge, Ethan Rinne, and Mithun Sinha

**Background:** Medical device-associated bacterial infections are a predominant source of healthcare-associated infections, often resulting in implant failure and disease. These infections result from the formation of complex communities of microorganisms known as biofilms, which adhere to surfaces and produce extracellular polymeric substances that shield bacteria from host immune response and antibiotics. Studying drugs that disrupt biofilm formation is challenging due to the lack of a standardized and efficient quantification method. Scanning electron microscopy (SEM) is regarded as the gold standard to verify the presence of biofilm. However, it is a qualitative approach. This study aimed to develop an artificial intelligence (AI) algorithm using the Nuclei Segmentation module in HALO AI to recognize and quantitate bacteria within biofilms captured by SEM.

**Methods:** SEM images of biofilm growth stages were collected and preprocessed. Manually annotated regions were used to train the AI, which extracted relevant characteristics from the images. The algorithm was validated using a separate set of SEM images. Performance was evaluated by comparing algorithm bacterial counts with hand-counts.

**Results:** The AI generated algorithm accurately identified and quantified bacteria on biofilm SEM images. The automated process allows for reliable and instant tracking of bacterial counts on biofilm. Allowing the algorithm to build a consensus via diverse training regions, multiple annotators, and regular validation were essential strategies to mitigate biases.

**Conclusion:** The developed AI algorithm offers a promising advancement in the optimization of a formerly tedious and subjective analysis method. By providing an efficient, consistent, and objective method for biofilm analysis, this approach enhances the accuracy of research on biofilms.

**Potential Impact:** Usage of AI in biofilm research can significantly improve the understanding and management of biofilm-associated infections. By automating SEM analysis, researchers can achieve consistent and objective results. This advancement has the potential to improve outcomes for patients with medical implants.

### **Impact of Social Determinants of Health on Referral Pattern and Surgical Outcomes in Children With Undescended testes**

**Deja Miller-Brooks**, Peter Arnold, Nikhil Batra, Pankaj Dangle

**Background:** The presence of undescended testis (UDT) warrants prompt evaluation and possible surgical correction to reduce risks of fertility impairment and testicular malignancy. According to the American Urological Association, if spontaneous testicular descent does not occur by six months, orchiopexy should be performed within 18 months. Healthcare access can be influenced by socioeconomic and health literacy disparities, so we investigated the association between Area Deprivation Index (ADI) and Health Literacy Estimate (HLE) on the timing of UDT referral and surgical correction. We hypothesized that patients with higher ADI and lower HLE are referred later and experience more complications.

**Methods:** We performed a retrospective chart review of patients who underwent surgical correction for UDT at a tertiary pediatric hospital from 2009 to 2024. Demographic data, surgical details, and ADI, a measure of socioeconomic disparities, were collected. We used the UNC Health Literacy Estimate map to estimate HLE. Outcomes of interest included age at referral, age at surgery, time between referral and surgery, and 30-day postoperative complications. Associations between high ADI, low HLE, and these outcomes were measured by chi-square tests and ANOVA.

**Results:** 1,493 patient charts were reviewed; 1,166 met the inclusion criteria of UDT diagnosis and orchiopexy. Patients were categorized by age at referral: 0-12 months, 12-24 months, and >24 months. Our analysis showed no significant difference between age at referral and race/ethnicity ( $p = .1136$ ), national-level ADI ( $p = 0.130$ ), postoperative complications ( $p = 0.2061$ ), timing between referral and surgery ( $p = .0942$ ), or health literacy ( $p = 0.9636$ ).

However, a significant association was found between state-level ADI and age at referral ( $p < 0.021$ ).

**Conclusion:** Our findings suggest that socioeconomic disparities within Indiana influence the timing of UDT referrals, with children from disadvantaged neighborhoods being referred later. Further research is needed to ensure timely intervention for children with UDT, reducing associated risks.

### **Late Antenatal Corticosteroid Treatment in Twin Pregnancies and Neonatal Outcomes: A Systematic Review and Meta-Analysis**

**Elizabeth Roy**, Victor Olafusi, Enaja Sambatur, Faezeh Aghajani, Moti Gulerson, Alireza Shamshirsaz, Asma Khalil, Vincenzo Berghella, Hiba J. Mustafa

**Objective:** To examine the impact of administering late-preterm corticosteroids on neonatal outcomes in twin pregnancies.

**Methods:** A systematic literature search was conducted in four databases from 2000-May 2024. Studies reporting on neonatal outcomes in twin pregnancies at risk of preterm birth receiving corticosteroid treatment for fetal lung maturity at the gestational age (GA) of 34 weeks and 0 days to 36 weeks and 6 days were included. Studies involving participants with specific conditions (twin-to-twin transfusion syndrome and intrauterine fetal demise of one fetus) were excluded. A random effect model was used to generate weighted mean differences (MD) and odds ratio (OR) with their 95% confidence intervals (CI). Heterogeneity was assessed using the I<sup>2</sup> value. The Newcastle-Ottawa Scale (NOS) was used for risk of bias assessment. The primary outcome was incidence of respiratory distress syndrome (RDS). Additional outcomes included need for mechanical ventilation, continuous positive airway pressure (CPAP), and neonatal hypoglycemia. Comparison groups included those receiving steroids vs those not.

**Results:** 267 abstracts were screened, of which 15 full-texts were fully reviewed. A total of 3 studies were included in the final analysis, which comprised 489 twin pregnancies receiving steroids and 2807 not receiving steroids. There were no differences in obstetric characteristics between groups, including maternal age, body mass index, pre-eclampsia, diabetes, and type of twin chorionicity. GA at delivery was earlier in the steroids group (MD -0.91, 95% CI [-1.50, -0.32]). For neonatal outcomes, there were no significant differences in incidence of RDS and need for mechanical ventilation between groups. There was higher incidence of CPAP use (OR 2.69, 95% CI [1.47, 4.92]) and neonatal hypoglycemia (OR 2.05, 95% CI [1.18, 3.56]) in the steroids group.

**Conclusions:** This study found that antenatal corticosteroid treatment during the late-preterm period in twin pregnancies was not associated with reduced neonatal respiratory complications.

## CMV Antigenic Stimulation in Disease Process of T Cell Large Granular Leukemia

Elizabeth Zenni, Bernhard Maier, Utpal Davé

**Background:** T cell large granular leukemia (T-LGL) is characterized by the clonal expansion of mature CD8+ cytotoxic T cells. Patients often present with anemia, neutropenia, and/or bone marrow infiltration. Most cases involve gain of function mutations in the STAT3 or STAT5b oncogene, which is pathognomonic for this neoplasm. T-LGL cells are clonal for specific T cell receptor (TCR) gene rearrangements, suggesting a role of TCR in disease pathophysiology. Here, we present the case of a 67-year-old male with T-LGL and severe neutropenia, hospitalized for recurrent febrile episodes and a perianal abscess. He had IgG antibodies against cytomegalovirus (CMV), a virus that establishes latency in the bone marrow and sporadically reactivates, thus restimulating CMV-specific memory T cells.

**Methods:** At the time of neutropenia, bone marrow aspiration and biopsy were performed. PBMCs were single-cell sorted for CD3+ T cells and TCR-clonotypes identified by targeted single-cell RNA-seq. TCR CDR3 similarities were searched in the VDJdb database to find potential antigenic epitopes. Epitope candidates were analyzed with the TCR Model web server to predict epitope binding to the patient's MHC and TCR. Patient PBMC gDNA was amplified in a nested PCR with CMV pp65-specific primers. Cytotoxicity assays were performed with patient CD3+ T cells and pp65-pulsed T2 cells.

**Results:** Alpha-beta TCR clonotype of the patient's T-LGL was identified and predicted (by VDJdb database) to be specific to CMV pp65 and IE1 epitopes and an autoimmune epitope, BST2. TCR model predicted epitope binding to the patient's MHC and TCR. Nested PCR detected the CMV pp65 gene in patient PBMCs.

**Conclusions:** Our data suggests a model for T-LGL pathogenesis where CMV reactivation could play a role in T-LGL initiation or autoimmune cytopenia. The identification of precise TCR sequences from leukemic T cell clones will guide development of clonotype-specific immunotherapeutic agents.

## Generation of Cholangiocyte Organoids Using Human Primary and Immortalized Intrahepatic Cholangiocytes

Emily H Chestnut, Minh-Uyen T. Le, Barry Wei, Ping Li, Burcin Ekser, Wenjun Zhang

**Background:** Developing cellular models for studying cholangiopathies has been challenging. Cholangiocyte (CHOL) organoids offer promise in recapitulating structure and function of the in vivo biliary tree. To enhance expansion, isolated CHOLs were immortalized using lentiviral vectors expressing human papillomavirus (HPV) E6/E7. It remains unclear whether immortalization alters other cellular properties. This study aims to determine whether immortalized CHOLs can self-organize into bile duct-like structures ex vivo, providing an avenue for modeling cholangiopathies and biliary tree development.

**Methods:** Human cholangiocytes were isolated from explanted liver tissue. 5,000 primary or immortalized CHOLs were seeded into a 24-well plate at 50ml/well in a mixture of Matrigel and supplemented media. At 10 days of growth, diameter and number of organoids from each condition were quantified. Expression of the key markers for CHOLs such as CK19, EpCAM, and others were measured by qPCR. Rhodamine123 transport assay was used to assess functionality of CHOL organoids.

**Results:** Fluorescent microscopy confirmed that cholangiocyte organoids generated with immortalized CHOLs express cholangiocyte-specific cell markers CK19 and CK7 and maintain p-glycoprotein function. However, organoids derived from immortalized CHOLs showed a significant reduction in diameter ( $12.68 \pm 2.4$  vs  $20.61 \pm 2.8$ ,  $p < 0.01$ ) and number per well ( $17.3 \pm 4.9$  vs  $27.0 \pm 3.2$ ,  $p < 0.02$ ) compared to organoids derived from primary CHOL. qPCR analysis revealed elevated expression of progenitor cell marker EpCAM and reduced expression of mature CHOL marker CK19 in organoids derived from immortalized cell, suggesting immortalization impaired differentiation of CHOLs.

**Conclusion:** Although establishing immortalized CHOL cell lines from human livers provides cellular models for studying cholangiopathies, caution should be exercised when using them for studies requiring functional, mature CHOL behavior/3D organization. Future work should focus on developing alternative immortalization methods that better preserve the functionality and differentiation of primary cholangiocytes in 3D culture.

**Outcomes Associated with Mechanical CPR Devices**

## Outcomes Associated with Mechanical CPR Devices

Erik Wilhelm, Amy Souers

**Background:** In the U.S. 350,000 out of hospital cardiac arrests (OHCA) occur annually with 90% resulting in mortality. Delivering timely, high-quality CPR is paramount in promoting favorable patient outcomes. Inherent difficulties in providing out of hospital CPR in addition to first responder shortages have increased mechanical CPR (mCPR) device utilization in out of hospital settings. Previous trials were conducted in urban areas and have shown no significant difference in efficacy, but smaller studies identified a greater risk of resuscitation related injuries with mCPR. We hypothesized that in a rural setting, mechanical would be

non-inferior to manual CPR for patient survival but would produce more resuscitation related injuries.

**Methods:** This IRB approved retrospective chart review considered all OHCA with attempted resuscitation by Parkview EMS from 1/1/2022–12/31/2023. Pediatric, pregnant, and Do-Not-Resuscitate patient charts were excluded. Traumatic and hypothermic cardiac arrests were also excluded. Data collection was completed via EMR reports. We collaborated with county coroners to obtain autopsy reports with information regarding resuscitation related injuries. Survivability was the primary outcome with cerebral performance category (CPC) scores and resuscitation related injuries as secondary endpoints. A t-test was used for continuous data. Chi-square, odds ratios, and confidence intervals were used for binary data ( $p < 0.05$  for significance).

**Results:** There were 160 manual and 21 mCPR patients. Injury data was obtained for 117 manual and 11 mCPR patients. 32/160 (20%) manual CPR patients survived and 1/21 (4%) mCPR patients survived ( $p = 0.089$ ). 22/160 (14%) manual CPR patients had favorable CPC scores compared to 1/21 (4%) mCPR patients ( $p = 0.245$ ). While not statistically significant, survival rates and CPC scores may be clinically significant. mCPR patients experienced splenic maceration, liver laceration, lacerated inferior vena cava, and lacerated pericardium significantly more than manual CPR ( $p = 0.001$ ).

**Conclusion:** The outcomes in this rural cohort demonstrated noninferiority of mCPR in comparison to manual CPR.

### **Exploring Lung Cancer Screening in the ED: Collecting Patient and Provider Insights**

**Erin O'Farrell**, Nicholas Pettit

**Background:** Lung cancer remains the primary cause of cancer-related death in adults, with 1.6 million deaths worldwide caused by this disease annually. The high morbidity and mortality associated with lung cancer underlies the importance of screening opportunities for detecting cancer early and improving overall rates of treating individuals. Despite this, only 5.8% of individuals who are eligible for a lung cancer screening participate. Many barriers may limit a patient's access to screening, among which may be lack of education regarding screenings and inability to receive a timely appointment. The ED may provide both education and referrals for screening. Research focuses on identifying effective methods to engage providers and ED patients, increasing education, and addressing concerns to enhance attendance at screenings and improve long-term patient outcomes.

**Methods:** Research involved conducting a preplanned topical analysis derived from semi-structured individual in-

terviews of one hundred participants. Participants included providers and ED patients. Participants provided information regarding potential ED intervention tools to increase lung cancer screening education and uptake alongside their subjective experiences and challenges with lung cancer screenings. Themes will be identified inductively utilizing constant comparative analysis.

**Results:** It is expected that patients and providers will express interest in learning about implementation of lung cancer screenings during an ED visit but will differ in the most effective method of lung cancer screening education. Findings will optimize interventions to increase lung cancer screening uptake among ED patients in a future randomized control trial.

**Conclusions:** This study will establish the feasibility of utilizing the ED to provide services for patient needs that are not emergencies, specifically the lung cancer screening. Implementation of lung cancer screening services in the ED will allow for earlier diagnosis of lung cancer and increase opportunities to treat this disease, bettering patient outcomes and improving quality of life.

### **Single-Cell Fixed RNA Gene Expression Profiling in Thoracic Aortopathy**

**Ethan H. Barksdale**, Benjamin J. Landis

**Background:** Thoracic aortic aneurysm (TAA) is characterized by aortic enlargement and may predispose to aortic dissection or rupture. The cellular mechanisms of TAA development and progression are incompletely understood. We aimed to develop single-cell fixed RNA profiling using human aortic tissues and cells, hypothesizing that cellular composition and gene expression are altered in TAA.

**Methods:** We investigated 3 human aortic cell preparation techniques for single-cell fixed RNA profiling with the Chromium Single Cell Gene Expression Flex assay (10X Genomics, Pleasanton, CA), starting with (A) flash frozen aortic tissues; (B) formalin-fixed aortic tissues; or (C) smooth muscle cells (SMCs) cultured directly from aortic tissues. The Flex assay was performed using cells that were dissociated from flash frozen aortic tissues. Data were processed with Cell Ranger and analyzed using Loupe Browser.

**Results:** Single-cell transcriptome data were generated from flash frozen aortic tissues for 10 TAA cases and 5 controls, identifying 19 unique cell clusters. Six clusters were provisionally assigned as SMCs, 3 as fibroblasts, 3 as endothelial cells, 2 as macrophages, and 5 uncertain. SMCs were the most common cell types in cases and controls. Multiple clusters included disproportional numbers of cells between TAA and controls, likely representing dysregulated cell states. Preliminary analysis of cells from formalin-fixed

tissues indicates a need for further technical optimization in preparation. Cultured aortic SMCs were successfully prepared for Flex assay RNA profiling.

**Conclusion:** These initial investigations of fixed RNA profiling in human aortopathy tissues and cells successfully generated single-cell transcriptomic data using flash frozen aortic tissues. The use of formalin-fixed aortic tissues and cultured aortic SMCs requires further development and Analysis. The application of fixed RNA profiling in human aortopathy has the potential to advance the understanding of disease mechanisms.

### **Efficient Adoption of Robotic Spine Surgery in 1 and 2-Level TLIF**

**Evan Brown**, Micah Smith

**Background:** Transforaminal lumbar interbody fusion (TLIF) is a critical procedure in modern spinal surgery, effectively addressing chronic back pain, restoring mobility, and improving patients' quality of life. It involves fusing adjacent vertebrae (1-Level or 2-Level TLIF) to treat conditions like anterolisthesis. TLIF can be performed through traditional open surgery or minimally invasive surgery (MIS), which uses smaller incisions and specialized tools to reduce tissue disruption and accelerate recovery. Both approaches incorporate advanced technologies such as fluoroscopy-guided surgery, computer navigation, and robotics, enhancing precision and outcomes. The integration of robotics in TLIF surgery, while requiring a learning curve, has shown promising results.

**Methods:** This study included 222 adult patients who underwent 1-2 level TLIFs from 2014 to 2024 at Parkview Hospital, all performed by Dr. Smith. It compared outcomes among open fluoroscopy, MIS, and robotic-assisted procedures.

**Results:** Significant findings indicated that robotic TLIF resulted in reduced operative time, hospital stay, and blood loss compared to open surgery for both 1-Level and 2-Level procedures. There was no significant difference in fluoroscopy time between open and robotic procedures. MIS robotic procedures showed shorter operation times compared to MIS fluoroscopy, but comparable outcomes in blood loss, hospital stay, and fluoroscopy time. Robotic screws used in TLIF are typically longer and wider, potentially reducing the need for revision surgeries by augmenting fixation. Common comorbidities among patients undergoing 1-Level TLIF included hypertension, respiratory conditions, and arthritis. Those undergoing 2-Level TLIF frequently had hypertension, arthritis, and diabetes mellitus.

**Conclusions:** In conclusion, the study supports that robotics in TLIF surgery improve patient outcomes, with the surgeon demonstrating rapid proficiency in their use. This

advancement marks a significant evolution in spinal surgery, promising enhanced recovery. The findings highlight robotics' potential to redefine standards in spinal fusion, ushering in a new era of precision and efficacy in spinal care.

### **The Impact of Neuritin 1 on Retinal Ganglion Cell Survival in Human Donor Glaucomatous Eyes using the Translaminar Autonomous System**

**Faith N. Mikolajczyk**, Shahna S. Hameed, Tasneem P. Sharma

**Background:** Glaucoma is a progressive optic neuropathy characterized by degeneration of retinal ganglion cells (RGCs), thinning of the retinal nerve layer, and atrophy of the optic nerve. Disease progression is characterized by increased intraocular pressure (IOP) and visual field loss. The only efficacious therapy for treating glaucoma is modification of IOP through pharmacological or surgical intervention. Although these interventions slow disease progression, they do not prevent RGC death entirely. Decreased axonal transport of essential neurotrophic factors contributes to RGC death. Neurotrophic factor supplementation has been shown to improve RGC survival and sustain retinal function. We have previously demonstrated that secreted human Neuritin-1 (hNRN1) exhibits neuroprotection, regeneration, and preservation of RGC function in non-glaucomatous human eyes perfused in the ex-vivo Translaminar Autonomous System (TAS). We will investigate the effects of hNRN1 in glaucomatous human donor eyes within the TAS to evaluate if hNRN1 can protect RGC loss in diseased retinas.

**Methods:** Three pairs of glaucomatous human donor eyes were obtained from eye banks in accordance with the Declaration of Helsinki. Posterior cups were perfused using the TAS for 6-7 days under high and normal pressures with and without hNRN1. We then assessed RGC survival by measuring apoptosis, inflammation, and retinal markers using qRT-PCR and immunostaining. Retinal activity was measured using the OcuScience® Ex Vivo electroretinogram.

**Results:** Posterior eye cups were successfully maintained in the TAS under normal and high-pressure conditions for 6-7 days. Human NRN1-treated eyes showed differential expression of various inflammatory and apoptotic markers. Decreased extracellular matrix deposition (Collagen, Fibronectin, Laminin) and improved retinal activity was seen within the treated glaucomatous eyes.

**Conclusions:** The TAS model can mimic pressure-induced pathogenesis in human glaucoma. Data from this study shows that hNRN1 may serve as a potential therapeutic target by promoting RGC survival in glaucoma patients.

## **Predictors of Discharge to Post-Acute Rehabilitation Following Spinal Surgery: Insights from a National Database Analysis**

**Fezaan Kazi**, Albert Yu, Muskan Bhatla, Mohamed A. Zaazoue, David Stockwell, Wael Hassaneen, Varun Rao, Munish C. Gupta

**Background:** A major area of delay and inefficiency in the United States healthcare system is patient discharge to post-acute rehabilitation services in the postoperative setting. Many patients may experience longer-than-necessary hospitalization following spinal surgery as a result of both evolving provider judgment regarding patient disposition and delays in securing discharge approval, insurance coverage, or facility acceptance for rehabilitation services. This study utilized a nationwide surgical database to examine various demographic and clinical factors that may predispose patients to such postoperative dispositions, in an attempt to increase predictability of requiring such services and streamline the process for patients.

**Methods:** Data was aggregated from the National Surgical Quality Improvement Program (NSQIP) database, focusing on patients who underwent spinal surgeries for deformity correction between 2006 and 2021, identified by specific CPT codes (22216, 22800, 22802, 22804, 22808, 22810, 22812, 22818, 22819, 22843, 22844, 22846, 22847). An analytical tool was developed to sift through thousands of patient records, identifying factors associated with discharge to post-acute rehabilitation (defined as care provided in inpatient rehabilitation units and facilities, skilled nursing facilities, long-term acute hospitals, and by home health services). Various pertinent demographic and clinical variables were analyzed, including age, sex, race, diabetes, transfusion history, functional status, bleeding disorders, and sepsis. The analysis included calculating the proportion of patients discharged to non-home locations within these subgroups, in order to classify patients as high, moderate, or low risk for such a disposition.

**Results:** Overall, 2808 patients underwent deformity spine surgery, of which 33% required postoperative discharge to rehab facilities or other non-home discharges. The proportion of patients discharged to rehabilitation facilities generally increased with age, rising from 0.578 in the 70–90 age group (n=690) to 0.75 in the 80–90 age group (n=104). Among patients with diabetes, females had a higher non-home discharge proportion (0.527) compared to males (0.446). Diabetes combined with a history of transfusion significantly increased the non-home discharge proportion regardless of sex (0.857, n=7). Black patients with diabetes were more likely than patients overall to require rehab (0.69, n=42, vs 0.493, n=351). Patients with both diabetes and bleeding disorders exhibited a high discharge proportion, especially if they did not have sepsis within 48 hours prior to surgery (0.91, n=11). Conversely, the proportion

was significantly lower for patients without diabetes, bleeding disorders, transfusion history, or sepsis.

**Conclusions:** The study identifies age, sex, race, diabetes status, functional status, transfusion history, bleeding disorders, and sepsis as significant factors influencing the likelihood of discharge to non-home locations post spinal surgery for deformity correction. These findings underscore the need for tailored discharge planning and early resource allocation to support high-risk patient groups effectively and efficiently. The use of a national database with thousands of patients confers additional reliability to the findings and allows for more confidence in pursuing pre-operative decisions regarding postoperative patient disposition for higher risk patients, thus mitigating additional patient risk by reducing delays and time in hospital.

## **Racial and Ethnic Disparities in Emergency Medical Transport: A Comparative Analysis of Trauma Admissions at a County Hospital and Academic Health Center**

**Fezaan Kazi**, Ajay Patel, Ali Sualeh, Jeff Kaihao Guo, Ahsan Siddiqui, Ammaar Basher, Mohamed A. Zaazoue, Muqsit Buchh, Varun Rao, Jamie Bradbury

**Background:** Trauma patients are often unable to communicate a preferred destination to emergency medical services (EMS) due to injuries or impairment. The destination hospital is thus determined by the EMS team transporting the patient. This study compares Level 1 trauma admissions in a major metro area at a county hospital (CH) and an academic health center (AHC) within two miles of each other.

**Methods:** We performed a retrospective analysis of patient charts and transport documentation to determine basic demographic and admission data for each patient. The analysis included location of EMS pickup, the facility the patient was taken to, and documented reasons for taking the patient to that specific facility.

**Results:** A total of 1520 patients were transferred to the CH and 625 to the AHC. The data suggests that more White patients were transported to the nearest hospital than minority patients (53.1% vs 46.4%, p=0.003) and fewer White patients bypassed the nearest hospital than minority patients (21.2% vs 33.0%, p < 0.001). Minorities were more likely to bypass AHC and be admitted to CH than White patients (46.6% vs 24.6%, p < 0.001); meanwhile only 3.8% of minorities bypassed CH to be admitted to AHC. We found that a higher proportion of AHC patients were Black compared to CH (47.4% vs 37.1%, p<0.001), but CH had a higher proportion of Hispanic patients than AHC (10.1% vs 5.6%, p<0.001). A higher proportion of patients at the AHC had Medicare (18.4 vs 10.9 %, p<0.001) and Medicaid (22.2 vs 12.8%, p<0.001). Meanwhile, more patients at the CH were classified as self pay (14.5% vs 11.8%, p = 0.027).

**Conclusions:** There is a significant difference in transport patterns between the two hospitals when it comes to patient race and ethnicity. Minority patients transported to CH were more likely than their white peers to bypass the nearest facility, after accounting for many established confounding factors.

### **A Clinically Interpretable Deep Learning Framework for the Detection and Grading of Diabetic Retinopathy**

**Frank Bogan,** Hunter Gill, Doaa Salem, Michael Happe, Sarath Janga, Amir Hajrasouliha

**Background:** One of the leading causes of blindness in working age adults is diabetic retinopathy (DR) which can result in vision loss if uncontrolled. DR can be detected and graded by fundus retinal imaging, however the amount of images requiring grading creates a burden on ophthalmologists. Thus, a growing demand exists for an optimized DR image reading process. To accomplish this, we propose the use of a deep learning artificial intelligence (AI) model to detect and grade DR using lesion feature extraction with clinical interpretation.

**Methods:** Retinal fundus images were collected from two sources for training (n=608): E-Ophthalmology, and a private Indiana University Eugene & Marilyn Glick Eye Institute dataset. Each dataset was divided into 70% (training), 20% (validation), and 10% (testing) subgroups. An external dataset, the UKBB, was also used (n=944) for evaluation. The AI model assigned images to 5 categories based on lesion features. The model operated through 2 stages: a multi-scale DeepLabV3+ to segment retinal lesions from input fundus images, followed by segmentation predictions for lesion. A classifier incorporates data to predict whether DR is present and the grade for images with DR.

**Results:** AI performance was analyzed using several metrics to compare against human grading. Developmental results for segmentation were: 0.88 (precision), 0.70 (recall), 0.78 (f1 score), 0.99 (accuracy), 0.94 (AUC), and 0.76 (IOU). Classification of DR results were: 0.89 (precision), 0.6 (recall), 0.78 (f1 score), 0.62 (accuracy), and 0.8 (AUC). External dataset results were: 0.47 (precision), 0.58 (recall), 0.52 (f1 score), 0.58 (accuracy), and 0.65 (AUC).

**Conclusions:** The proposed deep learning AI framework demonstrates good DR lesion detection and grading performance. Further improvement may allow AI to replace human grading, saving ophthalmologists time and standardizing the grading process. The current approach may be improved by including more lesion features and larger sample sizes.

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### **Information Sources for HPV Vaccination of Latinx Adults**

**Gabriela Mauro,** Niki Messmore, Monica Kasting

**Background:** Human papillomavirus (HPV) infection remains a significant public health concern in the United States, particularly affecting Latinx communities. HPV, which is preventable through a vaccine, refers to a group of viruses with over 100 types identified, some of which can cause genital warts or lead to cancer. Thus, it is important to recognize and address information barriers and Latinx-specific barriers these patients face when considering getting the HPV vaccine. This article explores the factors of HPV vaccination uptake among Latinx communities, emphasizing the role of trusted sources in promoting vaccine acceptance and uptake.

**Methods:** PubMed and Google Scholar were used to find literature on Latinx adult populations and examine information-seeking behavior to determine trusted sources or methods most conducive to vaccine uptake. Keywords included “Papillomavirus vaccines,” “Hispanic or Latino,” “information-seeking behavior,” and “information sources.” Findings were synthesized narratively to identify common themes and variations in HPV vaccine acceptance among Latinx adults.

**Results:** Positive correlations with perceived vaccine safety, benefits (genital HPV prevention), and severity of HPV risks are crucial in HPV-related cancer prevention efforts. Narrative formats such as *fotonovelas* effectively communicate health messages, while collaboration among physicians, nurses, *promotoras de salud*, and community partners strengthens outreach efforts. Texts delivered in recipients’ preferred language enhance communication effectiveness. Loss-frame messaging (emphasizing potential negative consequences of inaction) can effectively motivate behavior change in collectivist cultures. Cultural values, the influence of physician recommendations, and perceived transmission agencies are pivotal in shaping health behaviors and decisions within Latinx communities.

**Conclusion:** In conjunction with their delivery by a community partner or healthcare provider, community-specific patient literature or education materials can potentially increase HPV vaccination rates among the adult Latinx population. By utilizing these findings, public health endeavors can effectively increase HPV vaccine uptake in the Latinx community, thereby decreasing the disproportionate amount of HPV-related cancers in this group.

### **Gut-to-Brain Axis: The Protective Role of Gastrokine-1 from Parkinson’s Disease**

**Garrett Wolfram,** David Boone

**Background:** The purpose of this study was to understand how the gastric protein Gastrokine-1 (Gkn1) influences the development of Parkinson's disease (PD). We hypothesize that Gkn1 protects against  $\alpha$ -Synuclein deposition and PD symptoms.

**Methods:** Coordination Tests were taken separately for aged male and female mice on three tasks: time to travel 18 inches across a beam (counting slips), time to turn and descend 45 cm down a pole, and duration of holding onto a wire with front paws. Additionally, immunofluorescence images of frozen intestine and brain of adult Gkn1 WT and KO were incubated with Tyrosine Hydroxylase (TH) and  $\alpha$ -Synuclein aggregate antibodies.

**Results:** Male beam-crossing time was slower for Gkn1 KO than WT mice (6.4s vs 4.1s,  $p=.005$ ). In female mice, Gkn1 KO crossed slower than WT (4.4s vs 3.0s,  $p=.0004$ ) and slipped more often (2.1 vs 0.9,  $p=.007$ ). Other tests showed no significant findings. Sections of intestine stained with TH and  $\alpha$ -Synuclein fluoresced in submucosal tissue of duodenum, ileum, and colon. There was no noticeable difference in density of either TH or  $\alpha$ -Synuclein aggregates between Gkn1 WT or KO.  $\alpha$ -Synuclein aggregates were not visible in the brain sections of the specimens used.

**Conclusions:** The coordination tests indicate Gkn1 KO mice have decreased coordination in both sexes. This suggests the mice lacking Gkn1 could be developing PD or Parkinsonism. The immunofluorescent scans support the gut-to-brain hypothesis, showing more dopaminergic nerves and  $\alpha$ -Synuclein aggregation in the duodenum, which has the greatest vagal innervation in the intestine.  $\alpha$ -Synuclein aggregation was more prominent in the intestines than the brain, suggesting PD may start in the gut. Understanding the function of Gkn1 in the gut-to-brain axis may provide insights into the role of amyloid and  $\alpha$ -Synuclein etiology and management of PD symptoms.

### **Assessing Health Promotion Needs Among Immigrant Haitians in Central Indiana: A Literature Review**

**Gavin Thompson**

**Background:** The present study was aimed at investigating the health promotion intervention needs of the immigrant Haitian community in central Indiana. As the number of Haitians immigrating to the United States has increased in recent years, so too has the number of Haitians settling in Indiana, largely due to the lower cost of living and employment opportunities as compared to larger port cities. However, despite these attractants, Haiti immigrants to the Midwest still face a number of significant obstacles. This demographic influx has highlighted critical challenges, including language barriers and limited access to healthcare and economic integration opportunities.

**Methods and Results:** Conducted in collaboration with community stakeholders and organizations, this needs assessment identifies key health disparities and community priorities. The findings underscore the urgent need for tailored interventions to improve health outcomes and reduce disparities among Haitian immigrants in Indianapolis. Central to this research is the development of a Health Equity Hub, envisioned as a collaborative platform for stakeholders from academia, public health, healthcare systems, and social services. This hub aims to foster innovation and facilitate the implementation of culturally sensitive and effective health interventions. This research employed a Human-Centered Design approach by actively involving Haitian community members in the process. This model prioritized collaboration to clarify needs, generate ideas, and co-develop solutions with community partners. Facilitated by Research JAM sessions, these focus group workshops enabled researchers to pinpoint strategic priorities for advancing health equity within the Haitian community. Over the course of a year, three such sessions were conducted, resulting in the formulation of project concepts ready for grant proposal submissions.

**Conclusions:** By delineating the pressing issues faced by the Haitian immigrant community, this research provides a foundational understanding for future initiatives and policy interventions aimed at promoting health equity and enhancing community well-being.

### **Promoting Healthcare Careers for Minority Adolescents from the City of Gary**

**Gionté Mason, Jocelyn Chang-Stroman, Amy Han, Tatiana Kostrominova**

**Background:** Black and Hispanic individuals are underrepresented in medicine with several studies predicting a future deficit in Black and Hispanic physicians, especially when considering a growing proportion of the Hispanic population in the US. This study aims to determine whether early exposure to healthcare career options for low-income, minority adolescents can promote interest in the healthcare profession.

**Methods:** Two 45-minute presentations on health career options were given to a cohort of middle-schoolers ranging from 10-13 years old participating in the Kids College program in the medical track at Indiana University Northwest. A pre-survey and post-survey were given in the first five minutes and the last five minutes of a presentation on healthcare-related topics including career opportunities, a cast application demonstration, and ultrasound machine usage.

**Results:** Surveys showed that 5 out of the 7 medical track students wanted to pursue a career in healthcare both

before and after the presentations. The presurvey results showed that students learned about healthcare careers in a variety of ways before participating in the Kids College program.

**Conclusions:** Given the small sample size and knowledge before the presentations, it was difficult to conclude whether the exposure to healthcare-related topics provided by this program significantly increased the target audience's interest in future healthcare-related topics. A larger number of presentations and an increase in the number of participants is needed to reliably evaluate the effectiveness of this program in the promotion of interest in healthcare careers in minority adolescents. We are convinced that increased awareness of healthcare careers will promote interest in future careers in this area. This work was partially supported by the Trailblazer Planning Award from CTSI (T.K. and A.H.). G.M. and J.C. are medical students supported by the IMPRS program (CTSI grant UL1TR002529).

### **FoodRx: Exploring Disparities in Food Insecurity and Eye Health Conditions**

**Gloria V Cabrero**, LaKeisha Boyd, Deanna Reinoso, Richard J Holden, Daniel O Clark, Titus K Schleyer, Rebecca L Rivera

**Background:** Good nutrition and chronic disease management are important for eye health; however, little is known about the relationship between food insecurity and eye health outcomes. Marion County is designated as a medically underserved area, and 25% of families rely on food assistance. Additionally, Indianapolis is considered one of the least accessible American cities in terms of healthy food options.

**Objective:** My central research objective was to understand how food insecurity impacts eye health in medically underserved populations. This project had three specific aims: 1) understand the process of identifying food insecurity in an eye clinic setting; 2) implement food insecurity screening in a student run eye clinic; and 3) determine associations of food security status with eye health outcomes among Eskenazi Health patients.

**Methods:** In Aims 1 and 2, I consulted the literature and clinicians from the Eskenazi Health Department of Ophthalmology. I developed a protocol implementing food insecurity screening into the electronic health record of a student-run eye clinic using the clinic-based Hunger Vital Sign (HVS) 2-question screener. For Aim 3, I worked with a Regenstrief Data Core analyst to extract patient and community demographic information, eye health conditions, and food insecurity status from the Eskenazi Health Data Warehouse.

**Results:** I implemented the food insecurity protocol as a quality improvement project into the student-run eye clinic and to date, n=12 patients were screened. Additionally, I developed an analytical plan which included consolidating 1,073 eye-related ICD-10 codes into two groups: "nutrition-related eye disease" or "other eye disease."

**Conclusion:** These exploratory study findings will generate future research questions and quality improvement initiatives to further investigate tailored clinic-community prevention initiatives, such as extending the food insecurity screener to other healthcare settings and integrating community resources with health care.

### **Social Determinants of Vision Health: Characterizing Ophthalmic Readmissions in Northwest Indiana**

**Grace Armstrong**, Neon Calumpang, Jonathan Guerrero, Baraka Muvuka

**Background/Objective:** With aging populations and increasing life expectancy, the global disease burden of age-related conditions is expected to rise. In the United States, the number of individuals with visual impairment is projected to increase by 25% per decade to reach 6.95 million people by 2050. Timely care is essential for the prevention and treatment of vision loss, yet disparities in eye care access persist. This study investigates the social, demographic, and behavioral characteristics associated with ophthalmic readmissions as part of a participatory research partnership between Indiana University School of Medicine-Northwest and an urban health system in Northwest Indiana (NWI).

**Methods:** This retrospective study analyzed data collected from SDOH screenings in Epic using the Protocol for Responding to and Assessing Patients' Assets, Risks, and Experiences (PRAPARE) for all inpatient admissions across 3 NWI urban hospitals from January 2021 to April 2024. Data analysis included descriptive, bivariate (Chi-Square;  $p < 0.05$ ), and multivariate (binary logistic regression;  $p < 0.05$ ) analyses using SPSS 29.0. The study was exempted by the Indiana University Human Research Protection Program (IRB #14040).

**Results:** The study sample consisted of 338 ophthalmic patients who were predominantly White (59.5%) and older adults ( $79 \pm 18$ ). The bivariate analysis found a statistically significant association between ophthalmic readmissions with age ( $p = 0.026$ ), sex ( $p = 0.031$ ), hospital ( $p = 0.014$ ), and length of stay ( $p < 0.001$ ). After controlling for all covariates in the multivariate analysis, increased age (OR=1.016;  $p = 0.033$ ), Hospital C (small hospital in a medically underserved area) (OR=2.396;  $p = 0.006$ ), and prolonged hospital stay (OR=1.091;  $p = 0.002$ ) remained significantly associated with higher odds of ophthalmic readmissions.

**Conclusion/Implications:** These findings indicate a significant association between ophthalmic readmissions and several social determinants of health. Understanding predictors of ophthalmic readmissions is a key step towards developing more effective eye care delivery interventions.

### **Planning for Dementia Diagnoses: The Physician's Role in Developing Firearm Retirement Plans in Aging Populations**

**Haley Harkness**, Sam Kay, Ashley Meagher, Linda Schutzman

**Introduction:** Firearm ownership poses a critical risk to people living with dementia (PLWD) and their caregivers. Out of 241 veteran suicides that took place from 2001-2005, 73% were carried out using firearms, the majority of these suicides occurred in patients newly diagnosed with dementia. However, little is understood regarding how clinicians can effectively approach the subject of gun safety and cognitive decline.

**Methods:** A prospective survey was given to patients over 60 to assess attitudes and preferences regarding physician intervention in firearm safety planning in the case of cognitive decline. A second survey was distributed by the Marion County Youth Violence Prevention Coalition to determine the rate at which physicians discussed firearm safety with the caregivers of aging patients.

**Results:** Before participating in this study, 67% (n=12) of participants stated that they had never had a conversation about firearm safety and cognitive decline. 50% (n=9) reported that they were open to discussing firearm safety with their physician, with 11% (n=2) selecting that they were "undecided." After the survey, 72% (n=13) of participants planned on having a conversation related to firearm safety planning in the case of cognitive decline. The survey directed toward caregivers reported that 21% (n=5) of participants discussed firearm safety with a healthcare provider.

**Conclusion:** Before taking this survey, only 33% of participants had discussed firearm safety in the case of cognitive decline. After participating, 72% planned to have that conversation. We will continue this project by determining the preferences of caregivers regarding physician intervention in firearm safety planning and discovering the resources physicians need to assist in these conversations. When the most efficacious intervention strategy is understood, physicians can use their influential roles to equip aging populations with the ability to protect themselves and their families from firearm related injuries and deaths in the case of cognitive decline.

### **Comparative Analysis of Postoperative Outcomes at 6 Weeks: Basilar Thumb Reconstruction with**

### **Trapezium Excision and Fiberlock Internal Brace Reconstruction with Tenodesis versus Thumb Trapeziectomy with Ligament Reconstruction and Tendon Interposition**

**Hanna Malik**, Conor Ratigan, Derek Yocum, Sam Fuller, Aldebert Mencias

**Background:** Basilar Thumb Reconstruction (BTR) is a surgical procedure for the treatment of basilar thumb arthritis at the first carpometacarpal (CMC) joint of the thumb. There are a variety of surgical techniques that can be used in this procedure; however, they vary in post-operative outcomes of pain, function, recovery time, and strength. Optimizing surgical techniques in BTR is important for long-term patient outcomes, as the thumb is central for many activities of daily living. Research regarding the post-operative outcomes of BTR surgery with newer techniques, such as those with medical device implants, is crucial in determining the trajectory of this growing field.

**Methods:** Retrospective data was collected on 77 patients with thumb carpometacarpal (CMC) arthritis who underwent trapeziectomy with LRTI or Arthrex FiberLock™ Suspension Implants (Arthrex, Naples, FL, USA) Internal-Brace suspensionplasty with trapezium excision and side-to-side flexor carpi radialis tendon transfer. There were 38 LRTI and 39 FiberLock Internal Brace suspensionplasty procedures. Outcomes were measured using the Visual Analogue Scale (VAS) for pain, Quick Disabilities of the Arm, Shoulder, and Hand (QuickDASH) questionnaire, and Patient-Reported Outcomes Measurement Information System (PROMIS) v1.2 Upper Extremity (UE) item bank. Patient demographic data was also recorded.

**Results:** The PERMANOVA test revealed a significant difference in multivariate centroids between the groups ( $p < 0.01$ ). Approximately 31.29% of the variation in the dataset was explained by the grouping variable. However, post-hoc pairwise tests demonstrated no significant (All  $p > 0.05$ ) differences between groups for (VAS Pain 24 Hours, VAS Pain When Resting, VAS Pain When Active, PROMIS Upper Extremity, and Quick DASH).

**Conclusion:** Our analysis demonstrated LRTI patients may have more consistent outcomes 6-weeks after surgery compared to the newer FiberLock procedure. However, it is promising that no significant differences were seen between the patient outcome surveys of the two groups. Future research on long-term outcomes will be beneficial in comparing the effects of this new surgical technique.

### **Glaucomatous E50K Mutation in the Optineurin Gene Causes Mitophagy Defects for Retinal Ganglion Cells but Not for Motor Neurons**

**Harshavardhan Sanaka**, Michelle Surma, Leah La-  
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Cross, Kavitha Anbarasu, Arupratan Das

**Background:** Clearance of damaged mitochondria by lysosomes, known as mitophagy, is critical for maintaining mitochondrial homeostasis and cellular energy balance. Optineurin (Optn) is the central player for mitophagy found to be mutated among normal tension glaucoma (OPTNE50K) and in some familial forms of amyotrophic lateral sclerosis (OPTNE478G) patients. It is critical to understand how mitophagy mechanisms are altered for these inherited mutations in stem cells and differentiated neurons to gain insight into the disease's developmental aspect.

**Methods:** We utilized human embryonic stem cell-derived retinal ganglion cells (hRGCs) and induced motor neurons (iMNs) with and without the OPTNE50K mutation. The cells were treated with DMSO (vehicle control) or with 10 mM CCCP, an uncoupler that induces mitochondrial damage. We then analyzed the activation status of critical mitophagy players including Optn, Parkin, Pink and Lc3b. We further analyzed if OptnE50K mutant forms aggregate in iMNs as observed for hRGCs.

**Results:** We found that OPTNE50K mutation causes attenuated activation for Optn, Parkin, and LC3b in hRGCs under mitochondrial damage, while iMNs and hRGCs maintained healthy mitophagy. Additionally, mutant iMNs do not display distinct Optineurin aggregates, unlike in mutant hRGCs.

**Conclusion:** Our results suggest that the OptnE50K mutation may disrupt mitophagy in hRGCs but not in iMNs and stem cells. In addition, the lack of Optn aggregates in the OPTNE50K mutant iMNs suggests an alternative pathway that inhibits the aggregate formation, presumably for maintaining healthy mitophagy for longer survival.

**Impact:** The results from this project lay the groundwork for further investigation of the mechanisms behind mitophagy and its relation to glaucoma and ALS. Understanding what causes certain cell types to degrade while others remain healthy is key to understanding the genotype-phenotype specificity for inherited gene disorders.

### **Novel Role of Megakaryocytes in the Skeletal Response to Mechanical Loading**

**Ian M. Burke,** Amy Creecy, Sonali J. Karnik, Olatundun D. Awosanya, Tyler J. Hesselbrock, Sarah L. Mostardo, Kuldeep Yadav, Rachel J. Blosser, Pratibha Singh, Angela Bruzzaniti, and Melissa A. Kacena

**Background:** Megakaryocytes (MKs) are the largest and rarest of the cell types in bone marrow. MKs not only play a vital role in thrombopoiesis but are also known to regulate bone mass. Indeed, MKs stimulate osteoblast proliferation and bone formation through a direct cell-to-cell interaction.

Bone mass is regulated by mechanical stimulation, primarily through the mechanical sensing osteocytes. Interestingly, MKs are also known to be responsive to mechanical stimulation. Therefore, we hypothesized that bone formation induced by mechanical loading could be attributed, in part, to MK-mediated stimulation of bone formation.

**Methods:** We selectively ablated MKs (~50% reduction) in some mice using diphtheria toxin (DT). The right tibia of mice underwent mechanical loading 5 days/week for 2 weeks. Upon completion of the study, platelets and MKs were measured, and both loaded and non-loaded tibia were analyzed for bone-related parameters via microCT and histomorphometric assessments.

**Results:** Results indicated successful >50% reduction in MKs and platelets. Male and female mice showed no significant change in trabecular volume or thickness with loading but exhibited a trend of lower trabecular bone formation rate due to DT ablation. Female mice in the control group displayed increased number of osteoclasts per bone perimeter due to mechanical loading. This was not the same for the group treated with DT.

**Conclusion:** This suggests that MKs may play a role in bone remodeling due to mechanical loading. While more work is required to further elucidate these preliminary findings, it appears that reduced numbers of MKs for a short time minimally alters trabecular bone responses induced by mechanical stimuli. Importantly, dissecting the mechanisms responsible for skeletal changes may yield insights into potential therapeutic targets which could be developed to improve the bone mass and reduce osteoporotic related fractures in our aging demographic.

### **Induction of P53 in monocytes during co-culture of PBMCs with *P. falciparum* is partially mediated by IFN $\gamma$**

**Isabella Rodriguez,** Jyoti Bhardwaj, Tuan M. Tran

**Background:** Baseline activation of p53 pathways has been associated with decrease inflammatory responses to incident malaria infection in children. Using a mouse malaria model, we recently found that *Plasmodium* infection reliably upregulates p53 expression in peripheral blood mononuclear cells (PBMCs). We hypothesize that malaria infections induce p53 in monocytes to subsequently blunt the host inflammatory response. We have proposed three potential mechanisms of this upregulation that includes interferon (IFN)-dependent and/or IFN-independent pathways. An IFN-mediated pathway model is supported by previous evidence and established effects of type 1 IFNs on p53 protein levels and our data showing induction of p53 in monocytes upon IFN $\gamma$  stimulation. Here, we sought to explore the role of IFN $\gamma$ -mediated pathways in *Plasmodium falciparum* (Pf)-induced p53 expression in human PBMCs.

**Methods and Results:** Our initial co-culture experiments revealed that infected RBCs (iRBCs) induced p53 expression in CD14+ monocytes but not in other immune cell subsets of PBMCs however, p53 induction was absent in purified monocytes suggesting that signals from other cells are required for Pf-induced p53 expression in monocytes. Moreover, blockade of IFN $\gamma$  during PBMC co-culture with iRBCs partially abrogated p53 induction in monocytes. Based on this, we examined the cellular source of IFN $\gamma$  and revealed  $\gamma\delta$ T cells as major source of IFN $\gamma$  in iRBCs stimulated PBMCs. Subsequent co-culture experiments with  $\gamma\delta$ -T cell-depleted PBMCs showed reduced p53 expression compared to bulk PBMCs.

**Conclusion:** These findings suggest that crosstalk between  $\gamma\delta$ -T cells and monocytes via IFN $\gamma$  is crucial for parasite-induced p53 induction in monocytes. We are currently repeating these experiments and evaluating the effects of other stimulatory factors, including Type I IFN (IFN  $\alpha/\beta$ ) and pro-inflammatory cytokines like TNF, IL-1 $\beta$ , and IL-6 on p53 expression in PBMCs. Overall, these studies will provide important insights into the mechanisms underlying p53 upregulation in malaria-exposed children and help determine whether such upregulation affects malaria-induced inflammation.

### **Potential Biomarkers for Early Long-term Pulmonary Dysfunction Following Hematopoietic Stem Cell Transplantation**

**Isabella Small, Pi Chun Cheng, April Rahrig, Courtney Rowan**

**Background:** Pulmonary complications post-hematopoietic cell transplant (HCT) are common in children. The goal of this hypothesis-generating study is to identify potential risk biomarkers for long-term pulmonary dysfunction in children post-HCT.

**Methods:** This is a secondary analysis of a prospectively collected pediatric cohort. Pulmonary dysfunction within the first three months post-allogeneic HCT was evaluated using pulmonary function tests (PFTs) or requiring oxygen support at any during in the first 3 months post-HCT. Biomarker levels from days +7 and +14 plasma samples were measured using enzyme-linked immunosorbent assays (ELISAs). Biomarkers were chosen based on previous study and biologic plausibility, including soluble WAP-4 Disulfide Core Protein Domain-2 (WFDC2), Stimulation-2 (ST2), Tumor Necrosis Factor Receptor-1, Matrix metalloproteinase-2 and-9 (MMP2, MMP2), and Surfactant Protein D (SPD).

**Results:** Twenty-six patients were enrolled. The median age was 12 years. In the first 3 months post-HCT, 5 (19.2%) patients required oxygen support, 13 (50%) had a decreased FEV1/FVC ratio, and 6 (28.7%) patients had

PFT results indicative of restrictive lung disease. Those who required oxygen support had a trend toward higher SPD levels (20.82 ng/mL, (IQR:18.88, 20.84) vs 10.09 IQR:6.74, 19.15, p=0.11) and WFDC2 levels: 54,530.0 pg/mL (IQR:45,391, 90,214) vs 25,981 IQR:10,563, 44,344),p=0.006) Those with an impression of restrictive lung disease on PFT trended toward higher TNFR-1 (3,831.9 ng/mL, (IQR:2,945.8, 4,958.1) vs 2,880.3 (IQR:2,685.4, 3,643.8), p=0.08 ) and MMP2 (371 ng/ml (IQR:287.3-427.3) vs 303.7 (IQR: 278.8, 353.3), p=0.18). Those who had worsening FEV1/FVC at 3 months trended toward higher MMP9 (15,347.5 pg/mL (IQR: 9,392.2-22,525.3) vs 8,254.9 (5,445.5, 14,831.6), p=0.06 and ST2 (24,011 pg/mL (IQR:10,719.5, 68,354.5) vs 16,826 (IQR:9,333, 27,486), p=0.22).

**Conclusion:** This hypothesis-generating study demonstrated promising results for six biomarkers: SPD, WFDC2, TNFR-1, ST2, MMP2, and MMP9, for pulmonary dysfunction. Larger cohort studies are needed to determine true ability to detect risk for long-term pulmonary dysfunction.

### **Sensitization of APC knock-out cells to Doxorubicin in vitro using KU55933, an ATM inhibitor**

**Isaias F. Colón, Angelique R. Wise, Jenifer R. Prospero**

**Background:** Triple negative breast cancer (TNBC) has the lowest 5-year survival rate among breast cancer subtypes, with Adenomatous Polyposis Coli (APC) mutations/deletions found to be a leading cause of Doxorubicin (DOX) resistance. Additionally, increased expression of pATM/ATM in APC knock-out (APCKO) cells was previously observed, providing a possible explanation to chemotherapy resistance. We hypothesized that treatment with the ATM inhibitor, KU55933, would sensitize APCKO cells to DOX in vitro using  $\gamma$ H2AX as a marker of DNA damage.

**Methods:** The TNBC cell line, MDA-MB-231, was previously modified using CRISPR/Cas9 to knock out APC. The current study uses the non-targeting control (NTC) and 2 clonal knock-out cell lines (APCKO or clones 1 and 2). Cells were cultured in DMEM with 10% FBS, 1% penicillin/streptomycin, and Plasmocin, and treated with either H<sub>2</sub>O, DOX, KU, or DOX+KU for 24 hours. For western blot analysis of  $\gamma$ H2AX, membranes were blocked at room temperature in 5% nonfat dry milk and incubated with primary anti- $\gamma$ H2AX overnight at 4°C using actin as an internal control.

**Results:** Immunofluorescence studies included drug treatment of cells with the four previously mentioned treatments and probing for  $\gamma$ H2AX using anti- $\gamma$ H2AX antibody. Immunofluorescence studies displayed increased  $\gamma$ H2AX expression, indicating DNA damage in the combination (DOX+KU) treatment group in the APCKO cell lines.

Western Blot analysis showed a significant difference in the DOX treated 231 NTC and clone 2 cell lines vs H2O treated cells.

**Conclusion:** Data from this study will be used to pursue further research in the efficacy of KU in sensitizing AP-CKO cells to DOX treatment and have significant implications for the future of chemotherapy research and dosing for TNBC patients. Future studies may include testing the ability of KU to overcome DOX resistance in vivo and assessment of APCKO cell recovery after drug treatment in different growth media.

### **Impact of Social Determinants of Health on Stroke Severity in the Northwest Indiana Region**

**Jacobus Barnard**, David Lin, Grace Armstrong, Neon Calumpang, Miranda Cash, Amy Han

**Background/Objective:** Stroke significantly contributes to mortality and disability in the United States, yet geographical disparities exist across regions like Northwest Indiana, where stroke incidences and mortality rates are 2-4 times higher than the national average. Social and demographic determinants of health are known factors of stroke risk and outcomes. We aim to capture a more holistic and panoptic understanding of the specific patient population served by an individual hospital system by investigating the impact of stroke risk-specific social determinants of health on stroke incidence, severity, and outcomes.

**Methods:** Data elements were extracted from patients hospitalized at three Powers Health facilities between January 2022 and May 2024. Data was recorded with the AHA's GWTG Stroke Case Record Form. Our retrospective study conducted bivariate analysis, using R, on predictor variables of age, sex, race, Hispanic ethnicity, ZIP code, payment sources, and mode of arrival to the ordinal scores of the modified Rankin Scale (mRS) and the National Institutes of Health Stroke Scale (NIHSS).

**Results:** A total of 2,569 stroke patients from 46 ZIP Codes across 7 counties were analyzed. When age-adjusted, black or African American patients from Lake County, IN had higher mean initial and discharge NIHSS scores than white patients ( $p < 0.001$ ,  $p < 0.01$ ). Regarding incidence of NIHSS scores by categories of severity, white patients had higher rates of 'No Stroke Symptoms' while black or African American patients had higher rates of 'Minor Stroke Symptoms' ( $p < 0.02$ ,  $p < 0.01$ ). ZIP Codes with higher mean NIHSS stroke scale scores correlated significantly with ZIP Codes defined by lower median household income ( $r = -0.61$ ,  $p < 0.01$ ), lower education attainment ( $r = -0.71$ ,  $p < 0.001$ ), and higher percentages of minority group populations ( $r = 0.50$ ,  $p < 0.02$ ). Patients with higher mean scores across all measures were those associated with using Medi-

care versus private insurance ( $p < 0.0001$ ) and those arriving to the hospital via EMS versus private transport ( $p < 0.01$ ).

**Conclusions:** This research addresses the significance of surveying region-specific social determinants of health for its insight into clinical stroke care and future preventative and quality improvement initiatives. Implementation of interventions and policies can mitigate disparities and impact overall stroke management and prevention strategies.

### **Enhancing Inclusivity: Implementation of a DEI/Health Equity Checklist in Emergency Medicine Resident Didactic Presentations**

**Jared Clark**, Andreia Alexander

**Background:** In 2021, the Indiana University School of Medicine Department of Emergency Medicine developed a DEI/Health Equity checklist for residents presenting during weekly didactic sessions to improve inclusivity and Health Equity education in emergency medicine education. The purpose of this present study is to evaluate the implementation of the DEI/Health Equity checklist via trends in compliance with the checklist and qualitative analysis of the DEI/Health Equity content presented.

**Methods:** This was a mixed methods analysis using a concurrent nested design. The research team watched 50 randomly selected resident lectures, ten from each academic year from 2018-2023, except for the 2020-2021 academic year due to COVID-19. Each lecture was scored according to the DEI/Health Equity checklist. Quantitative analysis used descriptive statistics to identify trends in checklist compliance, with lower scores indicating higher compliance. Qualitative analysis used visual-verbal video analysis, a type of content analysis.

**Results:** Each year was assigned an average overall composite score according to the checklist items (0-10), with a score of zero indicating complete adherence to the checklist. After an initial negative deflection, overall scores indicated a trend toward checklist compliance: 2018-19: 1.8; 2019-20: 2.3; 2021-22: 2.3; 2022-23: 1.2; 2023-24: 0.8. Residents discussing how their topic may affect someone of a diverse background followed a similar trend: 70% in 2018-2019; 70% in 2019-20; 50% in 2021-22; 80% in 2022-23; and 80% in 2023-24. The percentage of presentations with a dedicated DEI/Health Equity slide gradually increased from 20% of lectures in 2018-19 to 80% in 2023-24. Qualitative analysis revealed residents transitioned from indirectly discussing DEI/Health Equity in 2018 to directly and intentionally addressing DEI/Health Equity from 2022-24.

**Conclusions:** Implementation of a DEI/Health Equity checklist for resident didactic presentations resulted in a general trend towards checklist compliance and increasing

attention to Health Equity topics among these residents. Residents showed more intentionality in approaching DEI topics in later years. Current medical education literature provides no widely agreed upon methodology for the development of inclusive didactics and the discussion of DEI/Health Equity in graduate medical education didactic sessions. This study provides a novel technique for operationalizing DEI/Health Equity in GME didactic presentations.

### **Piloting AAV infection of iPSC derived RGCs to investigate the effect of human neuritin on RGC survival**

**Jared DeBruin**, Shahna Hameed, Nicole Bodi, Nathan Hubbard, Tasneem Sharma

**Purpose:** Glaucoma is a leading cause of blindness worldwide. Even after decreasing intraocular pressure (IOP) through current treatment paradigms, retinal ganglion cell (RGC) degeneration progresses. Prior literature shows that neuritin (NRN1) promotes neurite outgrowth and prevents RGC apoptosis in rodent axonal injury models. Decreased expression of RGC markers (ISL-1 and RBPMS) along with decreased NRN1 was observed in glaucoma donor retinas compared to controls. We hypothesize that over-expressing or inhibiting human NRN1 (hNRN1) in iPSC derived RGCs can regulate pro-survival and regenerative pathways. We propose to utilize AAV infection for hNRN1 silencing and hNRN1 overexpression to study the impacts on iPSC derived RGC survival and regeneration.

**Methods:** Keratocytes from control and glaucomatous human eyes were reprogrammed to a pluripotent state then cultured as retinal organoids (ROs). After approximately 30-35 days in culture, we dissociated ROs with papain and plated RGCs on laminin-coated tissue slides. We then infected the RGCs with AAV2 containing GFP, scramble shRNA, IREShNRN1, and hNRN1 shRNA ( $n = 3$ ) at 100,000 MOI. We observed expression from GFP/RFP reporters, isolated the culture media for an MTT assay to assess cell viability, and examined RBPMS and NEFL expression as RGC identity and regeneration markers. All data processing and analysis was conducted in Excel, Fiji, and GPP.

**Results:** We were able to culture keratocytes and induce pluripotency from control and glaucomatous donors. There was a successful RO and subsequent RGC culture generation. Upon AAV transduction, we saw differences in formazan levels and RGC marker expression in the control and glaucomatous cells across the AAV treated groups.

**Conclusions:** Our study will lay the foundation to understand the impact of hNRN1 in iPSC derived RGCs through AAVs and for investigating hNRN1 as potential therapeutic target. Our future aim will be to treat our

AAV-infected iPSC derived RGCs with exogenous hNRN1 to test axon guidance and regeneration as well as inhibit downstream NRN1 pathway inhibitors like MEK, mTOR, PI3K.

### **Derivation of a Multivariable Model to Assist Emergency Department Triage of Heart Failure Patients by Their Diuretic Treatment Needs**

**Jiayu Tian**, Ivonne Cabrera, Chukwuebuka Ojukwu, Nicholas Harrison

**Background:** Emergency medicine physicians (EMP) treat 1 million patients with acute decompensated heart failure (ADHF) annually. After emergency department (ED) treatment, EMPs must determine the need for further intravenous loop diuretic (IVLD) therapy in dispositioning patients to home (no further IVLD treatment), short stay observation ( $\leq 24$ hrs treatment), or inpatient hospitalization ( $>48$  hours treatment). We hypothesized that EMPs overestimate IVLD needs, resulting in unnecessary admission, and derived a multivariable prediction model to aid EMP decision-making.

**Methods:** We prospectively enrolled 63 patients with ADHF. The primary predicted outcome was the number of guideline-based doses of IVLD (1 dose = 1x home furosemide dose) received during the total acute care encounter. Variables available prior to ED disposition (labs, imaging, risk-scores, structured physical exam {edema, JVP, orthopnea grade, hepatojugular reflux}, patient symptom scores) were used to derive a multivariable prediction model with linear regression. Control predictor models included A) ED physical exam + symptom score + natriuretic peptide (NP) and B) EMP disposition decision adjusted for risk of 30-day serious adverse events. Models were compared by adjusted R<sup>2</sup>.

**Results:** EMPs admitted 57 patients for full hospitalization, 5 for observation, and did not discharge any patients directly after ED IVLD treatment. Total-encounter IVLD requirements were median 2.5 guideline-standardized doses (IQR:0.8-4.5). ED disposition was poorly correlated with post-ED treatment needs, explaining only 2.1% of variance in IVLD requirements (i.e.  $R^2=0.021$ ). Physical exam, symptom score, and NP explained 24.7% of IVLD requirements. The new model (predictors: NP, BUN, sodium, troponin, heart rate, blood pressure, chest x-ray, medication adherence, edema severity) explained 54.7% of IVLD requirements.

**Conclusion:** EMPs may increase unnecessary hospitalizations by overestimating post-ED IVLD treatment needs. Our novel model, pending external validation in a new  $>5000$  patient sample, was 26 times more accurate than risk-adjusted ED disposition and twice as accurate as physical exam/symptom score/NPs.

## **Sociodemographic Disadvantaged Adolescent Attitudes on Healthy Lifestyle Education: Variances with Career Choice**

**Jocelyn Chang-Stroman**, Gionté Mason, Amy Han, Tatiana Kostrominova

**Background/Objective:** Children's and adolescents' physical and mental health have been declining for the past three decades. Several studies assessed the role of physical activity and nutritional programs on children's and adolescents' health in primarily white communities. Nevertheless, studies on the attitudes of children and adolescents regarding learning about a healthy lifestyle have been missing in the research, especially within predominantly non-Hispanic Black populations.

**Methods:** A 30-minute presentation on healthy lifestyles was given to 50 middle-schoolers ranging from ages 10-13 years old participating in the Kids College program at Indiana University Northwest from June 10 to June 21. A pre-survey and post-survey were given the first five minutes and last 5 minutes of the presentation, respectively. Based on the participant's listed profession, each survey was allocated to either the Health Professions group or the Non-Health Professions group. IRB: #19446 Kids College and Boys & Girls Club Presentations Surveys, approved on June 29, 2023.

**Results:** Adolescent interest in healthy lifestyle was highest amongst participants with future career aspirations in health professions (43.8% pre- and 75% post-presentation). Despite having low interest in the subject of healthy lifestyle, participants with non-health professional career aspirations showed an increase in interest from 8.8% to 35.3% after the presentation. Overall, interest in learning about healthy lifestyle increased from 20% to 39% in the participants.

**Conclusion/Implications:** Primarily non-Hispanic Black adolescents had a low interest in healthy lifestyle with existing knowledge relying primarily on schoolteachers. Expanding exposure to education on healthy lifestyle is essential to empowering adolescents to take control over their health, reducing health disparities by improving health behaviors, and setting strong foundations for adult health. This work was partially supported by the Trailblazer Planning Award from CTSI (T.K. and A.H.). G.M. and J.C. are medical students supported by the IMPRS program (CTSI grant UL1TR002529).

## **The Impact of Preoperative Weight Loss on 90-Day Complications Following Primary Total Knee Arthroplasty (TKA)**

**John Paul Lewis**, Mary Ziemba-Davis, Leonard T. Buller,  
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Kevin A. Sonn

**Background:** Access to primary TKA for morbidly obese (MO, BMI  $\geq 40$  kg/m<sup>2</sup>) patients is often restricted to minimize 90-day complication rates with patients asked to reduce their BMI preoperatively. We evaluated complication rates in patients who were MO or non-morbidly obese (NMO) at initial presentation to an arthroplasty surgeon based on whether their BMI had decreased by  $\geq 5\%$ , increased by  $\geq 5\%$ , or remained stable by the time of surgery hypothesizing that preoperative weight loss does not improve outcomes for either group.

**Methods:** Prospectively documented data for 1,070 unilateral, primary TKAs performed for osteoarthritis in 874 patients were retrospectively reviewed. Cases were performed between 2012 and 2022 at the same academic center by a single surgeon using standardized protocols. Increased, decreased or stable BMI between initial presentation and surgery was the independent variable. Outcomes included 90-day complications and reoperations. Outcome covariates included patient demographics and comorbidities and operative details such as anesthesia duration. Independent samples t-tests and Chi-squared tests were used for statistical analysis. Twenty-seven percent (n=294) were MO and 73% (n=776) were NMO at initial presentation. At the time of surgery, BMI had decreased by  $\geq 5\%$  for 29% of MO patients, with 5% experiencing an increase of  $\geq 5\%$  and 65% maintaining stable weight. For NMO patients, these statistics were 22%, 8%, and 70%, respectively.

**Results:** Overall, 90-day complication rates did not differ in MO patients with a  $\geq 5\%$  decrease (9.3%),  $\geq 5\%$  increase (6.3%), or stable (13.0%) BMI before surgery (P=.530). These statistics for NMO patients, 8.8%, 7.7%, and 6.9% respectively, also did not differ (P=.699). Reoperation within 90-days also did not differ based on weight change for MO or NMO patients (P $\geq$ .347).

**Conclusions:** Findings suggest that withholding surgery from MO patients clinically indicated for TKA pending weight loss may not be necessary to achieve good short-term postoperative outcomes.

## **Role of Aortic Hepatic Conduits in Liver Transplants**

**Jonathan Benitez**, Camila Samaniego, Burcin Ekser

**Background:** Aorta-hepatic conduits (AHC) also known as aortic jump grafts are used when the recipient's hepatic artery is unusable due to low flow, arterial wall dissection, and short and/or small arteries in liver transplantation (LT). AHCs are associated with low patency rates which ultimately lead to graft loss. Despite high complication rates, AHCs serve as an important life-saving procedure when

end-to-end arterial anastomosis or arterial reconstruction is not possible.

**Methods:** We systematically reviewed the literature between 1998 to 2024 on the role of AHCs in LT to identify risk factors associated with AHC-related complications. Data collected include the AHC implantation site, donor and recipient age, the material of the conduit, sutures used, thromboembolic prophylaxis, cause of transplant, and the type of immunosuppressive agents.

**Results:** Of 24,000 LTs, 2108 (8.7%) were with AHCs. We found a heavy association with the use of AHCs and re-transplants (33%). The infrarenal aorta was the most common implementation site (88%), followed by the supraceliac aorta (8%), and the common iliac artery (2%). Interestingly, there was no statistical difference regarding the patency of AHC when these three sites were compared ( $p=0.9$ ). We found that patency rates were significantly higher ( $>90\%$ ) when an allograft was used compared to a prosthetic conduit (Gore-tex, Dacron, or PFTE) ( $>30\%$ ) at 3-year follow-up. Aspirin use as an antithrombic prophylaxis was associated with lower occlusion rates (3.7%) compared to a group who did not receive aspirin (12%) ( $p=0.001$ ). Several risk factors were identified, such as (i) donor age  $>40$  years, (ii) no aspirin prophylaxis, and (iii) re-transplant, which have led to lower patency rates in AHCs and were all associated with increased patient mortality.

**Conclusion:** This study aimed to identify several variables leading to the decreased patency rates seen in AHCs in LT so that surgeons can identify the correct candidates for this procedure. AHCs are associated with several complications but serve an important role when a patient does not qualify for arterial reconstruction. By identifying influencing variables such as conduit placement, aspirin prophylaxis, and risk factors, an enhanced plan of treatment can be implemented for patients.

### **Rat Model of Elbow Ulnar Collateral Ligament Overuse**

**Jonathan Vore**, Riley Ables, Ben E. Loffin, Roufa Hanna, Stephen H. Schlecht

**Background:** Ulnar collateral ligament (UCL) injuries are relatively common among overhead throwing athletes of all ages. Accumulation of microdamage is a likely contributor to UCL injuries. To investigate the overuse injury mechanism and develop new diagnostics enabling clinical intervention prior to injury, an in vivo model is required. To accomplish this, we developed a novel murine loading model to submaximally fatigue the UCL using a clinically relevant injury diagnostic, the valgus stress maneuver.

**Methods:** Ten-week-old female Sprague-Dawley rats

( $n=28$ ) were used to validate force placement on the UCL via medial radiographic analysis of ulnohumeral joint space (JS) gapping. JS was determined as the distance from the distal, medial, humeral trochlea and the sublime tubercle of the ulna and the outlined area of the JS. This measurement was taken prior to, and following, UCL failure to validate an increase in joint gapping with injury. Elbows were then microdissected using stereomicroscopy to ensure tissue damage was isolated to the UCL. Using the rupture mechanics data, fresh arms ( $n=12$ ) were fatigued for 100 cycles at 60% of the average valgus angle. Elbows were then fixed, decalcified and microtomed at 5mm thickness. Tissue sections were then processed for immunofluorescence using a Cy3-conjugated collagen hybridizing peptide (CHP) that is specific to denatured collagen (molecular hallmark of overuse), to validate that UCL fatiguing was sufficient for generating collagen matrix damage.

**Results:** In the validation of force placement, a significant ( $p < 0.001$ ) increase JS width and area was quantified following UCL failure, compared to baseline. Upon microdissection of the elbow, 72% of all failures were noted to have occurred in the proximal third of the ligament. Failure occurred, on average, when the elbow reached a valgus angle of  $18.3^\circ$ . With immunofluorescence, fatigued UCLs showed 82% more denatured collagen compared to contralateral controls ( $p = 0.01$ ).

**Conclusion:** Outcomes from this study demonstrate that the rat elbow, though slightly anatomically different from the human elbow, reproducibly fatigues the UCL in the proximal third of the ligament. This valgus directed injury mechanism results in an increase in ulnohumeral joint space as observed clinically. This study provides proof-of-concept generating a similar fatigue injury in cadaveric human elbows to develop new diagnostic imaging protocols to evaluate and monitor low-grade UCL sprains, in the interest of mitigating damage progression and a catastrophic failure.

### **The Role of Cross-linked Actin Networks in the Proliferation and Senescence of Primary Human Trabecular Meshwork Cells**

**Joseph M. Dalloul**, Devon Harvey, Jiannong Dai, Chenna Kesavulu Sugali, Weiming Mao

**Background:** TGF $\beta$ 2 has been found to be elevated in the trabecular meshwork (TM) of patients with primary open-angle glaucoma. TM cells were treated with TGF $\beta$ 2 to form cross-linked actin networks (CLANs). These CLANs are a restructuring of the cells' actin cytoskeleton that appear as web-like (2D)/spherical (3D) structures. In this study, we used TGF $\beta$ 2-treated primary human TM (pHTM) cells to illuminate the relationship between CLAN formation and cell proliferation and senescence.

**Methods:** A characterized pHTM cell strain was seeded into a 96-well plate. Some cells were treated with 5ng/mL TGFβ2 for 1 week while the others served as a control. The cells were then fixed and immunostained for cell proliferation (Ki-67) and senescence (p21, H2AX, and β-galactosidase) markers. DAPI was also used to stain nuclei and phalloidin-Alexa-488 to stain F-actin/CLANs. Analysis was conducted through student's t-tests.

**Results:** TGFβ2-treated pHTM cells formed significantly more CLANs compared to control. The cell proliferation marker Ki-67 was rarely expressed in both groups (not statistically significant) but was mostly observed in CLAN-cells and seen only in the control. Ki-67 was almost completely absent in CLAN+ cells. Among senescence markers, none were expressed significantly differently between the two groups, however TGFβ2 led to an increase in p21 and β-gal. Most CLAN+ cells expressed p21. No cells expressed H2AX.

**Conclusions:** TGFβ2 increases the formation of CLANs in pHTM cells. It seems that CLAN formation inhibits cell proliferation. However, the effect of CLAN formation on cell senescence is not clear. More investigation is needed to help further understand the relationship between CLAN formation and cell proliferation and senescence.

### **Parent-Reported Outcomes Following Type B Ulnar Polydactyly Excision in the Clinic Versus the Operating Room**

**Joshua D. Gerstein**, Khoa Tran, Nikhi P. Singh, Gregory H. Borschel, Joshua M. Adkinson

**Background:** Ulnar polydactyly is the presence of an extra finger on the post-axial aspect of the hand. It is one of the most common congenital abnormalities and causes aesthetic and functional impairments that can be treated with surgical excision in the office or the operating room (OR). Our goal was to compare outcomes between type B ulnar polydactyly surgery performed in OR vs. office.

**Methods:** We reviewed treatment outcomes and administered a satisfaction survey via telephone or email link via REDCap to parents of children with type B ulnar polydactyly treated at Riley Children's Hospital between 2020 and 2024. We assessed satisfaction with treatment decisions, outcomes, and motivational factors. Outcomes were assessed via visual analog scale from 1 to 10; 1 equating to minimum satisfaction, 10 equating to maximum satisfaction.

**Results:** In total, 34 of the 165 (20%) parents agreed to participate in the study. Of those 34, 17 parents elected for excision in the OR and 17 chose the office. There were no significant differences in race, education, or marital status between groups. In total, 15 families had a history of polydactyly and chose the operating room 64.3% of the time

compared to 38.9% of the time from the families without a history of polydactyly. There was no significant difference in average comfort, satisfaction of outcome, function, and appearance VAS scores when stratified by family history of ulnar polydactyly. There were no significant differences in satisfaction between excision in the office or OR.

**Conclusions:** Office-based excision faces challenging logistics, sufficient lighting, staffing, and cooperation from parents and children. Parents who choose surgical excision in the office are satisfied with the treatment outcomes, would not change any of their treatment decisions, and would recommend their treatment process to others. While challenges exist, excision in the office may result in lower healthcare costs while providing similar outcomes.

### **CBD Mediated Lymphocyte Toxicity**

**Joshua Jun**, Matthew Miller, Sachiko Koyama, Debora Gisch, Michael T Eadon

**Background:** Calcineurin inhibitors, such as Tacrolimus, are the backbone of immunosuppressive treatment in solid organ transplant; however, they do not provide pain relief. Moreover, non-steroidal anti-inflammatory drugs (NSAIDs) cannot be used in kidney allografts. Cannabidiol (CBD) has known immunosuppressive and anti-inflammatory properties. We hypothesized that individuals taking CBD will have altered immune cell signatures and cytokine profiles.

**Methods:** In this clinical trial, subjects had lymphocytes isolated and cultured before and after a 14-day exposure to CBD. After lymphocytes were isolated, they were exposed to CD3/CD28 and concentrations of CBD varying from 0 - 10 uM. After a 48-hour incubation, lymphocytes were either sent for single-cell RNA sequencing or stained with MitoTracker to measure mitochondrial viability and NucBlue for nuclear identification. A Leica SP8 laser confocal microscope was used to capture images which were analyzed for fluorescence intensity and cell counts utilizing ImageJ. Media was then obtained from cultured lymphocytes for cytokine expression.

**Results:** Single cell RNA-sequencing found reduced gene expression indicative of proliferating T cells with concomitant increases in regulatory and memory T-cells. Monocyte populations were also found to be heavily upregulated. Cytokine studies corroborated these cell type differences. Immunofluorescent staining showed a mechanism by which these cellular changes occurred. We have found that mitochondrial fluorescent intensity decreases greatly with increasing concentrations of CBD. In the cells that were cultured before the patient consumed CBD, the lowest mitochondrial fluorescent intensity was 10% of peak intensity; whereas the lowest mitochondrial fluorescent intensity when CBD was allowed to reach steady state levels in plasma was 30%.

**Conclusions:** The data from this study can help establish CBD as a viable adjunct therapy for pain management. Additionally, the results suggest that tolerance develops within lymphocytes, which can help establish dosing regimens in the future.

### **Analyzing the Effectiveness of a Pre-Arrival Time-Out in Pediatric Trauma Resuscitations**

**Julian Spangler, Jodi Raymond, Matthew Landman**

**Background:** The surgical time-out is standard practice in the operating room. Time-out protocols have been associated with improved care and decreased complications in nonurgent care. However, the use of time-outs in trauma settings is not well studied and no standardized time-out exists. Early trauma time-out studies have found that these time-outs are perceived as effective and help reduce complications. The goal of this study was to draft a pre-arrival time-out protocol at Riley Hospital for Children (RHC), emphasizing introductions, patient details, and the patient's plan upon arrival.

**Methods:** In this study, pre-hospital preparation for trauma resuscitations were retrospectively reviewed using trauma video review (TVR). Resuscitations took place in one of four trauma bays at RHC. The TVR analyzed pre-hospital preparations before a formal time-out plan was drafted for items related to the trauma time-out. Twenty-four resuscitations with pre-arrival interactions were available in the TVR for analysis. At the conclusion of this project, a pre-arrival time-out plan was drafted and implemented by invested healthcare professionals.

**Results:** Before intervention, time-outs occurred 29.2% (7/24) of the time. Attendance at time-outs was  $76.2 \pm 11.7\%$ . The average length of time-outs was  $59.6 \pm 19.4$  seconds and the average time between the end of the time-out and patient arrival was 4 minutes 53.7 seconds  $\pm$  3 minutes 37.0 seconds. Introductions were fully completed in 16.7% (4/24) of all scenarios and 57.1% (4/7) of all scenarios with time-outs. A clear leader was identified in 29.2% (7/24) of cases. Discussions about the case occurred 83.3% (20/24) of the time. A stated need for an item occurred in 50.0% (12/24) of pre-hospital preparations.

**Conclusions:** The rates of time-outs, introductions, stating patient details, and stating equipment needs before patient arrival are less than desirable. The pre-arrival time-out intervention could be effective in increasing these rates. More data for post-intervention is needed.

### **Effects of Prostaglandin I2 Signaling on the Inflammatory Response of Dendritic Cells in Hypertensive and Normotensive Individuals**

**Justin Yu, Mahbub Ullah, Raghad AlMotiary, Allison Norlander**

**Background:** This study's aim is to evaluate the inhibitory effects of prostaglandin I<sub>2</sub> (PGI<sub>2</sub>) signaling on dendritic cells (DCs) via the IP receptor in hypertension using human and murine models. This study was specifically interested in measuring the expression and overall levels of pro-inflammatory cytokines in the DCs.

**Methods:** This research was accomplished through the isolation of CD11c-expressing cells, which are predominantly DCs, from mice that were engineered to have IP deficient DCs (IPflox x CD11cCre). These cells were compared to the IP-expressing cells from control mice (IPflox). Before isolation, both sets of mice were treated with either vehicle, as a control, or angiotensin II to induce hypertension. Following isolation, the CD11c-expressing cells were plated for 24 hours with varying levels of iloprost, a PGI<sub>2</sub> analog, and lipopolysaccharide (LPS) to induce an inflammatory state in the cells. An ELISA was performed on the resulting supernatant to measure the level of inflammatory cytokines, specifically IL-1 $\beta$ , IL-6, and TNF $\alpha$ , while a RT-PCR was performed on the isolated RNA to identify the expression levels of the same markers in the DCs. A similar experiment was run with human CD11c-expressing cells from both hypertensive and normotensive subjects. Likewise, STAT3 western blot optimization was performed to aid further studies into the development of tolerogenic DCs.

**Results:** Ultimately, the current data is inconclusive as larger sample sizes are still needed to infer any information, and the majority of this lab's current studies show that there are not any significant changes in inflammatory cytokine levels in response to PGI<sub>2</sub>.

**Conclusions:** The percentage of changes in total IL-1 $\beta$  concentration and the TNF $\alpha$  RT-PCR could suggest that there is a drop in the cytokine's levels with iloprost treatment under hypertensive conditions. Nonetheless, more research needs to be done, and all these experiments are still ongoing.

### **Using Implementation Science to Advance Hearing Health Equity in Older Adults**

**Kaitlyn O'Donnell, Rick Nelson, Irina Castellanos**

**Background/Objective:** Hearing loss is highly prevalent among the 1.2 million older adults who live in Senior Living Communities (SLCs). Under-detection of hearing loss and under-use of hearing devices among residents of SLCs is a significant healthcare disparity which places older adults at an increased risk for dementia, falls, and depression. Our long-term objective is to improve the hearing

health, emotional well-being, and quality-of-life of older adults living in SLCs by implementing hearing healthcare into standard clinical care.

**Methods:** We focused on the first two of the four inter-related phases of implementation science: exploration and initiation. We partnered with the largest SLC in Indiana and onboarded three of their communities. Each of these communities provide four levels of care, and residents vary across Social Determinants of Health (SDoH), allowing our team to compare hearing health outcomes as a function of residents' physical/cognitive abilities and SDoH.

**Results:** As part of the exploration phase, we identified five barriers to hearing healthcare in SLCs: 1) hearing health literacy in the care staff and residents, 2) poor management of hearing devices, 3) poor management of cerumen – ear hygiene – which hinders access to sound, 4) underuse of effective screening tools, and 5) lack of connections to an audiologist and neurotologist. As part of the initiation phase, we collaborated with community stakeholders to create the infrastructure for screening, referring, & implementation of clinical healthcare.

**Conclusions/Implications:** Implementation science is applying an already known evidence-based practice to a particular problem; in this case, we anticipate that providing effective screening tools, management of cerumen, and access to an audiologist and neurotologist will improve the hearing health, emotional well-being, & quality-of-life in older adults living in SLCs. Our research program will continue to develop, test, and refine our implementation strategies to achieve equity in hearing health outcomes.

### **Altered Reward Network Connectivity in Pregnant Women with Prenatal Opioid Exposure**

**Karena Dhamecha**, Ramana V. Vishnubhotla, Yi Zhao, Ashok Panigrahy, Senthilkumar Sadhasivam, Rupa Radhakrishnan

**Background:** The prescription rate and use of opioids during pregnancy continues to rise, following trends seen throughout the opioid crisis. Prenatal exposure in infants can cause congenital defects, Neonatal Abstinence Syndrome, and increases risk of preterm or stillbirth. In non-pregnant patients, opioid use has been linked to altered reward, emotion, stress, and cognitive control via reinforcement of specific networks; the same networks involved in maternal-infant bonding and responding to infant cues. Despite these risks, little research has been conducted with the pregnant population to fully understand the potential consequences of use in this cohort. We hypothesize that maternal opioid use in pregnant patients alters connectivity in the reward pathway.

**Methods:** Subjects in their 2nd and 3rd trimester were recruited and a BOLD functional MRI and a T1w sequence were taken. We processed the subject T1 MRIs and fMRIs by removing excess skull and head tissue. To register the fMRIs in standard space, the processed fMRI image was registered to the subject anatomical MRI, which was then registered to standard space using the MNI152 space. 20 regions associated with the reward network were chosen from the Automated Anatomical Labelling atlas 3 to analyze signal intensity differences between patients.

**Results:** The image analysis showed five pathways with significant increase in connectivity in the pregnant opioid users vs. pregnant non-users. This was between the right ventral tegmental area (VTA) and the right nucleus accumbens (NAcc), the right VTA and the left dorsal superior frontal gyrus (dSFG), the right VTA and the right dSFG, the right VTA and the left ventromedial prefrontal cortex, and between the right ventromedial prefrontal cortex and the left amygdala.

**Conclusions:** This study confirms dysregulation in reward network connectivity in pregnant patients with prenatal opioid exposure when compared to non-users. The reward network plays an important role in the development of maternal-infant connection, development of which begins prenatally. Research regarding this population is limited, with this study being one of the first to consider alterations and potential implications linked to opioid use.

### **MSC Secretome in Cardiomyocyte Mitochondrial Function: A Strategy to Improve DCD Heart Preservation**

**Karthik Annamalai**, JiaYue Luna Du, Qing Yu, Meijing Wang

**Background:** Heart transplantation saves the lives of patients with end-stage heart failure. Traditionally, heart transplants are from donations after brain death. However, with increasing demand and scarcity of organ supply, the donor criteria are extended to suboptimal groups, particularly for donations after circulatory death (DCD). Given that human mesenchymal stem cell (MSC) secretome (conditioned medium [CM]) protected donor heart performance against ex vivo cold storage/ischemia from our previous studies, we hypothesized that using MSC-CM can ameliorate ischemia-impaired mitochondrial function to improve DCD heart preservation.

**Methods:** Primary cardiomyocytes were isolated from male adult C57BL/6 mice. After calcium restoration, these cells were subjected to control, post-ischemia oxidative stress (90-min H<sub>2</sub>O<sub>2</sub>), or simulated ischemia (20-min) via a lactate/potassium media mimicking the interstitium of the myocardium following ischemia. The cardiomyocytes were then incubated with either vehicle (control media) or MSC-

CM. Mitochondrial membrane potential ( $\Delta\Psi_m$ ) was detected using JC-1 staining. Red-to-green fluorescence intensity (indicating  $\Delta\Psi_m$ ) was analyzed in individual cardiomyocytes (Fig. A) using ImageJ (NIH). Mitochondrial respiration was also measured with the Seahorse XF Cell Mito Stress Test. Data was analyzed using t-test or one-way ANOVA,  $n \geq 10$ /group and experiments were repeated four times from four mouse hearts,  $p < 0.05$  = statistical significance.

**Results:** Oxidative stress using H<sub>2</sub>O<sub>2</sub> induced cardiomyocyte mitochondrial dysfunction, as demonstrated by significantly decreased mitochondrial maximal respiration and spare respiratory capacity. Intriguingly, MSC-CM improved these metrics versus control (Fig. B, B1). Although similar trends of mitochondrial respiration were seen in the simulated ischemia group (Fig. C, C1), there was no statistical significance. Additionally, MSC-CM increased the red-to-green ratio in the simulated ischemia group (Fig. D), indicating improvement of  $\Delta\Psi_m$ .

**Conclusion:** Our data demonstrates that MSC-CM could ameliorate ischemia-impaired mitochondrial performance, thus likely promoting recovery of DCD hearts. This study opens the possibility of utilizing MSC-CM to improve preservation of DCD heart transplants.

### **Emergency Medicine Residency Program Expansion and Characteristics of Rural Rotations**

**Kayley Ryan**, Christine Motzkus, Aloysius Humbert

**Background:** Despite concerns surrounding a potential surplus of emergency medicine (EM) physicians through at least 2036, there has been no corresponding increase in the number of EM-trained physicians working in rural emergency departments. Previous studies suggest that the integration of rural rotations into EM residency curricula encourages more physicians to select rural EM positions. However, many EM residency programs do not offer rural rotations due to barriers such as insufficient finances, lack of resident interest, or lack of physician supervisors. No known studies since 2020 have explored rural rotations in EM residency programs. Following the COVID-19 impact, it is worth re-examining the current state of EM residency programs and exploring attitudes about implementing rural rotations into new and existing programs. Objectives include examining attitudes surrounding the expansion of EM residency programs and exploring characteristics of rural rotations in EM residency programs.

**Methods:** A Qualtrics survey was distributed through the Council of Residency Directors in Emergency Medicine (CORD-EM) listserv. Survey responses continue to be collected in order to analyze the trends present in the aggregate data.

**Results:** Data collection remains in progress regarding

availability, characteristics, and interest in rural rotations in EM residency programs. Data revealing attitudes surrounding the need for additional rural rotations in existing EM programs and the need for the development of new EM programs with a rural focus are also being collected.

**Conclusions:** Preliminary conclusions based on current data suggest that there are needs to increase EM resident interest in pursuing both rural rotations and jobs in rural sites, to find solutions to the barriers which hinder the implementation of rural rotations in EM residency programs, and to consider how future programs can incorporate a rural focus and address these issues.

### **Postoperative Depression Correlated with Obesity in Hip and Knee Osteoarthritis Patients Following Total Joint Arthroplasty Operation Using Real World Database**

**Keegan Leek**, Meagan McNicholas, Michael S. Roscoe, Arthur L. Chlebowski

**Background:** Obesity (OB) significantly contributes to worsening osteoarthritis (OA) as well as poor surgical outcomes following total joint arthroplasty (TJA). These reduced functional outcomes are also observed in patients with depression. In recent studies, TJA has been shown to decrease depressive symptoms in OA patients despite postoperative depression being a common complication. This study aims to investigate the relationship between obesity and postoperative depression following TJA in patients diagnosed with hip and/or knee OA.

**Methods:** Data was gathered from the RWEdatab Lab U.S. national Psychiatry database. Using ICD-10 and CPT codes, queries were generated to pull patients from the database with: hip and/or knee OA and TJA; hip and/or knee OA, TJA, and depression; and hip and/or knee OA, TJA, and OB. Data was extracted, organized, sorted, and Odds ratios were used to assess OA/TJA patients and the interaction between depression and obesity diagnoses.

**Results:** Odds ratios showed significant association between postoperative depression following TJA and an obesity diagnosis (1.20 95% CI (1.04-1.41)). Additionally, undergoing a TJA was shown to be protective against lifetime depression in all hip and/or knee OA patients (0.802 95% CI (0.75-0.86)) with more protection against lifetime depression being seen in non-obese patients (0.60 95% CI (0.63-0.76)). In all patients with hip and/or knee OA who underwent TJA, lifetime depression was significantly associated with the presence of an obesity diagnosis (2.21 95% CI (1.84-2.44)).

**Conclusion:** Data suggests a correlation of higher odds

that someone with hip and/or knee OA who underwent TJA will have postoperative depression if they also have a diagnosis of obesity. Findings convey the impact that obesity has not only on physical, but mental health impact in patients undergoing TJA surgery. Therefore, impacting that lifestyle and mental health of a patient may improve outcomes following surgery.

### **The Role of SHROOM3 in Congenital Heart Defects**

**Kevin Carthy**, Caelan Rathke, Róise Gribben, Mark Wakulchik, Catherine Guilfooy, Emma Kennedy, Omeed Mehrzad, Princess Murray, Inayat Arora, Stephanie Ware, Matthew Durbin

**Background:** Congenital heart defects (CHD) are the most common, and most frequently fatal birth defects, but most etiology remains unknown. Our prior research focused on a gene known as SHROOM3. The Stephanie Ware laboratory identified SHROOM3 variants in a patient with heterotaxy and CHD. This compelled us to utilize a SHROOM3-loss-of-function, gene trap mouse model (Shroom3gt) to demonstrate that Shroom3gt/gt embryos have CHDs. Additionally, analyzing sequencing data of 283 patients with heterotaxy, we identified 14 patients with rare, potentially damaging variants within SHROOM3. These observations have collectively led to the hypothesis that SHROOM3 is necessary for cardiac development and that disruption can contribute to CHD.

**Methods:** To test the hypothesis, we have leveraged the recent development of a novel in vivo model for conditional loss-of-function in Shroom3, (Shroom3flox/flox mice). We crossed Shroom3flox/flox mice to generate cohorts of embryos that have lineage-specific SHROOM3 deletion within the mesoderm (Mesp1-Cre), primary heart field (Nkx2.5-Cre), and neural crest (Wnt1-Cre). The embryos have been subjected to histological analysis at E14.5-17.5 to identify anatomical cardiac defects. Second, we developed CRISPR/Cas9 genome edited SHROOM3 patient variant iPSC lines and derived atrial cardiomyocytes (iPSC-aCM), ventricle cardiomyocytes (iPSC-vCM), and neural crest cells (iPSC-NCC). We assayed these patient SHROOM3 variant lines for disruption in cell shape, adhesion, movement, and function to elucidate a potential mechanism that may contribute to the development of CHD.

**Results:** This summer we analyzed patient SHROOM3 variant CRISPR/Cas9 cell lines. We also generated litters of embryos with lineage-specific Shroom3 deletion. Further analysis is ongoing.

**Conclusions:** This study will help to elucidate the role of SHROOM3 in CHD, with implications for our understanding of CHD inheritance, pathogenesis, and therapeutic development in humans.

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### **Exploring Barriers to Healthcare through the Transition of Care of Congolese Refugees: A Multi-Method Qualitative Study**

**Khunsha Ahmed**, Niki Messmore

**Background:** In recent years, the United States, and especially Indianapolis, has seen a rise in Congolese refugees. Refugees' experiences with the Congolese healthcare system and navigating their health, nutrition, and life are starkly different from those in the United States. The goal of this study is to understand the perspectives of Congolese refugees in Indianapolis and what needs to be done to help them navigate barriers to healthcare, especially as they are transferring from one healthcare system to another.

**Methods:** In order to understand perspectives that contribute to navigating the healthcare system, resettlement agency staff and healthcare providers in Indianapolis were interviewed using a semi-structured guided interview. The interviews were analyzed using a deductive approach to identify themes and sub-themes. These findings were then compared to major themes identified from the literature review focused on the Congolese refugee perspective of barriers to healthcare.

**Results:** The major themes identified from a thorough literature review of Congolese refugee perspectives in Indianapolis show that major barriers to healthcare include a language barrier, transportation, cultural differences, and difficulty navigating healthcare insurance. These themes correspond to major themes deduced from the interviews with the resettlement agency staff, however, the specific commentary and thoughts varied throughout the topics.

**Conclusions:** Moving forward, the resettlement agency has great programs in place to support Congolese refugees, but there can be expansion in some areas as well as further community education initiatives. For example, there can be inclusive translated video resources on topics that address cultural differences as individuals approach a new healthcare system, further dedicated Medicaid taxi trainings, and community education about in-person interpretation and its positive impact.

### **Exposure to and Helpfulness of Treatment Modalities in Patients with Chronic Pain**

**Kian Naimi Shirazi**, Michael A. Bushey

**Background:** Despite the availability of a wide array of treatment options, chronic pain, consisting of persistent pain for three months or longer, affects a large portion of the population. The Indiana University Health Pain Navigation Service (PNS) established a multidisciplinary pain evaluation clinic to address chronic pain comprehensively.

Since January 2023, PNS has integrated a structured intake process — a self-report questionnaire capturing symptom scales, patient demographics, pain characteristics, and treatment histories — including details on the prior helpfulness of over 80 treatment modalities.

**Methods:** A retrospective cohort study was conducted using the intake questionnaire completed by 226 patients at IU Health PNS between January 2023 and March 2024. The questionnaire, stored in a REDCap database, was utilized to separate which modality each patient tried and found helpful. Characteristics of patients who tried the top three most helpful treatments (massage therapy, oxycodone, and psychotherapy) were assessed by comparing sociodemographic variables. Independent sample Student's T-tests were used to compare continuous variables and chi-squared tests were used to compare categorical variables.

**Results:** Of triers, massage therapy was the highest-ranked treatment for helpfulness at 77%. Massage therapy triers had significantly higher formal education and had been living with pain longer than non-triers. 74% of Oxycodone triers reported its helpfulness, making it the second-ranked treatment. Compared to non-triers, oxycodone triers had half as many full-time workers and 3.5 times as many Social Security disability income receivers. Psychotherapy ranked third in helpfulness at 67%. Psychotherapy triers lived in significantly less deprived areas and had significantly higher formal education, in comparison with those who had not tried psychotherapy.

**Conclusions:** The three treatments with the highest proportion of patients reporting helpfulness represent three different classes of treatment (massage = complementary, oxycodone = medication, psychotherapy = mental health), emphasizing the importance of a multidisciplinary approach to pain treatment.

### **Neurofilament Light Chain and Delirium in ICU Patients: A Study on Neuronal Damage Indicators**

**Kyle Gannon**, Abigail Olbina, Brendan Devine, Sikandar H. Khan, Babar A. Khan

**Background:** Up to 70% of adults in the intensive care unit (ICU) experience delirium, and delirium is associated with post-ICU dementia. Plasma neurodegenerative biomarkers have recently been associated with dementia. Whether ICU delirium survivors experience elevated levels of Neurofilament Light chain (NfL) compared to subsyndromal delirium (SSD) is not known.

**Methods:** This is a secondary analysis of the IMPROVE trial. Participants included adults aged 50 years or older who experienced delirium or SSD and provided blood samples at hospital discharge. Delirium was assessed twice daily until discharge using the Confusion Assessment Method

for ICU (CAM-ICU). Subsyndromal delirium (SSD), a less severe form of delirium, was defined as any one CAM-ICU feature abnormal. Plasma NfL levels were measured using commercially available ELISA kits (Biotechne; sensitivity of 9.38 pg/mL). Values were reported in pg/mL and compared using the Wilcoxon Rank Sum Test (SAS).

**Results:** Of 68 subjects included, 37 (54%) experienced delirium while 31 (46%) experienced SSD. Subjects with SSD had a mean age of 63.7 years [SD 7.3] vs. 64.4 years [SD 7.1] in the delirium group ( $p=0.667$ ). Mean years of education in those with SSD was 13.6 years [SD 2.6] vs. 13.1 years [2.3] in delirious subjects ( $p=0.441$ ). NfL was detected in only 50% of the cohort with a median value of 2.30 pg/mL (IQR 1.87, 2.64). There were no statistical differences between the SSD [median 2.34 pg/mL (IQR 1.74, 3.05),  $n=16$ ] vs. delirium [2.26 pg/mL, (IQR 1.94, 2.54),  $n=18$ ] groups,  $p=.959$ .

**Conclusion:** No significant differences were found between in plasma NfL levels between patients with ICU delirium vs. SSD. Further research using more sensitive assays and multiple time points is needed to quantify NfL levels in ICU delirium survivors.

### **Sex-Dependent Effects of Irisin on Bone in an Aged Mouse Model**

**Kyle Richardson**, Anika Shimonty, Joshua Huot, Fabrizio Pin, Lynda Bonewald

**Background:** Irisin is a recently discovered protein that has garnered increasing attention due to its potential impact on metabolic health and disease prevention. This hormone, released from exercising skeletal muscle, is generated through the cleavage of the membrane protein FNDC-5 (fibronectin type III domain-containing protein 5). Irisin has been shown to play a role in the browning of white adipose tissue and serves as a mediator of exercise-induced metabolic improvements. Notably, bone and muscle tissues are known to communicate, influencing each other's physiology. Previous research on irisin demonstrated that in responding to stress, irisin's effects on bone exhibited sex-dependent differences. Specifically, female FNDC-5 knockout (KO) mice were protected from adverse bone phenotypes when subjected to a low calcium diet, while male FNDC-5 KO mice showed worse bone phenotypes at baseline, even before the diet began.

**Methods:** The prior study focused on 5-month-old mice. Our research aims to investigate the effects of FNDC-5 KO in aged mice, both at baseline and under stress conditions. We utilized 18-month-old wild-type (WT) and FNDC-5 KO male and female mice, feeding them a low calcium diet for 2 weeks.

**Results:** Our findings revealed similar results to the earlier study with younger mice: female FNDC-5 KO mice exhibited partial protection against the low calcium diet's adverse effects on bone and skeletal muscle.

**Conclusion:** These results suggest that age and sex are critical factors in the bone-muscle crosstalk mediated by Irisin, highlighting the need for personalized approaches in nutritional and exercise interventions. Future research should explore the underlying mechanisms and potential therapeutic applications of Irisin in metabolic and musculoskeletal health.

### **Atypical Presentation of IgG4-Negative Idiopathic Retroperitoneal Fibrosis**

**Kyra Colston**, Margaret Spolnik

**Background:** Retroperitoneal fibrosis (RPF) is a rare condition in which fibro-inflammatory tissue surrounds the iliac arteries and abdominal aorta. Ureteral obstruction is common, resulting in acute or chronic renal failure. Most cases are idiopathic and often develop alongside autoimmune conditions or IgG4-related disease. Clinical manifestations include fever, anorexia, and weight loss with back or flank pain.

**Case Description:** A 53-year-old African American male presented to the emergency room with extreme fatigue, worsening anorexia, and weight loss. Past medical history included hypertension, type 2 diabetes mellitus, obstructive sleep apnea, depression, and medication noncompliance. Physical exam was unremarkable and blood testing revealed serum creatinine of 5.28 (baseline 1.2), eGFR of 12.2 (68.6), and BUN of 35 (17). He denied flank pain, urinary symptoms, and history of kidney disease. Ultrasound showed moderate to severe bilateral hydronephrosis. CT scan of the abdomen and pelvis revealed no stones within the urinary tract but identified a retroperitoneal mass at the level of the aortic bifurcation. Following admission, bilateral upper pole percutaneous nephrostomy tubes and lower pole nephroureteral stents were placed. CT scan of the chest showed no evidence of malignancy. Two weeks later, diuretic renal scintigraphy determined renal function to be 68% (left) and 32% (right). Repeat CT abdomen/pelvis revealed improved hydronephrosis. Biopsy of the retroperitoneal mass showed myofibroblastic proliferation with thick collagen and inflammatory cells but rare IgG4-positive plasma cells. Treatment of idiopathic RPF was initiated with high dose corticosteroids. Serum creatinine has since decreased to 1.89, eGFR increased to 41.9, and BUN decreased to 22.

**Discussion:** This case illustrates the importance of maintaining a broad differential in the setting of AKI and considering rare causes for hydronephrosis. Idiopathic RPF can have a varied clinical presentation as seen in our patient

lacking back or flank pain despite extensive fibrosis causing hydronephrosis. Prompt recognition of idiopathic RPF is vital to early intervention and preservation of renal function.

### **Retrospective Analysis of Drug Overdose Deaths in Allen County, Indiana from 2008-2023**

**Lucas Boha**, Jana Sanders, Thomas Gutwein

**Background:** Deaths caused by drug overdose have been rising at the national, state, and local level. Research on drug overdose deaths at the local level is insufficient and not well understood. The aim of this study is to analyze and assess the drug overdose deaths in Allen County, Indiana from 2008-2023.

**Methods:** Data was collected from Allen County Coroner's Reports and Allen County Department of Health death certificates on 1,435 decedents. Data included decedent demographic information, employment, education level, and toxicology report results. Data was entered into a spreadsheet for analysis. Chi-squared analyses were completed to assess significance and descriptive statistics were completed.

**Results:** 1,435 drug overdose deaths were identified (1,298 accidental, 110 intentional, 27 undetermined) with a median age of death of 39. 66.4% of deaths were males. Multiple substances were found in nearly 67% of decedents. Race and ethnicity data reflected anticipated results for Allen County based on census data. Deaths in the study period tended to be accidental (83.6%) and most decedents had a high school education or less (71.1%) and were currently employed individuals (75.7%). Naloxone was found in twice as many toxicology reports after policy change occurred in 2015. There was a significant relationship between the age and manner of death in males and females with ages 64+ being more likely to die from an intentional overdose than those under 64,  $X^2 = 49.7$ ,  $p < 0.00001$ .

**Conclusion:** Governments can have an impact on drug overdose outcomes through policy change if demographic and locational information is better understood, and resources are allocated to at-risk populations. Education efforts should be focused on those with a high school education or less, additional attention should be made for those ages 64+, and naloxone distribution should be major points of emphasis going forward.

### **Factors Associated with Anemia in Infants with and without HIV Exposure in Western Kenya**

**Madeline M. Cory**, Eren Oyungu, Ziyi Yang, Emily Abuonji, Ananda R. Ombitda, Ben Mosong, Mary Ann Etling, Megan S. McHenry

**Background:** Anemia is a major global health problem

impacting morbidity and mortality, especially in children under 5 years of age. Children living with HIV are more likely to develop anemia, but little is known about children who are HIV-exposed but uninfected (HEU). The objective of this study is to evaluate rates of anemia and factors associated with anemia in a population of 6-month-old infants who are HEU and HIV-unexposed and uninfected (HUU) in western Kenya.

**Methods:** This study included a cross-sectional analysis of a large prospective cohort study. The study was conducted as part of the Academic Model Providing Access to Healthcare (AMPATH) and took place at Moi Teaching and Referral Hospital (MTRH) in Eldoret, Kenya. Only those participants with lab values were included in this analysis. Anemia was defined as hemoglobin level  $\leq 10.5$  g/dL. Data were analyzed from prenatal and birth records, questionnaires, anthropometric measurements, and blood samples. Two sample t-tests, chi-square, Fisher's exact tests, and logistic regression were used for analyses.

**Results:** Of the 586 infants with lab values, 95 had anemia (16.2%), with 38 (6.5%) meeting the threshold for moderate-to-severe anemia ( $\leq 9.4$  g/dL). Infant anemia was associated with male sex ( $p=0.02$ ) and stunting (low height-for-age) status ( $p=0.04$ ). Furthermore, infants with HIV exposure (OR=2.63, 95%CI: 1.29, 4.54), preterm birth (OR=3.92, 95%CI: 2.29, 6.70), high maternal blood pressure (OR=2.31, 95%CI: 1.05, 4.90), and interruption of breastfeeding before 6 months of age (OR=2.77, 95%CI: 1.29, 5.88) had increased odds of anemia, even after adjusting for covariates.

**Conclusions:** Infants who are HEU, born prematurely, exposed to maternal hypertension, and with interruption of breastfeeding were more likely to develop anemia, even when accounting for other factors. Health systems should monitor these risk factors to identify children at high risk for having anemia and ensure early referral for treatment.

### **Optimizing CT Surveillance for Thymic Epithelial Tumors Based on Recurrence Characteristics**

**Mae Shu**, Mohammed Ghazali, Hannah Davis, Rohan Maniar, and Patrick Loehrer

**Background:** Thymic epithelial tumors (TETs), including thymoma and thymic carcinoma, are rare malignancies originating from the thymus gland epithelium. Surgery is the primary treatment for early-stage disease, and post-operative surveillance is crucial for early detection of recurrence, which enhances eligibility for curative-intent treatments.

**Purpose:** The National Comprehensive Cancer Network (NCCN) recommends chest CT scans every 6 months for 2 years, then annually for 10 years for thymoma, and annual-

ly for 5 years for thymic carcinoma. However, the optimal duration, frequency, and type of imaging for TET surveillance remain undetermined in published studies. This study hypothesizes that postoperative CT scan surveillance can be tailored based on WHO classification, Masaoka-Koga staging, resection margin status, and common sites of metastasis.

**Methods:** The REDCap database includes 1,089 TET patients seen at IU. Applying inclusion criteria of histological classification as thymoma or thymic carcinoma, surgical resection, and documented recurrence yielded 190 patients. Disease characteristics collected included WHO classification, Masaoka-Koga staging, resection margin status, and common sites of metastasis. Time to recurrence was categorized as early ( $<2$  years), late (2-10 years), or very late ( $>10$  years). ANOVA assessed associations between time to recurrence and disease characteristics.

**Results:** WHO classification was the most significant predictor of recurrence timing ( $p = 0.0465$ ), with higher classifications indicating earlier recurrences. Other disease characteristics were not significant predictors. Eight patients experienced recurrence beyond 10 years. Metastatic sites in 11% of thymomas and 19% of thymic carcinomas were detected via abdominal CT scans, highlighting gaps in current guidelines.

**Conclusion:** The study emphasizes the need to tailor postoperative surveillance based on WHO classification. Findings suggest extending surveillance beyond 10 years and incorporating abdominal imaging to detect metastases. These insights recommend that the NCCN update current guidelines, aiming to improve long-term outcomes for TET patients. Future research will include expanding the cohort to non-recurrent cases to better assess recurrence risk characteristics.

### **Sociodemographic and Behavioral Determinants of Hospitalizations for Labor and Delivery Complications in an Urban Health System**

**Maggie Sullivan**, Alexis Dres, Skyler Thompson, Jonathan Guerrero, Baraka Muvuka

**Background/Objective:** The United States (US) has the highest maternal mortality ratio (MMR) among high-income countries, with Indiana having the 3rd highest MMR in the US. For every maternal death, 20 to 30 more experience life-threatening complications. Labor and delivery complications are key contributors to severe maternal morbidity and mortality, costing over \$30 billion. Identifying and addressing underlying social determinants of health (SDOH) are high-impact strategies for improving maternal health outcomes. This study examined a comprehensive group of socio-demographic and behavioral determinants of hospitalization for labor and delivery complications in an

urban health system in Northwest Indiana (NWI).

**Methods:** This retrospective study analyzed data generated from inpatient SDOH screenings in EPIC™ at an urban health system in NWI between January 2021 and April 2024, using the Protocol for Responding to and Assessing Patients' Assets, Risks, and Experiences (PRAPARE). Complications of labor and delivery were determined using ICD-10 Codes. Data analysis utilized IBM SPSS V. 29.0 to produce descriptive statistics, bivariate analysis (Chi-Square, Mann-Whitney, Kruskal Wallis;  $p < 0.05$ ), and multivariate analysis (binary logistic regression;  $p < 0.05$ ).

**Results:** The sample consisted of 2873 patients who received labor and delivery services, 89% of whom experienced complications. Patients were predominantly White (52.3%) with a median age of 28.9. The bivariate analysis revealed statistically significant associations between labor and delivery complications and age ( $p < 0.001$ ), veteran status ( $p = 0.014$ ), social connections risk ( $p = 0.021$ ), smoking ( $p = 0.037$ ), length of stay ( $p < 0.001$ ), and BMI ( $p < 0.001$ ). The multivariate analysis found that family income 1500 to 24999 (OR=0.437,  $p = 0.029$ ), family income 25000 to 34999 (OR=0.388,  $p = 0.011$ ), family income 50000 to 74999 (OR=0.318,  $p = 0.005$ ), length of stay (OR=1.670,  $p < 0.001$ ), veteran status (OR=0.180,  $p = 0.012$ ), BMI overweight (OR=2.355,  $p = 0.002$ ), and BMI obese (OR=5.450,  $p < 0.001$ ) remained significant.

**Conclusion/Implications:** Routine hospital-based SDOH screenings and referrals can help identify nonmedical risk and protective factors for complicated labor and delivery, which in turn informs multi-level strategies to improve maternal health outcomes. Future research will validate these findings and further explore SDOH in larger, more diverse samples.

### **Mental Health Literacy Assessment Among Black Girls Ages 6-16**

**Makala Blakely**, Midtzar Alexis, Niki Messmore

**Background:** Girls STEM Institute (GSI) is a nonprofit organization designed to expose girls and young women of African American descent to STEM based topics and careers. GSI launched their first STEM intensive summer institute 11 years ago and has since served more than 200 youth in the greater Indianapolis area through both their summer institute and Super Saturdays programs.

**Method:** Participants ( $n = 40$  for pre and post surveys) were divided into two groups: junior and senior scholars based on age. A seven question pre survey was administered to determine a baseline level of mental health literacy, thoughts regarding mental health topics and disorders, and knowledge about resources available in the community. Furthermore, the survey consisted of both positive and

negative statements about mental health. The presurvey was followed by a 30-minute presentation on mental health literacy. This interactive presentation discussed the difference between mental health and mental health disorders, stigmas within the black community, seeking help, and coping mechanisms. Following this, the same survey was administered to gauge students' thoughts and perceptions compared to before the presentation.

**Results/Conclusion:** Overall, the post survey indicates a positive trend in mental health literacy when compared to the presurvey. Based on this information and the data, conversations regarding mental health could be beneficial for adolescents to increase their comfortability with discussing mental health topics, coping mechanisms to maintain good mental health habits.

### **Temporal Changes in Neuronal Innervation during Human Inner Ear Organoid Development**

**Maria Martinez**, Shweta Reddy, and Eri Hashino

**Background/Objective:** Ribbon synapses are specialized synapses in sensory systems, crucial for tonic neurotransmitter release. Neuronal refinement, involving synaptic elimination and strengthening, is essential for nervous system development. While vestibular neuronal refinement is not well understood, cochlear maturation in mice provides reference for investigation. This study aims to test whether neuronal refinement/pruning, similar to those seen in the mouse inner ear, takes place in human pluripotent stem cell-derived inner ear organoids during development.

**Methods:** A 3D differentiation strategy developed in the laboratory was used to generate inner ear organoids, followed by tissue clearing and immunofluorescence labeling. Confocal microscopy was used to capture 3D volumetric images of vestibular hair cells and neurons at days 80, 120, and 200. Hair cell innervation was quantified by manually counting direct contact points between neurons and hair cells in 3D. NIS Elements annotation software was employed for accurate quantification.

**Results:** The mean number of neuron contacts per hair cell significantly decreases from day 80 to day 200 ( $\bar{x} = 2.56, 1.89, \text{ and } 1.60$ ) respectively. The variability in these contacts reduces, as indicated by the standard deviations ( $\sigma = 1.131, 0.8570, \text{ and } 0.7107$ ). Despite this, there is persistent non-normal distribution of neuronal contact.

**Conclusion/Implications:** This study identifies temporal changes in neuronal contacts with hair cells in the human in vitro model of inner ear development, which is similar to neuronal refinement/pruning in the mouse inner ear during development. Observations include decreased neuronal contacts after differentiation day 80, branching refinement at day 120, and stabilization until day 200. The

findings suggest varied maturation rates but increasing system uniformity over time. These results suggest that human inner ear organoids can be used to recapitulate normal and pathological development of ribbon synapses and neuronal innervation, essential components for sensory transduction in the human inner ear.

### **Social Determinants of Health and Their Effects on Readmission and 30-Day Readmission in Patients with a History of Cardiovascular Interventions**

**Mark Delos Reyes**, Baraka Muvuka, Jonathan Guerrero

**Background/Objective:** 30-day readmission is a quality indicator impacting patients and healthcare systems. Medicare patients accounted for 2.3 million 30-day readmissions, costing \$35.7 billion 4 years following the 2012 Hospital Readmission Reduction Program (HRRP) launch. Three of six HRRP measures are cardiovascular: myocardial infarction, Heart Failure, and Coronary Artery Bypass Graft Surgery. This study examined relationships between social determinants of health (SDOH), demographics, and behavioral factors on readmission and 30-day readmission among patients with a cardiovascular intervention history in partnership with an urban Northwest Indiana (NWI)-based health system.

**Methods:** This retrospective study analyzed de-identified data from inpatient SDOH screenings in Epic using the Protocol for Responding to and Assessing Patients Assets, Risks and Experiences (PRAPARE) at 3 urban hospitals between January 2021 and April 2024. Data analysis included descriptive, bivariate (Chi-Square, Mann-Whitney U, Kruskal Wallis;  $p < 0.05$ ), and multivariate (binary logistic regression;  $p < 0.05$ ) analyses in SPSS 29.0. This study was exempted by the Indiana University Human Research Protection Program (IRB #14040).

**Results:** The sample comprised 3717 patients, the majority White (70.2%), publicly insured (87.4%), and older adults (73+17). Readmissions represented 43.5% of admissions, 19.8% being 30-day readmissions. Bivariate analysis revealed significant associations between readmission and age ( $p < 0.001$ ), ethnicity ( $p = 0.001$ ), race ( $p < 0.001$ ), sex ( $p < 0.001$ ), sexual orientation ( $p = 0.007$ ), insurance type ( $p < 0.001$ ), financial resource risk ( $< 0.001$ ), housing risk ( $p = 0.05$ ), smoking status ( $p = 0.041$ ), BMI ( $p < 0.001$ ), hospital ( $p < 0.001$ ), and comorbidities ( $p = 0.027$ ). Sex, insurance type, sexual orientation, BMI, and hospital were also associated with 30-day readmission. Multivariate analysis revealed significantly higher odds of readmission with prolonged hospital stay (OR=1.051;  $p < 0.001$ ), former smoking (OR=1.759;  $p = 0.039$ ), and patients at a small, lower SES-serving hospital (OR=1.473;  $p < 0.001$ ).

**Conclusions/Implications:** Social-behavioral factors

were associated with readmissions and 30-day readmissions among patients with a history of cardiovascular interventions. Integrating SDOH and behavioral screenings and interventions into hospital readmission reduction initiatives could strengthen these programs.

### **Sexual Dimorphism in the Skeleton of Adult and Aged Mice with Alzheimer's Disease-Related Mutations**

**Mark Zhang**, Gabriel Ramirez, Alix Teal, Roquelina Pianeta, Lakshmi Chellaganapathy, Dan Horan, Chiaki Yamada, Alyson Essex, Alexandru Movila, Lilian I. Plotkin

**Background:** Alzheimer's disease (AD) is a progressive neurological disease characterized by gradual impairment in cognition and memory. Osteoporosis is another common degenerative disease in aging populations. Recent research has uncovered links between AD and bone biology, as well as potential sex-linked differences in disease progression, but the mechanisms behind this are yet to be fully understood. We hypothesize that at both 4 and 13 months of age, female mice with AD-related mutations will have more age-related adverse effects on bone microstructure and geometry than their male counterparts.

**Methods:** Male and female mice expressing humanized forms of AD-linked mutations (Swedish/Arctic/Austrian) in the Amyloid Precursor Protein (APP-SAA) were raised until either 4 or 13 months of age to accelerate plaque formation. Dxa/Piximus data was collected for body weight, total bone mineral density (BMD), femur BMD, and spine BMD for both age groups and sexes. Trabecular bone from distal femora and cortical bone from femoral mid-diaphyses were then analyzed by  $\mu$ CT. Sexes were analyzed separately by 2-way ANOVA (Tukey's post-hoc multiple comparisons) or unpaired t-test.

**Results:** Our results show that among mice with AD-related mutations, female sex is associated with more pronounced age-related effects on bone. Both sexes displayed increases in tissue and marrow area, point of maximal inertia, and tissue mineral density, but females showed a more detrimental effect with age. The deleterious effects of age were more apparent in trabecular bone than cortical, with female APP-SAA mice also displaying significantly lower BV/TV, Tb.N., Tb.Th., and higher Tb.Sp. than male APP-SAA mice at both ages.

**Conclusion:** AD and osteoporosis are prevalent and debilitating diseases affecting millions of patients throughout the United States. The results from this study will help to understand the relationship between them and identify potential interactions between sex and disease progression.

## Exploring Motivations for a Career in Geriatrics

Mary O'Connor, Kathleen Unroe

**Background:** Recently published literature has reported declining numbers of medical students and trainees choosing to pursue a fellowship in geriatric medicine. The few published, qualitative studies that seek information as to why medical students and trainees choose geriatrics tend to focus on what the subjects dislike about the field. The purpose of this study is to determine common factors that motivated recent medical residency or fellowship graduates to pursue a career in geriatrics and gather information on some of the positive aspects of a career in geriatrics.

**Methods:** Thirteen eligible participants were interviewed, each being a current geriatric fellow or having graduated from an accredited geriatric fellowship in the U.S. within the last 6 years. Interviews were transcribed and coded by the research team.

**Results:** There were 18 codes identified that were then divided into four themes: 1) personal experiences with older adults and geriatricians; 2) distinguishing characteristics of geriatrics as a specialty; 3) benefits and challenges of a career in geriatric medicine; and 4) expectations and recommendations for the future of geriatrics. Responses suggested close relationships with older adults, early clinical experiences in geriatrics, and having geriatrician mentors were common motivating factors. Participants highlighted a patient-centered, “what matters most” approach, which sets geriatrics apart from much of their previous medical training. Benefits of a career in geriatrics, including good work-life integration, flexible career paths, supportive work environments, appreciative patients and caregivers, and making an impact, were met with challenges related to increased medical complexity and working in a system that does not value preventative care or the needs of older adults. Participants discussed the need for increased exposure to geriatrics in medical training and the need for geriatrics to further evolve as a specialty.

**Conclusions:** Common motivating factors included early personal relationships with older adults and early clinical exposure to geriatrics. Findings suggest that participants consider their work to be rewarding with many lifestyle benefits, and the declining number of medical trainees pursuing geriatrics should be met with efforts to increase exposure to the field early on in medical training.

## US ADI, Healthcare Usage and Other SES Factors? Impact on Antimicrobial Resistant Bacteria Cholangitis

Mateo Blair, Nicolas Barros

**Background and Hypothesis:** Cholangitis is inflam-

mation of the biliary tree that is most commonly caused by bacterial infection of the biliary tree. Management of cholangitis is typically a regiment of broad spectrum antibiotics, but it is not uncommon for cholangitis to be caused by a resistant microbe. The purpose of this project is to examine socioeconomic factors that may impact the incidence of antibacterial resistant microbes causing cholangitis. In comparison to cholangitis patients with a lower ADI and higher healthcare usage, there will be a greater incidence of antibacterial resistant microorganisms in patients with a higher ADI score.

**Methods:** Bile samples had previously been collected from cholangitis patients. The infecting organisms were identified and then classified as VRE, MRSA, ESBL or not resistant. Race, age, gender, socioeconomic status (SES) and healthcare usage were collected and compared to resistant organism incidence to measure correlation. SES was approximated using ADI.

**Results:** Of all patients with ESBL, there was a higher proportion of ESBL patients (50%) in the lowest ADI range than there was in the highest ADI range (5%). The decrease was not linear and with no discernable pattern. In patients with VRE a similar trend was found, at the lowest ADI range the proportion was 33% whereas in the highest ADI range the proportion was 20%. This trend—or lack thereof—continued across all other categories of resistant organisms.

**Conclusion and Potential Impact:** This study did not find a connection between any factors of the social determinants of health and incidence of antimicrobial resistant organisms. This is the opposite of what was expected. These results indicate that there is no link between these factors in the population of our investigation. This investigation should be repeated with a more racially and socioeconomically diverse group.

## Through a Different Lens: Assessing Patient and Clinician Diversity in Medical Education Clinical Practice Media

McKenna Major, Stacey Dunham, Valerie O'Loughlin

**Background:** As demands grow for inclusivity and representation in the workplace, schools, and various other settings, an increased focus has been placed on the lack of diversity in health multimedia. Specifically, textbooks utilized in medical school curriculum often lack photos that depict diverse skin tones, body shapes, sexes, and genders. However, past studies did not analyze the most recent clinical textbooks or emerging clinical video databases. This research focuses on examining patient and clinician clinical diversity in two clinical education resources: Bates' Guide to Physical Examination and History Taking 13th edition (2021 e-text) and Bates' Visual Guide to Physical Examina-

tion (video series).

**Methods:** We developed a coding scheme for photos and videos based on previous literature that analyzes age, gender, sex, health state, skin tone, hair texture, body composition, SES, and the presence of tattoos and/or piercings. The coding scheme underwent 2 rounds of testing and subsequent modifications with a smaller sample. The final validated scheme was used to assess 576 photos and videos.

**Results:** Of the photos and videos, only 18% exhibited individuals with curly or wavy hair, 1% included individuals with a darker skin tone, and 0.3% of individuals had a larger body type. There were no intersex or nonbinary individuals included. None of the individuals had tattoos, and all the piercings displayed were earlobe piercings, with all but 1 of the individuals being female.

**Conclusions:** These findings reflect conclusions from previous studies, demonstrating that diversity and representation in medical textbooks can still be improved. Although there was some diversity in the photos and videos, several of the same models were used throughout the sources, which limits the application of such images to a range of diverse individuals. By advancing the diversity of medical school curriculum materials, students can provide more competent and compassionate care.

### **Use of Crescent(TM) RA Dual Lumen Catheter for VV ECMO Cannulation in Pediatric Patients: A Review of Early Outcomes**

**Michael Chmiel**, Michael Sobolic, Yujin Park, Ryan Barbaro, Ameer Bigelow, Laura Boomer, Michael Buoncristiani, Dan Byron, Jolynne Carl, Nicholas C. Carr, Stephanie Chao, Anthony Chin, Katherine Clement, Goeto Dantes, William Dugal, Sharada Gowda, Senan Hadid, Justin Henson, Laura Hollinger, Swosti Joshi, Harry Kallas, Vinay Kalvacherla, Sarah Keene, Laura Kenny, Eric Lloyd, Dimitra Lotakis, Ogechukwu Menkiti, Laura Metzler, William Middlesworth, Mark Molitor, Brie Ochoa, Meagan Peterson, Thomas Pranikoff, Vilmaris Quinones Cardona, Eric Rellinger, Dan Scheese, Nick Schmoke, Brian W. Gray

**Introduction:** Venovenous (VV) extracorporeal membrane oxygenation (ECMO) is paramount in supporting pediatric patients with respiratory failure. Compared to venoarterial (VA) ECMO, VV-ECMO is associated with decreased neurological complications in pediatric and neonatal patients as well as decreased mortality in neonatal patients with respiratory failure. Since 2018, the only VV-ECMO cannula available for pediatric and neonatal patients was the bicaval VV cannula which carries increased risk of complications like atrial perforation. In 2021, however, the Crescent(TM) Right Atrial (RA) cannula was developed and made available in 13Fr, 15Fr, and 19Fr sizes, as the only VV cannula designed for placement in the right atrium.

This study aims to evaluate patient outcomes and cannula-related complications during the first two years of use following the introduction of the Crescent(TM) RA cannula.

**Methods:** This was a multicenter retrospective cohort study looking at 165 pediatric and neonatal patients placed on VV-ECMO using the Crescent(TM) RA cannula from September of 2021 to August of 2023. Using a Redcap survey, data from these patients were collected from 20 medical institutions across the United States of America. Collected data included: patient characteristics, cannulation parameters, length of ECMO runs, flow data, complications, and survival. Descriptive statistics were calculated using Microsoft Excel.

**Results:** The median duration of ECMO runs was 7 days [interquartile Range (IQR): 4, 11]. Migrations occurred in 20.6% of patients and repositioning of the cannula transpired in 17.6% of patients. Cannula-related cardiovascular (CV) injuries occurred in 5.5% of patients. Of these patients with cannula-related CV injuries, 22.2% of these CV injuries occurred during cannulation, 33.3% occurred within the first 24 hours of the ECMO run, and 44.4% occurred greater than 48 hours from the initiation of ECMO. 1.8% of the total patients died as a direct result of cannula-related CV injuries. 78.2% of patients survived to decannulation, while 70.3% survived to hospital discharge.

**Conclusions:** The first two years of use of the novel Crescent(TM) RA cannula indicate that it is a safe and reliable tool for neonatal and pediatric VV-ECMO cannulation. In addition, this cannula addresses a significant gap in neonatal and pediatric care in its offering of a dual lumen VV-ECMO cannula designed to position its tip within the right atrium. Given the incidence of cannula-related CV injuries, increased education is necessary to reduce their prevalence.

### **Effect of Decreased Oxygen Tension on Glioblastoma Cell Migration**

**Michael Sundahl**, Elise O'Herron, Scott Cooper, Angela M. Richardson

**Background and Hypothesis:** Glioblastoma (GBM) is the most common primary malignant brain tumor in adults. Despite the current standard of care, outcomes for these patients remain poor. Current preclinical models for glioblastoma utilize cells that have been exposed to ambient air. However, previous research in both hematopoietic stem cells and breast cancer cells has shown that cells undergo changes when exposed to higher oxygen tensions. These studies have shown that cells demonstrate differences in stemness, expression of signaling pathways, and proliferation when comparing normoxia (21% oxygen) and physoxia (2-6% oxygen). We sought to determine if decreased oxygen tension affects glioblastoma cell migration. The differ-

ences seen between cells at normoxia and physoxia may explain why preclinical successes have not translated into effective therapies for patients with glioblastoma.

**Methods:** In this study we used different assays to determine if the oxygen tension that cells are exposed to affects cellular function. Cells used for all experiments were from the human glioblastoma cell line, GB10. Cells for physoxia experiments were grown and maintained at 5% oxygen and normoxia cells were grown and maintained at 21% oxygen. Growth curves were performed in order to compare the growth rate of cells in physoxia and normoxia. Transwell migration assays were utilized to compare the migration of cells. Images were taken from the middle of the well and cells were counted in order to compare conditions. Finally, wound healing of cells was measured by performing a scratch assay. Upon measuring wound distance at each time point, percent wound closure was measured.

**Results:** In this study, we found that differences do exist when glioblastoma cells are processed and maintained in lower oxygen concentrations. GB10 cell growth was decreased in cells that were maintained at physoxia. Scratch assay data demonstrated greater wound closure at 24 hours for GB10 cells that were maintained in physoxia. Results from the transwell migration assay showed that migration of the cells in physoxia was decreased when compared to normoxia.

**Potential Impact:** This study highlights the importance of establishing a more accurate preclinical model for glioblastoma. We demonstrated that differences do exist between cells maintained at physoxia and those maintained at normoxia. The next step is to repeat these experiments on additional GBM cell lines in order to verify the results. Cell lines created from patient tumor samples can also be used to repeat the experiments.

### **The Impact of Social Demographics, Disease Activity, and Organ Damage on Time to Diagnosis in Pediatric Systemic Lupus Erythematosus**

**Michaela Harter**, Rebecca Hetrick, Kiana Johnson, Martha Rodriguez

**Background:** Pediatric Systemic Lupus Erythematosus (pSLE) is a systemic autoimmune disease with variable clinical presentation. Untreated SLE can cause significant impairment, making early recognition and diagnosis critical in preventing irreversible organ damage. This study aims to understand the relationship between sociodemographic factors, disease activity at diagnosis, and time to diagnosis.

**Methods:** A retrospective chart review of 156 pSLE patients evaluated by the Department of Pediatric Rheumatology at Riley Hospital for Children between 2017 and 2023 examined various sociodemographic and disease-related variables: race, ethnicity, preferred language, **88 | Insight Vol. 7**

sex, insurance type, Area of Deprivation Index, disease activity (SLEDAI-2K score), and cumulative organ damage (SLICC/ACR Damage Index). SLEDAI-2K scores were calculated for 132 (84.6%) of the patient cohort. Time to diagnosis was calculated in weeks from symptom onset to diagnosis. Multiple regressions analysis was conducted using time to diagnosis as the dependent variable and social demographic variables as predictors. Data was collected with REDCap and analyzed with IBM SPSS Statistics (Version 28).

**Results:** No significant correlation was found between time to diagnosis and: age at diagnosis, type of insurance, ethnicity, preferred language, state ADI decile, sex, or SLICC/ACR Damage Index. There was a significant correlation between time to diagnosis and SLEDAI-2K disease activity score calculated at time of diagnosis (Pearson Correlation= -0.245,  $p < 0.005$ ).

**Conclusions:** The study showed no significant correlation between time to diagnosis and several sociodemographic variables. These findings suggest that pSLE patients from racial and ethnic minority groups and those with public insurance may have equitable access to care compared to non-minoritized groups and those with private insurance in Indiana. Additionally, the study did show a significant negative correlation between time to diagnosis and disease activity. Future work can include strategies to find and diagnose low-disease activity patients earlier.

### **The Use of High-Flow Nasal Cannula in Children with Immunocompromising Conditions: A novel score associated with intubation**

**Michelle Mai**, Colin M. Rogerson, MD, MPH, Courtney Rowan, MD, MS

**Background:** Exposure to heated, humidified, high-flow nasal cannula (HFNC) before intubation has been associated with increased mortality in children with immunocompromising conditions (ICC). We sought to describe the rate of HFNC failure in this population, defined as need for intubation. Further, we aimed to develop a novel metric of HFNC respiratory support and determine its association with HFNC failure in a cohort of children with ICC.

**Methods:** A single center, retrospective cohort study was conducted involving children and young adults (aged 0-26 years) with ICCs who used HFNC between 2021-2023 at a Quaternary Children's hospital. No interventions were performed.

**Results:** Ninety-three subjects were included. Forty-four (47.3%) failed HFNC. PICU mortality rate was 14% ( $n=13$ ). The median duration of HFNC was 18.7 hours (IQR: 6.0, 40.4). The median PICU stay was 6 days (IQR: 3,15). We then developed the novel score termed FLOX

((flow rate Liters/minute)/ weight (kg))\*FiO<sub>2</sub>) and analyzed its association with HFNC failure. Median FLOX score was higher in those that failed HFNC at initiation (p=0.04), 2 hours (p=0.03), 4 hours (p=0.05), and 6 hours (p=0.05). Using Liu's index to identify an optimal FLOX cutpoint of  $\geq 0.20$ , those with a high FLOX were more likely to fail HFNC. Adjusting for PRISM, the odds of HFNC failure with a FLOX score ( $\geq 0.20$ ) were as follows: Initiation OR=2.5 (95%CI: 1.03, 5.9), p=0.042; 2 hours of HFNC, OR 4.3 (95%CI: 1.7, 10.9), p=0.002; 4 hours of HFNC, OR=6.5 (95%CI: 2.5, 16.8), p<0.001; and 6 hours of HFNC, OR=4.9 (95%CI: 1.9, 12.7), (p=0.001).

**Conclusions:** In children with ICCs, the HFNC failure rate is high, and mortality is high in those who fail HFNC. The novel FLOX score, specifically a FLOX  $\geq 0.20$ , is associated with increased odds of failing HFNC in our ICC cohort. These results should be explored in an external cohort for validation.

### **Impact of Race and Industry on Stroke Incidence on Patients in Northwest Indiana – A Report to Advocate for Targeted Community-Based Interventions**

**Miranda M. Cash, Sahar A. Abdullah,** Amy Han

**Background:** Stroke is a leading cause of death and disability in the US and studies have shown racial/ethnic disparities in stroke, including in Hispanics/Latinos: the fastest growing segment of the US population. St. Catherine Hospital is located in East Chicago, Indiana and the majority population is Hispanic/Latino (54.8%) and is disproportionately at risk of stroke with a death rate of 79 per 100,000 people. With such disparities in stroke mortality across Northwest Indiana, especially among minority patients, we aim to report which zip codes show particular associations in stroke incidence and report possible social determinants of health (SDoH) between White, Black/African American, and Hispanic/Latino patients that receive treatment at St. Catherine Hospital.

**Methods:** Powers Health System provided data from St. Catherine Hospital in East Chicago, Indiana from January 2022 - March 2024 collecting socio-demographic data from 304 patients residing in the greater Northwest Indiana area. We calculated odds ratios to investigate associations in stroke outcome, race, and zip codes.

**Results:** In Whiting, IN, stroke is less likely to occur in Hispanics/Latinos compared to Whites. In South Chicago, stroke is more likely to occur in Hispanics/Latinos compared to Blacks/African Americans. Based on U.S. Census Bureau metrics, residents of South Chicago face more negative SDoH than residents of Whiting.

**Conclusion:** Northwest Indiana has the largest steel mak-

ing facility in North America; this study aims to provide St. Catherine Hospital with a better understanding of which patients may be at particular risk of stroke based on SDoH (type of employment, pollution levels, and population density) that contribute to increased stroke incidence. Targeted community outreach efforts, such as policy change, patient education/training, and a stroke support group at St. Catherine Hospital, are future steps to increase positive SDoH.

### **MRTX1133, a KRASG12D Inhibitor, Exhibits Significant Antitumor Activity and Enhances Nanoparticle-Paclitaxel-Based Chemotherapy Response in Pancreatic Cancer**

**Mitchel Ramos,** Niranjana Awasthi

**Background:** Pancreatic ductal adenocarcinoma (PDAC) is one of the most challenging malignancies with an extremely grim prognosis. Nab-paclitaxel plus gemcitabine (NPT-GEM) represents the standard treatment, yielding a median survival of ~8.5 months. Genetic studies have identified KRAS, TP53, p16/CDKN2A, and SMAD4 as the most common mutated genes in PDAC, with KRAS mutations present in over 90% of cases, driving tumorigenesis. The most prevalent KRAS-mutation subtypes in PDAC include G12D (~49%), G12V (~30%), and G12R (~12%). MRTX1133 targets the KRASG12D mutation in both active and inactive states, selectively inhibiting KRASG12D mutant tumor cells while sparing wild-type KRAS, highlighting its significant therapeutic potential for PDAC.

**Methods:** In vitro proliferation of KRASG12D-mutant (AsPC-1, HPAF-II, SW-1990), KRASG12C-mutant (MiaPaCa-2) and KRASwt (BXPC-3) cell lines was performed by colorimetric WST-1 assay. Protein expression was measured by Immunoblot analysis. Tumor growth studies were conducted using NOD/SCID mice with AsPC-1 subcutaneous xenografts.

**Results:** In vitro assays demonstrated dose-dependent inhibition of proliferation in KRASG12D-mutant cells with both NPT-GEM and MRTX1133, exhibiting a synergistic effect when used in combination. MRTX1133 alone had minimal effect on KRASG12C-mutant and KRASwt cell lines. Immunoblot analysis of KRASG12D-mutant AsPC-1 and HPAF-II cells revealed decreased expression of phospho-ERK, phospho-AKT, phospho-S6, phospho-MEK, phospho-RAF, and an increase in apoptosis markers cleaved-PARP-1 and cleaved-caspase-3. Tumor growth inhibition studies exhibited significant delays in tumor growth with MRTX1133 and NPT-Gem and their combination had synergistic effect. Average net tumor growth compared to control (327 mm<sup>3</sup>) was reduced to 129 mm<sup>3</sup> by NPT-Gem, 56 mm<sup>3</sup> by MRTX1133 and -4 mm<sup>3</sup> (tumor regression) by the combination therapy. Tumor weight data from subcutaneous xenograft experiments corroborated the tumor growth inhibition findings. IHC analysis of tumor

tissue to examine the mechanism of action of MRTX1133 is currently ongoing.

**Conclusion:** These findings underscore the therapeutic potential of MRTX1133 for clinical therapy of KRASG12D-mutant PDAC patients.

### **Feasibility of Implementing a Hospital-Wide Ultrasound-Guided Peripheral Intravenous Access Training Program for Nurses**

**Mitchell Holland**, Benjamin Nti

**Background:** Difficult intravenous access (DIVA) in pediatric patients is a significant barrier to care, negatively influencing therapeutic interventions, diagnostic procedures, patient experience, and staff workflow. Ultrasound-guided peripheral intravenous access (USGPiV) improves IV access and longevity in DIVA patients.

**Methods:** We implemented a novel approach to USGPiV training across multidisciplinary pediatric nursing staff and assessed the impact of this program on patient care. This is a prospective observational study of multidisciplinary nurses at an urban quaternary children's hospital with no prior training program. Our training program took place from January 2023 to June 2024. We included Multidisciplinary pediatric nurses and Maternal-Fetal Medicine nurses with at least 6 months of nursing experience in placing standard PiVs. The curriculum consisted of 3 phases: 1. Initial didactics and phantom practice; 2. Supervised cannulation, and 3. Unsupervised cannulation. Participants were required to complete a pre-survey, pass a skills and knowledge assessment, and complete a post-survey following completion of the training.

**Results:** Ninety-eight nursing staff with limited to no prior USGPiV experience from various disciplines voluntarily enrolled in the training, with most having professional experience in the 5-to-10-year range. Evaluation of pre- and post-training surveys of nursing staff showed improvements in competence, comfort, and expertise. During the period of data collection, 623 USGPiVs were performed by the trained nursing staff, 73% of which were placed on DIVA patients or patients with emergent IV access needs.

**Conclusions:** Implementation of our hospital-wide training program successfully equipped nurses with the necessary skills to perform USG-PiV, resulting in improved IV access and patient care outcomes. These findings suggest that a structured USG-PiV training program can enhance the competency of nursing staff while streamlining workflow in pediatric care settings.

### **A Predictive Model for Surgical Resectability in Thymic Epithelial Tumors Using Clinical Data: A Step Towards Integrating Radiomics and Histopa-90 | Insight Vol. 7**

## **thology**

**Mohammed Ghazali**, Mae Shu, Rohan Maniar, Patrick Loehrer, DuyKhanh Ceppa

**Background:** Thymic epithelial tumors (TETs) are rare, heterogeneous malignancies. Surgery is the primary treatment for early-stage TETs, while induction strategies aim to reduce tumor mass and improve R0 resection likelihood. However, treating borderline resectable TETs remains a challenge. Machine learning (ML) can offer insights beyond traditional methods and the field of RaPtomics applies ML to radiologic and pathological images. Establishing a baseline model will allow future evaluation of hidden features like texture and homogeneity against current clinical standards. To start, we hypothesize that a clinical model can accurately predict surgical resectability in TET patients.

**Methods:** From a REDCap database of 1089 TET patients at Indiana University's thoracic oncology clinic, 143 patients met the following criteria: confirmed Masaoka stage I-III TET, confirmed resection status, and surgery with curative intent. Nine clinical data points, including tumor size and WHO Staging, were used to encode 18 features. Patients were divided into cohorts based on resection: R0 resection (92 patients) and R1/R2 resection (51 patients). Five ML models were assessed via stratified cross-validation, evaluating accuracy and AUC.

**Results:** The Random Forest Classifier achieved 75.9% accuracy and an AUC of 0.774, indicating the model has a 72.6% chance of distinguishing between R0 and R1/R2 resection cases. A sensitivity of 0.80 for R1/R2 indicates that the model effectively identified unresectable cases, highlighting a use case in helping avoid unnecessary surgeries. Top contributing features included WHO and Masaoka staging, and notably, second-largest tumor dimension, implying that volume may be a more significant indicator for resectability than primary tumor length.

**Conclusion:** This study establishes a foundational ML model for predicting surgical resectability in TETs. Future work will address current model limitations by incorporating RaPtomics features and expanding the cohort to differentiate between direct-to-surgery and neoadjuvant chemotherapy patients. This may enhance decision-making for neoadjuvant therapy and improve R0 resection likelihood.

### **A Case Report: Synergistic Benefit of Levofloxacin-Azithromycin Combination Therapy in Severe Legionella Pneumonia**

**Molly Beatty**, Nicole Libiran, Elle Zenni, Anna Montelongo, Graham Carlos

**Background:** Studies have shown no significant difference between fluoroquinolone versus macrolide use in reducing

mortality in patients with *Legionella* pneumonia. However, the effects of using both antibiotics simultaneously are not well elucidated. A study analyzing in vitro synergy reported significant synergy for clarithromycin-levofloxacin and azithromycin-levofloxacin against *Legionella* strains, and with similar findings in other in vitro studies, combination therapy has been suggested to enhance bactericidal activity in severe cases of *Legionella*.

**Case description:** A 58-year-old female presented to the emergency department for worsening shortness of breath, productive cough, and diarrhea. Chest X-ray (CXR) showed multifocal airspace disease, concerning for multifocal pneumonia. Blood cultures were drawn while azithromycin and ceftriaxone were started. The patient's status worsened, and vancomycin and piperacillin/tazobactam were added. A basic metabolic panel (BMP) revealed hyponatremia, and a urine test for the *Legionella* antigen was positive. Antibiotics except for azithromycin were discontinued. Repeat CXR showed worsening infiltrates, acute respiratory distress syndrome (ARDS) criteria were met, and intubation was performed due to increased oxygen requirements. Without improvement with azithromycin, levofloxacin was added. The next day, CXR showed improved infiltrates while the patient began to display signs of clinical stability.

**Conclusion:** Observing the patient's improvement after the addition of levofloxacin to azithromycin, we hypothesize a synergistic relationship between the antibiotic pair. Prior case studies on severe *Legionella* pneumonia have likewise demonstrated the efficacy of combination therapy with macrolides plus quinolones as both patients survived. Like the case presented here, combination therapy was successful when monotherapy with levofloxacin or azithromycin failed.

**Clinical Significance:** In severe *Legionella*, physicians should consider macrolide-quinolone dual therapy when macrolide alone initially fails. It is unclear if the patient presented would have survived without adding levofloxacin to the antibiotic regimen.

### **Changes in Contraceptive Methods Choices following Indiana abortion legislation in a Statewide Contraceptive Access Initiative: PATH4YOU**

**Molly Ruggles**, Brownsyne Tucker Edmonds, Jeffrey Peipert, Rebecca Evans, Maria Fernandez, Kathleen Wendholt, Surya S. Bhamidipalli, Tracey A. Wilkinson, Caitlin Bernard

**Background:** The Dobbs v. Jackson Women's Health decision significantly impacted abortion access, and Indiana was the first state to enact an abortion ban in August 2022. The objective of this study was to evaluate changes in contraceptive method choice among participants using our statewide contraceptive access initiative, PATH4YOU. Our

hypothesis was that more people would choose contraceptive methods with higher effectiveness due to concern for lack of abortion access in case of unintended pregnancy.

**Methods:** We analyzed programmatic data of 2,039 reproductive-age people receiving care through PATH4YOU from September 2021 to August 2024, including 1,072 pre-Indiana abortion ban and 967 post-Indiana abortion ban. All participants received pregnancy intention screening, comprehensive contraceptive counseling and same-day contraception access at no cost. We analyzed the study population via age and zip code, including the social deprivation index (SDI), and the contraceptive method mix before and after the Indiana abortion ban.

**Results:** Overall, the average age of participants was 27.7 years; 79.7% received care in-person, 20.3% via telehealth. Based on zip code, 82.7% were urban. Participants chose 50.9% LARC, 34.1% pill/patch/ring, 11.8% injectable, 2.6% barrier/EC, and .6% other. After Indiana's abortion ban, more participants chose LARC (52.5% vs 49.4%,  $p$ -value = .151) via the significant increase in implants (39.7% vs 32.0%,  $p < .001$ ). The average age of participants significantly decreased from 28.1 to 27.2 ( $p = .004$ ). There was a significant increase in mixed and rural geographic patient population (18.6% vs 10.5% and 3.5% vs 2.7%,  $p < .001$ ), respectively.

**Conclusions:** The change in abortion access, both nationally and within Indiana, is associated with contraceptive method choice for participants in PATH4YOU.

### **Determining the Therapeutic Effect of Human Neuritin 1 on the Restoration of Degenerated Retinal Ganglion Cells from Glaucoma Patients**

**Nathan Hubbard**, Shahna Hameed, Tasneem Sharma

**Background and Hypothesis:** Glaucoma is a group of optic neuropathies that affects approximately 76 million people worldwide. The main risk factor is elevated intraocular pressure (IOP) which predominantly affects retinal ganglion cells (RGC), resulting in cell death and permanent vision loss. Current therapeutics for glaucoma involve reducing IOP and halting progression of disease, but no current treatments can revive degenerated RGCs. Our project aims to evaluate the therapeutic effect of human Neuritin 1 (NRN1) in regenerating and protecting RGC loss in glaucoma. By administering NRN1 to the RGCs in culture, we hope to elucidate the efficacy in helping glaucomatous RGCs recover from cell death.

**Methods:** Immunofluorescence (IF), gene expression, and karyotyping experiments were performed on iPSCs to confirm they were successfully reprogrammed from donor keratocytes. The iPSCs were differentiated to retinal organoids (RO) to generate RGCs in vitro. After around 30

days of differentiation, the ROs were dissociated to isolate RGCs. The RGCs were seeded at one end of three different in vitro collagen scaffolds. The first received no NRN1 treatment, the second received NRN1 at the cell body, and the third received NRN1 at the opposite end. IF was done on RGC-seeded scaffolds with RBPMS and NEFL antibodies to confirm RGC marker expression and neurite growth.

**Results:** The iPSCs were successfully reprogrammed from donor keratocytes. We successfully generated RGCs from both non-glaucomatous and glaucomatous donor iPSCs. The RGCs effectively integrated within the collagen scaffolds. After NRN1 treatment, non-glaucomatous and glaucomatous RGCs demonstrated differential expression of RGC specific markers.

**Conclusions and Potential Impact:** Our study demonstrates that NRN1 exhibits a therapeutic effect on glaucomatous RGCs. This study lays the foundation that NRN1 could potentially restore vision in glaucoma patients. Additionally, iPSC-derived RGCs can successfully be obtained from human donor eyes and cultured for future research for testing therapeutics.

### **“I Simply Don’t Trust It”: Exploring How Artificial Intelligence Fits in The Education of Healthcare Professionals**

**Nathan Pairitz,** Kyle Robertson, Fiona Kolbinger

**Background:** Artificial Intelligence (AI) has the potential to transform medicine by enhancing patient care, research, and education. However, computational tools are poorly integrated into medical curricula. Large language models (LLMs) like ChatGPT and BERT can personalize study plans, analyze program effectiveness, and support research, making them promising for medical education. This project aims to demonstrate how LLMs can be integrated into medical education and investigate their effect on student self-efficacy in using AI.

**Methods:** A quasi-experimental study was conducted in the D528: Anatomy for Health Care Professionals course at Indiana University School of Medicine (May 15 - August 5, 2024, N=130). Participation was voluntary and had no effect on standings within the class. Two educational modules on LLMs and prompt engineering were implemented. Self-efficacy was measured through surveys at the end of each of the four course content blocks corresponding to exams, with gift cards as incentives. Data was preliminarily placed into Excel, and two questions from the survey were chosen to create line charts displaying student self-efficacy.

**Results:** A total of 46 students participated, with 24 completing all three surveys. Early results indicate students have increasing belief that AI can help them gain confidence with learning anatomical content, as mean Likert-scale

responses increased from 2.0 to 2.3 across the three surveys. However, belief that AI can aid in performance on the anatomy practical exam remained low, with mean responses between 1.5-1.8.

**Conclusion:** Preliminary results suggest mixed student beliefs on how AI can build student self-efficacy after two learning modules over AI. While students see potential in AI for learning anatomical content, they remain skeptical about its usefulness for practical exams. Further analysis at the study’s conclusion in early August will provide more definitive results.

### **Primary Hyperparathyroidism Delays to Surgical Visit: Associations with Socioeconomic Status**

**Nathaniel Lin,** Meghan Lark, Caroline Vieira, Kristen Kaiser, Hannah Allison, Signe Braafladt, Alexandria McDow

**Background:** Primary Hyperparathyroidism (PHPT) is a common endocrine disorder associated with significant morbidity if left untreated. The only curative treatment is parathyroidectomy. Prior studies suggest Black and Hispanic patients tend to experience delays in care and have more comorbidities at surgical consult. This study aims to identify factors associated with delays from referral to surgical consult in patients with PHPT at our institution.

**Methods:** A retrospective chart review was conducted on patients with PHPT who underwent parathyroidectomy performed by two endocrine surgeons at University and Eskenazi Hospitals in 2023. Demographics collected included race, sex, ethnicity, and age. Patients were grouped by days from referral to consult (< 60 and ≥60). Patients with Area of Deprivation Index (ADI) ≥75 were considered to have low socioeconomic status (SES). Charlson Comorbidity Index (CCI) was used to model comorbidity level.

**Results:** Of the 73 patients with PHPT, 52 (73%) were White, 58 (75%) were female, and average age was 63 years (SD=12). The majority of patients (89%) were referred by medical endocrinologists. Forty-nine percent of patients were seen over 60 days past referral. Patients who were seen past 60 days of referral were more likely to be Black (25% vs. 17%, p=0.026\*) compared to those seen within 60 days. They trended towards being Hispanic (14% vs. 2.7%, p=0.11) and towards having a high ADI (53% vs. 32%, p=0.082). No differences in time to clinic visit were associated with gender, age, referral source, referring physician specialty, alcohol use, or tobacco use. Median CCI were similar between groups (3.0 vs. 3.0, p=0.5).

**Conclusions:** Black patients and patients with high ADI were more likely to have delays from referral to clinic visit. Future work will incorporate a larger sample size to further explore these associations.

## Demographic, Social, and Behavioral Predictors of Readmission for Neurodegenerative Diseases in Northwest Indiana

Neon Calumpang, Grace Zhou Armstrong, Jonathan Guerrero, Baraka Muvuka, Kyle Gospodarek

**Background:** Neurodegenerative diseases, such as Alzheimer's and Parkinson's disease, pose significant challenges given their progressive nature and multifaceted care needs. This research examined the intricate interplay between social determinants of health (SDOH) and hospital readmissions among individuals with neurodegenerative diseases. It is part of a Participatory Research partnership between Indiana University School of Medicine-Northwest and an urban health system in Northwest Indiana (NWI).

**Methods:** This retrospective study analyzed a dataset generated from routine SDOH screenings and referrals in Epic using the Protocol for Responding to and Assessing Patients' Assets, Risks, and Experiences (PRAPARE) for inpatient admissions from 3 NWI urban hospitals between January 2021 to April 2024. Data analysis was conducted in SPSS 29.0 with descriptive statistics, bivariate analysis (Chi-square), and multivariate analysis (binary logistic regression). This study received exemption from Indiana University Human Research Protection Program (IRB #14040).

**Results:** The sample consisted of 1,338 patients admitted for neurodegenerative diseases. Patients were predominantly White (68.9%), older adults ( $73 \pm 14$ ), and publicly insured (91.5%). The bivariate analysis found that readmission was significantly associated with age ( $p < 0.001$ ), insurance type ( $p = 0.003$ ), hospital ( $p < 0.001$ ), physical activity level (0.034), and length of stay ( $p < 0.001$ ). The multivariate analysis found higher odds of hospital readmission among patients with public insurance (OR=76.1%;  $p = 0.028$ ), prolonged hospital stay (OR=8.5%;  $p < 0.001$ ), and admission at a small hospital in a medically underserved area (OR=69.6%;  $p < 0.001$ ).

**Conclusion:** Understanding the impact of SDOH on hospital readmissions is crucial for developing targeted interventions to improve outcomes and reduce healthcare costs. These factors can profoundly influence disease management, adherence to treatment plans, and overall health outcomes. Findings from this research underscore the critical need for integrated approaches addressing SDOH as part of comprehensive disease management strategies. By addressing these SDOH, healthcare systems can potentially reduce readmissions, enhance quality of life, and promote health equity.

### Health Insurance Status is Independently Associated with Testing for Hepatitis B in Pregnancy

Nicholas Imperiale, Michael Santoro, Mackenzie Fahey, Suneetha Mekala, Erin Cleary, Brittney Akerson, Naga

Chalasan, Ashina Singh

**Background:** Testing for chronic hepatitis B (HBV) in pregnancy is guideline-recommended to prevent vertical transmission to the newborn. We conducted a study to determine the frequency of selected demographics and socioeconomic variables associated with HBV testing in pregnant women who delivered at IU Health. We also examined whether HBV positivity is associated with adverse maternal and fetal outcomes.

**Methods:** We conducted a retrospective cohort study using IU Health data from 1/2022 to 12/2023. We identified the number of women who were tested for HBV during pregnancy and used logistic regression to examine the association between selected demographics and socioeconomic variables and HBV testing. Subsequently, we compared adverse maternal and fetal outcomes between hepatitis B positive pregnant women and a random sample of 100 pregnant women who concurrently tested negative (controls).

**Results:** Of 15,899 pregnant women seen during the study period, 12,756 were tested for HBV during pregnancy (80.2%). With White patients as reference, Asian patients were significantly more likely (OR: 1.26 [95% CI: 1.00-1.58],  $p = 0.048$ ) and Black patients were significantly less likely to be tested (OR:0.68 [95% CI: 0.61-0.77],  $p < 0.001$ ). Using commercial insurance as reference, patients with Medicaid (OR:0.31 [95% CI: 0.28-0.33],  $p < 0.001$ ) or either Medicare or self-pay (OR: 0.28 [95% CI: 0.22-0.33],  $p < 0.001$ ) were also less likely to be tested. In the multivariable analysis, Medicaid (OR: 0.33 [95% CI: 0.30-0.36],  $p < 0.001$ ) and either Medicare or self-pay (OR: 0.27 [95% CI: 0.22-0.33],  $p < 0.001$ ) were independently associated with lower likelihood of HBV testing. 16 pregnant women (0.13%) were positive for HBV. There were no significant differences in pregnancy-related complications between HBV positive pregnant women and their controls. Recommended HBV prophylaxis was administered to 11 (68.7%) of 16 neonates at birth.

**Conclusion:** Twenty percent of women were not tested for HBV during pregnancy. Lack of commercial insurance was significantly associated with not receiving HBV testing.

### It is all about POCUS!: Participant survey data from a statewide gastric POCUS workshop

Nicole Bianca Libiran, Mohammed Azam, Tanner Brandon, Boyer Tanna, Packiasabapathy Senthil

**Background:** POCUS education has grown significantly in the past two decades, impacting various medical specialties. This study aimed to assess anesthesia faculty's comfort, knowledge, and skill in performing gastric POCUS before and after a focused workshop.

**Methods:** Participants in the 2024 Indiana Society of An-

esthesiologists annual meeting attended a hands-on gastric point-of-care ultrasound workshop. They completed pre- and post-workshop surveys to assess their knowledge and confidence with gastric ultrasound. A knowledge test was also given post-workshop to evaluate their ability to identify structures. This study is a prospective analysis of pre- and post-workshop survey data. Data was analysed using two-tailed Fisher's exact tests, with statistical significance set at  $p < 0.05$ .

**Results:** 37 participants completed the pre-workshop survey, and 25 completed the post-workshop survey. Statistically significant differences were found in physicians' confidence with obtaining gastric images ( $p < 0.0001$ ), interpreting gastric ultrasound ( $p < 0.0001$ ), and confidence in incorporating gastric POCUS into practice ( $p = 0.0003$ ). No significant difference was found in general POCUS comfort ( $p = 0.5336$ ).

**Conclusions:** Prior studies implementing POCUS into medical education through standardized workshops have been shown to improve knowledge and POCUS comfort. In one study, implementation of a 6-hour-workshop with faculty showed increased confidence in teaching POCUS to medical students, a 36% increase in POCUS knowledge, and an increase in correct identification of anatomic structures. Likewise, hands-on training and asynchronous online modules increased PGY-1 residents' confidence in obtaining POCUS images, recognizing anatomical structures, and incorporating POCUS into clinical practice. Our study reinforces these findings in the population of practicing anesthesiologists, with an emphasis on the use of gastric ultrasound. Gastric ultrasound can be a vital tool for anesthesiologists in determining an appropriate anesthesia induction and maintenance technique when a patient's fasting status is uncertain.

### **Single Institution Retrospective Review of Inflammatory Myofibroblastic Sarcoma**

David Randall, **Pari Revankar**, Fariba Rana, Samantha Armstrong

**Background:** Inflammatory Myofibroblastic Sarcoma (IMS) is a rare mesenchymal tumor that occurs in pediatric or young adults. Diagnosis is confirmed pathologically through the presence of spindle cell proliferation within myxoid stroma admixed with inflammatory cells. Common genetic markers in the literature have revealed positivity for ALK, ROS1, or NTRK. Molecular testing confirms ALK fusion or ROS1 fusion mutations. Prognosis is usually good, with most patients requiring little or no neoadjuvant therapy, and surgical resection is often curative. However, recurrence rates are 25% and active surveillance is necessary. Epithelioid is a more aggressive subset of IMS.

**Methods:** In this single-institution retrospective analysis, **94 | Insight Vol. 7**

patients with inflammatory myofibroblastic sarcomas were identified between 2002-2024. Patient data was extracted from the electronic medical record. Relevant clinical factors including demographics, age of diagnosis, stage, location of primary tumor, pathology and associated molecular testing, surgery details, lines of systemic therapy, and outcomes were obtained. Overall survival (OS) is defined as the length of time from the date of diagnosis of IMS that patients are still alive.

**Results:** Seventeen patients with pathologically confirmed IMS were identified at Indiana University Simon Cancer Center and Riley Children's Hospital. Median age was 8.5 years, ranging from 1.25-24 years. 76% of the patients were White, 11% were Black, and 11% were Asian. Biological sex ratio was 8M:9F. Most common sites of the primary tumor were the Abdomen (N=4) and Bladder (N=3), and only 1 patient had more than 1 primary tumor at diagnosis. All tumors were locally advanced stage without lymphatic spread or distant metastatic disease. Two epithelioid IMS cases were identified. Twelve patients underwent molecular testing to confirm driving mutations, of these, 75% (N=9) had +ALK staining, 3 of which had confirmed ALK fusions, 1 ROS1 fusion, and 1 with NTRK fusion. The NTRK fused patient received neoadjuvant therapy (Larotrectinib) with significant reduction of tumor burden, and all patients underwent surgical resection of their IMS tumor. Average time for recurrence was 8.25 months (N=4), with 50% of receiving Crizotinib first line systemic therapy. Of the four patients on systemic salvage therapy or who underwent second resection have no current evidence of active disease. One patient is deceased, and was treated with combination therapy vincristine, Actinomycin D, and cyclophosphamide. The median OS for the living cohort (N=16) is 67.5 months (range <1mo-170 months).

**Conclusion:** To date, this is the largest single institution reporting on IMS with 17 patients treated over 22 years. As noted in the literature, most cases were ALK driven, primary treatment was surgical resection and targeted therapy toward the driving mutation provided successful neoadjuvant and salvage treatment if recurrence occurred. Our population's mOS was 67.5 months.

### **Spiritual Distress in Caregivers of Patients with Cleft and Craniofacial Anomalies—a Single-Center Cross-Sectional Study**

**Patrick F. Mercho**, Khoa D. Tran, Rodica I. Muraru, Emma J. Cordes, Sunil Tholpady, Katelyn G. Makar

**Background/Objective:** Spiritual distress describes an "impaired ability to experience and integrate meaning and purpose," frequently occurring after receipt of a major diagnosis. We measured spiritual distress in caregivers of children presenting to a multidisciplinary cleft and craniofacial clinic, hypothesizing that a significant percentage of

caregivers would demonstrate spiritual distress.

**Methods:** Caregivers were surveyed utilizing the Functional Assessment of Chronic Illness Therapy—Spiritual Well-Being scale (FACIT-Sp 12), the PHQ-8 and GAD-7, as well as questions evaluating caregiver health, financial strain, and religiosity measured by the Duke Religion Index. Logistic regression with cluster adjustment was used to control for demographic and clinical variables. Setting: A multidisciplinary cleft and craniofacial clinic. Patients, Participants: All caregivers able to read English were surveyed. 149/191 completed the survey (response rate=78.0%). Main Outcome Measure(s): Caregiver spiritual distress, as measured by the FACIT-Sp 12.

**Results:** The median age of caregivers was 33 (IQR 25-39). Most were female (76.7%), white (86.7%), non-Latino (91.1%), and Christian (76.7%). Most patients were seen for a cleft diagnosis (90.8%). Thirty percent of caregivers demonstrated spiritual distress. Depression was indicated in 16.1% and moderate to severe anxiety in 18.1%. On adjusted analysis, Christianity was associated with lower odds of spiritual distress (OR 0.32,  $p=0.039$ ).

### **Predicting Hypocalcemia in Multiple Myeloma Patients Undergoing Autologous Stem Cell Collection**

**Prabhjot Singh Chahal**, Esther Soundar

**Background:** Multiple myeloma is a plasma cell dyscrasia that can be treated with an autologous stem cell transplant, which involves the harvest of autologous hematopoietic cells by apheresis following induction therapy. Citrate anticoagulation-induced hypocalcemia is more common with large volume apheresis, which is defined as processing 3 or more total blood volumes. Although calcium is given parenterally to mitigate this complication, about a third of this patient population still experiences symptoms of hypocalcemia. Total calcium to ionized calcium ratio (T:iCa) has been employed widely to predict iatrogenic hypocalcemia induced by citrate anticoagulation during renal dialysis. Our aim is to assess the utility of total to ionized calcium ratio to predict hypocalcemia in multiple myeloma patients during autologous stem cell collection by leukapheresis.

**Methods:** A retrospective chart review study of a cohort of patients with multiple myeloma, who underwent autologous stem cell collection over a period of 6 months from October 2023 to March 2024, was conducted after an institutional review board approval. Demographic, clinical and laboratory data were obtained from the electronic medical record. The cohort was categorized into two groups: T:iCa  $\geq 2.00$ , and T:iCa  $< 2.00$ . The binary outcome variable measured was the presence or absence of symptoms of hypocalcemia. A 2x2 table was constructed to examine the relationship between the two categorical variables.

**Results:** A total of 22 multiple myeloma patients that underwent apheresis for the harvest of autologous stem cells were identified. About 55% of the patients were female; the median age of the patients was 56 years (IQR, 48-62) and the median weight of the patients was 79 kg (IQR, 72-100). The pre-procedure median peripheral CD34+ cell count was 46 cells/ $\mu\text{L}$  (IQR, 33-72), the median pre-procedure ionized calcium was 1.14 mmol/L (IQR, 1.1-1.2), and the median pre-procedure total calcium was 9.2 mg/dL (IQR, 8.8-9.4). The median duration of the apheresis procedure was 329 mins (IQR, 286-365). During apheresis, the median number of total blood volumes processed was 4.25 (IQR, 3.43-4.88), and the median volume of ACD-A infused was 1504 mLs (IQR, 1241-1914). The overall prevalence of symptoms of hypocalcemia was 27% during the apheresis procedure. The median T:iCa was calculated to be 1.96 (IQR, 1.89-2.06). Results of the analysis of the 2x2 table are as follows: sensitivity 50%, specificity 62.5%, positive predictive value 0.33, and negative predictive value 0.77 using a T:iCa cut-off of 2.00.

**Conclusions:** Hypocalcemia is highly prevalent among multiple myeloma patients undergoing apheresis for hematopoietic stem cell collection. A third of the patient cohort have an increased probability of developing symptoms of hypocalcemia with a T:iCa of  $\geq 2$ . Additional calcium supplementation in this subset of patients may be helpful in mitigating hypocalcemia during the procedure. A majority of the patient population who have T:iCa of  $\geq 2$  are likely to undergo autologous stem cell collection without experiencing symptoms of hypocalcemia.

### **Breast Implant Illness – Long-term Impact of Explantation and Capsulectomy**

**Princess ViLan Ferguson-Nguyen**, Ravi Bamba, Christine Kelley

**Background:** Breast implant illness (BII) refers to an array of non-specific symptoms that patients associate with their breast implants. Although poorly defined, there is a growing effort to establish the etiology, symptoms, diagnostic criteria, and treatments for BII. Proposed etiology ranges from autoimmune diseases to biofilms to psychosomatic causes. Explantation and capsulectomy has yielded symptom reduction in most patients in short term studies, but there are no long-term patient reported outcomes. This study aims to evaluate long term patient reported outcomes after breast explantation and capsulectomy in the setting of BII.

**Methods:** A longitudinal study was performed to determine if patients with BII had symptom improvement after breast implant explantation and capsulectomy. An extensive questionnaire was issued to patients before implant removal and at least one year following the procedure. Surveys were administered via email and completed in REDCap. A total

of 61 symptoms were presented. Patients rated the frequency of their current symptoms on a scale of 1-5, with 1 being “not at all” and 5 being “very much”. A difference matrix was created to visualize the change in symptom frequency. The difference between postoperative and preoperative results were calculated. A reduction in symptom frequency was defined as a negative value and increased symptom frequency was a positive value. Statistical analysis included a paired two-tailed t-test to analyze pre- and post-explantation survey data.

**Results:** A total of 36 surveys were used to analyze post-explantation and capsulectomy data. The eyes, skin, musculoskeletal, digestive, endocrine, and general body systems constitute the majority of symptoms experienced after implant removal. Low libido, joint pain/swelling, brain fog, and bloating were the most frequently reported. At least one year following explantation, overall symptom improvement was reported by 91.9% of patients. Additionally, 83.3% of patients rated the magnitude of improvement a 5 or above, with 0 being no improvement and 10 being complete improvement. Compared to preoperative surveys (n=33), in all but three of the symptoms evaluated, frequency was significantly different ( $p < 0.05$ ) before and after explantation. Specifically, the symptom frequency decreased across each symptom evaluated.

**Conclusions:** Breast implant explantation and capsulectomy provides long-term BII-related symptom relief in patient reported outcomes. A large majority of patients reported overall symptom improvement, as there was a reduced symptom frequency and severity. Thus, our results further support the long-term effectiveness of explantation and capsulectomy in the setting of breast implant illness and other related complications.

### **Kidney Function and Mortality Following Two-Stage Revision Total Joint Arthroplasty for Periprosthetic Joint Infection**

**Rilee L. Epley**, T. Kyle Stoops, Leonard T. Buller, Evan R. Deckard, Peter Caccavallo, R. Michael Meneghini

**Background and Hypothesis:** Periprosthetic joint infection (PJI) after total hip and knee arthroplasty (THA, TKA) is reported in up to 2% of cases yet remains a serious complication. The current gold standard of treatment consists of a two-stage surgery involving intravenous antibiotic therapy between stages of implant resection and reimplantation. In addition, studies on the effects of these antibiotics on kidney function after two-stage treatment for PJI are limited. This study evaluated kidney function and mortality before, during, and after two-stage revision for PJI. The hypothesis of the study was that the antibiotics part of the treatment course would not lead to an increased risk of kidney injury.

**Methods:** Clinical data on 160 THAs and TKAs undergoing two-stage treatment for PJI were retrospectively reviewed. Standardized protocols were used for all cases consisting of robust medical optimization by a dedicated perioperative medicine specialist and 6-weeks of intravenous antibiotics prior to reimplantation. Kidney function metrics of serum creatinine (Cr), estimated glomerular filtration rate (eGFR), and blood urea nitrogen (BUN) were collected from routine labs in the electronic medical record along with mortality data. A p-value of 0.05 was considered statistically significant.

**Results:** No significant differences were observed in mean serum Cr (1.10, 1.12, 1.13 mg/dL), eGFR (78.6, 77.7, 74.8 mL/min/1.73m<sup>2</sup>), or BUN levels (19.8, 18.9, 19.0 mg/dL) between pre-resection, the inter-stage period, or post-reimplant, respectively ( $P \geq 0.432$ ; Power  $\geq 85.3\%$ ). Mortality was 0% within 90-days of resection and 1.4% (2/138) within 1-year of resection (both cardiac events unrelated to kidney function). Kaplan-Meier survivorship estimates were 98% at 2-years and 86% at 5-years post-resection.

**Potential Impact:** Kidney function was not adversely impacted by the antibiotics associated with the two-stage revision procedure for PJI. With proper medical management, the two-stage revision for PJI remains the preeminent treatment for PJI following TJA.

### **ABCCCP: A Large-Scale Breast and Cervical Cancer Co-Screening Program in Western Kenya**

**Ryan McArdle**, Lucy Wabende, Kapten Muthoka, Naftali Busakhala, Peter Itsura, Philip Tonui, Elkanah Omenge Orang’o, Patrick Loehrer, Darlene R. House, Archana Shrestha, Jennifer Morgan

**Background:** Oncology care in low- and middle-income countries (LMICs) presents a pressing global concern, with a massive mortality burden predicted in LMICs by 2030. In 2017, oncologists from Moi Teaching and Referral Hospital (MTRH) in Kenya and Indiana University partnered to create the AMPATH Breast and Cervical Cancer Control Program (ABCCCP), a novel breast and cervical cancer screening and early detection program in Western Kenya.

**Methods:** This project presents a retrospective review of ABCCCP data from 2017-2022 and analyzes key lessons learned before presenting the ABCCCP program’s successor, the Kenya-Nepal Oncology Network (KENON). ABCCCP utilized clinical breast examination (CBE) for breast cancer screening and visual inspection with acetic acid (VIA) for cervical cancer screening.

**Results:** A total of 113,525 women were screened: 6,679 for breast cancer alone, 42,232 for cervical cancer alone, and 64,614 for both breast and cervical cancer. Notably, 94.1% of co-screening occurred on the same day. Screening

resulted in the early detection of 715 cases of breast cancer and 416 cases of cervical cancer, yielding positivity rates of 1.00% and 0.39%, respectively.

**Conclusions:** ABCCCP demonstrated the feasibility of large-scale, same-day breast and cervical cancer co-screening in an LMIC setting. Building on the lessons learned, KENON will aim to incorporate more sensitive screening methods (mammography and point of care ultrasound for breast cancer and human papillomavirus testing for cervical cancer), implement more robust patient navigation and community engagement to decrease loss to follow-up, and expand to a new site in Nepal, leveraging the strength of triangular partnership to improve patient care.

### **A Novel, Low-Cost Corneal Aesthesiometer for Enhanced Diagnosis and Monitoring of Neurotrophic Keratopathy**

Brooke Stephanian, **Sabin Karki**, Gregory Borschel

**Background:** Neurotrophic Keratopathy (NK) is a rare but debilitating condition affecting 1 in 2000 individuals globally. Characterized by reduced or absent corneal sensation, NK leads to corneal ulceration, scarring, and potential blindness if undiagnosed or untreated. The current diagnostic standard, the Cochet-Bonnet Aesthesiometer (CBA), is hindered by high cost, non-sterilizability, and mechanical degradation due to repeated use, reducing accessibility globally and increasing infection risk to patients. To address these limitations, we developed a novel, low-cost, single-use corneal aesthesiometer to enhance NK diagnosis and management.

**Methods:** We employed an iterative design process informed by surgeon feedback to refine usability, ergonomics, and comfort. Prototypes were fabricated using high-resolution 3D printing of acrylonitrile butadiene styrene (ABS) filament to achieve economical component design and production consistency. The device was designed as a hollow tube with a manual slider that controls a nylon monofilament bidirectionally to deliver forces for corneal sensation testing. Unlike the CBA, the nylon filament and encasement are disposable, eliminating the need for sterilization and preventing mechanical warping associated with repeated use.

**Results:** Preliminary qualitative testing shows similar actuation to the existing CBA standard, demonstrating no degradation or warping over multiple tests. The ergonomic design and the single-use format were recognized as important to clinicians, offering a critical improvement in reducing infection risk and ensuring consistent performance.

**Conclusions:** The design of a novel, disposable corneal aesthesiometer addresses key limitations of the CBA by offering a sterile, low-cost, and reliable alternative for corneal

sensation assessment. The use of a nylon monofilament and 3D-printed design ensures reproducible mechanical performance and eliminates risks associated with repeated use. This device can enhance early NK diagnosis, improve patient outcomes, and increase accessibility to quality ocular care in all settings, including potential applications in aerospace medicine. Future work will involve clinical testing to demonstrate the level of correlation between measurements from the new device and the CBA as well as larger trials to further validate the device's performance and optimize its integration into clinical practice.

### **Multiple Myeloma is Associated with Lower Serum Zinc and Selenium Levels and a Higher Cu/Zn Ratio**

**Savannah Cook**, John Oyelakin-Ogunbileje, Michelle Zimmerman, Rejwi Dahal

**Background:** Multiple myeloma (MM) is a neoplastic proliferation of plasma cells in the bone marrow, often associated with monoclonal protein (M-protein) and end-organ damage. Recent research has explored the connection between cancer physiology and trace metals like copper (Cu), zinc (Zn), and selenium (Se). We hypothesize that patients with monoclonal gammopathy of undetermined significance (MGUS) or MM will exhibit different mean levels of serum Zn, Cu, and Se compared to controls and have higher Cu/Zn ratios.

**Methods:** 1035 serum samples were analyzed by ICP-QQQ (inductively coupled plasma-tandem mass spectrometry) to measure Zn, Cu, & Se concentrations. Based on chart reviews, specimens were categorized as control (normal serum protein electrophoresis pattern, no history of M-protein; n=357, mean age=61±16years), MM (n=410, mean age=68±10years), or MGUS (n=81, mean age=72±11years). One-way ANOVA tests were performed to evaluate the relationship between patient status and serum trace metal concentrations.

**Results:** Statistical analysis showed lower Zn in the MM group compared to controls and MGUS ([Zn] in MM, MGUS, and control were 86.86±23.35µg/dL, 96.43±25.34µg/dL, & 96.58±23.37µg/dL, respectively, control vs MM (p<0.001); MM vs MGUS (p=0.003)). Cu/Zn ratios in the MM group was higher compared to control and MGUS (MM:1.35±0.52; MGUS: 1.16±0.31; control:1.20±.36, respectively, control vs MM (p<.001) and MM vs MGUS (p=0.001). [Se] was lower in the MM group compared to controls (128.78±35.9µg/L in MM and 139.82±34.31µg/L in control, p<0.001).

**Conclusions:** The significantly lower serum concentrations of Zn and Se and a higher Cu/Zn ratio in MM or MGUS patients suggest they may play a role in MM's

disease pathophysiology. Understanding trace metal levels in this population can aid in elucidation of mechanisms of neoplastic development, biomarker generation for earlier detection, improve MGUS to MM prognostics, and possibly suggest new therapeutic approaches.

### **Assessing Child Sexual Abuse Preventative Education Programs and Factors of Disclosure Rates**

**Sebastian Castillo**, Niki Messmore

**Background:** Child Sexual Abuse (CSA) is a widespread issue that organizations like Holly's House and the Mama Bear Effect address through awareness campaigns and preventive measures. Resistance from parents to implementing such education stems from believing that CSA is not a concern for their children or that the subject is too mature. This literature review aims to examine the efficacy and effects of CSA preventive education on children and identify factors influencing their likelihood of disclosing abuse.

**Methods:** A comprehensive literature review was undertaken to investigate pediatric sexual abuse, with a specific focus on the effectiveness of preventive education, the long-term behavioral effects of such education, and the factors that may influence disclosure rates among children who have experienced abuse. To identify reliable and informative sources, PubMed was utilized for biomedical literature, CALIO for child abuse-specific journals, and Google Scholar for a broader search encompassing journals not found in other databases.

**Results:** This study demonstrates that CSA prevention programs yield positive outcomes for participating children, evidenced by their retention of knowledge and acquisition of self-protective skills. Regarding behavioral changes, most studies indicate either no changes or no emergence of new negative behaviors following preventive CSA education. Disclosure rates are significantly influenced by factors such as the child's perceived parental support, concerns about being believed, power differentials between abuser and victim, and the child's ability to articulate the incident.

**Conclusions:** With further evidence supporting the positive outcomes and harm reduction from preventive education, parents and educators should feel more confident in teaching children to protect themselves from CSA. Self-education, resource-seeking, active child protection, and vigilance can enhance a child's safety and ability to handle abuse. Strong family communication is also crucial for encouraging children to disclose abuse and providing necessary details for prosecution and justice.

### **Social Determinants of Health Factors Associated with Breast Cancer Screening in Underserved Communities of Northwest Indiana**

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**Seth Boucher**, Basem Altarshan, Pooja Patel, Amy Han

**Background/Objective:** Despite breast cancer being the second most common type of cancer found in female patients, a large number of female patients have not received a mammogram in the past two years. This disparity is partly due to factors related to social determinants of health. The effects of social determinants of health on positive breast cancer screenings are clearly present in Northwest Indiana, a region containing vastly differing communities with a wide range of income levels and diversity. Nearly two decades of patient data from this area can inform us which social determinants of health are associated with increased risk for breast cancer.

**Methods:** "Hospital System A", located in Lake County, Indiana, provided data from 111,564 mammograms from the year 2006 to the end of 2023. These 18 years of data provide patient zip code, age, race, insurance category, and screening results. A proportion of positive screenings was calculated for each group and compared using Chi-Square tests. Census information such as mean household income, race, and age was gathered for each zip code in Northwest Indiana and was tested on proportion of positive screenings by regression analysis.

**Results:** When comparing zip codes of Northwest Indiana, lower mean household income was associated with higher rates of breast cancer (p-value = 0.0049). Medicare and Medicaid patient groups both had significantly higher rates of breast cancer than private and self-pay groups (p-value =  $1.35 \times 10^{-10}$ , p-value = 0.0032). Race had almost no impact on breast cancer rates.

**Conclusion/Implications:** Income level has the greatest impact on breast cancer rates. We hypothesize that this relationship may be related to decreased access to care and unhealthy lifestyles because of economic restraints. Additionally, race has little influence on breast cancer rates, which may explain that society may have a greater role in health than individual characteristics.

### **Social, Demographic, and Behavioral Determinants of Primary Admission and Prolonged Hospital Stay of Postoperative Complications in an Urban Acute Care Hospital**

Alexis Dres, **Skyler Thompson**, Maggie Sullivan, Baraka Muvuka, Jonathan Guerrero, Josh Mangum, Kyle Godspodek

**Background/Objective:** The influence of social determinants of health (SDOH) on hospital readmission rates is a broadly discussed topic in current literature. However, further exploration is required into the influence of SDOHs on readmission rates for postoperative complications. In 2012, the Hospital Readmission Reduction Program was

created to reduce patient readmissions which are linked to adverse health outcomes and mortality. This study aims to understand the influence of SDOH, demographics, and health behaviors on readmission rates with postoperative complications in urban care centers. This study is part of a multi-phased Community-Based Participatory Research (CBPR) partnership between IUSM-NW and Power Health in Northwest Indiana.

**Methods:** This retrospective study analyzed a limited dataset generated by SMMC from EPIC™ with SDOH, demographic, health behavior, and health outcomes data obtained from adult inpatients between January 2021 and April 2024. Data analysis occurred on a subset of readmitted patients and patients admitted within 30 days. Data analysis utilized SPSS 29.0 to produce frequencies, Chi-Square tests ( $p < 0.05$ ), and a binary logistic regression ( $p < 0.05$ ). This study was exempted by Indiana University Human Research Protection Program (IRB # 14040).

**Results:** This study included 565 patients involving predominantly adults over 50 (81.8%), White (69.4%), and publicly-insured patients (74.8%). The bivariate analysis revealed significant associations between postoperative complication readmissions and age ( $p < 0.001$ ), veteran status ( $p = 0.022$ ), insurance type ( $p < 0.001$ ), smoking tobacco use ( $p < 0.001$ ), BMI ( $p = 0.002$ ) and length of stay ( $p = 0.003$ ). The multivariate analysis for all readmission lengths found that former smoking tobacco use ( $OR = 2.144, p < 0.001$ ), underweight BMI ( $OR = 4.131, p = 0.006$ ), and publicly-insured patients ( $OR = 3.295, p < 0.001$ ) remained significant. The multivariate analysis for 30-day readmission revealed that only public insurance ( $OR = 2.844, p = 0.021$ ) and former smoking tobacco ( $OR = 1.875, p = 0.037$ ) remained significant.

**Conclusion/Implications:** This study found multiple SDOH and health behaviors associated with increased risk for readmission with postoperative complications. Policies and interventions targeting SDOH and health behaviors before and after surgery may reduce hospital readmissions due to postoperative complications.

### **Potential Role of Cigarette Smoke Exposure on Elastin Sensitization and Aortic Pathophysiology in a Mouse Model of Abdominal Aortic Aneurysm**

**Supriya Chittajallu**, Jacob Saliba, Madelyn Fairbairn, Jennifer Stashevsky, Theresa Doiron, Steven J. Miller, Kelly Schweitzer, Michael P. Murphy

**Background:** In the US, 200,000 people annually are diagnosed with abdominal aortic aneurysm (AAA) and it accounts for over 15,000 deaths per year. The current paradigm for AAA progression includes cytotoxic T cell activation inducing inflammatory monocyte and macrophage recruitment. These cells secrete collagen and elastin degrading enzymes, leading to loss of structural

integrity, aortic dilatation, and eventual rupture. Studies in AAA patients show an increase in cytotoxic T lymphocyte number and activity, a significant decrease in the number and immuno-suppressive activity of the T-regulatory (Treg) cells responsible for governing autoimmune responses, and decreased levels of circulating IL-10. Data from our group suggest that the immune system is sensitized to elastin in patients with early AAA. Cigarette smoking is one of the strongest risk factors for development of AAA in humans and smoke exposure has been shown to exacerbate aneurysm formation in mice. Our working hypothesis is that cigarette smoke causes lung damage via activation of tissue proteases which in turn generates antigenic elastin fragments that trigger an inflammatory reaction in the abdominal aorta resulting in an aneurysm. The current study will evaluate the effect of cigarette smoke exposure in mice on the relative ratios of populations of pro-inflammatory and anti-inflammatory T-cell subtypes, serum levels of IL-10, miRNA related to IL-10, aortic pathology, and an assessment of potential self-sensitization to elastin. The results of this study will be used to develop a delayed-type hypersensitivity (DTH) assay for elastin that could be used to easily assess the presence of AAA in human patients.

**Methods:** C57BL/7 mice were subjected to cigarette smoke exposure using a TE-10 smoking machine for 5 hours per day, Monday to Friday for 28 days. A DTH assay was conducted by injecting 30  $\mu$ L of elastin into the left ear pinna and 30  $\mu$ L of phosphate-buffered saline (PBS) into the contralateral ear on day 28. On day 30, animals were sacrificed to obtain tissues. Formalin fixed paraffin embedded (FFPE) tissue sections were stained with Hematoxylin and Eosin (H&E), Picrosirius Red, or Verhoeff-Van Gieson and used to assess aortic pathology. Changes in mRNA expression were determined by quantitative real-time PCR using TaqMan primer/probe expression assays.

**Results:** The DTH test, evaluated through ear mass and thickness, showed no significant findings, suggesting that the model had not generated sufficient antigenic elastin fragments to trigger an inflammatory response. The mRNA expression of molecules mediating pro- and anti-inflammatory responses, including pro-inflammatory IL-6 and anti-inflammatory markers TSG-6 and IL-10, showed a trend toward increased expression in the aortas of smoke-exposed mice compared to controls. Aortic pathology revealed no qualitative differences in aortic structure, collagen content, or elastin content between smoke-exposed and non-smoke-exposed mice.

**Conclusions:** These results suggest initial molecular changes but no detectable morphological changes in the aorta of the smoking cohort compared to the non-smoking cohort. These results indicate that a successful AAA model could be established through increasing the total time of smoking exposure to enhance lung damage and elastin fragment release.

## **Effectiveness of Universal Testing Legislation on Indiana's Childhood Blood Lead Level Testing Rates: Facilitators and Barriers to Implementation**

**Susie Kim**, Mark Fox, Heidi Beidinger-Burnett

**Background:** Disparities in lead exposure and social determinants of health – including housing, environmental conditions, and nutrition security – influence developmental and health outcomes, as well as academic achievement and socioeconomic status through generations. Blood lead testing and follow-up care are essential safety nets for children who may already be lead-exposed. Although Indiana Department of Health reports that Indiana's universal testing statute, House Enrolled Act 1313, has facilitated a statewide testing increase in its first year (2023), lack of implementation direction plus data inconsistencies may hinder decision making at local levels. The research studies the interpretation and implementation of universal testing by health care practices in Michiana, serving legacy cities, including South Bend, with widespread lead-based paint hazards and proximity to lead crises in East Chicago, Indiana, and Flint, Michigan.

**Methods:** Semi-structured interviews were conducted with Michiana key informants selected through purposive sampling for their knowledge of the subject. Frameworks of street-level bureaucracy and WHO's building blocks of well-functioning health systems guide analysis.

**Results:** Twelve interviewees spoke of varying testing processes and awareness of the new law. Implementation barriers include ambiguous state guidelines, CHIRP reporting issues, and persistent health inequities in primary care access. Although in-office point-of-care analyzers reduce access barriers, the detection limit of 3.3 mcg/dL bars distinction of lead levels below this threshold. Facilitators include adequately staffed workforces, communication with local social services (e.g., WIC and Head Start) and schools, and increased funding for families.

**Conclusions:** Clear implementation directions are needed to improve service delivery of lead testing by practices, while barriers in information systems, leadership and governance, and medical technologies must be addressed to support medical and environmental management of lead-exposed families. Gaps in well-child care and health system fragmentation are major barriers to lead testing, necessitating expansion of public health services and collaboration with primary care practices to reach underserved communities.

## **Evaluating the Efficacy and Utilization of Financial Assistance in the Justice-Involved Recovery Population**

**Suzanne Scanameo**, Niki Messmore

**Background:** Over 70 million Americans, or 1 in 3 US adults, have a criminal record. Involvement with the justice system has overarching effects on quality of life and especially on employment and wages. Recovery Café Indy (RCI) is a nonprofit organization that serves adults in recovery. The Member Financial Assistance program (MFA) provides up to \$500 per month for five months of financial support for justice-involved members to assist in overcoming these barriers. Evaluation of MFA will allow more members to benefit from its assistance.

**Methods:** Members across sixteen Cafés in Indiana were enrolled in MFA from October 2022-June 2024. Data was collected by Café staff and recorded on a spreadsheet, and images of spreadsheets were evaluated. Average spending, how funds were spent, and disenrollment and graduation rates were analyzed.

**Results:** The trend in spending across the sixteen Cafés showed that members on average underutilized between \$750-\$1000 of their allotted \$1500 in the first three quarters of MFA. In the fourth quarter and beyond, members decreased this number to \$250 and below. Twelve of the sixteen Cafés recorded more members disenrolling from MFA than graduating. For RCI specifically, spending on rent and utilities decreased from 58% in the first quarter to 14% in the fourth quarter while spending on food and groceries increased from 16%-41%.

**Conclusions:** MFA is not being utilized to its fullest potential by members, both in the amount of money and time spent in the program. At RCI, spending trends have shifted from a higher percentage spent on rent to more spent on groceries and food. Interviewing members on entrance and exit from the program would provide an understanding of motivations behind spending and reasons for disenrollment from MFA. This would allow for the program to improve and more members to benefit.

## **Characterization of 297 NICU Patients with Congenital Anomalies Evaluated with Genome Sequencing**

**Tejasvi Kakani**, Caroline Parker, Benjamin Helm, Samardeep Gurudatta, Lindsey Helvaty, Liesbeth Vossaert, Matthew Durbin, Theodore Wilson, Stephanie Ware, Kristen Suhrie

**Background:** Congenital anomalies remain a common indication for Neonatal Intensive Care Unit (NICU) admission. It is well-established that many congenital anomalies are caused by underlying genetic disease. However, there are limited studies describing the types of congenital anomalies in a NICU cohort or diagnostic variants identified following genomic testing. In this prospective cohort study,

we describe the types of congenital anomalies, diagnostic yield, diagnostic variants, and hospital outcomes of NICU patients who underwent genome sequencing (GS).

**Methods:** This cohort included 297 patients admitted to three NICUs at Riley Children's Hospital, in Indianapolis, Indiana from May 2022 to November 2023. Patients received GS from Baylor Laboratories due to the presence of at least one congenital anomaly identified through manual chart review. Prior to testing, each patient had a list of Human Phenotype Ontology (HPO) terms created. Each patient's Human Phenotype Ontology (HPO) terms were then mapped to body systems and validated by an internal software ('Phenobert'). The body systems of interest included musculoskeletal, nervous, genitourinary, digestive, cardiovascular, head/neck/eye/ear, pulmonary, or other. Patients with anomalies in multiple body systems constituted the "More than One System" category. Patients with anomalies isolated to one body system constituted the "Isolated System" category. From positive genetic diagnoses, diagnostic variants were described by genotype characteristics: Single Nucleotide Variants (SNVs) or Copy Number Variants (CNVs). CNVs were organized as microduplications, microdeletions, or aneuploidies. SNVs were classified as intronic or exonic and further as substitutions, insertions, deletions, or indels, with biological roles analyzed via Panther. Length of stay (LOS) was the primary hospital outcome studied. Chi-squared, Fisher's exact, Mantel-Haenszel, and Wilcoxon tests were used to assess statistical differences in the genetic diagnosis rates and LOS among comparison groups.

**Results:** The majority of the cohort had anomalies in multiple systems compared to a single system (59% vs. 41%), with a higher genetic diagnosis rate in the "More Than One System" group compared to the "Isolated System" group (32% vs. 21.3%,  $p=0.04$ ). Of the cohort, 71.4% had anomalies in cardiac, 12.8% in digestive, 29.0% in genitourinary, 29.3% in head/neck/eye/ear, 20.9% in musculoskeletal, 13.8% in nervous, 10.8% in pulmonary, and 5.4% in other. Among the 82 diagnosed patients, 38 CNVs (60.5% microdeletions) and 47 SNVs (87.2% exonic, 63.8% substitutions) were identified. Panther analysis of 41 unique SNV genes showed the top three biological processes were cellular processes, biological regulation, and developmental processes (63.4%). In the "Isolated System" group, patients with a genetic diagnosis had a longer LOS (median 94 vs. 16 days,  $p = 0.005$ ). In the "More Than One System" group, the presence or absence of a genetic diagnosis did not affect LOS (median 30.5 vs. 35 days,  $p > 0.05$ ).

**Conclusions:** NICU patients present with a wide range of congenital anomalies across organ systems. While anomalies in multiple organ systems predicted a greater chance of a genetic diagnosis after GS, a significant number of patients with anomalies in one organ system received a genetic

diagnosis, highlighting the utility of GS in this population. Genes linked to congenital anomalies in a NICU cohort are often involved in ubiquitous cellular functions expressed across multiple organ systems and cause early symptomatic disease when carrying pathologic variants. While most patients had SNVs, a significant minority had CNVs, highlighting the superiority of GS to detect a variety of genetic mechanisms which result in congenital anomalies. Patients with congenital anomalies had LOSs extending beyond the neonatal period, with patients having an isolated system anomaly and a genetic diagnosis experiencing the longest.

### **The Efficacy of an FQHC's Homeless Initiative Program in Reducing Emergency Department Recidivism for Unhoused Populations**

**Thomas McEvilly**, Niki Messmore, HealthNet Bloomington

**Background/Objective:** A man presents with long-standing Wagner Grade 3 diabetic ulcers. He experiences chronic homelessness in a city he doesn't feel he belongs. His worsening memory impairs his ability to take his medication and manage these ulcers. When wounds don't heal, where do you go? What do you do? Emergency departments (ED) often serve as primary care points for people experiencing homelessness (PEH), a population incurring higher healthcare costs yet poorer health outcomes. PEH face many barriers to primary and preventive care, leading to frequent ED use. Street medicine (SM), which brings health care and social work directly to PEH, has shown potential in reducing hospital visits and improving health outcomes. This study evaluates the impact of HealthNet's Homeless Initiative Program (HIP) on ED recidivism rates and overall healthcare utilization among unhoused individuals in Bloomington, Indiana.

**Methods:** This retrospective cohort study ( $n = 84$ ) utilizes EMR data to track the frequency of ED visits within HIP's client population. Criteria for inclusion in the study required that the participant used medical services in Bloomington for at least one year prior to the introduction of HIP and has been a client of HIP for at least 180 days. Frequency of ED visits within a 24-month period before and after the implementation of HIP were adjusted for the COVID-19 pandemic and assessed.

**Results and Conclusion/Implications:** By comparing healthcare utilization before and after the implementation of HIP, this study seeks to provide evidence on SM's effectiveness in reducing ED recidivism and improving the wellbeing of PEH. Initial observation reveals a 4.4% reduction in ED visits in the post-HIP period, and adjusting for national ED trends during the COVID-19 pandemic amplifies this to a 13.7% decrease in monthly visits. These findings support the development of SM programs in order to improve healthcare services and decrease personal and

institutional expenditures.

### **Community Gardening: Strengthening a Rural Community-Academic Partnership**

**Tien-Lu Huang**, Katherine Pope, Temitope Erinosho

**Background:** High rates of childhood obesity, specifically in rural communities, are an urgent public health concern that need to be addressed. In recent years, community engagement in research and multi-level interventions have been shown to be effective at addressing a variety of public health concerns, including childhood obesity. However, these techniques have not been used in interventions for obesity prevention targeted at rural children aged 2- to 5-years old. The long-term goal of community and academic partners working in Greene County, Indiana, is to develop a rural, multi-level, obesity prevention intervention for children aged 2-5 years old.

**Methods:** To achieve this and to strengthen the partnership in the immediate term, the community and academic partners have been collaboratively working together to establish a community garden at the Bloomfield Public Library in Greene County to provide children and families with access to healthy foods and nutrition education. Community engagement activities have included scheduled meetings between the community and academic partners, as well as partner involvements in the cultivation, promotion, maintenance, harvesting, and distribution of the garden produce.

**Results:** Thus far, this partnership has led to the cultivation of seven garden beds (two raised and five elevated beds), two successful planting days with participation from community and academic partners representing at least 10 organizations, and three one-hour nutrition education sessions offered. Thus, there has been active partner engagement in this community garden initiative.

**Conclusions:** The current study will end in September 2024 and exit interviews will be conducted with partners to garner insight into the aspects of community engagement that did and did not work. Community and academic partners have begun conversations about expanding the garden, developing a multi-level intervention, and seeking external grant funds for the intervention.

### **Reminder Recall to Increase Vaccination Rates within Allen County**

**Tyra Grischke**, Sarah GiaQuinta

**Background:** No childhood vaccinations are required between 18 months and 4 years old, resulting in children falling behind after turning 4. Super Shot Fort Wayne, a nonprofit, works to make vaccinations accessible and af-

fordable. They have implemented reminder recall methods to increase vaccination rates, but there is uncertainty about the best practice. Previous studies show that repeat phone calls are the most effective method, followed by mailed flyers; however, there is little data on text messaging. This quality improvement project evaluated which reminder recall methods are effective in terms of outcomes, time, and cost.

**Methods:** We conducted a randomized controlled trial including 488 Super Shot's patients, aged 4-6, who were behind on at least one vaccine and have valid contact information. Participants were distributed into experimental groups based on available contact information. Interventions included: control, phone calls (two calls at different times), text messages (two messages in English and Spanish at different times) and mailed flyers (single flyer sent in English and Spanish). Outcomes were measured as a vaccination appointment being scheduled and the time-of-day calls were answered; both were analyzed using the Chi-Squared Test. Time and cost of Super Shot's staff were also compared.

**Results:** Chi-squared yielded a significant difference upon comparison of all experimental groups ( $p=0.048$ ). In total, 37 (37%) phone calls were answered with no significant difference between time frames ( $p=0.22$ ). Only speaking directly versus voicemail led to significantly more appointments scheduled ( $p<0.01$ ). The cost of required services was highest for text messaging, cost of staff and time spent were highest for phone calls.

**Conclusion:** Phone calls, regardless of time frame, were shown to be the most effective reminder recall method in terms of outcomes. Voicemails did not increase scheduling; therefore, it is not indicated that automated calling services would be impactful.

### **Comparative Risk of Stroke in Patients Undergoing Transcatheter Aortic Valve Replacement Versus Surgical Aortic Valve Replacement**

**Victoria Wichard**, Sydney Young

**Background:** The aortic valve is the most commonly replaced heart valve, traditionally through surgical aortic valve replacement (SAVR). However, transcatheter aortic valve replacement (TAVR) has become increasingly prevalent. This study evaluates ischemic stroke rates associated with SAVR and TAVR, providing critical insights for clinical decision-making and highlighting the impact on patient safety and long-term outcomes.

**Methods:** Data was sourced from the Indiana University School of Medicine RWEdataLab (CRC/Sidus Insights) Cardiology dataset, containing de-identified records from 3.36 million patients with cardiology-related diagnoses

across the United States. Two cohorts were identified: patients who underwent a TAVR procedure and those who underwent a SAVR procedure. Odds ratios assessed ischemic stroke likelihood in TAVR versus SAVR patients, stratified by age groups: 50-59, 60-69, 70-79, and 80+ years of age.

**Results:** Patients undergoing TAVR demonstrated a significantly higher risk of ischemic stroke (OR: 3.45; CI [2.86-4.16]) compared to those undergoing SAVR (OR: 1.76; CI [1.29-2.39]). When stratified by age, patients 80 years and older who underwent TAVR also faced a notably elevated stroke risk (OR: 2.79; CI [2.26-3.43]) compared to patients in the same age cohort undergoing SAVR (OR: 1.23; CI [0.82-1.82]).

**Conclusion:** TAVR is associated with a significantly higher risk of ischemic stroke across all age groups, indicating that SAVR may be a more suitable option for patients with comorbidities that heighten stroke risk. When determining the optimal procedure, clinicians must carefully consider factors such as the patient's age, overall health, and the invasiveness of the procedure.

### **Subdural Hematoma Risk in Patients on Antiplatelet and Anticoagulant Therapy: An Analysis Using Real-World Evidence**

**Whitney Brown**, Meagan McNicholas, Micheal Roscoe, Eric Goebel

**Background/Objective:** Antiplatelet and anticoagulation therapy is widely used for treatment and prevention of various medical conditions. However, there remains on-going debate regarding the safest medication, particularly considering the increased risk of intracranial hematomas. Our study aims to use real-world evidence to analyze the odds of developing a subdural hematoma among patients prescribed antiplatelet or anticoagulant therapy, compared to the general population.

**Methods:** Data was gathered from a national electronic health records database containing de-identified electronic medical records from nearly 5 million patients in the United States receiving psychiatric, mental health, and counseling care. Patients were isolated by diagnosis history using International Classification of Disease, 10th revision (ICD-10) codes. Contingency tables were created to compare the incidence of subdural hematomas (ICD-10: S06.5-S06.599, I62.01) between patients prescribed antiplatelets or anticoagulant and those who were not. Antiplatelet medications analyzed include aspirin and clopidogrel, while anticoagulant medications examined were warfarin, low molecular weight heparin (LMWH), rivaroxaban, and apixaban. Odds ratios and confidence intervals (CI) were calculated to assess the relationship between subdural hematoma diagnosis and each drug.

**Results:** All calculated odds ratios were statistically significant. Patients on antiplatelet therapy had an increased odds of developing a subdural hematoma, with odds ratios of 1.76 for aspirin (95% CI: 1.68-1.83) and 2.25 for clopidogrel (95% CI: 2.10-2.41). Among anticoagulants, the odds ratios were 2.92 for warfarin (95% CI: 2.67-3.19), 5.34 for LMWH (95% CI: 4.21-6.27), 1.96 for rivaroxaban (95% CI: 1.74-2.20), and 2.57 for apixaban (95% CI: 2.37-2.79).

**Conclusion/Implications:** Antiplatelet agents should be prescribed cautiously in patients with an increased risk for subdural hematomas (fall risk, occupation, etc.). When anticoagulation is required, clinicians should consider transitioning from warfarin and LMWH to rivaroxaban, with a preference over apixaban, for long-term management. Additionally, alternative forms of venous thromboembolism prophylaxis should be considered for patients at elevated risk of cranial bleeding.

### **Pediatric Histoplasmosis in the Midwest: A Retrospective Chart Review**

**Wynne Milhouse**, Alex Smith, Christian Huntington, Aneesha Kamath, Jackson Schneider, John Christenson, L. Joseph Wheat, Lindsey Kirkpatrick

**Background:** *Histoplasma capsulatum* is the most prevalent endemic mycosis in North America, particularly in the Ohio and Mississippi River Valleys. Disease severity ranges from asymptomatic to life-threatening, with up to 90% of residents in endemic areas exposed to *H. capsulatum*. While Histoplasmosis in adults is well-studied, pediatric data are limited. This study aims to elucidate the disease course, health outcomes, diagnosis, and epidemiology of Histoplasmosis in children through a retrospective chart review, intending to enhance diagnosis and recognition in this population. Future research will investigate whether the enzyme immunoassay antibody test is more sensitive than other modalities for pediatric diagnosis.

**Methods:** We retrospectively reviewed charts of pediatric patients ( $\leq 18$  years old) diagnosed with Histoplasmosis at IU Health-affiliated centers between 2010 and 2021 ( $n=100$ ). Data on *Histoplasma* testing (antibody, antigen, histopathology, cytology), epidemiology, clinical manifestations, outcomes, treatment course, and immune status were collected. Chi-squared tests were used to determine relationships between categorical variables in our preliminary analysis. In the future, we will ascertain the sensitivity for each testing modality and conduct more comprehensive analyses of the clinical data.

**Results:** Preliminary findings illustrate the demographics and clinical manifestations of pediatric Histoplasmosis, identifying cough, fever, and headache as the most common symptoms, with mediastinal and hilar lymphadenopathy

being the predominant lymphatic manifestations. The liver and spleen were the primary sites of extrapulmonary dissemination. Chi-squared analysis confirmed our sample's representativeness of the Indiana population in terms of race, ethnicity, and residence. Interestingly, a relationship between gender and disease severity/classification emerged, necessitating further investigation.

**Potential Impact:** Our understanding of adult Histoplasmosis is extensive, but limited data in the pediatric population has led to a lack of pediatric-specific protocols. This study, comprising the largest cohort of pediatric histoplasmosis cases in the US, aims to expand our knowledge to improve early recognition and diagnosis of pediatric Histoplasmosis.

### **Evaluating the Role of Pretherapy Scans in Post-Thyroidectomy Thyroid Cancer Management: Predictive Value, Management Impact, and Efficacy**

**Yousif Mukatash**, Mark Tann

**Background:** Thyroid cancer management typically involves radioiodine ablation (RAI) therapy post-thyroidectomy to eliminate residual thyroid tissue and cancerous cells. Pretherapy imaging and dose selection are contentious subjects. This study evaluates the comparative effectiveness of different imaging modalities and doses.

**Methods:** This retrospective IRB-approved study included ninety-eight thyroid cancer cases of patients who underwent ablation therapy from January 2022 onwards. Data was collected through the electronic health record system. Imaging studies were evaluated by two separate readers. Thirty-nine cases were excluded for imaging congruency due to the absence of SPECT/CT. Cure rate analysis excluded fifteen cases due to missing post-ablation Tg levels. The data was stratified into N1b (metastasis to cervical lymph nodes) and non-N1b cancer.

**Results:** Results indicate that pretherapy planar and SPECT/CT imaging findings were congruent in the non-detection of extrathyroidal disease. Both I-123 and I-131 isotopes demonstrated high congruence with post-planar scans, with I-123 showing 85.48% congruency and I-131 showing 82.86% congruency. Cure rates varied only minimally by RAI dosage with the highest cure rates observed in the 33-56 mCi range (92.31%) and the lowest in the 110+ mCi range (81.82%). In N1b cases, the highest cure rate was 100% in the 33-56 mCi range, while non-N1b cases showed the highest cure rate of 94.12% in the 56-110 mCi range.

**Conclusions:** No advantage was found using SPECT/CT or I-123 for detecting extra-thyroidal diseases. Higher treatment doses beyond 110 mCi do not yield better outcomes.

The study's findings underscore important considerations regarding cost-effectiveness of imaging and appropriate dose selection in thyroid cancer ablation management.