## Optimizing Outcomes for a Pregnant Patient with Congenital Heart Disease

Eckert NL, Jones TK, Okoruwa OP, Rouse CE

Case Description: A 24 yo F with complex congenital heart disease (CHD), modified WHO (mWHO) class III, presented for prenatal care in the first trimester. Her history was complicated by hypoplastic right heart syndrome with pulmonary atresia for which she had undergone multiple surgical procedures in childhood, including ultimately extracardiac lateral tunnel Fontan. Additional comorbidities included epilepsy, mild cerebral palsy, scoliosis, irritable bowel syndrome, asthma, and anxiety. Her pregnancy was managed by a multidisciplinary team, including Maternal-Fetal Medicine, Adult CHD Cardiology, Neurology, Obstetric Anesthesia, and Social Work. A cesarean delivery was performed at 32+4 weeks for fetal growth restriction with non-reassuring fetal testing without complications. Her postpartum course was complicated by pericarditis which was managed medically. The infant stayed in the NICU due to prematurity but was otherwise healthy.

**Conclusion:** A multidisciplinary team approach to the care of pregnant patients with complex CHD supports development of comprehensive, patient-specific assessments and plans for each stage of pregnancy, thereby minimizing risks of negative outcomes. Having extensive knowledge of high-risk care and applying the mWHO risk assessment helped the team ensure that the patient received appropriate counseling, monitoring, and management for a healthy pregnancy with minimal complications.

**Clinical Significance:** Prior to the utilization of high-risk multidisciplinary care teams, many women with congenital heart defects were discouraged from attempting pregnancy following the Fontan procedure. As the population of women who have undergone the Fontan procedure grows, it is critical to implement a multidisciplinary approach to care with intent to empower women with congenital heart defects to achieve successful pregnancies while minimizing pregnancy-related mortality and morbidity.

## Approach to Treatment of Cervical Pregnancy: A Case Report

Campbell M, Chaudhary A, Pandhiri T, Tominack H, Rouse CE

Case Description: A 25 yo G1 at 11wk4d dated by last menstrual period and confirmed with a 10-week ultrasound presented with a possible cervical ectopic pregnancy. Past medical, surgical, and OBGYN histories were unremarkable. A cervical pregnancy was suspected on ultrasound due to low implantation of the gestational sac, and a significant posterior bulge with an hourglass shaped uterus. MRI suggested implantation of the placenta in the posterior uterine and cervical walls due to extreme thinning of these structures. Our institution had previously created a protocol for multidisciplinary management of cesarean scar and cervical pregnancies. The patient desired fertility preservation, and so consented to combined local and systemic treatment with methotrexate (MTX). Preprocedural Beta-

hCG was 81,514.8 mU/mL. Ultrasound-guided transvaginal intragestational sacinjection of MTX was performed without complication, though cardiac activity was still present at the conclusion of the procedure. The patient also received an intramuscular injection of MTX before discharge. Serial Beta-hCGs are still being followed and are trending towards 0.

**Conclusion:** The optimal management for cervical pregnancies is not known, and decisions around type of management are informed by the patient's desire for fertility preservation. In this case, a protocol created by a multidisciplinary team was used to guide treatment. This protocol using MTX successfully treated a cervical pregnancy at 11wk4d and avoided a surgery that could complicate future fertility.

**Clinical significance:** Due to the rare occurrence of cervical pregnancy, there is not a universally accepted treatment protocol. This case shows that medical management can be successful for cervical pregnancies. Clear guidelines must be established for cervical pregnancies to optimize outcomes, decrease maternal morbidity and mortality, and preserve future fertility.

### Assaults in Schools: Findings Using a National Database

Loder RT, Farooq H, Gianaris JB

**Background:** Assaults can occur at schools/educational facilities involving students, teachers, and other school employees. The purpose of this study was to correlate injury patterns with patient demographics in school assault victims. Understanding injury patterns with their associated demographics will not only be useful for healthcare providers but can also assist in proposing prevention strategies for both students and school employees.

**Methods:** Emergency department (ED) data from the National Electronic Injury Surveillance System All Injury Pro-gram for years 2005-2015 were used in this study. Statistical analyses were performed with SUDAAN software to account for the weighted, stratified nature of the data.

**Results:** There were an estimated 852,822 ED visits for school assaults. The median age was 13.8 years, with 81.3% of participants between 5-19 years old. 64.4% of participants were male. After age 4, the number of females proportionately increased with increasing age. The most common diagnosis was a contusion/abrasion (38.6%). The injuries occurred in the head/neck (63.9%), upper extremity (19.0%), upper trunk (6.6%), lower trunk (5.5%), and lower extremity (4.9%). Firearm violence accounted for 0.1% of the assaults. Human bites occurred in 3.7%. Sexual assault was rare and proportionally the highest in those  $\leq$ 4 years of age. Internal organ injuries were more common in females (13.1% vs 3.55%) and for those admitted to the hospital (29.9% vs 19.9%). The incidence of ED visits for school assault decreased 50% from 2005 to 2015.

**Conclusions:** This study analyzed ED visits due to assaults occurring in schools. Firearm violence accounted for only 0.1% of the injuries,

in contrast to media coverage regarding school assaults. The most common injury location was the head/neck, and the most common diagnosis was a contusion/abrasion. This data can also serve as a baseline for further studies and the impact of potential reduction strategies.

## Utilization of Free Clinics by Underinsured and Uninsured Populations and their Impact on Community Health

Wickstrom M, Gong S, Burrow Z, Stoll K

**Case:** A 50-year-old female presented with suspected "thyroid issues," which consisted of lower extremity edema, insomnia, alopecia, dry skin, cold intolerance, extreme fatigue, and anxiety/ depression. Review of systems was significant for pallor of skin and conjunctiva, thymus of normal size without nodules, alopecia, and bilateral lower extremity edema. Family history was significant for hypothyroidism. The patient was furloughed by her employer during the COVID-19 pandemic.

**Conclusion:** This patient was underinsured and furloughed by her employer, leaving her with no source of income and limited access to healthcare. Fortunately, with access to a free clinic, she was able to obtain lab work at zero cost to her, which revealed extremely low hemoglobin and hematocrit levels. She was advised to go to the emergency department the day that results were obtained, where she was diagnosed with a GI bleed, given iron supplementation, and 3 units of blood.

Clinical Significance: A survey conducted by the US Department of Health and Human Services estimated that 30 million Americans lived uninsured in the first half of 2020, leaving many Americans living without primary health care services due to fear of out-of-pocket expenses. Individuals lacking insurance are more likely to identify as African American or Latino, be young adults, have lower incomes, and live in states that have not implemented Medicaid expansion. Free clinics provide a number of basic medical services which can be of significant benefit to patients who are unable to regularly access healthcare. This case demonstrates a scenario in which a patient's life was likely saved due to her access to a free clinic and the services therein. As is evident, free clinics are an integral part of closing the uninsurance gap and ensuring quality healthcare access to those who require it regardless of ability to pay.

#### A Plan for Progress: Indiana Women's Health Center of Excellence Five-Year Plan

Clodfelter K, Emerick S, Farris K, Stoll K, Peipert J

**Background:** Strategic plans are useful for setting ambitious goals as they allow the organization of timelines, encourage interdepartmental collaboration, and create a basis for funding to reach goals. Indiana University Health and the Indiana University School of Medicine have developed a strategic five-year plan to enhance the Center of Excellence in Women's Health (WH-CoE). The vision for WH-CoE and the goal of the strategic plan is that the center will be a leader in women's health and a premier destination for the prevention, treatment, and cure of women's health disorders. Attention to Indiana women's health is necessary as certain health outcomes in the state fall low on national rankings. Indiana has an infant mortality rate 20% higher than the national average, ranks 28th for infants born preterm, and has the third highest maternal mortality rate in the United States.

**Intervention:** The five-year strategic plan aims to position WH-CoE as a recognized leader and primary destination for women's health disorders. This task will be accomplished through the completion of yearly goals established by the foundation in areas of clinical care, research, and education, which were identified by a committee of leaders from various women's health disciplines. The plan is broken down into six centers of focus: chronic pain, cardiovascular disease, breast health, endocrine/polycystic ovarian syndrome (PCOS), oncofertility, and substance use disorders.

**Results:** The timeline was developed to give priority to initiatives which were multidisciplinary and the most feasible for the given timeframe. Research efforts are built into the five-year plan to evaluate the plan's efficacy and impact on women's health.

**Conclusion:** As healthcare providers in Indiana, we have a duty to our patients to improve our women's healthcare. Our hopes are that the successes and failures of this plan may be built upon by other programs to improve women's healthcare across the nation.

#### Use of Nasal Septal Grafts in Substitution Urethroplasties: An Early Series

**Arnold PJ,** Soyster ME, Burns RT, Mantravadi AV, McDonald CJ, Mellon MJ

**Overview:** Substitution urethroplasty remains one of the most effective treatments of urethral strictures, especially in cases of elongated stricture length. While oral mucosa is the gold standard graft for repairs, buccal mucosa grafts (BMG) are associated with significant post-operative morbidity. This series is the first to review the use of nasal septal cartilage for augmentation urethroplasty.

**Methods:** All patients undergoing nasal septal graft substitution urethroplasty from December 2020 to February 2022 were identified. Institutional Review Board exempt status was granted for the conduct of this study. Septal graft harvesting was performed by two otolaryngologists, and urethroplasty was performed by a single surgeon at a tertiary care referral center. The novel nature of the technique was explained to all patients who expressed understanding and willingness to proceed. Descriptive analyses were performed, and postoperative retrograde urethrograms (RUG) were analyzed.

**Results:** Four patients were identified with an average follow-up time of 12 months. The average stricture length was 2.6 cm. Three patients had bulbar urethral strictures; one patient had a perineal urethrostomy stricture. The largest nasal perichondral harvest was 3x5 cm. At 4 weeks, two patients had no leak on RUG with successful catheter removal. One patient had a minor contained leak and catheter was removed at 6 weeks without imaging. One patient had a leak at their 4- and 6-week RUG, with no leak and catheter removal at week 10. Notably, this patient had a prior BMG urethroplasty. Patients reported associated pain ("2-4/10"), difficulty breathing, and epistaxis as side effects.

**Conclusions:** Further study of this technique and longer follow-up are required to determine long-term efficacy. Still, this initial data suggests that nasal septal substitution urethroplasty may be a viable surgical approach to treating urethral strictures, especially for patients wishing to avoid morbidity associated with BMG urethroplasty or those unable to undergo BMG harvesting.

## A Case of Plaque-Like CD34+ Dermal Fibroma Masquerading as Granuloma Annulare

Skorobogatko V, Spaulding R, Alomari A, Umphress B

**Background:** Plaque-like CD34+ dermal fibroma, also known as "medallion-like dermal dendrocyte hamartoma (MLDDH)," is a rare cutaneous lesion found predominantly in females. It often presents as a solitary, erythematous, and circumscribed atrophic plaque. Histologically, lesions demonstrate a bandlike proliferation of bland fibroblast-like cells within the upper dermis. CD34 is positive with variable expression of FXIIIa. Here, we report the case of a patient who presented with a long-standing and asymptomatic erythematous,

firm annular plaque without scaling. The plaque was located on the lower extremity and clinically resembled granuloma annulare. Biopsies revealed dermal spindle cell proliferation with interspersed collagen and CD34 reactivity. Given the findings, a diagnosis of plaque-like CD34+ dermal fibroma was favored with differential diagnostic considerations including fibroblastic connective tissue nevus and dermatomyofibroma.

**Conclusion:** Our aim is to increase awareness of this rare diagnostic entity, highlight distinguishing features from its histologic mimickers, and further illuminate one of the possible clinical presentations.

## Analysis of Neutral Lipid Accumulation in Hepatic Lineage Cells to Study NAFLD/NASH

**Bolujo I,** Park Y, Isidan K, Lopez K, Cross-Najafi A, Li P, Zhang W, Ekser B

**Background:** Nonalcoholic fatty liver disease (NAFLD) is the leading cause of liver disease in the United States and is often associated with obesity and type 2 diabetes. NAFLD may progress to Nonalcoholic Steatohepatitis (NASH), which is characterized as lobular inflammation and apoptosis leading to fibrosis, cirrhosis, and/or hepatocellular carcinoma (HCC). Although it is well established that lipid deposition in hepatocytes plays a critical role in the pathogenesis of NAFLD/NASH, the effects of accumulation of neutral lipids in other liver cell types, including liver endothelial cells and cholangiocytes, are poorly understood.

**Methods:** Primary human hepatocytes, cholangiocytes, and liver endothelial cells were seeded on a collagen-coated plate prior to being incubated with vehicle alone (control, 1% BSA) or different concentrations of free fatty acids (FFA - oleic acid and palmitic acid 2:1; 160 M, 320 M, 500M and 1mM) for 24 hours. After treatment, the cells were subjected to BODIPY493/503 staining to determine lipid droplet accumulation within the cells. Hoechst was used to stain the cell nuclei. Images were captured with a Leica fluorescence microscope and imaging system. Fluorescence intensity was measured with Image J software.

**Results:** Following treatment, especially with higher FFA concentrations, lipid accumulation (BODIPY493/503, green fluorescence) was augmented in all three cell types (Figure 1). In addition, treating the cells with 1 mM FFA led to reduced Hoechstlabeled cell nuclei and increased cell detachment in all three cell types, which indicated high levels of lipid-mediated cell toxicity.

**Conclusions:** We developed an in vitro model to examine lipid accumulation in different liver cell types, which could be used to determine the adaptive responses within different hepatic lineage cells in NAFLD/NASH progression.

#### Patients Don't Read Textbooks: The Impact of Medical and Social Biases on the Diagnosis of Cushing's Syndrome

Patel S, Young A, Cooper S, Love E, Saeed Z

**Background:** We present the case of a 66-year-old African American female with severe Cushing's syndrome (CS) who remained undiagnosed for several years. The patient had a history of an unsuccessful Roux-en-Y gastric bypass nine years ago. The patient also had type 2 diabetes, hypertension, unexplained hypokalemia, and a past history of unprovoked PE and DVT. She presented with acute onset headache. MRI of the brain revealed a 1.4x1.7 cm macroadenoma. On exam, the patient did not have the classic Cushingoid appearance. In particular, she did not have "moon facies," facial plethora, supraclavicular fullness, or any evidence of a dorsocervical fat pad ("buffalo hump"). Work-up was consistent with severe ACTH-dependent CS with random serum cortisol of 58.6 mCg/dL, ACTH of 300 pg/mL (reference range 7.5-63 pg/mL), 24hour urine free cortisol of 1,608 mCg (normal: <45 mCg), and 1 mg dexamethasone suppression test with no reduction in cortisol. The diagnosis was delayed for ten years, but the patient was later found to have a pituitary tumor causing excessive ACTH secretion which caused her symptoms.

**Conclusions:** Awareness of medical and social biases is crucial when evaluating a patient. CS is a treatable condition and delays in diagnosis correlate with increased morbidity and mortality (Neiman et al). This case demonstrates the importance of recognizing disease presentation beyond textbook characterization and recognizing potential biases held by providers. CS is caused by excessive production or exposure to glucocorticoids (Sharma et al). This disorder commonly presents with weight gain, "moon facies," and dorsal fat pads, although the presentation can be variable. Though patient sex, age, and disease etiology have not been found to influence diagnosis timing, the impact of race and bias has not yet been described (Rubinstein et al). Medical training may overemphasize "buzzwords" and textbook presentations causing physicians to misattribute a patient's symptoms to another pathology.

#### Establishment and Characterization of Patient-Derived Xenograft from Leptomeningeal Spread of Rare Pediatric Anaplastic Pleomorphic Xanthoastrocytoma (PXA) Bearing CDC42SE2-BRAF Fusion

**Damayanti NP**, Saadatzadeh RM, Dobrota E, Ordaz JD, Bailey B, Pandya P, Alfonso A\*, Keir S, Zhang ZY, Balsara KE, Pollok KE

**Background:** Pleomorphic xanthoastrocytoma (PXA) is a rare subset of primary pediatric glioma with 70% 5-year disease-free survival. Up to 20% of cases can recur and/or undergo malignant transformation into a more aggressive type, anaplastic PXA (AXPA). The understanding of disease etiology and the mechanisms that drive PXA and APXA are limited. Therefore, there is a need to develop preclinical models to investigate molecular underpinning and guide therapeutic approaches.

**Methods:** We established and characterized a patient-derived xenograft (PDX) from a leptomeningeal spread of a patient with recurrent APXA bearing novel type of CDC42SE2-BRAF fusion. Characterization was done to assess the model fidelity in genomic, transcriptomic, and proteomic landscape.

Results: Histological features were conserved between the PDX and matched human tumors throughout serial passages. Whole exome sequencing (WES) demonstrated a high degree of conservation in small variants (Pearson's r=0.794-0.839), tumor mutational burden, and mutations in MAPK family genes between PDX and patient tumor. Chromosomal gain in chromosomes 4-9, 17, and 18 and loss in chromosome 9p associated with homozygous 9p21.3 deletion involving CDKN2A/B locus, were identified in both patient tumor and PDX sample. Chromosomal rearrangement involving 7q34 fusion; CDC42SE-BRAF t (5;7) (q31.1, q34) (5:130,721,239, 7:140,482,820) was identified in PDX tumor, xenoline, and matched human tumor. Transcriptomic profile of the original patient tumor was retained in PDX (Pearson r=0.88) and in xenoline (Pearson r= 0.63), as well as preservation of enriched signaling pathways (FDR Adjusted P<0.05). Both xenoline (IC50= 200nM) and PDXs did not respond to MEK inhibitor recapitulating patient insensitivity to similar treatments in the clinic. Multi-omics data integration was used to deduce potential actionable pathways (FDR<0.05) including; KEGG01521, KEGG05202, and KEGG05200.

**Conclusion:** This set of PDX and stable xenolines will serve as a preclinical resource for developing novel therapeutics for rare APXA and other pediatric high-grade gliomas bearing the BRAF fusion.

## Translocation RCC: Progression-Free and Overall Survival by Tumor Stage and Surgical Procedure at a High-Volume Academic Center

Drake CJ, Farrow JM, Bahler CD, Sundaram CP

**Background**: Translocation Renal Cell Carcinoma (RCC) is a rare variant and is estimated to represent 2-5% of RCC diagnoses. Prior studies characterizing the clinical behavior of translocation RCC are limited and stage-by-stage prognostication for adult patients remains uncertain.

**Methods:** Patients diagnosed with localized translocation RCC that underwent either partial or radical nephrectomy between 2004 and 2021 were reviewed. Standard clinico-pathologic characteristics were included. Progression-free and overall survival were estimated using Kaplan-Meier curves. Non-parametric tests in SAS were used, with statistical significance set at 0.05.

**Results**: A total of 59 patients were identified. Age at surgery and body mass index were balanced across pathological stage. Tumor complexity increased with stage, as did adverse pathological features (Fuhrman Grade 3-4, lymphovascular invasion, and margin positivity). Both progression-free and overall survival were worse with higher stage disease. Of note, low-stage disease had favorable long-term survival, approaching 90%; there was no difference in overall survival between partial or radical nephrectomy for low-stage disease.

**Conclusion:** Translocation tumors predictably demonstrate worse pathological features with stage progression. Interestingly, those patients with low-stage disease had durable treatment responses with either partial or radical nephrectomy, suggesting minimally invasive approaches may be preferred to limit perioperative morbidity without sacrificing oncologic outcomes.

# Participatory Design and Development of a Mobile App to Improve Kangaroo Mother Care in Kenya Using the People at the Center Of Mobile Application Development (PACMAD) Framework Young A, Dolan M, Esamai F, Purkayastha S, Bucher S

Background: Prematurity is the leading cause of death worldwide for children under five. 15 million babies are born prematurely each year, and 2.4 million children die during their first month of life. Neonatal hypothermia is a contributing factor, particularly in low-and-middle income countries (LMICs), where incubators may be less available or overcrowded. To address the global burden of neonatal hypothermia among premature infants, the Neolnnovate Collaborative Consortium has developed a suite of innovations to provide automated thermal support and facilitate the uptake of and compliance to Kangaroo Mother Care/Skin-to-skin care (KMC/STS). This integrated intervention features a wearable baby warmer ("NeoWarm") and a suite of smart-phone applications to increase access to KMC/STS, as well as provide vital sign updates to healthcare workers. We describe on-going multidisciplinary efforts to

utilize human-centered participatory design techniques to develop a feasible and acceptable mobile phone app ("NeoRoo") for parents and healthcare providers of premature infants in LMICs.

**Methods:** Participatory design is a human-centered design technique that involves stakeholders in the design process itself, with the goal of creating a solution that better addresses users' needs and context. For this study, 10 healthcare workers and 10 parents of premature infants from 3 hospitals in Western Kenya will be asked to navigate through the app as they "think aloud" about its features and function. Next, a facilitator will conduct semi-structured interviews while instructing participants to complete tasks. Their responses will be further analyzed using the People at the Center of Mobile Application Development (PACMAD) model.

**Conclusion:** Integration of direct stakeholder feedback into subsequent iterations of the application is anticipated to increase the functionality and usability of NeoRoo for targeted users. Results will be utilized to further iterate the existing NeoRoo prototypes, and then perform an A/B evaluation.

## Candida Rugosa: An Atypical Cause of Vulvovaginal Candidiasis

Crawford JD, Weber L, Wickstrom MJ, Burrow ZM, Neal CM

**Case Description:** A 20-year-old female presented with recurrent bacterial vaginosis and incomplete resolution of symptoms after treatment. She reported multiple episodes of green vaginal discharge with odor and vaginal pruritus. Her symptoms began two years prior and never completely resolved after treatments with metronidazole. History and physical exam were noncontributory. Vaginal microscopy was normal. Culture and staining showed 1+ Candida albicans and 1+ Candida rugosa.

**Conclusion:** Because C. rugosa is an atypical pathogen for candidiasis, the treatment plan had to be altered, and the patient was placed on boric acid vaginal suppositories once daily for 14 days. As diagnoses and treatments for typical pathogens are well established, atypical pathogens are a growing problem, due in part to reduced susceptibility to normal treatments for candidiasis.

Clinical Significance: C. rugosa was first isolated in 1917. It is a poorly studied fungus and not typically implicated in vulvovaginal candidiasis (WC), which is a challenging long term condition characterized by inflammation secondary to fungal colonization. Current challenges to treatment include social barriers to care, azole resistance, and emergence of new fungal species. Identification and research of emerging fungal strains are critical contributions to the literature since these strains are not well studied, continue to arise in practice, and are problematic for diagnosis and treatment. There are few reports in recent literature of patients diagnosed with C. rugosa WC. However, there are numerous recent studies of C. rugosa using lipase as a means of the fungus' drug resistance, making this an important topic for further research. There have also been a growing number of fungi with similar characteristics identified in recent case

reports. Their susceptibility to antifungals is particularly important as it seems to be an emerging cause of both localized and disseminated fungal infections worldwide.

#### Multilevel Factors Underlying Adolescent Retention and Disengagement in HIV Care Across Global Settings: A Mixed-Methods Systematic Reviewl

**Risk N,** Toromo J, Bosma C, Misquith C, Apondi E, Wools-Kaloustian K, Vreeman RC, Enane LA

**Background:** Adolescents living with HIV (ALHIV, aged 10-19) are at risk for disengagement from care, resulting in poor health outcomes and potential for viral transmission. We investigated multilevel barriers and facilitators to retention in HIV care for ALHIV across global settings to inform strategies to better retain this group.

**Methods:** We conducted a systematic review of publications between 1994-2022 that reported factors associated with retention or disengagement from HIV care for ALHIV. Our search included terms for concepts of antiretroviral therapy (ART), treatment adherence, and barriers to care. Quantitative and qualitative barriers and facilitators to retention at multiple levels were synthesized using a convergent integrated approach, assessing themes, promising interventions, and needs for research or implementation.

Results: 8,564 records were screened, 333 full-text articles assessed, and 98 included. Studies were conducted in Africa (n=53), the Americas (n=36), Asia (n=5), Europe (n=2), and multiple regions (n=2). Barriers to retention included: older adolescence; female sex; pregnancy; racial, ethnic, sexual, or gender minority status; orphan status; no initiation of ART; advanced immunosuppression; mental health factors; lack of social support; financial challenges; unstable living conditions; nondisclosure of HIV status to the adolescent or household; negative experiences with providers; rural clinic site; school-related factors; and pervasive HIV stigma. Facilitators to retention included: adolescent disclosure; having a family member with HIV; supportive relationships with family or providers; adolescent-friendly services including peer support, dedicated clinic hours, and case management; appointment reminders and follow-up after missed appointments; and financial or social support interventions.

**Conclusion:** Improving adolescent retention requires addressing multilevel factors associated with disengagement, which reflect multiple axes of social, financial, and medical vulnerability. Beyond provision and scale-up of comprehensive adolescent-friendly services, peer, social, or financial support interventions may be promising to mitigate various challenges across settings. Rigorous intervention studies are needed as well as strategies for implementation and scale-up.

#### Food Banks and Food Insecurity: A Measure of Hope and Resiliency Haas AN, Mulcahey CT

**Background:** Food bank utilization has increased in America due to the COVID-19 pandemic and is closely associated with food insecurity. The very state of being food insecure may affect one's outlook for a better future, their hope, or their ease in overcoming obstacles. To investigate these themes, two food banks in South Bend, IN were surveyed using validated stigma, hope, resiliency, and food insecurity scales. Additionally, special attention was given to the COVID-19 pandemic effects on relationships, given the resource shortage and collective emotional trauma experienced disproportionally by those of lower socioeconomic status.

**Methods:** This quantitative study was conducted between June-August 2021 in South Bend, IN at the Clay Church Food Pantry and the Food Bank of Northern Indiana. This study included 433 individuals and investigated hope and resiliency between stratified levels of self-reported food insecurity, as well as COVID-19 effects on relationships and quality of life.

**Results:** Of the total respondents, 33.8% reported being severely food insecure, 26.3% moderately, 23.4% somewhat, and 16.4% had no food insecurity. Hope was measured on the Trait Hope Scale, with a mean hope score of 43.7 (SD=12.9), in the hopeful range. There was no statistically significant difference in hope scores when comparing severity of food insecurity. Post COVID-19 effects on relationships show that family and friend relationships were worse in only 22.1% and 27.6% of respondents, respectively. Quality of life measures, physical health, mental health, and financial situation were worse in 23.5%, 24.2%, and 43.1% of respondents, respectively.

**Conclusion:** Most local food bank clients are severely food insecure. In addition, these clients rate overall in the "hopeful category." Although food insecurity remains a concern, food bank clients largely did not report negative COVID-19 effects on quality of relationships, physical health, mental health, or financial resources.

#### Surgeon Values vs Clinical Practice: Do We Assess the Right Clinical Factors when Deciding to Initiate Enteral Nutrition in Surgical Neonates?

**Anderson C,** Bhatia M, Fisher S, Joplin TS, Hunter-Squires J, Saula P, Gray B

**Background:** Enhanced Recovery After Surgery (ERAS) guidelines recommend enteral nutrition (EN) initiation within 48 hours following neonatal surgical procedures; however, this practice has not been widely adopted by pediatric surgeons. We aimed to understand if surgeon-ranked patient factors were similar to observed clinical factors when initiating EN in surgical neonates.

**Methods**: Following institutional review board approval, neonates (admitted at <30 days) treated at a quaternary referral center in July 2021 (n=10) were enrolled in an observational study. Clinical factors and nutrition status were recorded electronically for 30 days or until discharge. Results were analyzed using SPSS 27 and SAS 9.4, with p<0.05 indicating significance. Concurrently, pediatric surgeons and fellows from this and a neighboring institution (n=10, response rate 67%) completed an online survey to assess their feeding practices in surgical neonates.

**Results:** Patient diagnoses included congenital diaphragmatic hernia (n=2), gastroschisis (n=4), spontaneous intestinal perforation (n=3), and umbilical cord hernia (n=1). The average time until EN initiation was 11.2  $\pm$  14.0 days. Only two neonates received EN within 48 hours of their operation. Univariate analysis demonstrated that top clinical factors predictive of EN administration were passage of stool (OR 12.99 [5.95-27.78], p<0.001) and hemodynamic stability (OR 8.62 [2.07-35.71], p=0.003). On average, surgeons (n=8) ranked hemodynamic stability and gastric tube output volume as the top two essential factors, respectively. When multiple clinical factors were combined in stepwise multivariate regression, stool within the past 24 hours (OR 27.02 [8-125], p=0.022), lower gastric tube output volume (OR 0.85 [0.79-0.90], p=0.032), and higher postoperative day (OR 1.09 [1.04-1.15], p=0.001) were significantly associated with EN.

**Conclusion:** Surgeon ranking of patient factors for initiation of EN did not exactly match clinical observations, emphasizing the subjectivity of the decision. Goal-based nutrition protocols may reduce variability and ambiguity when advancing neonatal nutrition.

#### Intramedullary Nailing Achieves Comparable Reductions to Plate Fixation in Complete Intraarticular Distal Femur Fractures

Poirier JL, Lopas L

**Background:** Intraarticular distal femur fractures (AO/OTA type 33C) are an uncommon and challenging injury to treat. Achieving adequate reduction while minimizing soft tissue injury requires balancing potentially competing interests. Traditionally, 33C type injuries have been treated with various plating constructs due to the belief that adequate reductions could not be obtained or maintained

with alternative methods. Intramedullary nailing (IMN) is potentially more biologically favorable and is preferred to plate fixation in a variety of different orthopedic injuries. The purpose of this study is to evaluate the quality of the reduction obtained for 33C type injuries when treated primarily with a plate vs IMN.

**Methods:** This retrospective study identified patients 17 years of age who sustained a 33C type fracture from 2013-2020. Patients with incomplete radiographic follow-up were excluded from the study. 42 patients who underwent plating and 142 patients who underwent IMN met criteria. Patient demographics and radiographic data including posterior distal femoral angle (PDFA) and lateral distal femoral angle (LDFA) were collected. T-Tests and descriptive statistics were performed to assess difference; significance was set at p=0.05.

**Results:** Mean PDFA at most recent radiographic follow-up was not different between plating and IMN (82.8 vs 83.1, p=0.706). Mean LDFA at last follow-up was not different between plating and IMN (81.9 vs 82.8, p=0.2684). Mean follow-up for the plating cohort was 366 days and 307 days for the IMN cohort (p=0.3178).

**Conclusion:** Both radiographic measures showed no difference between the alignment obtained between IMN and plating. This suggests that based on radiographic alignment, plating and IMN may be similar. Future studies will compare the difference in LDFA and PDFA from initial postoperative imaging to last known follow-up as well as evaluate for differences in patient reported outcomes.

#### Instability Risk Factors for Conservative Therapy-Refractory Chronic Lateral Ankle Instability Poirier JL, Porter D

**Background:** Most acute lateral ankle sprains are treated nonoperatively; however, up to 20% of acute sprains develop Chronic Lateral Ankle Instability (CLAI) requiring surgical reconstruction. CLAI risk factors have not been analyzed in the context of a multifactorial system. This study aims to identify a model to identify patients who are at increased risk for CLAI after acute lateral ankle sprains utilizing clinical and radiographic findings.

**Methods:** This retrospective study identified 78 patients who presented with acute lateral ankle sprains and 50 patients with CLAI who underwent lateral ankle reconstruction (LAR), diagnosed between 2010-2020. Patients' clinical exam findings and radiographic data were collected. Descriptive statistics were utilized to determine difference; significance was set at p<0.05.

**Results**. Of 50 CLAI patients who failed conservative therapies and required LAR, 48% had a clinical diagnosis of lateral ankle impingement (LAI) as compared to 18% of acute sprains (p=0.0003). A clinical diagnosis of subtalar instability was made in 32% of CLAI patients as compared to 2.5% of acute sprains (p=0.0001). Assessment of calcaneal pitch yielded a significant difference between CLAI [ $\mu$ =30.7, median=30.9] and acute sprains [ $\mu$ =25.8, median=25.8] (p<0.0001).

**Conclusion:** Clinical diagnosis of LAI is a significant risk factor for developing CLAI necessitating LAR. Furthermore, subtalar instability is a difficult clinical diagnosis that is nonetheless a significant risk factor for developing long term CLAI. High calcaneal-pitch angle is associated with CLAI and can be a prognostic indicator after acute sprain encounters. The presence of any of these risk factors at time of acute LAS necessitates closer patient follow-up, monitoring, and more extensive preventative intervention. Future studies aim to identify candidates for early surgical intervention.

## Variables Contributing to Missed Appointments in a Free Clinic

Stoll K, Black M, Hopf B, Nunez A, Smeltzer K

**Background:** In a free clinic, missed primary care appointments often result in the absence of prevention and treatment of chronic diseases. Underserved communities are particularly vulnerable, and providers for this population have an obligation to contact patients for follow up and aid. Mollie Wheat Memorial Clinic (MWMC) performed a qualitative study to evaluate variables contributing to missed appointments. The results of this study can serve as a benchmark for deriving solutions used to provide a high quality of care to the Wabash River Valley.

Intervention/Innovation: MWMC is a student-run clinic open every other Saturday. Patients who presented from February 2021 to April 2022 with an appointment ("show") or as a walk-in ("walk-in") were surveyed on barriers to care and demographics. Patients who failed to present for a scheduled appointment ("no-shows") were contacted via phone for a brief interview highlighting reasons for missing the appointment. Comparisons between "show" and "no-show" groups were made to evaluate variables contributing to missed appointments.

**Results**: 53 "show/walk-in" patients have been surveyed and 6 "no-show" patients have been interviewed. Preliminary data analysis of surveys has highlighted several variables patients encounter when trying to attend appointments. Phone interviews have provided insight on ways that MWMC can work to mitigate some of the challenges patients are facing.

**Conclusion:** Transportation, lack of internet access, proximity to affordable healthcare, and socioeconomic status were all variables encountered by our patients. Since access to care at the clinic was presumably affected as a result, we proposed the introduction of a text message system reminding patients of their scheduled appointment and new clinic hours that differ from what we currently offer. The text messaging system was recently implemented, and missed appointments are repeatedly tracked to evaluate efficacy.

#### Acute Urinary Retention Seen in a Pediatric Male Patient After the Administration of Afrin During Intra-arterial Chemotherapy

Smith TE, Kritzmire S, Tejada JG, Martinez ML

**Case Description:** A 3-year-old male patient underwent selective ophthalmic artery infusion chemotherapy (SOAIC) for retinoblastoma (RB). A "generous amount" of intranasal oxymetazoline (INO) was administered via both nostrils after intubation. The patient underwent SOAIC twice without incident or adverse complications. After the third session, the mother of the patient noted he had issues with voiding over the next 24 hours, which eventually resolved on their own. The same experience was noted after SOAIC #4. However, the patient was unable to obtain relief from his symptoms and was taken to the emergency room, where a postvoid residual volume of >200 mL was noted. The symptoms resolved on their own. Prior to SOAIC #5, the parents brought this to the attention of the team. After completion of the procedure, the patient underwent straight catheterization and was kept for a period of observation. After awakening, the patient immediately complained of an inability to urinate and was found to have a postvoid residual volume of 100 mL. Upon returning home, the patient continued to have voiding issues and was subsequently prescribed Tamsulosin 0.4 mg daily. Approximately two hours after administration, he was able to urinate normally. The patient required three days of treatment with Tamsulosin.

**Conclusion:** Adverse events from adjunctive techniques used to optimize outcomes of SOAIC for the treatment of RB are rare. In the case of our patient, we suspect that oxymetazoline's affinity for adrenergic receptors played a role in the voiding dysfunction. Clinical Significance: Although adverse events following INO administration during SOAIC procedures for RB are rare, increased awareness of adverse effects can help with prevention and/or treatment. Moreover, there is a need for more research pertaining to the pharmacokinetics, dosing, adverse effects, and benefits of common adjunctive agents being used in SOAIC.

### Caregiver Experiences with Accessing Sickle Cell Care and the Use of Telemedicine

Feliciano A, Jacob SA, Daas R, LaMotte JE, Carroll AE

**Background:** Sickle cell disease (SCD) is associated with a wide range of complications. However, a multitude of barriers prevent SCD patients from receiving adequate healthcare, including difficulties with transportation and lack of provider knowledge about disease sequelae. Importantly, studies have demonstrated the benefits of telemedicine in addressing barriers to healthcare. While previous studies have identified barriers to care through quantitative methods, few studies have explored barriers which affect the pediatric SCD patient population in the Midwest, wherein the geographical landscape can prohibit healthcare access. Furthermore, few studies have established acceptability of telemedicine among caregivers and patients with SCD.

**Methods:** This study aims to increase understanding of barriers to care and

perceptions of telemedicine by caregivers of pediatric SCD patients in a medically under-resourced area in the Midwest. Researchers conducted semi-structured interviews with caregivers of children with SCD. The interviews were audio-recorded and transcribed. Thematic analyses were performed.

**Results:** Researchers interviewed 16 caregivers of 15 children with SCD. Thematic analyses of the interview transcripts revealed four broad themes regarding caregiver burden/stress, both facilitators and barriers to SCD healthcare, and general thoughts on the acceptability/usefulness of telemedicine.

**Conclusion:** This qualitative study describes common burdens faced by caregivers of SCD, barriers to and facilitators of SCD care in the Midwest, and caregiver perceptions of the usefulness and efficacy of telemedicine for SCD care.

## Characterization of Voluntary Social Distancing and Vaccination Trends Among Workers From May 2020-June 2021

Waggoner C, Gidley S, Garcia K

**Background:** Vaccine hesitancy has become an important topic of discussion during the COVID-19 pandemic. The purpose of this study was to determine the relationship between early adherence to COVID-19 mitigation measures (before vaccine availability) and later vaccination status (after vaccines were widely available) in the Southwest Indiana workforce population.

**Methods:** This study focused on secondary analysis of existing data from two surveys of the same workforce population, spanning manufacturing, finance, healthcare, and service industries. As part of a COVID-19 prevalence study conducted in May 2020, participants were asked to provide information about demographics, social distancing behaviors, and health status. As part of a follow-up study

conducted in June 2021, the same cohort was invited to complete an online survey focused on mental health. The latter survey also asked participants to report information about their work environment and vaccination status. Groups were compared using Chi Square and Kruskall-Wallis or Mann-Whitney U where appropriate.

**Results:** Significant differences in age (p=0.016) and education (p=0.011), but not rurality (rural, rural/mixed, or urban county based on zip code of residence), were observed between the vaccinated and unvaccinated groups. Furthermore, comparison of vaccinated and unvaccinated groups found significantly different responses to the degree of social distancing self-reported in early 2020.

**Conclusions:** Consistent with previous studies, we found that demographic characteristics such as age and education may influence vaccination status. Furthermore, our data suggest an association between willingness to socially distance at the beginning of the pandemic and willingness to receive the COVID-19 vaccine.

#### Sexual Dysfunction in Male Childhood Cancer Survivors (CCS) and Adolescent and Young Adult (AYA) Survivors of Hematologic Malignancies Crist N, Bernie H

Abstract: Sexual health is an important aspect of overall health and quality of life (QoL) among adolescents and young adults (AYA), as well as childhood cancer survivors (CCS). Sexual health encompasses the psychosocial, physical, developmental, emotional, and relationship factors that impact sexual function. Cancer and its associated treatments are associated with negative effects on sexual health, body image, and relationships, as well as overall physical and mental health. Data shows that CCS are known to experience diminished QoL compared to their peers. However, limited information is available to guide the assessment and treatment of sexual dysfunction (SD) in AYA and CCS. Further, exploration into specific cancer types, treatment methods, and their resultant effects on sexual function within these populations is far more limited. We conducted an extensive review of the literature that focused on SD in male survivors of hematologic malignancies (HM). Our review identified an increased incidence of SD within male AYA and CCS of HM, and the negative impact this has on overall QoL. Our results show the degree to which survivors of HM experience increased SD, and the therapies and pathophysiologic mechanisms that may contribute to the development of SD within this population. These findings highlight the lack of research on this topic and the need for further exploration into AYA and CCS sexual health to improve patient care and close the knowledge gaps to better assess and treat SD in this patient population.

#### Systems Modeling of Gut Microbiome Regulation of Estrogen Receptor Beta Signaling in Ulcerative Colitis

Trinh A, Munoz J, Cross TW, Brubaker D

**Introduction:** A sex-bias exists in ulcerative colitis (UC), a chronic inflammatory disorder in the colon, with men 20% more likely to develop UC. A possible explanation for the difference is the anti-inflammatory and epithelial-protective role of estrogen signaling via estrogen receptor beta (ESR2) in the gut. To understand microbiome regulation of ESR2 signaling in UC, we developed a partial least squares path modeling (PLS-PM)-inspired microbiome multi-omic modeling framework.

Materials and Methods: Gut metabolomic, colorectal transcriptomic, and stool 16S rRNA-seq data from 35 unique UC or non-IBD controls subjects were obtained from the Inflammatory Bowel Disease Multi-Omics Database. We built regularized sparse PLS regression (sPLSR) models predicting ESR2DN scores from 16S or metabolomic data. A linear regression meta-model with independent variables consisting of patient LV scores of metabolites and 16S data variables, sex, and UC status was built to predict ESR2DN activity. Significance testing on regression coefficients identified LV interactions synergistically predictive of ERb pathway activity.

**Results and Discussion:** The meta-model was significantly predictive of ESR2DN pathway activity, implicating main effects of microbiotaLV1 (p =0.004), metabolitesLV2 (p=0.004), and diagnosis and the interaction effects of metabolites:microbiotaLV1 (p=0.005), microbiota:UC in LV1 (p=0.014), microbiota:sex in LV2 (p=0.017), and metabolites:UC in LV2 (p=0.035) in predicting ESR2DN pathway status. Utilizing the metamodel and loadings from sPLSR, many interesting metabolites were identified via spearman correlation of highly-loaded taxa and metabolites and Mann-Whitney tests of metabolite abundance by sex or disease status. L-histidine, a metabolite predicted by our model to have a differential effect on ESR2 activity based on patient sex, was validated in literature to show association with reduced colonic inflammation.

**Conclusions:** We demonstrated the effectiveness of a PLS-PM based meta-model for modeling relationships between host signaling and microbiome multi-omics data and quantified significant multi-omic microbiome interactions that can aid in identifying new therapeutics for UC.

## Progression of Paraneoplastic Vitelliform Retinopathy: A Case Study

Minturn R, Minturn J

**Case Description:** A 62-year-old patient with metastatic cutaneous melanoma presented with difficulty seeing at night and blurring of vision, OS > OD. He had a past medical history of prostate cancer with no pertinent ocular, cardiovascular, or smoking history. Bestcorrected vision at the initial visit was 20/30 OD and 20/25 OS. Indirect ophthalmoscopy showed evidence of multiple flat subretinal yellow foci, suspicious of vitelliform dystrophy. At 2-week followup, the patient noted persistent difficulty in low light and difficulty accommodating. Best-corrected vision worsened to 20/60 OS and indirect ophthalmoscopy showed increased layering of subretinal material in the inferior macula. At 8-month follow-up, the patient had no significant vision changes; however, best-corrected vision showed improvement to 20/25 OS. Indirect ophthalmoscopy showed resolution of the material in the inferior macula and continued absence of choroidal metastasis. However, there was presence of new lipofuscin material in the superior macula. At 26-month follow-up, the patient noted no significant vision changes, no changes in visual acuity, and complete resolution of subretinal deposits. This was the last visit with the patient, unfortunately, the patient passed 8 months later.

**Conclusion:** Paraneoplastic vitelliform retinopathy is a rare autoimmune phenomenon caused by antibodies targeting cancer cells which cross-react causing degradation of bipolar cells, rods, and cones leading to deposition of lipofuscin in the subretinal space. While it may lead to visual distortion, visual acuity changes are transient and resolve on their own as the lipofuscin deposits resolve.

**Clinical Significance:** Here, we reported the progression and subsequent regression of the macular-associated retinopathy over the course of a 2-year follow-up. While clinically paraneoplastic vitelliform retinopathy leads to visual disturbances such as vision color change, visual distortion, and blurred vision, given time it will regress without intervention. In this case, visual changes were mild with full resolution of subretinal deposits.

#### Non-metastatic Colon Cancer Model C26 Upregulates Glycolysis in Osteocytes in vitro and Bone in vivo

Tollar MR, Prideaux M, Pin F, Bonewald L

**Background:** Developing effective treatments for musculoskeletal complications in cancer patients requires understanding metabolic effects of cancer on bone, and particularly osteocytes, the most abundant bone cell and key regulator of bone remodeling. However, little is known regarding how cancer impacts normal osteocyte energy metabolic pathways, such as glycolysis. Given that changes in metabolism are important regulators of cellular function, it is essential to determine how osteocyte metabolism is disrupted by cancer and how this may impact skeletal and whole body health.

**Methods:** Mice inoculated with saline (N=5) or C26 cells (N=6) were sacrificed after 2 weeks. Bones were harvested for metabolic profiling by GC-MS, gene expression by RT-PCR, and bone morphology by  $\mu$ CT. Differentiated IDG-SW3 osteocyte-like cells were cocultured with C26 cells for 12-24hrs and metabolites and gene expression analyzed by GC-MS and RT-PCR.

Results: Trabecular bone mass was significantly decreased in the C26 mice. GC-MS analysis revealed decreased glucose in C26 mice tibiae, but no change in lactate. The bone resorption promoting gene Rankl was upregulated, whereas the inhibitor Opg was unchanged. Bone mineralization regulators Mepe and Phex were decreased. In vitro metabolic studies revealed increased glucose and lactate in IDG-SW3 cell lysate; culture media glucose levels were decreased whereas lactate was increased in the co-cultures with C26 cells. RT-PCR demonstrated increases in the glycolysis promoter Hif1-alpha in addition to glycolysis pathway genes including Glut1, Hk2, Slc16a3 and Pdk1. Rankl was also increased in the IDG-SW3 cells co-cultured with the C26 cells whereas Opg, Phex, and Mepe were downregulated.

**Conclusion:** Glycolysis is upregulated in mouse bone and in vitro IDG-SW3 cells exposed to cancer. Our study provides novel understanding for how cancer affects bone metabolism. Integrating these results with whole body metabolism will aid in the development of novel therapeutic strategies to target musculoskeletal and systemic complications of cancer.

## The Importance of Sleep in Total Joint Arthroplasty: A Review

**Gregory B,** Deans C, Stahl SM, Buller LT

**Background:** Total joint arthroplasty (TJA) procedures are among the fastest growing and most cost-effective surgeries in the US. With the desire to optimize outcomes, the association of sleep and TJA has relatively little focus and requires proper assessment. This review serves to assess the current state of the literature regarding sleep in the perioperative period: importance of sleep, etiologies of sleep disturbance, and pre-operative, intraoperative, and postoperative

interventions that may improve our patients' sleep quality and duration after surgery.

**Methods:** A review of the literature was conducted using the PubMed database. A total of 120 articles were used wherein inclusion criteria was determined based on the relevance of content pertaining to TJA and sleep. Preference was placed towards articles of recent publication.

Results: Disturbances in normal sleep structure related to comorbid conditions and surgical intervention play a multifactorial part in TJA recovery, most notably with pain perception. Sleep and pain act in a bidirectional fashion, whereas a decline in one adversely affects the other, and vice versa. Several aspects play a role in sleep quality such as perioperative pain, alteration in sleep structure, and the body's physiologic response to surgery. Improvements of sleep focus on perioperative pain control, the type of anesthesia used, environmental conditions, and pharmacologic intervention, as well as cognitive therapy and meditation.

**Conclusion:** The findings from this review indicate the importance of sleep on recovery and outcomes in patients undergoing TJA. While sleep is a complex process, modifications to enhance sleep and thus decrease pain may prove to be a beneficial and necessary intervention in improving overall outcomes.

# Relationship of Speech Language Pathology with Physical Outcomes in Spinal Cord Injury Patients with Cognitive-Communication Limitations and Traumatic Brain Injury: The SCIRehab Project Leonard PM, Littell K, Whiteneck G, Foster J

**Objective:** Examine the impact of speech therapy (SLP) services on physical outcomes with acute traumatic spinal cord injury (SCI) during acute inpatient rehabilitation with concurrent diagnosis of cognitive-communication limitations (CCL) and traumatic brain injury (TBI).

**Methods:** Using the SCIRehab database from six participating rehabilitation centers, comparison was done with patients who had SCI with CCL that received SLP services during their acute inpatient rehabilitation stay and those who did not receive SLP. A propensity analysis was used to control for heterogeneity of the initial groups with n=190 in each paired group. A subset was then completed to include the diagnosis of TBI with concurrent CCL, n=85 in each pair.

**Results:** Data was obtained from the SCIRehab database using a propensity score analysis and analyzed with a logistical regression model with variable predictors, including admission cognitive and physical FIM, ASI neurologic group, total PT/OT hours, and several other metrics. Patients receiving SLP were randomly matched with similar controls, forming nearest neighbor pairs. In total, for SCI/CCL with and without SLP, there were 380 subjects or 190 matched pairs for primary analysis. Pairs were formed similarly in the SCI/CCL+TBI group forming 85 pairs, or 170 subjects with and without SLP.

Differences in FIM motor scores between admission and discharge were analyzed using a one-sample t-test. In the SCI/CCL group, no significant difference was found in motor FIM improvement, with a p-value of 0.72. Similarly, with the SCI/CCL+TBI group, no significant difference was found in motor FIM improvement, with a p-value of 0.87.

**Conclusion:** SLP remains an important tool in the care for SCI and TBI patients with and without CCL. Though the impact of SLP was not shown in motor FIM improvement in this study, future studies may be better able to associate such treatment with improved outcomes.