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HENRY FORD HEALTH

Henry Ford Health Publication List – June 2024

This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, meeting abstracts, book chapters, books and other works published by Henry Ford Health personnel. Searches were conducted in PubMed, Embase, Web of Science, and CINAHL during the month, and then imported into EndNote for formatting. There are 332 unique citations listed this month, including 110 articles and 222 conference abstracts.

Articles are listed first, followed by conference abstracts. Because of various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health authors.

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Articles

Conference Abstracts

Articles

Administration

Kaur N, **Patel K**, **Lu M**, **Dababneh Y**, **Jomaa D**, **Nagirimadugu A**, **Oruganti P**, and **Yee K**. Enhancing Community-Based Specialty Access Through Virtual Care. *NEJM Catal Innov Care Deliv* 2024; 5(6):1-1. PMID: Not assigned. Full Text

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In December 2020, the authors set out to improve access to tertiary care at Henry Ford Health by creating a network of virtual care clinics to overcome the challenges of home-based virtual care, including broadband access or the need for physical examination. These clinics provided connectivity to the tertiary specialist, vital sign assessment, physical examination, and facilitation of diagnostic testing at a location convenient to the patient. Each clinic was staffed by an on-site team including medical assistants and a single advanced practice provider; the tertiary specialists were present only virtually. For example, a patient with complex Crohn's disease requiring surgery and parenteral nutrition is best served by a tertiary specialist and multidisciplinary team. These patients require frequent, thorough follow-up visits, including blood pressure checks to assess hydration, catheter site checks, and physical examination to assess healing after surgery, in addition to medical management of Crohn's disease by a tertiary specialist. Each of these parameters is clinically paramount and not optimally assessed during a home-based video visit. In this clinical scenario, the medical assistant telepresented the patient to the off-site specialist, checked vital signs, and showed the specialist the catheter and surgical site. The clinical consultation took place in the local clinic facility, with the support of the on-site team. Laboratory testing and imaging studies were coordinated through community settings, and tertiary site-based surgical, health psychology, and nutritional teams also followed up with this patient via virtual care clinic visits. By providing these clinical services closer to the patient's home through a clinical facility, numerous objectives were achieved: (1) patients received thorough clinical assessment and care plans; (2) patients were less likely to use the hospital or ED; (3) patients were more likely to remain in the workforce; and (4) community health care was off-loaded, reducing burnout and improving workforce retention. This approach combines virtual care with a cooperative care delivery model, where the aim is not to shift patient care from one provider to another, but to expand access for patients and to create both new and clinically appropriate care for each care participant, with the aim that improved access will lead to enhanced care outcomes and more efficient care utilization. Telemedicine endeavors have increased dramatically in the past few years, and to the best of the authors' knowledge, no other health system or hospital has expanded specialty services into rural communities in this collaborative manner. The novel approach to health care delivery outlined herein provides a model to improve access to specialty care and patient outcomes, and could be replicated in other regions. Collaboration across institutions, cooperation among leaders and physicians, and commitment to serve communities are the keys to success.

Administration

Suleyman G, **McCormick ME**, **McLenon N**, **Chami E**, **Pollak E**, and **Dabaja AA**. Urinary catheter alleviation navigator protocol (UCANP): Update to the hospital-wide implementation at a single tertiary health care center. *Am J Infect Control* 2024; Epub ahead of print. PMID: 38876167. Full Text

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BACKGROUND: Catheter-associated urinary tract infections (CAUTIs) are commonly reported healthcare-associated infections. It was demonstrated that the urinary catheter alleviation navigator protocol (UCANP) pilot resulted in a reduction of catheter utilization and catheter days. METHODS: Quality improvement initiative that was implemented at a single urban, tertiary health care center, focusing on early discontinuation of indwelling urinary catheters (IUC) and avoidance of reinsertion. Protocol was expanded hospital-wide September 2020-April 2022. We compared IUC utilization, IUC standardized utilization ratio (SUR) and CAUTI standardized infection ratio (SIR) in the pre-intervention period (March 2020-August 2020) to the post-intervention period (May 2022-October 2022). RESULTS: Pre-implementation, 2 patients with IUC removal were placed on UCANP. Post-implementation, 835 (45%) patients with IUC removal participated in the protocol. Number of patients requiring IUC reinsertion did not differ among the 2 groups. IUC utilization was significantly decreased from 0.28 to 0.24 with 14% reduction (p=0.025). SUR decreased by 11% from 0.778 to 0.693 (p=0.007) and SIR by 84% from 0.311 to 0.049 (p=0.009). CONCLUSION: Our protocol significantly reduced IUC utilization and SUR after hospital-wide implementation. UCANP is a safe and effective strategy that can potentially decrease unnecessary IUCs in patients with transient urinary retention.

Allergy and Immunology

Afshan TS, **Kulkarni A**, Smith JM, Tesson E, Blackshere T, **Joseph C**, **Zoratti EM**, Rivera-Spoljaric K, Hartert T, Gern JE, and Singh AM. Research protocol and recruitment redesign of a study of pregnant women and their infants during the COVID-19 pandemic: Childhood Allergy and the NeOnatal Environment (CANOE). *J Allergy Clin Immunol Glob* 2024; 3(3):100270. PMID: 38881739. Full Text

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BACKGROUND: Recruitment for research studies is a challenging endeavor that was further complicated by the coronavirus disease 2019 pandemic. We launched a new multicenter birth cohort, Childhood Allergy and the NeOnatal Environment (CANOE), supported by the National Institutes of Health in January 2020 across 4 sites. Although the pandemic temporarily halted clinical research, we restructured the study and instituted novel recruitment methods that we hypothesized would enable brisk enrollment when research activities resumed. OBJECTIVE: We sought to develop protocol modifications and recruitment methods that promote successful recruitment of diverse populations in clinical research despite a global pandemic. METHODS: Even though study activities were suspended, we modified recruitment strategies to limit in-person contact, shifting toward alternative HIPAA-compliant methods such as clinician referrals, institutional social media, and telemedicine screening and consent procedures. Protocol changes included reducing the frequency of in-person visits, leveraging clinical care visits to collect biospecimens, expanded self-collection of samples at home, and making study materials available online. RESULTS: Remote methods, including targeted social media posts, mailed letters, and email, combined with in-clinic recruitment with modifications for social distancing led to successful recruitment at all sites. Rates of consent have been similar across recruitment sites, with the highest rates of enrollment of mother-infant dyads realized by sites that implemented multiple recruitment strategies. CONCLUSIONS: Study procedures that prioritize health and safety measures such as social distancing, study participant convenience, and use diverse recruitment strategies enable successful enrollment of pregnant women and their newborns into clinical research while adhering to public health restrictions during a global pandemic.

Allergy and Immunology

Biagini JM, Martin LJ, He H, Bacharier LB, Gebretsadik T, Hartert TV, Jackson DJ, **Kim H**, Miller RL, Rivera-Spoljaric K, Schauberger EM, Singh AM, Visness CM, **Wegienka G**, **Ownby DR**, Gold DR, Martinez FD, Johnson CC, Wright AL, Gern JE, and Khurana Hershey GK. Performance of the Pediatric Asthma Risk Score across Diverse Populations. *NEJM Evid* 2023; 2(10):EVIDoa2300026. PMID: 38320177. Full Text

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BACKGROUND: Methods to determine whether a toddler is likely to develop asthma are of value to parents and clinical trialists testing primary prevention strategies. The Pediatric Asthma Risk Score (PARS) is a 14-point score of six factors designed to predict asthma in early life. PARS was developed and validated in relatively homogenous populations, so its generalizability is unknown. METHODS: We computed PARS using the six factors of self-declared race (parent-reported as “Black” or “not Black”), parental asthma, eczema, any wheezing, wheezing without a cold, and polysensitization in 5634 children from birth to 3 years of age. The primary outcome of our analysis was the ability of PARS to predict asthma development at 5 to 10 years of age using the area under the receiver operating curve in each cohort and across all cohorts with varying ethnicity, sex, cohort type, birth decades, missing PARS factors, and polysensitization definition. We also performed a meta-analysis across all the cohorts. Finally, we compared PARS predictive ability with the binary Asthma Predictive Index (API). RESULTS: Across 10 cohorts, the area under the receiver operating curve for PARS was 0.76. PARS performance did not differ by ethnicity, sex, cohort type, enrollment decade, missing PARS factors, or polysensitization definition (all P>0.05). The weights of each factor in the meta-analysis were similar to the original PARS weights. PARS and API equally identified children at high risk for developing asthma or not; API missed 31% of children at moderate asthma risk. CONCLUSIONS: PARS provided robust estimates of asthma risk in children from a wide range of ethnicities, backgrounds, and susceptibility. (Funded by the National Institute of Allergy and Infectious Diseases and others.)

Allergy and Immunology

Ryan PH, Zanobetti A, Coull BA, Andrews H, Bacharier LB, Bailey D, Beamer PI, Blossom J, Brokamp C, Datta S, Hartert T, Khurana Hershey GK, Jackson DJ, **Johnson CC**, **Joseph C**, Kahn J, Lothrop N, Louisias M, Luttmann-Gibson H, Martinez FD, Mendonça E, Miller RL, Ownby D, Ramratnam S, Seroogy CM, Visness CM, Wright AL, **Zoratti EM**, Gern JE, and Gold DR. The Legacy of Redlining: Increasing Childhood Asthma Disparities Through Neighborhood Poverty. *Am J Respir Crit Care Med* 2024; Epub ahead of print. PMID: 38869320. Full Text

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RATIONALE: Identifying the root causes of racial disparities in childhood asthma is critical for health equity. OBJECTIVES: To determine if the 1930's racist policy of redlining led to present-day disparities in childhood asthma by increasing community-level poverty and decreasing neighborhood socioeconomic position (SEP). METHODS: We categorized census tracts at birth of participants from the Children's Respiratory and Environmental Workgroup birth cohort consortium into A, B, C, or D categories as defined by the Home Owners Loan Corporation (HOLC), with D being the highest perceived risk. Surrogates of present-day neighborhood-level SEP were determined for each tract including the percentage of low-income households, the CDC's social vulnerability index (SVI), and other tract-level variables. We performed causal mediation analysis, which, under the assumption of no unmeasured confounding, estimates the direct and mediated pathways by which redlining may cause asthma disparities through census tract-level mediators adjusting for individual-level covariates. MEASUREMENTS AND MAIN RESULTS: Of 4,849 children, the cumulative incidence of asthma through age 11 was 26.6% and 13.2% resided in census tracts with a HOLC grade of D. In mediation analyses, residing in grade D tracts (aOR = 1.03 [95%CI 1.01,1.05]) was significantly associated with childhood asthma, with 79% of this increased risk mediated by percentage of low-income households; results were similar for SVI and other tract-level variables. CONCLUSIONS: The historical structural racist policy of redlining led to present-day asthma disparities in part through decreased neighborhood SEP. Policies aimed at reversing the effects of structural racism should be considered to create more just, equitable, and healthy communities.

Anesthesiology

Abou Daher L, **Heppell O**, **Lopez-Plaza I**, and **Guerra-Londono CE**. Perioperative Blood Transfusions and Cancer Progression: A Narrative Review. *Curr Oncol Rep* 2024; Epub ahead of print. PMID: 38847973. Full Text

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PURPOSE OF REVIEW: To examine the most recent evidence about known controversies on the effect of perioperative transfusion on cancer progression. RECENT FINDINGS: Laboratory evidence suggests that transfusion-related immunomodulation can be modified by blood management and storage practices, but it is likely of less intensity than the effect of the surgical stress response. Clinical evidence has questioned the independent effect of blood transfusion on cancer progression for some cancers but supported it for others. Despite major changes in surgery and anesthesia, cancer surgery remains a major player in perioperative blood product utilization. Prospective data is still required to strengthen or refute existing associations. Transfusion-related immunomodulation in cancer surgery is well-documented, but the extent to which it affects cancer progression is unclear. Associations between transfusion and cancer progression are disease-specific. Increasing evidence shows autologous blood transfusion may be safe in cancer surgery.

Anesthesiology
Grinman L, Elmore B, Ardon AE, **Hussain A**, Malik MF, Hernandez N, and Jacoby MJ. Use of Peripheral Nerve Blocks for Total hip Arthroplasty. *Curr Pain Headache Rep* 2024; Epub ahead of print. PMID: 38907794. Full Text

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PURPOSE OF REVIEW: The purpose of this review is to summarize the recent literature regarding regional anesthesia (RA) techniques and outcomes for total hip arthroplasty (THA) in the face of changing surgical techniques and perioperative considerations. RECENT FINDINGS: Based on large meta-analyses, peripheral nerve blocks are indicated for THA. Each block has its own risks and benefits and data for outcomes for particular techniques are limited. New surgical techniques, improved use of multimodal analgesia, and improved ultrasound guided regional anesthetics lead to better pain control for patients undergoing THA with less associated risks. Block selection continues to be influenced by provider comfort, surgical approach, patient anatomy, and postoperative goals. Head-to-head studies of particular nerve blocks are warranted.

Anesthesiology
Mosalpuria Y, **Ibrahim M**, Fayed M, **Guruswamy J**, and **DePorre AR**. Massive Hemoptysis: An Unusual Complication of Left Atrial Appendage Occlusion Device in Two Patients. *Cureus* 2024; 16(5):e61451. PMID: 38947731. Request Article

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Left atrial appendage occlusion (LAAO) devices have emerged as a promising alternative for stroke prevention in non-valvular atrial fibrillation (NVAF) patients with contraindications to chronic anticoagulation therapy. The most common life-threatening procedural complications described in the

literature include pericardial effusion, air embolism, and stroke. We here present a case report of two patients who experienced identical but rare post-procedural complications of pulmonary venous bleed, presenting as hemoptysis.

Anesthesiology
Vaidyanathan A, **Guruswamy J**, **Saluja A**, Eng M, and **Szymanski T**. Use of Pleth Variability Index as a Non-invasive, Dynamic Indicator of Left Atrial Pressure Change During MitraClip: Transcatheter Mitral Valve Repair. *Semin Cardiothorac Vasc Anesth* 2024; Epub ahead of print. PMID: 38864441. Full Text

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BACKGROUND: Transcatheter edge-to-edge repair (TEER) with MitraClip is a safe and effective alternative to surgical mitral valve repair/replacement in patients with high operative risk. Pleth Variability Index (PVI) is a non-invasive, dynamic index based on analysis of the respiratory variations in the plethysmographic waveform recorded transcutaneously by the pulse oximeter. OBJECTIVES: The objective of the study was to evaluate if the hemodynamic effect of improved left-sided output after successful transcatheter mitral valve repair would lead to a significant change in PVI, and if it would correlate with the decrease in left atrial pressure (LAP). DESIGN: Prospective, observational cohort study (ClinicalTrials.gov NCT03993938). SETTING: Single academic hospital in Detroit, Michigan (USA), from October 2019 to February 2021. PARTICIPANTS: The authors included adult patients with severe mitral regurgitation who underwent successful MitraClip placement. MEASUREMENTS AND MAIN RESULTS: Of 30 patients, all components of the LAP (a wave, v wave, and mean) decreased significantly after successful MitraClip placement ($P < .01$). The median (IQR) PVI increased from 21 (11-35) to 23 (13-38) after clip placement; however, this change was not statistically significant ($P = .275$). No significant correlation between change in PVI and change in LAP was observed ($P = .235$). CONCLUSIONS: In patients with severe mitral regurgitation, successful MitraClip resulted in a significant reduction in LAP without a significant change in PVI. A larger sample size may provide more insight on the utility of using PVI as an indicator of LAP change in patients with mitral regurgitation.

Anesthesiology
Weinstein JL, Ali H, **Mitchell JD**, Sarwar A, Palmer MR, MacLellan C, Matyal R, and Ahmed M. Analyzing the Evolution of Needle and Ultrasound Probe Manipulation Skills of Interventional Radiology Trainees With Time and Experience. *Simul Healthc* 2024; Epub ahead of print. PMID: 38922448. Full Text

From the Department of Radiology (J.W., H.A., A.S., M.R.P., C.M.L., M.A.), Beth Israel Deaconess Medical Center, Boston, MA; Department of Anesthesiology (J.D.M.), Henry Ford Health, Detroit, MI/Michigan State University CHM, Grand Rapids, MI; and Department of Anesthesia (R.M.), Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA.

PURPOSE: To test the hypothesis that hand motion analysis can measure the progression of needle and ultrasound probe manipulation skills of interventional radiology trainees in central venous line placement. MATERIALS AND METHODS: An expert cohort of 6 interventional radiologists and 4 anesthesiologists and a trainee cohort of 6 novice trainees (<50 central lines) and 5 experienced trainees (>50 central lines) performed simulated central venous access. Four novices and 1 experienced trainee repeated the task 1 year later. An electromagnetic motion tracking system tracked the needle hand and ultrasound probe. Path length, translational, and rotational movements were calculated separately for the needle hand and probe sensor. These metrics were used to calculate motion metrics based scores on a scale of 0 to 3 for each sensor. Nonparametric statistics were used, and the data are reported as median ± interquartile range. RESULTS: Comparing novice and experienced trainees, there was a significant difference in probe scores (experienced vs. novice: 1 ± 2 vs. 0 ± 0, $P = 0.04$) but not in needle-hand scores (1 ± 1.5 vs. 0 ± 1, $P = 0.26$). Trainees showed a significant increase in probe scores at the 1-year follow-up (baseline vs. follow-up: 0 ± 1 vs. 2.5 ± 1.8, $P = 0.003$), but no significant difference was observed in the needle manipulation metrics. Experts differed significantly from experienced trainees for all metrics for both sensors ($P < 0.05$), with the exception of the path length of the probe. CONCLUSIONS: Acquisition of

improved dexterity of the probe may occur before improvement in the dexterity with the needle hand for interventional radiology trainees.

Behavioral Health Services/Psychiatry/Neuropsychology
Murray MF, **Pearl ES**, **Zelenak L**, **Hamann A**, **Sehgal M**, **Braciszewski JM**, **Carlin AM**, and **Miller-Matero LR**. COVID-19-Related Increases in Depressive and Anxious Symptoms Are Associated with Maladaptive Eating Among Patients up to 4 years Post-bariatric Surgery. *Obes Surg* 2024; Epub ahead of print. PMID: 38839635. Full Text

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INTRODUCTION: Depressive and anxious symptoms and maladaptive eating behaviors fluctuate with stressful events for patients seeking bariatric surgery. These associations are less clear for patients postoperatively. Using the COVID-19 pandemic as a frame, we examined associations between changes in depressive and anxious symptoms and maladaptive eating behaviors between up to four years postoperatively. METHODS: Participants (N = 703) who underwent surgery between 2018 and 2021 completed web-based questionnaires between 2021 and 2022. Demographic and surgical data were obtained from electronic health records. Participants reported whether depressive and anxious symptoms increased or were stable/decreased during the COVID-19 pandemic, and completed eating behavior measures. RESULTS: Many participants reported increased depressive (27.5%) and anxious (33.7%) symptoms during the COVID-19 pandemic. Compared to those who reported stable or decreased symptoms, these participants were as follows: (1) more likely to endorse presence of binge, loss-of-control, graze, and night eating; (2) reported higher emotional eating in response to anger and frustration, depression, and anxiety; and (3) reported higher driven and compulsive eating behaviors. Frequency of binge, loss-of-control, graze, and night eating episodes did not differ between groups (e.g., increased vs. stable/decreased anxious symptoms) among participants who endorsed any episodes. CONCLUSION: A large portion of the sample reported increased depressive and anxious symptoms during the COVID-19 pandemic, and these increases were associated with maladaptive eating behaviors. Depressive and anxious symptoms and eating behaviors should be assessed postoperatively as significant stressors may be associated with increased distress and maladaptive eating behaviors that can affect postoperative outcomes. Postoperative interventions may be useful at simultaneously targeting these concerns.

Behavioral Health Services/Psychiatry/Neuropsychology
Patel S, Tareen K, Patel C, and Rosinski A. Herbal and Non-Herbal Dietary Supplements for Psychiatric Indications: Considerations in Liver Transplantation. *Curr Psychiatry Rep* 2024; Epub ahead of print. PMID: 38941032. Full Text

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PURPOSE OF REVIEW: Traditional, complementary, and integrative medicine (TCIM) modalities are widely employed. However, TCIM, specifically herbal and non-herbal dietary supplements, can pose challenges in the context of organ transplantation. In this review, we discuss common supplements used for psychiatric purposes and highlight important considerations for candidates and recipients of liver transplants. RECENT FINDINGS: Ashwagandha, kava kava, green tea extract, skullcap, turmeric, and valerian have known idiosyncratic hepatotoxic potential and may complicate the liver transplantation course. Multiple supplements reportedly carry a lower risk of hepatotoxicity, though evidence for

widespread use in those at risk for or with hepatic impairment is limited. Psychiatrists caring for candidates and recipients of liver transplants must recognize that patients may find supplements helpful in alleviating psychiatric symptoms, despite an overall limited evidence base. Evaluating benefit versus risk ratios and reviewing drug-drug interactions is essential to promote transplant candidacy and mitigate the possibility of native or graft liver dysfunction.

Behavioral Health Services/Psychiatry/Neuropsychology

Sullivan MD, Wilson L, Amick M, **Miller-Matero LR**, Chrusciel T, Salas J, **Zabel C**, Lustman PJ, **Ahmedani B**, Carpenter RW, and Scherrer JF. Social support and the association between post-traumatic stress disorder and risk for long-term prescription opioid use. *Pain* 2024; Epub ahead of print. PMID: 38833573. Full Text

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Post-traumatic stress disorder (PTSD) is common in patients with chronic pain, adversely affects chronic pain outcomes, and is associated with opioid use and adverse opioid outcomes. Social support is a robust predictor of PTSD incidence and course as well as chronic pain outcome. We determined whether the association between PTSD and persistent opioid use was modified by emotional support in a cohort of patients receiving opioids for noncancer pain. Eligible participants were ≥18 years and had completed a new period of prescription opioid use lasting 30 to 90 days. Bivariate associations between cohort characteristics and each key variable was assessed using $\chi 2$ tests for categorical variables and t-tests for continuous variables. Interaction between PTSD and emotional support was assessed by a priori stratification on low vs high emotional support. Participants (n = 808) were 53.6 (SD ± 11.6) years of age, 69.8% female, 69.6% White, and 26.4% African American. Overall, 17.2% had probable PTSD. High emotional support was significantly ($P < 0.0001$) more common among those without probable PTSD. Prescription opioid use at 6-month follow-up was significantly ($P = 0.0368$) more common among patients with vs without probable PTSD. In fully adjusted models, PTSD was no longer associated with opioid use at 6-month follow-up among participants with high emotional support. Among those with lower emotional support, PTSD was significantly associated with opioid use at 6-month follow-up in unadjusted (odds ratio = 2.40; 95% confidence interval: 1.24-4.64) and adjusted models (odds ratio = 2.39; 95% confidence interval: 1.14-4.99). Results point to the hypothesis that improvement of emotional support in vulnerable patients with chronic pain and PTSD may help reduce sustained opioid use.

Cardiology/Cardiovascular Research

Aggarwal V, Giri J, Visovatti SH, Mahmud E, Matsubara H, Madani M, Rogers F, Gopalan D, Rosenfield K, and McLaughlin VV. Status and Future Directions for Balloon Pulmonary Angioplasty in Chronic Thromboembolic Pulmonary Disease With and Without Pulmonary Hypertension: A Scientific Statement From the American Heart Association. *Circulation* 2024; 149(15):e1090-e1107. PMID: 38450477. Full Text

Balloon pulmonary angioplasty continues to gain traction as a treatment option for patients with chronic thromboembolic pulmonary disease with and without pulmonary hypertension. Recent European Society of Cardiology guidelines on pulmonary hypertension now give balloon pulmonary angioplasty a Class 1

recommendation for inoperable and residual chronic thromboembolic pulmonary hypertension. Not surprisingly, chronic thromboembolic pulmonary hypertension centers are rapidly initiating balloon pulmonary angioplasty programs. However, we need a comprehensive, expert consensus document outlining critical concepts, including identifying necessary personnel and expertise, criteria for patient selection, and a standardized approach to preprocedural planning and establishing criteria for evaluating procedural efficacy and safety. Given this lack of standards, the balloon pulmonary angioplasty skill set is learned through peer-to-peer contact and training. This document is a state-of-the-art, comprehensive statement from key thought leaders to address this gap in the current clinical practice of balloon pulmonary angioplasty. We summarize the current status of the procedure and provide a consensus opinion on the role of balloon pulmonary angioplasty in the overall care of patients with chronic thromboembolic pulmonary disease with and without pulmonary hypertension. We also identify knowledge gaps, provide guidance for new centers interested in initiating balloon pulmonary angioplasty programs, and highlight future directions and research needs for this emerging therapy.

Cardiology/Cardiovascular Research
Ahmed O, **Singh H**, **Bai S**, **Maraj D**, **Qureshi MA**, **Hawes E**, **Alamelumangapuram C**, and **Othman H**. Delayed Presentation of a Post-infarction Ventricular Septal Rupture. *J Investig Med High Impact Case Rep* 2024; 12:23247096241262514. PMID: 38904301. Full Text

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Ventricular septal rupture, a formidable complication of acute myocardial infarction (AMI), is linked to significant morbidity and mortality. The clinical manifestation typically involves pronounced hemodynamic compromise necessitating prompt surgical intervention. This report outlines the case of a 60-year-old male presenting with acute heart failure 3 weeks post a presumed AMI. On evaluation, a substantial ventricular septal defect with left-to-right shunt was observed. The patient, although hemodynamically stable with mild symptoms, underwent surgical closure of the defect and coronary artery bypass graft for multivessel coronary artery disease. This case contributes to the literature on the delayed presentation of post-myocardial infarction (MI) ventricular septal rupture, a scenario deviating from the anticipated severe hemodynamic instability given the timing of the MI and the extent of the septal defect.

Cardiology/Cardiovascular Research
Alonso WW, **Keteyian SJ**, Leifer ES, Kitzman DW, and Sachdev V. Adherence to Exercise in Adults With Heart Failure. *J Cardiopulm Rehabil Prev* 2024; Epub ahead of print. PMID: 38870066. Full Text

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Cardiology/Cardiovascular Research
Ayyad M, **Jabri A**, Khalefa BB, Al-Abdouh A, Madanat L, Albandak M, Alhuneafat L, Sukhon F, Shahrori Z, Mourid MR, Mhanna M, **Giustino G**, **Wang DD**, Hanson ID, Abbas AE, **AlQarqaz M**, and **Villablanca P**. Efficacy and safety of TAVR versus SAVR in patients with small aortic annuli: A systematic review and meta-analysis. *Int J Cardiol* 2024; 132243. Epub ahead of print. PMID: 38851542. Full Text

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INTRODUCTION: Patients with a small aortic annulus (SAA) undergoing aortic valve replacement are at increased risk of patient-prosthesis mismatch (PPM), which adversely affects outcomes. Transcatheter aortic valve replacement (TAVR) has shown promise in mitigating PPM compared to surgical aortic valve replacement (SAVR). METHODS: We conducted a systematic review and meta-analysis following PRISMA guidelines to compare clinical outcomes, mortality, and PPM between SAA patients undergoing TAVR and SAVR. Eligible studies were identified through comprehensive literature searches and assessed for quality and relevance. RESULTS: Nine studies with a total of 2476 patients were included. TAVR demonstrated similar 30-day and 2-year mortality, myocardial infarction, and stroke rates compared to SAVR. However, TAVR showed significant advantages in reducing moderate survival post SAVR, the observed hemodynamic outcomes may potentially contribute to substantial survival variations between TAVR and SAVR during extended follow-up periods.(22) Furthermore, previous studies found comparable 30-day and 2-year mortality rates between TAVR and SAVR, with no significant differences across annulus sizes.(22, 23) Stroke and myocardial infarction incidences and severe PPM and lowering rates of major bleeding at both 30 days and 2 years. Conversely, SAVR had better outcomes in 30-day permanent pacemaker implantation. Echocardiographic outcomes were comparable between the two interventions. CONCLUSION: Our findings suggest that both TAVR and SAVR are viable options for treating AS in patients with a small aortic annulus. TAVR offers advantages in reducing PPM and major bleeding, while SAVR performs better in terms of pacemaker implantation. Future studies should focus on comparing newer generation TAVR techniques and devices with SAVR. Consideration of patient characteristics is crucial in selecting the optimal treatment approach for AS.

Cardiology/Cardiovascular Research

Berkowitz JL, Kennedy KF, Font C, **Nerenz DR**, Abbott JD, and **Aronow HD**. Limited English proficiency, cardiovascular risk factors, cardiovascular disease, and in-hospital COVID-19 outcomes. *Am J Manag Care* 2024; 30(6):251-256. PMID: 38912951. Full Text

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OBJECTIVES: Cardiovascular risk factors and history of cardiovascular disease are associated with greater morbidity and mortality in patients hospitalized with COVID-19. Limited English proficiency (LEP) has also been associated with worse outcomes in this setting, including requiring intensive care unit (ICU) level of care and in-hospital death. Whether non-English-language preference (NELP) modifies the association between cardiovascular risk factors or disease and outcomes in patients hospitalized with COVID-19 is unknown. STUDY DESIGN: Retrospective cohort study of adult patients admitted to a large New England health system between March 1 and December 31, 2020, who tested positive for COVID-19. NELP was defined as having a preferred language that was not English noted in the electronic health record. METHODS: Cardiovascular risk factors, history of cardiovascular disease, and NELP were related to the primary composite clinical outcome-death or ICU admission-using multivariable binary logistic regression adjusted for demographic and clinical characteristics. Interaction terms for NELP and model covariates were evaluated. RESULTS: Of 3582 patients hospitalized with COVID-19, 1024 (28.6%) had NELP; 812 (79.3%) of the patients with NELP received interpreter services. Death or ICU admission occurred in 794 (22.2%) of the hospitalized patients. NELP was not significantly associated with the primary composite outcome in unadjusted or adjusted analyses. In the adjusted analyses, only male gender, coronary artery disease, pulmonary circulatory disease, and liver disease significantly predicted the primary outcome. NELP did not modify the effect of these associations. CONCLUSIONS: NELP was not significantly associated with odds of death or ICU admission, nor did it modify the association between cardiovascular risk factors or history of cardiovascular disease and this composite outcome. Because most patients with NELP received interpreter services, these findings may support the role of such services in ensuring equitable outcomes.

Cardiology/Cardiovascular Research

Cherabuddi MR, **Goodman B**, **Ayyad A**, **Almajali DA**, **Nadeem O**, **Bradley P**, **Russell C**, and **Ouellette D**. Association of Area Deprivation Index with Adherence to Proposed Regimen in Patients with Sarcoidosis in Detroit, Michigan. *Sarcoidosis Vasc Diffuse Lung Dis* 2024; 41(2):e2024031. PMID: 38940707. Full Text

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BACKGROUND AND AIM: Social predictors affect severity of sarcoidosis, with Black patients, older individuals, those with lower income, and those without insurance having greater severity. This study aimed to explore potential disparities affecting access to care in sarcoidosis patients with a primary focus on metrics such as area deprivation index (ADI) and its association with adherence to the proposed regimen. METHODS: A retrospective chart review study of all patients seen in pulmonary clinics at a large urban tertiary care center over 2 years with sarcoidosis patients identified with International Classification of Diseases diagnosis code D86. Data collected included age, race, sex, ADI, insurance, online patient portal usage, chest x-rays, pulmonary function tests, missed visits, hospitalizations, positive biopsy, communication and visits around bronchoscopy. Categorical variables were described using frequency and percentage. Numerical variables were described using median, mean and standard deviation. Statistical analysis included chi-square test, two-sample T-test and Wilcoxon rank sum test. Multivariate logistic regression analysis was performed to model independent association with 12 month no-show occurrence as a metric of adherence to the proposed regimen. RESULTS: Among sarcoidosis patients (N = 788), univariate models showed the presence of active online patient portal use among younger patients (58.6 years with portal vs. 65.1 years without portal, $p < 0.001$), those with lower ADI (73 with portal vs. 92 without portal, $p < 0.001$) and with commercial insurance (48.5% with portal vs. 20.7% without portal, $p < 0.001$); more x-rays (45.6% with x-rays vs. 36.6% without x-rays, $p = 0.018$) and hospitalizations (50.3% with hospitalizations vs. 36.2% without hospitalizations, $p < 0.001$) in Medicare patients. Sarcoidosis patients with positive biopsies on file from 2013-2023 were more likely to be male (44.19% with positive biopsy vs. 33.91% without positive biopsy, $p = 0.006$), White (36.29% with positive biopsy vs. 22.9% without positive biopsy, $p < 0.001$) or other races (3.23% with positive biopsy vs. 2.25% without positive biopsy, $p < 0.001$), younger (55.8 years with positive biopsy vs. 61.7 years without positive biopsy, $p < 0.001$) and belonged to lower national ADI ranks (73 with positive biopsy vs. 80 without biopsy, $p = 0.041$). A multivariate analysis was done with those variables found to be significant in the univariate analyses, which revealed that higher ADI national was associated with failure to adhere to the proposed regimen. CONCLUSIONS: We identified intricate patterns of sociodemographic variables affecting access to care in sarcoidosis patients, especially higher ADI national associated with failure to adhere to the proposed regimen, raising concerns for potential healthcare barriers. Understanding these barriers is vital for equitable high-quality care, assisting in timely and efficient management of the patient's disease.

Cardiology/Cardiovascular Research

Ellauzi R, Erdem S, Salam MF, Kumar A, **Aggarwal V**, **Koenig G**, **Aronow HD**, and **Basir MB**. Mechanical Circulatory Support Devices in Patients with High-Risk Pulmonary Embolism. *J Clin Med* 2024; 13(11). PMID: 38892871. Full Text

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI 48202, USA.
Department of Internal Medicine, Detroit Medical Center, Wayne State University, Detroit, MI 48202, USA.
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Pulmonary embolism (PE) is a common acute cardiovascular condition. Within this review, we discuss the incidence, pathophysiology, and treatment options for patients with high-risk and massive pulmonary embolisms. In particular, we focus on the role of mechanical circulatory support devices and their possible therapeutic benefits in patients who are unresponsive to standard therapeutic options. Moreover,

attention is given to device selection criteria, weaning protocols, and complication mitigation strategies. Finally, we underscore the necessity for more comprehensive studies to corroborate the benefits and safety of MCS devices in PE management.

Cardiology/Cardiovascular Research
Goel R, Sartori S, Vogel B, Okoli K, Franklin-Bedel K, Ortega R, **Wang DD**, Douglas PS, Wang TY, and Mehran R. Geographic Mapping of Gender Disparities in Authorship of Cardiovascular Literature. *J Am Coll Cardiol* 2024; 83(24):2458-2468. PMID: 38866449. Full Text

Center for Interventional Cardiovascular Research and Clinical Trials, Icahn School Medicine at Mount Sinai, New York, New York, USA; Department of Internal Medicine, SUNY Downstate Health Sciences University, Brooklyn, New York, USA.
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BACKGROUND: Women in cardiology experience considerable gender disparities in publications, which hinders their career advancements to higher faculty and senior leadership positions. However, the extent of these disparities across different types of cardiovascular literature is not well understood. OBJECTIVES: We investigated gender differences in authorship across various cardiovascular publications over a decade and examined geographic variations in the representation of women authors. METHODS: All papers published from January 1, 2010, to December 31, 2019, in 4 major cardiovascular journals (Journal of the American College of Cardiology, European Heart Journal, Journal of the American Medical Association Cardiology, and Nature Reviews Cardiology) were reviewed. RESULTS: Of the 18,535 papers with 111,562 authors, 20.6% of the authors were women, and 47.7% of the papers had no women authors. Over 10 years, the proportion of women authors remained low (20.7% in 2010 to 21.4% in 2019), with the lowest proportion in editorial papers (14.8%) and the highest in research papers (21.8%). More women as first (34.6%) and last (47.6%) authors were affiliated with institutions in the United States compared with other countries. The proportion of women middle-order authors was higher on papers with women as first authors (29.4% vs 20.5%) or last authors (30.6% vs 21.3%), compared with papers with men as first or last authors, respectively. CONCLUSIONS: Over the past decade, the proportion of women authors across all article types in major cardiovascular journals remained low. A call to action is needed to promote women in cardiology and provide them with equitable opportunities.

Cardiology/Cardiovascular Research
Gornik HL, **Aronow HD**, Goodney PP, Arya S, Brewster LP, Byrd L, Chandra V, Drachman DE, Eaves JM, **Ehrman JK**, Evans JN, Getchius TSD, Gutiérrez JA, Hawkins BM, Hess CN, Ho KJ, Jones WS, Kim ESH, Kinlay S, Kirksey L, Kohlman-Trigoboff D, Long CA, Pollak AW, Sabri SS, Sadwin LB, Secemsky EA, Serhal M, Shishehbor MH, Treat-Jacobson D, and Wilkins LR. 2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS Guideline for the Management of Lower Extremity Peripheral Artery Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol* 2024; Epub ahead of print. PMID: 38752899. Full Text

AIM: The "2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS Guideline for the Management of Lower Extremity Peripheral Artery Disease" provides recommendations to guide clinicians in the treatment of patients with lower extremity peripheral artery disease across its multiple clinical presentation subsets (ie, asymptomatic, chronic symptomatic, chronic limb-threatening ischemia, and acute limb ischemia). METHODS: A comprehensive literature search was conducted from October 2020 to June 2022, encompassing studies, reviews, and other evidence conducted on human subjects that was published in English from PubMed, EMBASE, the Cochrane Library, CINHL Complete, and other selected databases relevant to this guideline. Additional relevant studies, published through May 2023 during the peer review process, were also considered by the writing committee and added to the

evidence tables where appropriate. STRUCTURE: Recommendations from the "2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease" have been updated with new evidence to guide clinicians. In addition, new recommendations addressing comprehensive care for patients with peripheral artery disease have been developed.

Cardiology/Cardiovascular Research
Gornik HL, **Aronow HD**, Goodney PP, Arya S, Brewster LP, Byrd L, Chandra V, Drachman DE, Eaves JM, **Ehrman JK**, Evans JN, Getchius TSD, Gutiérrez JA, Hawkins BM, Hess CN, Ho KJ, Jones WS, Kim ESH, Kinlay S, Kirksey L, Kohlman-Trigoboff D, Long CA, Pollak AW, Sabri SS, Sadwin LB, Secemsky EA, Serhal M, Shishehbor MH, Treat-Jacobson D, and Wilkins LR. 2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS Guideline for the Management of Lower Extremity Peripheral Artery Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2024; Epub ahead of print. PMID: 38743805. Full Text

VESS representative.
Layperson or patient representative.
SVS representative.
AACVPR representative.
APMA representative.
AHA/ACC Joint Committee on Clinical Practice Guidelines liaison.
SVM representative.
ABC representative.
SCAI representative.
SVN representative.
SIR representative.

AIM: The "2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS Guideline for the Management of Lower Extremity Peripheral Artery Disease" provides recommendations to guide clinicians in the treatment of patients with lower extremity peripheral artery disease across its multiple clinical presentation subsets (ie, asymptomatic, chronic symptomatic, chronic limb-threatening ischemia, and acute limb ischemia). METHODS: A comprehensive literature search was conducted from October 2020 to June 2022, encompassing studies, reviews, and other evidence conducted on human subjects that was published in English from PubMed, EMBASE, the Cochrane Library, CINHL Complete, and other selected databases relevant to this guideline. Additional relevant studies, published through May 2023 during the peer review process, were also considered by the writing committee and added to the evidence tables where appropriate. STRUCTURE: Recommendations from the "2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease" have been updated with new evidence to guide clinicians. In addition, new recommendations addressing comprehensive care for patients with peripheral artery disease have been developed.

Cardiology/Cardiovascular Research
Gupta RC, **Singh-Gupta V**, **Szekely KJ**, **Zhang K**, **Lanfear DE**, and **Sabbah HN**. Dysregulation of cardiac mitochondrial aldehyde dehydrogenase 2: Studies in dogs with chronic heart failure. *J Mol Cell Cardiol Plus* 2024; 8. PMID: 38938550. Full Text

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Mitochondrial (MITO) dysfunction occurs in the failing heart and contributes to worsening of heart failure (HF). Reduced aldehyde dehydrogenase 2 (ALDH2) in left ventricular (LV) myocardium of diabetic hearts has been implicated in MITO dysfunction through accumulation of toxic aldehydes including and elevated levels of 4-hydroxy-2-nonenal (4HNE). This study examined whether dysregulation of MITO ALDH2 (mALDH2) occurs in mitochondria of the failing LV and is associated with increased levels of 4HNE. LV tissue from 7 HF and 7 normal (NL) dogs was obtained. Protein quantification of total mitochondrial

ALDH2 (t-mALDH2), phosphorylated mALDH2 (p-mALDH2), total MITO protein kinase c epsilon (t-mPKCε), phosphorylated mPKCε (p-mPKCε) was performed by Western blotting, and total mALDH2 enzymatic activity was measured. Protein adducts of 4HNE-MITO and 4HNE-mALDH2 were also measured in MITO fraction by Western Blotting. Protein level of t-mALDH2 was decreased in HF compared with NL dogs (0.63 ± 0.07 vs 1.17 ± 0.08, $p < 0.05$) as did mALDH2 enzymatic activity (51.39 ± 3 vs. 107.66 ± 4 nmol NADH/min/mg, $p < 0.05$). Phosphorylated-mALDH2 and p-mPKCε were unchanged. 4HNE-MITO proteins adduct levels increased in HF compared with NL (2.45 ± 0.08 vs 1.30 ± 0.03 du, $p < 0.05$) as did adduct levels of 4HNE-mALDH2 (1.60 ± 0.20 vs 0.39 ± 0.08, $p < 0.05$). In isolated failing cardiomyocytes (CM) exposure to 4HNE decreased mALDH2 activity, increased ROS and 4HNE-ALDH2 adducts, and worsened MITO function. Stimulation of mALDH2 activity with ALDA-1 in isolated HF CMs compared to NL CMs improved ADP-stimulated respiration and maximal ATP synthesis to a greater extant (+47 % and +89 %, respectively). Down-regulation of mALDH2 protein levels and activity occurs in HF and contributes to MITO dysfunction and is likely caused by accumulation of 4HNE-mALDH2 adduct. Increasing mALDH2 activity (via ALDA-1) improved MITO function in failing CMs.

Cardiology/Cardiovascular Research

Hollis IB, Jennings DL, Krim S, Ton VK, Ducharme A, **Cowger J**, Looby M, Eulert-Green JJ, Bansal N, Horn E, Byku M, Katz J, Michaud CJ, Rajapreyar I, Campbell P, Vale C, Cosgrove R, Hernandez-Montfort J, Otero J, Ingemi A, Raj S, Weeks P, Agarwal R, Martinez ES, Tops LF, Ahmed MM, Kiskaddon A, Kremer J, Keebler M, and Ratnagiri RK. An ISHLT consensus statement on strategies to prevent and manage hemocompatibility related adverse events in patients with a durable, continuous-flow ventricular assist device. *J Heart Lung Transplant* 2024; Epub ahead of print. PMID: 38878021. Full Text

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Tufts Medical Center, Boston, Massachusetts.
Baptist Health Medical Center, Little Rock, Arkansas.
The Prince Charles Hospital, Chermside, Queensland, Australia.
Cornerstone Specialty Hospital/University of Arizona College of Pharmacy, Tucson, Arizona.
Baylor Scott and White Health for Central Texas and Greater Austin, Temple, Texas.
AdventHealth Littleton Hospital, Littleton, Colorado.
Sentara Norfolk General Hospital, Norfolk, Virginia.
NH Health, Bangalore, India.
Memorial Hermann-Texas Medical Center, Houston, Texas.
Duke University Medical Center, Durham, North Carolina.
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Life expectancy of patients with a durable, continuous-flow left ventricular assist device (CF-LVAD) continues to increase. Despite significant improvements in the delivery of care for patients with these devices, hemocompatability-related adverse events (HRAEs) are still a concern and contribute to significant morbility and mortality when they occur. As such, dissemination of current best evidence and practices is of critical importance. This ISHLT Consensus Statement is a summative assessment of the current literature on prevention and management of HRAEs through optimal management of oral anticoagulant and antiplatelet medications, parenteral anticoagulant medications, management of patients at high risk for HRAEs and those experiencing thrombotic or bleeding events, and device management outside of antithrombotic medications. This document is intended to assist clinicians caring for patients with a CF-LVAD provide the best care possible with respect to prevention and management of these events.

Cardiology/Cardiovascular Research

Miller J, **Cook B**, **Gandolfo C**, Mills NL, Mahler S, Levy P, **Parikh S**, **Krupp S**, **Nour K**, **Klausner H**, **Gindi R**, **Lewandowski A**, **Hudson M**, **Perrotta G**, **Zweig B**, **Lanfear D**, **Kim H**, Dangoulian S, **Tang A**, **Todter E**, **Khan A**, Keerie C, **Bole S**, **Nasseredine H**, **Oudeif A**, **Abou Asala E**, **Mohammed M**, **Kazem A**, **Malette K**, **Singh-Kucukarslan G**, Xu N, Wittenberg S, **Morton T**, **Gunaga S**, **Affas Z**, **Tabbaa K**, Desai P, **Alsaadi A**, **Mahmood S**, **Schock A**, **Konowitz N**, **Fuchs J**, **Joyce K**, Shamoun L, Babel J, Broome A, **Digiacinto G**, **Shaheen E**, **Darnell G**, **Muller G**, **Heath G**, **Bills G**, **Vieder J**, **Rockoff S**, **Kim B**, **Colucci A**, **Plemmons E**, and **McCord J**. Rapid Acute Coronary Syndrome Evaluation Over One Hour With High-Sensitivity Cardiac Troponin I: A United States-Based Stepped-Wedge, Randomized Trial. *Ann Emerg Med* 2024; Epub ahead of print. PMID: 38888531. Full Text

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STUDY OBJECTIVE: The real-world effectiveness and safety of a 0/1-hour accelerated protocol using high-sensitivity cardiac troponin (hs-cTn) to exclude myocardial infarction (MI) compared to routine care in the United States is uncertain. The objective was to compare a 0/1-hour accelerated protocol for evaluation of MI to a 0/3-hour standard care protocol. METHODS: The RACE-IT trial was a stepped-wedge, randomized trial across 9 emergency departments (EDs) that enrolled 32,609 patients evaluated for possible MI from July 2020 through April 2021. Patients undergoing high-sensitivity cardiac troponin I testing with concentrations less than or equal to 99th percentile were included. Patients who had MI excluded by the 0/1-hour protocol could be discharged from the ED. Patients in the standard care protocol had 0- and 3-hour troponin testing and application of a modified HEART score to be eligible for discharge. The primary endpoint was the proportion of patients discharged from the ED without 30-day death or MI. RESULTS: There were 13,505 and 19,104 patients evaluated in the standard care and accelerated protocol groups, respectively, of whom 19,152 (58.7%) were discharged directly from the ED. There was no significant difference in safe discharges between standard care and the accelerated protocol (59.5% vs 57.8%; adjusted odds ratio (aOR)=1.05, 95% confidence interval [CI] 0.95 to 1.16). At 30 days, there were 90 deaths or MIs with 38 (0.4%) in the standard care group and 52 (0.4%) in the accelerated protocol group (aOR=0.84, 95% CI 0.43 to 1.68). CONCLUSION: A 0/1-hour accelerated protocol using high-sensitivity cardiac troponin I did not lead to more safe ED discharges compared with standard care.

Cardiology/Cardiovascular Research

Sukul D, Albright J, Thompson MP, **Villablanca P**, **Keteyian SJ**, Yaser J, Berkompas D, DeLucia A, Patel HS, Chetcuti SJ, and Grossman PM. Predictors and Variation in Cardiac Rehabilitation Participation After Transcatheter Aortic Valve Replacement. *JACC Adv* 2023; 2(8):100581. PMID: 38938330. Full Text

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BACKGROUND: Cardiac rehabilitation (CR) is strongly recommended for a spectrum of cardiovascular conditions and procedures including aortic valve replacement. OBJECTIVES: The purpose of this study was to characterize patient and hospital factors associated with CR participation after transcatheter aortic valve replacement (TAVR) and determine which factors explain hospital-level variation in CR participation. METHODS: We linked clinical and administrative claims data from patients who underwent TAVR at 24 Michigan hospitals between January 1, 2016 and June 30, 2020 and obtained rates of CR enrollment within 90 days of discharge. Sequential mixed models were fit to evaluate hospital variation in 90-day post-TAVR CR participation. RESULTS: Among 3,372 patients, 30.6% participated in CR within 90-days after discharge. Several patient factors were negatively associated with CR participation after TAVR including older age, Medicaid insurance, atrial fibrillation/flutter, dialysis use, and slower baseline 5-m walk times. There was substantial hospital variation in CR participation after TAVR ranging from 5% to 60% across 24 hospitals. Patient case mix did not explain hospital variation in CR across hospitals with median OR numerically increasing from 2.11 (95% CI: 1.62-2.67) to 2.13 (95% CI: 1.61-2.68) after accounting for patient-level factors. CONCLUSIONS: Less than 1 in 3 patients who underwent TAVR in Michigan participated in CR within 90-days of discharge. Although several patient factors are associated with CR participation, hospital-level variation in CR participation after TAVR is not explained by patient case mix. Identifying hospital processes of care that promote CR participation after TAVR will be critical to improving CR participation after TAVR.

Cardiology/Cardiovascular Research

Terré JA, Torrado J, George I, Harari R, Cox-Alomar PR, **Villablanca PA**, Faillace RT, Granada JF, Dangas G, Garcia MJ, Latib A, and Wiley J. Aortic Stenosis Management in Patients With Acute Hip Fracture. *JACC Adv* 2024; 3(5):100912. PMID: 38939644. Full Text

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The treatment of severe aortic stenosis (SAS) has evolved rapidly with the advent of minimally invasive structural heart interventions. Transcatheter aortic valve replacement has allowed patients to undergo definitive SAS treatment achieving faster recovery rates compared to valve surgery. Not infrequently, patients are admitted/diagnosed with SAS after a fall associated with a hip fracture (HFx). While urgent

orthopedic surgery is key to reduce disability and mortality, untreated SAS increases the perioperative risk and precludes physical recovery. There is no consensus on what the best strategy is either hip correction under hemodynamic monitoring followed by valve replacement or preoperative balloon aortic valvuloplasty to allow HFx surgery followed by valve replacement. However, preoperative minimalist transcatheter aortic valve replacement may represent an attractive strategy for selected patients. We provide a management pathway that emphasizes an early multidisciplinary approach to optimize time for hip surgery to improve orthopedic and cardiovascular outcomes in patients presenting with HFx-SAS.

Center for Health Policy and Health Services Research

Berkowitz JL, Kennedy KF, Font C, **Nerenz DR**, Abbott JD, and **Aronow HD**. Limited English proficiency, cardiovascular risk factors, cardiovascular disease, and in-hospital COVID-19 outcomes. *Am J Manag Care* 2024; 30(6):251-256. PMID: 38912951. Full Text

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OBJECTIVES: Cardiovascular risk factors and history of cardiovascular disease are associated with greater morbidity and mortality in patients hospitalized with COVID-19. Limited English proficiency (LEP) has also been associated with worse outcomes in this setting, including requiring intensive care unit (ICU) level of care and in-hospital death. Whether non-English-language preference (NELP) modifies the association between cardiovascular risk factors or disease and outcomes in patients hospitalized with COVID-19 is unknown. STUDY DESIGN: Retrospective cohort study of adult patients admitted to a large New England health system between March 1 and December 31, 2020, who tested positive for COVID-19. NELP was defined as having a preferred language that was not English noted in the electronic health record. METHODS: Cardiovascular risk factors, history of cardiovascular disease, and NELP were related to the primary composite clinical outcome-death or ICU admission-using multivariable binary logistic regression adjusted for demographic and clinical characteristics. Interaction terms for NELP and model covariates were evaluated. RESULTS: Of 3582 patients hospitalized with COVID-19, 1024 (28.6%) had NELP; 812 (79.3%) of the patients with NELP received interpreter services. Death or ICU admission occurred in 794 (22.2%) of the hospitalized patients. NELP was not significantly associated with the primary composite outcome in unadjusted or adjusted analyses. In the adjusted analyses, only male gender, coronary artery disease, pulmonary circulatory disease, and liver disease significantly predicted the primary outcome. NELP did not modify the effect of these associations. CONCLUSIONS: NELP was not significantly associated with odds of death or ICU admission, nor did it modify the association between cardiovascular risk factors or history of cardiovascular disease and this composite outcome. Because most patients with NELP received interpreter services, these findings may support the role of such services in ensuring equitable outcomes.

Center for Health Policy and Health Services Research

Bobb JF, Idu AE, Qiu H, Yu O, Boudreau DM, Wartko PD, Matthews AG, McCormack J, Lee AK, Campbell CI, Saxon AJ, Liu DS, Altschuler A, Samet JH, Northrup TF, **Braciszewski JM**, Murphy MT, Arnsten JH, Cunningham CO, Horigian VE, Szapocznik J, Glass JE, Caldeiro RM, Tsui JI, Burganowski RP, Weinstein ZM, Murphy SM, Hyun N, and Bradley KA. Offering nurse care management for opioid use disorder in primary care: Impact on emergency and hospital utilization in a cluster-randomized implementation trial. *Drug Alcohol Depend* 2024; 261:111350. PMID: 38875880. Full Text

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BACKGROUND: Patients with opioid use disorder (OUD) have increased emergency and hospital utilization. The PROUD trial showed that implementation of office-based addiction treatment (OBAT) increased OUD medication treatment compared to usual care, but did not decrease acute care utilization in patients with OUD documented pre-randomization (clinicaltrials.gov/study/NCT03407638). This paper reports secondary emergency and hospital utilization outcomes in patients with documented OUD in the PROUD trial. METHODS: This cluster-randomized implementation trial was conducted in 12 clinics from 6 diverse health systems (March 2015-February 2020). Patients who visited trial clinics and had an OUD diagnosis within 3 years pre-randomization were included in primary analyses; secondary analyses added patients with OUD who were new to the clinic or with newly-documented OUD post-randomization. Outcomes included days of emergency care and hospital utilization over 2 years post-randomization. Explanatory outcomes included measures of OUD treatment. Patient-level analyses used mixed-effect regression with clinic-specific random intercepts. RESULTS: Among 1988 patients with documented OUD seen pre-randomization (mean age 49, 53 % female), days of emergency care or hospitalization did not differ between intervention and usual care; OUD treatment also did not differ. In secondary analyses among 1347 patients with OUD post-randomization, there remained no difference in emergency or hospital utilization despite intervention patients receiving 32.2 (95 % CI 4.7, 59.7) more days of OUD treatment relative to usual care. CONCLUSIONS: Implementation of OBAT did not reduce emergency or hospital utilization among patients with OUD, even in the sample with OUD first documented post-randomization in whom the intervention increased treatment.

Center for Health Policy and Health Services Research

Haley EN, Dolbier CL, Campbell LC, Carels RA, and **Braciszewski JM**. Brief Self-Compassion Intervention for Women of Higher Weight and Internalized Weight Bias: A Randomized Pilot Study. *Int J Behav Med* 2024; Epub ahead of print. PMID: 38839712. Request Article

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BACKGROUND: Internalized weight bias (IWB) negatively impacts mental and physical health, and disproportionately affects women of higher weight. Although self-compassion training may be advantageous for reducing IWB and associated sequalae, further examination of its clinical significance and cultural acceptability is warranted. METHOD: A randomized pilot study was conducted to evaluate the feasibility, including cultural acceptability, and clinical significance of a 3-session self-compassion intervention (SCI) for women with IWB. Women with BMIs of > 25 and IWB (N = 34) were randomly

assigned to the SCI or a waitlist control group. Participants completed pre, post, and 1-month follow-up surveys on IWB, self-compassion, body image, eating behaviors, physical activity, and affect. Analyses of covariance were employed and percentages of change were calculated to examine post-intervention between-group differences in outcomes. Cultural acceptability was evaluated through participants' ratings of the perceived inclusivity and relevancy of the SCI. RESULTS: There were 59% (n = 10) and 47% (n = 8) completion rates in the SCI and waitlist control groups, respectively. Compared to the waitlist control group, SCI participants reported greater pre-post improvements in self-compassion, IWB, body shame and surveillance, uncontrolled eating, and physical activity with medium to large effect sizes, and emotional eating with small effects. The SCI was perceived to be beneficial overall, and cultural acceptability ratings were mostly favorable despite individual differences. CONCLUSION: This brief SCI may be beneficial for women impacted by weight stigma and IWB. Attention to increased diversity and cultural acceptability is warranted in future trials.

Center for Health Policy and Health Services Research
Kahn GD, **Lockhart E**, Simon GE, Owen-Smith AA, Rossom RC, Beck AL, Lynch FL, Daida YG, Lu CY, Waring S, **Yeh HH**, and **Ahmedani BK**. Recorded Diagnosis of Gender Identity Disorder Is Strongly Associated with Suicide Mortality. *Transgend Health* 2023. PMID: Full Text

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We assessed the association between gender identity disorder (GID) diagnosis and suicide in a retrospective case-control study (N = 300,364) from nine health care systems between 2000 and 2015. Adjusting for age and sex, the odds ratio for GID was 18.6 (95% confidence interval 7.0-49.5). Adjusting additionally for comorbid psychiatric diagnoses, the odds ratio was 4.75 (1.78-12.68), higher than depressive (3.96, 3.64-4.31), alcohol use (3.42, 3.04-3.84), bipolar (2.42, 2.10-2.80), and psychotic disorders (1.44, 1.22-1.70). These U.S. data support prior research demonstrating increased suicide risk among patients with diagnosed GID, who may benefit from targeted screening and intervention within health care systems.

Center for Health Policy and Health Services Research
Lockhart E, Turner D, Guastaferro K, Szalacha LA, Alzate HT, Marhefka S, **Pittiglio B**, **Dekker M**, **Yeh HH**, **Zelenak L**, **Toney J**, **Manogue S**, and **Ahmedani BK**. Increasing pre-exposure prophylaxis (PrEP) in primary care: A study protocol for a multi-level intervention using the multiphase optimization strategy (MOST) framework. *Contemp Clin Trials* 2024; 143:107599. PMID: 38848935. Full Text

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BACKGROUND: In the United States, over 1.2 million people are living with HIV. This disease disproportionately affects men who have sex with men (MSM), people of color, youth and young adults, and transgender individuals. Pre-exposure prophylaxis (PrEP) is an effective HIV prevention method. Barriers exist for both primary care providers (PCPs) to prescribe PrEP and prevent patients from initiating PrEP. METHODS: This study, MOST: PrEP, follows the multiphase optimization strategy (MOST) framework. The purpose is to identify a multi-level intervention among patients and PCPs to increase PrEP prescriptions in primary care. First, feedback will be obtained from providers and patients via focus groups, then, suggestions related to the context-specific (provider and individual level) factors of intervention component delivery will be incorporated. Subsequently, a rigorous experiment will be conducted using a 2(4) factorial design focusing on priority populations for PrEP initiation. Provider components include computer-based simulation training and a best practice alert. Patient components include a tailored PrEP educational video and HIV risk assessment. Finally, the facilitators and barriers to implementing the intervention components will be qualitatively examined. CONCLUSION: In this protocol paper, we describe the one of the first known multilevel MOST optimization trial in healthcare. Intervention components are to be delivered to patients and providers in a large healthcare system, based in an HIV Ending the Epidemic priority jurisdiction. If effective, this multi-level approach could be disseminated to providers and patients in other large healthcare systems to make a significant impact on HIV prevention.

Center for Health Policy and Health Services Research
Murray MF, **Pearl ES**, **Zelenak L**, **Hamann A**, **Sehgal M**, **Braciszewski JM**, **Carlin AM**, and **Miller-Matero LR**. COVID-19-Related Increases in Depressive and Anxious Symptoms Are Associated with Maladaptive Eating Among Patients up to 4 years Post-bariatric Surgery. *Obes Surg* 2024; Epub ahead of print. PMID: 38839635. Full Text

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INTRODUCTION: Depressive and anxious symptoms and maladaptive eating behaviors fluctuate with stressful events for patients seeking bariatric surgery. These associations are less clear for patients postoperatively. Using the COVID-19 pandemic as a frame, we examined associations between changes in depressive and anxious symptoms and maladaptive eating behaviors between up to four years postoperatively. METHODS: Participants (N = 703) who underwent surgery between 2018 and 2021 completed web-based questionnaires between 2021 and 2022. Demographic and surgical data were obtained from electronic health records. Participants reported whether depressive and anxious symptoms increased or were stable/decreased during the COVID-19 pandemic, and completed eating behavior measures. RESULTS: Many participants reported increased depressive (27.5%) and anxious (33.7%) symptoms during the COVID-19 pandemic. Compared to those who reported stable or decreased symptoms, these participants were as follows: (1) more likely to endorse presence of binge, loss-of-control, graze, and night eating; (2) reported higher emotional eating in response to anger and frustration, depression, and anxiety; and (3) reported higher driven and compulsive eating behaviors. Frequency of binge, loss-of-control, graze, and night eating episodes did not differ between groups (e.g., increased vs. stable/decreased anxious symptoms) among participants who endorsed any episodes. CONCLUSION: A large portion of the sample reported increased depressive and anxious symptoms during the COVID-19

pandemic, and these increases were associated with maladaptive eating behaviors. Depressive and anxious symptoms and eating behaviors should be assessed postoperatively as significant stressors may be associated with increased distress and maladaptive eating behaviors that can affect postoperative outcomes. Postoperative interventions may be useful at simultaneously targeting these concerns.

Center for Health Policy and Health Services Research
Poland CA, Shadur JM, Cinader M, and **Felton JW**. Co-Locating Obstetrics and Addiction Medicine Clinics to Improve Attendance in Services for Pregnant People with Opioid Use Disorder. *Psychiatr Res Clin Pract* 2024; 6(2):36-41. PMID: 38854870. Full Text

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OBJECTIVE: Pregnant people receiving treatment for opioid use disorders (OUD) are at significant risk of return to use during the postpartum period. Recently, practice groups and other national organizations have called for the co-location of addiction medicine and obstetric care to reduce the burden on pregnant and postpartum people with OUD associated with engaging in treatment. This paper examines the effectiveness of co-locating services in retaining pregnant people with OUD in care following childbirth. METHODS: A records review of pregnant people receiving medication for OUD between 2012 and 2017 in stand-alone addiction medicine clinic (n = 23) and from 2017 to 2021 following the creation of an integrated addiction medicine-obstetric care clinic (n = 67) was conducted to compared rates of attendance in both obstetric and addiction medicine services. RESULTS: Findings from this study suggest that individuals receiving services in a co-located clinic had significantly fewer missed appointments during the postpartum period relative to individuals who sought care at separate addiction medicine and obstetric care clinics. CONCLUSIONS: Results from this study support the potential for co-locating clinics to reduce barriers to accessing obstetric and addiction medicine services, as well as support continued attendance in care across a vulnerable period.

Center for Health Policy and Health Services Research
Sullivan MD, Wilson L, Amick M, **Miller-Matero LR**, Chrusciel T, Salas J, **Zabel C**, Lustman PJ, **Ahmedani B**, Carpenter RW, and Scherrer JF. Social support and the association between post-traumatic stress disorder and risk for long-term prescription opioid use. *Pain* 2024; Epub ahead of print. PMID: 38833573. Full Text

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Post-traumatic stress disorder (PTSD) is common in patients with chronic pain, adversely affects chronic pain outcomes, and is associated with opioid use and adverse opioid outcomes. Social support is a robust predictor of PTSD incidence and course as well as chronic pain outcome. We determined whether

the association between PTSD and persistent opioid use was modified by emotional support in a cohort of patients receiving opioids for noncancer pain. Eligible participants were ≥18 years and had completed a new period of prescription opioid use lasting 30 to 90 days. Bivariate associations between cohort characteristics and each key variable was assessed using $\chi 2$ tests for categorical variables and t-tests for continuous variables. Interaction between PTSD and emotional support was assessed by a priori stratification on low vs high emotional support. Participants (n = 808) were 53.6 (SD ± 11.6) years of age, 69.8% female, 69.6% White, and 26.4% African American. Overall, 17.2% had probable PTSD. High emotional support was significantly ($P < 0.0001$) more common among those without probable PTSD. Prescription opioid use at 6-month follow-up was significantly ($P = 0.0368$) more common among patients with vs without probable PTSD. In fully adjusted models, PTSD was no longer associated with opioid use at 6-month follow-up among participants with high emotional support. Among those with lower emotional support, PTSD was significantly associated with opioid use at 6-month follow-up in unadjusted (odds ratio = 2.40; 95% confidence interval: 1.24-4.64) and adjusted models (odds ratio = 2.39; 95% confidence interval: 1.14-4.99). Results point to the hypothesis that improvement of emotional support in vulnerable patients with chronic pain and PTSD may help reduce sustained opioid use.

Center for Health Policy and Health Services Research

Vanderziel A, Maslovich MM, and Alshaarawy O. A feasibility study to assess the recruitment and retention of pregnant patients who regularly use cannabis. *BMC Res Notes* 2024; 17(1):177. PMID: 38918795. Full Text

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OBJECTIVE: To assess first-trimester recruitment and retention of pregnant patients who regularly used cannabis, but not other substances, measured by willingness to participate in a research study, completion of self-administered electronic questionnaires, and willingness to provide urine samples during each trimester of pregnancy. We designed and launched a prospective feasibility study titled, Cannabis Legalization in Michigan (CALM) - Maternal & Infant Health (MIH), in two Michigan clinics after the recreational use of cannabis became legal for adults 21 years and older. RESULTS: Over half (52%) of patients asked to participate in CALM-MIH were consented to the study. Two-thirds (66%) of screened patients initiated prenatal care during their first trimester of pregnancy and 50% used cannabis, of which the majority did not concurrently use other substances. Of those recruited into the prospective study, all participants completed the first-trimester questionnaire and provided urine samples. Study retention was 80% and all participants who completed follow-up assessments were willing to provide urine samples.

Clinical Quality and Safety

Suleyman G, **McCormick ME**, **McLenon N**, **Chami E**, **Pollak E**, and **Dabaja AA**. Urinary catheter alleviation navigator protocol (UCANP): Update to the hospital-wide implementation at a single tertiary health care center. *Am J Infect Control* 2024; Epub ahead of print. PMID: 38876167. Full Text

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BACKGROUND: Catheter-associated urinary tract infections (CAUTIs) are commonly reported healthcare-associated infections. It was demonstrated that the urinary catheter alleviation navigator protocol (UCANP) pilot resulted in a reduction of catheter utilization and catheter days. METHODS:

Quality improvement initiative that was implemented at a single urban, tertiary health care center, focusing on early discontinuation of indwelling urinary catheters (IUC) and avoidance of reinsertion. Protocol was expanded hospital-wide September 2020-April 2022. We compared IUC utilization, IUC standardized utilization ratio (SUR) and CAUTI standardized infection ratio (SIR) in the pre-intervention period (March 2020-August 2020) to the post-intervention period (May 2022-October 2022). RESULTS: Pre-implementation, 2 patients with IUC removal were placed on UCANP. Post-implementation, 835 (45%) patients with IUC removal participated in the protocol. Number of patients requiring IUC reinsertion did not differ among the 2 groups. IUC utilization was significantly decreased from 0.28 to 0.24 with 14% reduction (p=0.025). SUR decreased by 11% from 0.778 to 0.693 (p=0.007) and SIR by 84% from 0.311 to 0.049 (p=0.009). CONCLUSION: Our protocol significantly reduced IUC utilization and SUR after hospital-wide implementation. UCANP is a safe and effective strategy that can potentially decrease unnecessary IUCs in patients with transient urinary retention.

Dermatology

Armstrong AW, Reddy R, Khan S, Chovatiya R, Green L, **Gold LS**, Kwong P, Lebwohl M, and Kircik L. Consensus Statements on the Use of Corticosteroid-Containing Topical Medications in Psoriasis. *J Drugs Dermatol* 2023; 22(8):736-741. PMID: 37556522. Request Article

This article aims to provide consensus statements on the use of corticosteroid-containing topical medications for the management of psoriasis. This Psoriasis Expert Group (PEG) includes dermatologist voting members with expertise in psoriasis who convened and evaluated the use of topical medications and previously published guidelines. A modified Delphi process was conducted to reach consensus results. Two rounds of voting were conducted for each topic and panel consensus was determined. Nine statements were developed regarding topical medication efficacy, patient quality of life, frequency of application, medication "feel", and safety and tolerability. Dermatologist experts voted on the statements separately. Patients were not polled. All items received agreement: 15 with high consensus and 1 with moderate consensus. For the treatment of psoriasis, the PEG agreed that patients and physicians prefer topical medications that are effective, provide long-lasting results, have a quick onset of action, and "feel good on the skin" with few adverse effects. The developed consensus statements provide guidance on the topical treatment of psoriasis, including combination therapies, such as a vitamin D and topical corticosteroid analog. These recommendations will be continuously reviewed and updated as more evidence continues to emerge. April W. Armstrong AW, Reddy R, Khan S, et al. Consensus statements on the use of corticosteroid-containing topical medications in psoriasis. J Drugs Dermatol. 2023;22(8):736-741. doi:10.36849/JDD.7453.

Dermatology

Bouazzi D, Andersen RK, Vinding GR, Medianfar CE, Nielsen SM, Saunte DML, Chandran NS, van der Zee HH, Zouboulis CC, Benhadou F, Villumsen B, Alavi A, Ibekwe PU, **Hamzavi IH**, Ingram JR, Naik HB, Garg A, Boer J, Christensen R, and Jemec GBE. The Global Hidradenitis Suppurativa Atlas Methodology: Combining Global Proportions in a Pooled Analysis. *Dermatology* 2024; 240(3):369-375. PMID: 38354718. Request Article

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INTRODUCTION: Data concerning the global burden of hidradenitis suppurativa (HS) are limited. Reported prevalence estimates vary between 0.0003% and 4.1%, and data from various geographical regions are still to be collected. Previously reported prevalences have been limited by the methodological approach and source of data. This has resulted in great heterogeneity as prevalence data from physician-diagnosed cases poorly match those of self-reported apparent HS disease. METHODS: The Global Hidradenitis Suppurativa Atlas (GHiSA) introduces an innovative approach to determine the global prevalence of HS. This approach involves using a previously validated questionnaire to screen apparently healthy adults accompanying a patient to a non-dermatological outpatient clinic visit in a hospital or a private/family medicine clinic. The screening questionnaire (i.e., the index test) is combined with a subsequent physician-based in-person validation (i.e., the reference standard) of the participants who screen positive. Approximately ten percent of the screen-negative participants are also clinically assessed to verify the diagnostic precision of the test. The local prevalence (pi) will be estimated from each country that submits the number of patients who are HS positive according to the index test and clinical examination (n), and the corresponding total number of observations (N). CONCLUSION: The GHiSA Global Prevalence studies are currently running simultaneously in 58 countries across six continents (Africa, Europe, Australia, North America, South America, and Asia). The goal of the combined global proportion is the generation of a single summary (i.e., proportional meta-analysis), which will be done after a logit transformation and synthesized using a random-effects model. The novel standardization of the Global Prevalence Studies conducted through GHiSA enables direct international comparisons, which were previously not possible due to substantial heterogeneity in past HS prevalence studies.

Dermatology

Dreno B, Passeron T, Puig S, **Lim HW**, Goh CL, Kang HY, Ly F, Morita A, Ocampo-Candiani J, Schalka S, Wei L, Demessant AL, Le Floc'h C, Kerob D, and Krutmann J. Are people more concerned about photoaging than skin cancer when raising awareness about risks of skin exposure? *Clin Exp Dermatol* 2024; Epub ahead of print. PMID: 38838203. Full Text

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Dermatology
Lyons AB, **Karim MS**, and **Mohammad TF**. Fragmented Facial Flushing: A Quiz. *Acta Derm Venereol* 2024; 104:adv40665. PMID: 38850054. Full Text

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Dermatology
Masson R, Seivright J, Grogan T, Atluri S, **Hamzavi I**, Hogeling M, Shi VY, and Hsiao JL. Ustekinumab in Hidradenitis Suppurativa: A Systematic Review and Meta-analysis. *Dermatol Ther (Heidelb)* 2024; Epub ahead of print. PMID: 38907878. Full Text

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INTRODUCTION: Hidradenitis suppurativa (HS) is a frequently debilitating, inflammatory skin condition. Patients may have a limited response to adalimumab, currently the only Food and Drug Administration (FDA)-approved biologic treatment for HS. Ustekinumab is an interleukin-12/23 inhibitor that has been utilized in HS, but there is a lack of an updated systematic review on its efficacy and safety. The aim of this study is to perform a systematic review and meta-analysis of the literature on the efficacy and safety of ustekinumab for HS. METHODS: In October 2022, MEDLINE and Embase databases were searched for articles on ustekinumab in HS. Data extraction was performed on relevant articles by two reviewers. The primary study outcome was the pooled response rate of HS to ustekinumab. A fixed-effects meta-analysis was performed, and Cochran's Q statistic and I squared index were used to assess heterogeneity. Statistical significance was determined at $p < 0.05$. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors. RESULTS: From 2012 to 2022, ten articles (nine case series and one prospective trial) with 88 patients met the inclusion criteria. Patients with reported disease severity had Hurley stage II (17.6%, 12/68) or III (82.4%, 56/68) disease. The majority (80.7%, 71/88) had previously failed at least one biologic treatment. A meta-analysis of all ten studies showed a pooled response rate of 67% (95% CI 0.57-0.76). Study limitations include a small number of patients and randomized controlled trials (RCTs). CONCLUSIONS: Ustekinumab may be a helpful treatment option to consider for HS that is recalcitrant to first-line biologic therapies, but RCTs are needed to determine optimal dosing regimens and the specific patient populations that would benefit the most from this agent.

Dermatology
Novice T, **Vellaichamy G**, McCalmont TH, and Moesch J. Cutaneous "Microcystic" Microsecretory Adenocarcinoma With Marked Adnexal Hyperplasia: A Simulant of Microcystic Adnexal Carcinoma. *Am J Dermatopathol* 2024; Epub ahead of print. PMID: 38941552. Full Text

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Microsecretory adenocarcinoma (MSA) was first described in 2019 as a low-grade salivary gland neoplasm of intraoral origin with distinct histopathologic features and a characteristic MEF2C::SS18 fusion. Recently, skin was also identified as a primary site for MSA in a report by Bishop et al. Due to its rarity and resemblance to other adnexal tumors, MSA is a challenging diagnosis. Herein, we present a case of cutaneous MSA that was unique for the presence of a significant microcystic component and marked adnexal hyperplasia, which mimicked myxoid microcystic adnexal carcinoma (MAC). A 58-year-old presented with a 1 year history of an enlarging eyelid nodule. Histopathologic analysis revealed dermal tumor composed of small tubules containing inspissated bluish mucinous material. Accompanying marked adnexal hyperplasia and many microcysts were also present. Tumor cells expressed S100 protein, which is distinct from MAC, while p63 immunohistochemistry showed marked loss of myoepithelial labeling, as is common in primary adenocarcinomas. Next generation gene sequencing detected the characteristic MSA fusion protein MEF2c::SS18. We report a novel presentation of MSA that simulated MAC because of the presence of associated microcystic change. The presence of S100 immunopositivity and the identification of MEF2C::SS18 fusion confirmed the diagnosis of cutaneous MSA.

Dermatology
Passeron T, Ezzedine K, **Hamzavi I**, van Geel N, Schlosser BJ, Wu X, Huang X, Soliman AM, Rosmarin D, Harris JE, Camp HS, and Pandya AG. Once-daily upadacitinib versus placebo in adults with extensive non-segmental vitiligo: a phase 2, multicentre, randomised, double-blind, placebo-controlled, dose-ranging study. *EClinicalMedicine* 2024; 73:102655. PMID: 38873632. Full Text

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BACKGROUND: Janus kinase (JAK) inhibition is a promising approach for treating vitiligo. We aimed to assess the efficacy and safety of upadacitinib, an oral selective JAK inhibitor, in adults with non-segmental vitiligo. METHODS: This was a phase 2, multicentre, randomised, double-blind, placebo-controlled, dose-ranging study completed at 33 clinical centres in the United States, Canada, France, and Japan. Eligible patients were aged 18-65 years with non-segmental vitiligo and had a Facial Vitiligo Area Scoring Index (F-VASI) ≥0.5 and a Total Vitiligo Area Scoring Index (T-VASI) ≥5. Patients were randomly assigned (2:2:2:1:1) using an interactive response technology to receive upadacitinib 6 mg (UPA6), upadacitinib 11 mg (UPA11), upadacitinib 22 mg (UPA22), or placebo (PBO; preassigned to switch to either UPA11 or UPA22 in period 2) once daily for 24 weeks (period 1). For weeks 24-52 (period 2), patients randomly assigned to upadacitinib continued their treatment, and patients receiving PBO switched to their preassigned upadacitinib dose in a blinded fashion. The primary endpoint was the percent change from baseline in F-VASI at week 24. Efficacy was analysed in the intention-to-treat population, and safety was examined in all randomly assigned patients who received at least one dose of study drug. This study is registered with ClinicalTrials.gov, number NCT04927975. FINDINGS: Between June 16, 2021, and June 27, 2022, 185 patients (including 115 [62%] who were female and 70 [38%] who were male) were randomly assigned to UPA6 (n = 49), UPA11 (n = 47), UPA22 (n = 43), or PBO (n = 46).

At week 24, the LS mean difference versus PBO in the percent change from baseline in F-VASI was -7.60 (95% CI -22.18 to 6.97; p = 0.3037) for UPA6, -21.27 (95% CI -36.02 to -6.52; p = 0.0051) for UPA11, and -19.60 (95% CI -35.04 to -4.16; p = 0.0132) for UPA22. The LS mean difference versus PBO in the percent change from baseline in T-VASI was -7.45 (95% CI -16.86 to 1.96; p = 0.1198) for UPA6, -10.84 (95% CI -20.37 to -1.32; p = 0.0259) for UPA11 and -14.27 (95% CI -24.24 to -4.30; p = 0.0053) for UPA22. Ongoing treatment with upadacitinib induced continuous skin repigmentation over time without reaching a plateau through week 52. The rates for study drug discontinuation and serious treatment-emergent adverse events (TEAEs) were higher in the UPA22 group than in the UPA11 and UPA6 groups. Eight serious TEAEs, including one death of unknown cause and one case of infiltrating lobular breast carcinoma, were reported through 52 weeks; only two serious TEAEs (coronary artery arteriosclerosis [UPA6 (n = 1)] and non-fatal ischemic stroke [UPA11 (n = 1)]) were deemed by the investigator to have a reasonable possibility of being related to study drug. The one case of breast cancer in the UPA11 group was deemed unrelated to study drug, and the one death of unknown cause in the UPA22 group was reviewed and adjudicated and was deemed to be unrelated to study drug. The most common TEAEs were COVID-19, headache, acne, and fatigue. No new safety signals were observed. INTERPRETATION: Upadacitinib monotherapy led to substantial repigmentation of both facial and total body vitiligo lesions and may offer an effective treatment option for adults with extensive non-segmental vitiligo. Based on these findings, upadacitinib 15 mg is being investigated in adults and adolescents with non-segmental vitiligo in an ongoing phase 3 randomised controlled trial. FUNDING: AbbVie Inc.

Dermatology

Sampath AJ, Westerkam LL, Blum FR, Alhusayen R, Bechara FG, Caffrey J, Carmona-Rivera C, Chandran NS, George R, Goldberg SR, Gudjonsson JE, Hansen SL, Ingram JR, Kirby B, Marzano AV, Matusiak Ł, Orgill DP, Prens E, van der Zee HH, van Straalen KR, Zouboulis CC, Byrd AS, Frew JW, Anne Lowes M, Naik HB, Sokumbi O, **Mi QS**, Miedema JR, Googe PB, and Sayed CJ. Standardized Protocols for Clinical and Histopathological Characterization of Hidradenitis Suppurativa Tissue Specimens. *J Invest Dermatol* 2024; Epub ahead of print. PMID: 38901775. Full Text

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Methods for describing and reporting the clinical and histological characteristics of cutaneous tissue samples from patients with hidradenitis suppurativa (HS) are not currently standardized, limiting clinicians' and scientists' ability to uniformly record, report, and communicate about the characteristics of tissue used in translational experiments. A recently published consensus statement outlined morphological definitions of typical HS lesions, but no consensus has been reached regarding clinical characterization and examination of HS tissue samples. Here we aimed to establish a protocol for reporting histopathologic and clinical characteristics of HS tissue specimens. This study was conducted from May 2023 to August 2023. Experts in clinical care, dermatopathology, and translational research were recruited, and a modified Delphi technique was used to develop a protocol for histologic reporting and clinical characterization of submitted tissue specimens from HS patients. A total of 27 experts participated (14 dermatologists, 3 fellowship-trained dermatopathologists, 3 plastic surgeons, 3 general surgeons, and 4 research scientists) in creating and reviewing protocols for the clinical and histopathological examination of HS tissue specimens. The protocols were formatted as a synoptic report and will help consistently classify specimens in biobanks based on histological features and more accurately report and select samples used in translational research projects.

Dermatology
Shivaram K, **Edwards K**, and **Mohammad TF**. An update on the safety of hydroquinone. *Arch Dermatol Res* 2024; 316(7):378. PMID: 38850450. Full Text

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Hydroquinone has been used for years for multiple conditions, including melasma, post-inflammatory hyperpigmentation, dyschromia from photoaging, and solar lentigines. It is known to be a very effective lightening agent, but several concerns have been raised about this widely used agent. The recent U.S. ban on over-the-counter skin lightening products containing hydroquinone has prompted further questioning of the safety of this widely used agent. While there have been prior informative, large-scale reviews on the safety of hydroquinone, new findings have since been reported. Here, we provide an updated review of studies published in the past 15 years on hydroquinone safety.

Dermatology
Xue GR, **Hamzavi IH**, **Kohli I**, and **Mohammad TF**. Challenges of tinted sunscreen in skin of color. *Int J Dermatol* 2024. PMID: Not assigned. Full Text

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Emergency Medicine
Chaudhary AJ, **Joyce KM**, **Haq K**, Qureshi MH, and **Donthireddy V**. Non-alcoholic Wernicke's Encephalopathy Masquerading As CNS Relapse of Acute Myeloid Leukemia. *Cureus* 2024; 16(5):e61184. PMID: 38933646. Request Article

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While Wernicke's encephalopathy (WE) is mostly caused by thiamine deficiency secondary to chronic alcohol use, other conditions that may affect one's nutritional status, such as bariatric surgery, hyperemesis gravidarum, chronic gastrointestinal disease, HIV/AIDS, and certain malignancies, may also lead to this outcome. We are discussing one such case, WE, in a young man with acute myeloid leukemia (AML) who underwent chemotherapy. The patient presented with blurred vision, paresthesia, weakness, and vomiting. Although he denied alcohol abuse, his symptoms, physical exam findings, and MRI results were consistent with WE. Treatment with thiamine resulted in a significant improvement in his visual disturbances and mental status. The authors highlight the importance of recognizing WE in non-alcoholic patients, particularly those undergoing prolonged hospitalization and chemotherapy, as nutritional deficiencies can develop. They recommend thiamine supplementation for patients receiving chemotherapy and those with poor oral intake. The case underscores the need for high clinical suspicion and early intervention in atypical cases of WE.

Emergency Medicine

Dugar SP, **Jayaprakash N**, Reilkoff R, and Duggal A. Hospital-onset sepsis: Why the brouhaha? *Chest Physician* 2024; 19(6):16-17. PMID: Not assigned. Full Text.

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Emergency Medicine

Miller J, **Cook B**, **Gandolfo C**, Mills NL, Mahler S, Levy P, **Parikh S**, **Krupp S**, **Nour K**, **Klausner H**, **Gindi R**, **Lewandowski A**, **Hudson M**, **Perrotta G**, **Zweig B**, **Lanfear D**, **Kim H**, Dangoulian S, **Tang A**, **Todter E**, **Khan A**, Keerie C, **Bole S**, **Nasseredine H**, **Oudeif A**, **Abou Asala E**, **Mohammed M**, **Kazem A**, **Malette K**, **Singh-Kucukarslan G**, Xu N, Wittenberg S, **Morton T**, **Gunaga S**, **Affas Z**, **Tabbaa K**, Desai P, **Alsaadi A**, **Mahmood S**, **Schock A**, **Konowitz N**, **Fuchs J**, **Joyce K**, Shamoun L, Babel J, Broome A, **Digiacinto G**, **Shaheen E**, **Darnell G**, **Muller G**, **Heath G**, **Bills G**, **Vieder J**, **Rockoff S**, **Kim B**, **Colucci A**, **Plemmons E**, and **McCord J**. Rapid Acute Coronary Syndrome Evaluation Over One Hour With High-Sensitivity Cardiac Troponin I: A United States-Based Stepped-Wedge, Randomized Trial. *Ann Emerg Med* 2024; Epub ahead of print. PMID: 38888531. Full Text

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STUDY OBJECTIVE: The real-world effectiveness and safety of a 0/1-hour accelerated protocol using high-sensitivity cardiac troponin (hs-cTn) to exclude myocardial infarction (MI) compared to routine care in the United States is uncertain. The objective was to compare a 0/1-hour accelerated protocol for evaluation of MI to a 0/3-hour standard care protocol. METHODS: The RACE-IT trial was a stepped-wedge, randomized trial across 9 emergency departments (EDs) that enrolled 32,609 patients evaluated

for possible MI from July 2020 through April 2021. Patients undergoing high-sensitivity cardiac troponin I testing with concentrations less than or equal to 99th percentile were included. Patients who had MI excluded by the 0/1-hour protocol could be discharged from the ED. Patients in the standard care protocol had 0- and 3-hour troponin testing and application of a modified HEART score to be eligible for discharge. The primary endpoint was the proportion of patients discharged from the ED without 30-day death or MI. RESULTS: There were 13,505 and 19,104 patients evaluated in the standard care and accelerated protocol groups, respectively, of whom 19,152 (58.7%) were discharged directly from the ED. There was no significant difference in safe discharges between standard care and the accelerated protocol (59.5% vs 57.8%; adjusted odds ratio (aOR)=1.05, 95% confidence interval [CI] 0.95 to 1.16). At 30 days, there were 90 deaths or MIs with 38 (0.4%) in the standard care group and 52 (0.4%) in the accelerated protocol group (aOR=0.84, 95% CI 0.43 to 1.68). CONCLUSION: A 0/1-hour accelerated protocol using high-sensitivity cardiac troponin I did not lead to more safe ED discharges compared with standard care.

Emergency Medicine

Seligowski AV, Harnett NG, Ellis RA, Grasser LR, Hanif M, Wiltshire C, Ely TD, Lebois LAM, van Rooij SJH, House SL, Beaudoin FL, An X, Neylan TC, Clifford GD, Linnstaedt SD, Germine LT, Bollen KA, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Jr., Hendry PL, Sheikh S, Jones CW, Punches BE, Swor RA, Hudak LA, Pascual JL, Seamon MJ, Harris E, Pearson C, Peak DA, Merchant RC, Domeier RM, Rathlev NK, O'Neil BJ, Sergot P, Sanchez LD, Bruce SE, Harte SE, Koenen KC, Kessler RC, McLean SA, Ressler KJ, Stevens JS, and Jovanovic T. Probing the neurocardiac circuit in trauma and posttraumatic stress. *J Psychiatr Res* 2024; 176:173-181. PMID: 38875773. Full Text

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The neurocardiac circuit is integral to physiological regulation of threat and trauma-related responses. However, few direct investigations of brain-behavior associations with replicable physiological markers of PTSD have been conducted. The current study probed the neurocardiac circuit by examining associations among its core regions in the brain (e.g., insula, hypothalamus) and the periphery (heart rate [HR], high frequency heart rate variability [HF-HRV], and blood pressure [BP]). We sought to characterize these associations and to determine whether there were differences by PTSD status. Participants were N = 315 (64.1 % female) trauma-exposed adults enrolled from emergency departments as part of the prospective AURORA study. Participants completed a deep phenotyping session (e.g., fear conditioning, magnetic resonance imaging) two weeks after emergency department admission. Voxelwise analyses revealed several significant interactions between PTSD severity 8-weeks posttrauma and psychophysiological recordings on hypothalamic connectivity to the prefrontal cortex (PFC), insula, superior temporal sulcus, and temporoparietaloccipital junction. Among those with PTSD, diastolic BP was directly correlated with right insula-hypothalamic connectivity, whereas the reverse was found for those without PTSD. PTSD status moderated the association between systolic BP, HR, and HF-HRV and hypothalamic connectivity in the same direction. While preliminary, our findings may suggest that individuals with higher PTSD severity exhibit compensatory neural mechanisms to down-regulate autonomic imbalance. Additional study is warranted to determine how underlying mechanisms (e.g., inflammation) may disrupt the neurocardiac circuit and increase cardiometabolic disease risk in PTSD.

Family Medicine

Lockhart E, Turner D, Guastaferro K, Szalacha LA, Alzate HT, Marhefka S, **Pittiglio B**, **Dekker M**, **Yeh HH**, **Zelenak L**, **Toney J**, **Manogue S**, and **Ahmedani BK**. Increasing pre-exposure prophylaxis (PrEP) in primary care: A study protocol for a multi-level intervention using the multiphase optimization strategy (MOST) framework. *Contemp Clin Trials* 2024; 143:107599. PMID: 38848935. Full Text

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BACKGROUND: In the United States, over 1.2 million people are living with HIV. This disease disproportionately affects men who have sex with men (MSM), people of color, youth and young adults, and transgender individuals. Pre-exposure prophylaxis (PrEP) is an effective HIV prevention method. Barriers exist for both primary care providers (PCPs) to prescribe PrEP and prevent patients from initiating PrEP. METHODS: This study, MOST: PrEP, follows the multiphase optimization strategy (MOST) framework. The purpose is to identify a multi-level intervention among patients and PCPs to increase PrEP prescriptions in primary care. First, feedback will be obtained from providers and patients via focus groups, then, suggestions related to the context-specific (provider and individual level) factors of intervention component delivery will be incorporated. Subsequently, a rigorous experiment will be conducted using a 2(4) factorial design focusing on priority populations for PrEP initiation. Provider components include computer-based simulation training and a best practice alert. Patient components include a tailored PrEP educational video and HIV risk assessment. Finally, the facilitators and barriers to implementing the intervention components will be qualitatively examined. CONCLUSION: In this protocol paper, we describe the one of the first known multilevel MOST optimization trial in healthcare. Intervention components are to be delivered to patients and providers in a large healthcare system, based in an HIV Ending the Epidemic priority jurisdiction. If effective, this multi-level approach could be disseminated to providers and patients in other large healthcare systems to make a significant impact on HIV prevention.

Gastroenterology
Abusuliman M, **Jamali T**, and **Elatrache M**. Esophageal Obstruction After Bleeding Within an Esophageal Duplication Cyst. *Gastrointest Endosc* 2024; Epub ahead of print. PMID: 38879043. Full Text

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Gastroenterology
Abusuliman M, **Jamali T**, and **Elatrache M**. Heterotopic Pancreatic Tissue Containing a Mucinous Cystic Neoplasm Within the Duodenum With Fish-Mouth Appearance on Endoscopy. *Gastrointest Endosc* 2024; Epub ahead of print. PMID: 38876264. Full Text

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Gastroenterology
Chaudhary AJ, **Khan MZ**, Sohail A, Zaidi SMH, Denha E, and **Venkat D**. Acute onset nitrofurantoin-induced autoimmune hepatitis after urinary tract infection treatment. *Clin Case Rep* 2024; 12(6):e9050. PMID: 38868111. Full Text

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KEY CLINICAL MESSAGE: This case signifies the importance of recognizing DIAIH within the context of antibiotic therapy, especially in older adults and even shortly after common drug exposures for treating UTI. ABSTRACT: Various drugs can induce immune-mediated liver damage and in rare instances may lead to autoimmune hepatitis. Here we report an 84-year-old woman who developed autoimmune hepatitis less than 3 weeks after treatment for urinary tract infection with the antibiotic nitrofurantoin. She presented with jaundice, right upper quadrant abdominal pain, nausea, and vomiting. In the absence of a history of an autoimmune disorder or elevated liver enzymes in the past; elevated liver enzymes after a short course of Nitrofurantoin and the presence of smooth muscle antibodies strongly suggested autoimmune hepatitis, which was confirmed through biopsy sample analysis. The patient scored 7 points on the Naranjo adverse reaction probability scale. The patient's rapid recovery within 1 month of prednisone therapy supports the association of liver damage with nitrofurantoin use.

Gastroenterology
Kaur N, **Patel K**, **Lu M**, **Dababneh Y**, **Jomaa D**, **Nagirimadugu A**, **Oruganti P**, and **Yee K**. Enhancing Community-Based Specialty Access Through Virtual Care. *NEJM Catal Innov Care Deliv* 2024; 5(6):1-1. PMID: Not assigned. Full Text

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In December 2020, the authors set out to improve access to tertiary care at Henry Ford Health by creating a network of virtual care clinics to overcome the challenges of home-based virtual care, including broadband access or the need for physical examination. These clinics provided connectivity to the tertiary

specialist, vital sign assessment, physical examination, and facilitation of diagnostic testing at a location convenient to the patient. Each clinic was staffed by an on-site team including medical assistants and a single advanced practice provider; the tertiary specialists were present only virtually. For example, a patient with complex Crohn's disease requiring surgery and parenteral nutrition is best served by a tertiary specialist and multidisciplinary team. These patients require frequent, thorough follow-up visits, including blood pressure checks to assess hydration, catheter site checks, and physical examination to assess healing after surgery, in addition to medical management of Crohn's disease by a tertiary specialist. Each of these parameters is clinically paramount and not optimally assessed during a home-based video visit. In this clinical scenario, the medical assistant telepresented the patient to the off-site specialist, checked vital signs, and showed the specialist the catheter and surgical site. The clinical consultation took place in the local clinic facility, with the support of the on-site team. Laboratory testing and imaging studies were coordinated through community settings, and tertiary site-based surgical, health psychology, and nutritional teams also followed up with this patient via virtual care clinic visits. By providing these clinical services closer to the patient's home through a clinical facility, numerous objectives were achieved: (1) patients received thorough clinical assessment and care plans; (2) patients were less likely to use the hospital or ED; (3) patients were more likely to remain in the workforce; and (4) community health care was off-loaded, reducing burnout and improving workforce retention. This approach combines virtual care with a cooperative care delivery model, where the aim is not to shift patient care from one provider to another, but to expand access for patients and to create both new and clinically appropriate care for each care participant, with the aim that improved access will lead to enhanced care outcomes and more efficient care utilization. Telemedicine endeavors have increased dramatically in the past few years, and to the best of the authors' knowledge, no other health system or hospital has expanded specialty services into rural communities in this collaborative manner. The novel approach to health care delivery outlined herein provides a model to improve access to specialty care and patient outcomes, and could be replicated in other regions. Collaboration across institutions, cooperation among leaders and physicians, and commitment to serve communities are the keys to success.

Gastroenterology

Nimri F, **Ichkhanian Y**, Shinn B, Kowalski TE, Loren DE, Kumar A, Schlachterman A, Tantau A, Arevalo M, **Taha A**, **Shamaa O**, Viales MC, Khashab MA, **Simmer S**, **Singla S**, **Piraka C**, and **Zuchelli TE**. Comprehensive analysis of adverse events associated with transmural use of LAMS in patients with liver cirrhosis: International multicenter study. *Endosc Int Open* 2024; 12(6):E740-e749. PMID: 38847015. Full Text

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Background and study aims Endoscopic ultrasound (EUS)-guided transmural (TM) deployment of lumen-apposing metal stents (LAMS) is considered relatively safe in non-cirrhotic patients and is cautiously offered to cirrhotic patients. Patients and methods This was a retrospective, multicenter, international matched case-control study to study the safety of EUS-guided TM deployment of LAMS in cirrhotic patients. Results Forty-three cirrhotic patients with model for end-stage liver disease score 12.5 ± 5, with 23 having ascites and 16 with varices underwent EUS-guided TM LAMS deployment, including 19 for pancreatic fluid collection (PFC) drainage, 13 gallbladder drainage, six for endoscopic ultrasound-directed transgastric endoscopic retrograde cholangiopancreatography (ERCP), three for EDGI, one for endoscopic ultrasound-directed transenteric ERCP, and one postsurgical collection drainage. Technical failure occurred in one LAMS for PFC drainage. Clinical failure was encountered in another PFC. Nine adverse events (AEs) occurred. The most common AE was LAMS migration (3), followed by non-bleeding mucosal erosion (2), delayed bleeding (2), sepsis (1), and anesthesia-related complication (pulseless

electrical activity) (1). Most AEs were graded as mild (6), followed by severe (2), and moderate (1); the majority were managed conservatively. On univariable comparison, risk of AE was higher when using a 20 × 10 mm LAMS and the absence of through-the-LAMS plastic stent(s). Conditional logistic regression of matched case-control patients did not show any association between potential predicting factors and occurrence of AEs. Conclusions Our study demonstrated that mainly in patients with Child-Pugh scores A and B cirrhosis and despite the presence of mild-to-moderate ascites in over half of cases, the majority of AEs were mild and could be managed conservatively. Further studies are warranted to verify the safety of LAMS in cirrhotic patients.

Gastroenterology

Younossi ZM, AlQahtani SA, Funuyet-Salas J, Romero-Gómez M, Yilmaz Y, Keklikkiran C, Alswat K, Yu ML, Liu CJ, Fan JG, Zheng MH, Burra P, Francque SM, Castera L, Schattenberg JM, Newsome PN, Allen AM, El-Kassas M, Treeprasertsuk S, Hameed S, Wai-Sun Wong V, Zelber-Sagi S, Takahashi H, Kawaguchi T, Castellanos Fernández MI, Duseja A, Arrese M, Rinella M, Singal AK, **Gordon SC**, Fuchs M, Eskridge W, Alkhouri N, Cusi K, Loomba R, Ranagan J, Kautz A, Ong JP, Kugelmas M, Eguchi Y, Diago M, Gerber L, Lam B, Fornaresio L, Nader F, Spearman CW, Roberts SK, Chan WK, Silva M, Racila A, Golabi P, Ananchuensook P, Henry L, Stepanova M, Carrieri P, and Lazarus JV. The impact of stigma on quality of life and liver disease burden among patients with nonalcoholic fatty liver disease. *JHEP Reports* 2024; 6(7). PMID: Not assigned. Full Text

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Background & Aims: Patients with nonalcoholic fatty liver disease (NAFLD)/metabolic dysfunction-associated steatotic liver disease (MASLD) face a multifaceted disease burden which includes impaired health-related quality of life (HRQL) and potential stigmatization. We aimed to assess the burden of liver disease in patients with NAFLD and the relationship between experience of stigma and HRQL. Methods: Members of the Global NASH Council created a survey about disease burden in NAFLD. Participants completed a 35-item questionnaire to assess liver disease burden (LDB) (seven domains), the 36-item CLDQ-NASH (six domains) survey to assess HRQL and reported their experience with stigmatization and discrimination. Results: A total of 2,117 patients with NAFLD from 24 countries completed the LDB survey (48% Middle East and North Africa, 18% Europe, 16% USA, 18% Asia) and 778 competed CLDQ-NASH. Of the study group, 9% reported stigma due to NAFLD and 26% due to obesity. Participants who reported stigmatization due to NAFLD had substantially lower CLDQ-NASH scores (all $p < 0.0001$). In multivariate analyses, experience with stigmatization or discrimination due to NAFLD was the strongest independent predictor of lower HRQL scores (beta from -5% to -8% of score range size, $p < 0.02$). Experience with stigmatization due to obesity was associated with lower Activity, Emotional Health, Fatigue, and Worry domain scores, and being uncomfortable with the term “fatty liver disease” with lower Emotional Health scores (all $p < 0.05$). In addition to stigma, the greatest disease burden as assessed by LDB was related to patients’ self-blame for their liver disease. Conclusions: Stigmatization of patients with NAFLD, whether it is caused by obesity or NAFLD, is strongly and independently associated with a substantial impairment of their HRQL. Self-blame is an important part of disease burden among patients with NAFLD. Impact and implications: Patients with nonalcoholic fatty liver disease (NAFLD), recently renamed metabolic dysfunction-associated steatotic liver disease (MASLD), may experience impaired health-related quality of life and stigmatization. Using a specifically designed survey, we found that stigmatization of patients with NAFLD, whether it is caused by obesity or the liver disease per se, is strongly and independently associated with a substantial impairment of their quality of life. Physicians treating patients with NAFLD should be aware of the profound implications of stigma, the high prevalence of self-blame in the context of this disease burden, and that providers’ perception may not adequately reflect patients’ perspective and experience with the disease.

Hematology-Oncology

Bueno ES, Neto CD, Rodrigues A, Sousa TC, Hinokuma KD, **de Aquino AM**, Scarano WR, Brandt JZ, and Mendes LD. Assessment of prostate tissue remodeling in rats exposed to bisphenol A and the phytoestrogens genistein and indole-3-carbinol during the perinatal period. *Ciencia Rural* 2024; 54(8):9. PMID: Not assigned. Full Text

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Bisphenol A (BPA) is a compound known for its direct action on the prostate. Prostatic morphogenesis is a critical period when interference by any compound could permanently damage the organ. As such, the present study evaluated the morphological aspects resulting from gestational and lactational administration of BPA, indole-3-carbinol (I3C) and genistein (GEN) in prepubescent male rats. Pregnant Sprague Dawley females were allocated into 4 experimental groups and received the following: C: Control (no treatment); B: BPA (10 mu g/Kg); BG: BPA+GEN (5 mg/Kg); BI: BPA+I3C (20 mg/Kg) from gestation day (GD) 17 to postnatal day (PND) 21. After euthanasia on PND22, the prostate was collected and processed. When administered alone, BPA reduced the stromal compartment when compared to group C ($P = 0.039$). This decline was reversed in the groups submitted to GEN ($P = 0.019$) or I3C ($P = 0.017$). The groups treated with BPA ($P < 0.0001$) and the phytoestrogens ($P < 0.0001$) exhibited decreased epithelial height in relation to the control group. These changes were observed in stereological and morphometric analyses, but not in fractal analysis ($P = 0.569$). The area occupied by collagen increased in groups treated with BPA ($P < 0.0001$) and phytoestrogens ($P < 0.0001$) in relation to controls, while collagen distribution values were higher in all the treated groups ($P < 0.0001$), according to fractal analysis. Thus, BPA induced prostrate stroma remodeling with no influence from the phytoestrogens, which may affect glandular development and cause histopathological changes in adulthood.

Hematology-Oncology

Chaudhary AJ, **Joyce KM**, **Haq K**, Qureshi MH, and **Donthireddy V**. Non-alcoholic Wernicke's Encephalopathy Masquerading As CNS Relapse of Acute Myeloid Leukemia. *Cureus* 2024; 16(5):e61184. PMID: 38933646. Request Article

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While Wernicke's encephalopathy (WE) is mostly caused by thiamine deficiency secondary to chronic alcohol use, other conditions that may affect one's nutritional status, such as bariatric surgery, hyperemesis gravidarum, chronic gastrointestinal disease, HIV/AIDS, and certain malignancies, may also lead to this outcome. We are discussing one such case, WE, in a young man with acute myeloid leukemia (AML) who underwent chemotherapy. The patient presented with blurred vision, paresthesia, weakness, and vomiting. Although he denied alcohol abuse, his symptoms, physical exam findings, and MRI results were consistent with WE. Treatment with thiamine resulted in a significant improvement in his visual disturbances and mental status. The authors highlight the importance of recognizing WE in non-alcoholic patients, particularly those undergoing prolonged hospitalization and chemotherapy, as nutritional deficiencies can develop. They recommend thiamine supplementation for patients receiving chemotherapy and those with poor oral intake. The case underscores the need for high clinical suspicion and early intervention in atypical cases of WE.

Hematology-Oncology

Cho BC, Lu S, Felip E, Spira AI, Girard N, Lee JS, Lee SH, Ostapenko Y, Danchaivijitr P, Liu B, Alip A, Korbenfeld E, Mourão Dias J, Besse B, Lee KH, Xiong H, How SH, Cheng Y, Chang GC, Yoshioka H, Yang JC, Thomas M, Nguyen D, Ou SI, Mukhedkar S, Prabhash K, D'Arcangelo M, Alatorre-Alexander J, Vázquez Limón JC, Alves S, Stroyakovskiy D, Peregudova M, Şendur MAN, Yazici O, Califano R, Gutiérrez Calderón V, de Marinis F, Passaro A, Kim SW, **Gadgeel SM**, Xie J, Sun T, Martinez M, Ennis M, Fennema E, Daksh M, Millington D, Leconte I, Iwasawa R, Lorenzini P, Baig M, Shah S, Bauml JM, Shreeve SM, Sethi S, Knoblauch RE, and Hayashi H. Amivantamab plus Lazertinib in Previously Untreated EGFR-Mutated Advanced NSCLC. *N Engl J Med* 2024; Epub ahead of print. PMID: 38924756. Full Text

From the Division of Medical Oncology, Yonsei Cancer Center, Yonsei University College of Medicine (B.C.C.), Samsung Medical Center, Sungkyunkwan University School of Medicine (S.-H.L.), and the Lung Cancer Center, Asan Medical Center Cancer Institute (S.-W.K.), Seoul, the Department of Hematology-Oncology, Seoul National University Bundang Hospital, Seongnam (J.-S.L.), and the Medical Department, Chungbuk National University Hospital, Cheongju (K.-H.L.) - all in South Korea; the Department of Medical Oncology, Shanghai Chest Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai (S.L.), Harbin Medical University Cancer Hospital, Harbin (B.L.), the Department of Medical Oncology, Huizhou Municipal Central Hospital of Guangdong Province, Huizhou (H.X.), and Jilin Cancer Hospital, Changchun (Y.C.) - all in China; the Medical Oncology Service, Vall d'Hebron Barcelona Hospital Campus-Vall d'Hebron University Hospital, Barcelona (E. Felip), and the Medical Oncology Department, Hospital Regional Universitario de Málaga y Virgen de la Victoria, Institute of Biomedical Research of Malaga, Malaga (V.G.C.) - both in Spain; Virginia Cancer Specialists, Fairfax (A.I.S.); Institut Curie, Institut du Thorax Curie-Montsouris, Paris (N.G.), and Paris-Saclay University, Université de Versailles Saint-Quentin-en-Yvelines, Versailles (N.G.), and Paris-Saclay University and Institut Gustave Roussy, Villejuif (B.B.) - all in France; the National Cancer Institute, Kyiv, Ukraine (Y.O.); the Division of Medical Oncology, Department of Medicine, Siriraj Hospital Faculty of Medicine, Mahidol University Bangkok Noi Campus, Bangkok, Thailand (P.D.); the Clinical Oncology Unit, Faculty of Medicine, University of Malaya, Kuala Lumpur (A.A.), and the Department of Internal Medicine, Division of Respiratory Medicine, International Islamic University Malaysia Medical Specialist Center, Pahang (S.-H.H.) - both in Malaysia; British Hospital of Buenos Aires, Central British Hospital, Buenos Aires (E.K.); the Department of Medical Oncology, Barretos Cancer Hospital, São Paulo (J.M.D.); the School of Medicine and Institute of Medicine, Chung Shan Medical University, and the Division of Pulmonary Medicine, Department of Internal Medicine, Chung Shan Medical University Hospital, Taichung (G.-C.C.), and the Department of Medical Oncology, National Taiwan University Cancer Center, Taipei (J.C.-H.Y.) - both in Taiwan; the Department of Thoracic Oncology, Kansai Medical University Hospital, Hirakata (H.Y.), and the Department of Medical Oncology, Kindai University Faculty of Medicine, Osaka (H.H.) - both in Japan; the Department of Thoracic Oncology, Thoraxklinik, Heidelberg University Hospital, and the National Center for Tumor Diseases Heidelberg, German Center for Lung Research, Heidelberg, Germany (M.T.); City of Hope National Medical Center, Duarte (D.N.), Chao Family Comprehensive Cancer Center, University of California, Irvine, School of Medicine, Orange (S.-H.I.O.), and Janssen Research and Development, San Diego (E. Fennema, D.M., S.M.S.) - all in California; St. John of God Murdoch Hospital, Murdoch, WA, Australia (S.M.); the Department of Medical Oncology, Division of Adult Solid Tumor, Tata Memorial Center and Homi Bhabha National Institute, Mumbai, India (K.P.); the Local Health Unit Authority of Romagna, Ravenna Hospital and Department of Onco-Hematology, Santa Maria delle Croci Hospital of Ravenna, Ravenna (M. D'Arcangelo), and the Division of Thoracic Oncology, European Institute of Oncology IRCCS, Milan (F.M., A.P.) - both in Italy; Health Pharma Professional Research, Mexico City (J.A.-A.), Oncología Médica, Antiguo Hospital Civil de Guadalajara "Fray Antonio Alcalde," Guadalajara, and Universidad de Guadalajara, Guadalajara (J.C.V.L.) - all in Mexico; Instituto Português de Oncologia do Porto, Porto, Portugal (S.A.); Moscow City Oncology Hospital No. 62 (D.S.) and the Medical Center in Kolomenskoe (M.P.) - both in Moscow; the Department of Medical Oncology, Ankara Bilkent City Hospital and Ankara Yıldırım Beyazıt University (M.A.N.Ş.), and the Department of Medical Oncology, Gazi University Faculty of Medicine (O.Y.) - both in Ankara, Turkey; the Department of Medical Oncology, Christie NHS Foundation Trust and Division of Cancer Sciences, University of Manchester, Manchester, United Kingdom (R.C.); the Division of Hematology-Oncology, Henry Ford Cancer Institute, Henry Ford Health, Detroit (S.M.G.); Janssen Research and Development, Raritan, NJ

(J.X., T.S., M.M., M. Daksh, M.B.); Janssen Research and Development, Spring House, PA (M.E., R.I., P.L., S. Shah, J.M.B., S. Sethi, R.E.K.); and Johnson and Johnson Clinical Innovation, Campus Basel, Allschwil, Switzerland (I.L.).

BACKGROUND: Amivantamab plus lazertinib (amivantamab-lazertinib) has shown clinically meaningful and durable antitumor activity in patients with previously untreated or osimertinib-pretreated EGFR (epidermal growth factor receptor)-mutated advanced non-small-cell lung cancer (NSCLC). METHODS: In a phase 3, international, randomized trial, we assigned, in a 2:2:1 ratio, patients with previously untreated EGFR-mutated (exon 19 deletion or L858R), locally advanced or metastatic NSCLC to receive amivantamab-lazertinib (in an open-label fashion), osimertinib (in a blinded fashion), or lazertinib (in a blinded fashion, to assess the contribution of treatment components). The primary end point was progression-free survival in the amivantamab-lazertinib group as compared with the osimertinib group, as assessed by blinded independent central review. RESULTS: Overall, 1074 patients underwent randomization (429 to amivantamab-lazertinib, 429 to osimertinib, and 216 to lazertinib). The median progression-free survival was significantly longer in the amivantamab-lazertinib group than in the osimertinib group (23.7 vs. 16.6 months; hazard ratio for disease progression or death, 0.70; 95% confidence interval [CI], 0.58 to 0.85; P<0.001). An objective response was observed in 86% of the patients (95% CI, 83 to 89) in the amivantamab-lazertinib group and in 85% of those (95% CI, 81 to 88) in the osimertinib group; among patients with a confirmed response (336 in the amivantamab-lazertinib group and 314 in the osimertinib group), the median response duration was 25.8 months (95% CI, 20.1 to could not be estimated) and 16.8 months (95% CI, 14.8 to 18.5), respectively. In a planned interim overall survival analysis of amivantamab-lazertinib as compared with osimertinib, the hazard ratio for death was 0.80 (95% CI, 0.61 to 1.05). Predominant adverse events were EGFR-related toxic effects. The incidence of discontinuation of all agents due to treatment-related adverse events was 10% with amivantamab-lazertinib and 3% with osimertinib. CONCLUSIONS: Amivantamab-lazertinib showed superior efficacy to osimertinib as first-line treatment in EGFR-mutated advanced NSCLC. (Funded by Janssen Research and Development; MARIPOSA ClinicalTrials.gov number, NCT04487080.).

Hematology-Oncology
Dziadziuszko R, Peled N, Mok T, Peters S, Aix SP, Alatorre-Alexander J, Vicuna BD, Maclennan M, Bhagawati-Prasad V, Shagan SM, Schleifman E, Ruf T, Mathisen MS, and **Gadgeel SM**. High-dose alectinib for RET fusion-positive non-small cell lung cancer in the Blood First Assay Screening Trial. *Contemp Oncol (Pozn)* 2023; 27(4):217-223. PMID: 38405208. Full Text

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INTRODUCTION: This paper presents results from Cohort B (rearranged during transfection [RET], fusion-positive) of the Blood First Assay Screening Trial in patients with advanced non-small cell lung cancer (NSCLC) screened for genetic alterations using blood-based next-generation sequencing. MATERIAL AND METHODS: Adults with advanced RET fusion-positive NSCLC received alectinib 900 mg twice daily (BID) in Phase I. Enrolment closed prematurely with Phase II uninitiated. RESULTS:

Among eight treated patients, confirmed best overall responses in evaluable patients were stable disease (4/5) and progressive disease (1/5). One dose-limiting toxicity (death, unknown cause) was considered by the investigator to be related to treatment and underlying disease. Serious adverse events (SAEs) occurred in five patients, and SAEs that may be related to treatment occurred in two patients. CONCLUSIONS: Alectinib showed limited activity in advanced RET fusion-positive NSCLC, and further investigation was not conducted due to the development of selective RET inhibitors pralsetinib and selpercatinib. No new safety signals were observed, and the safety profile of alectinib was in line with previous reports at the 600 mg BID dose.

Hematology-Oncology

Felip E, Cho BC, Gutiérrez V, Alip A, Besse B, Lu S, Spira AI, Girard N, Califano R, **Gadgeel SM**, Yang JC, Yamamoto S, Azuma K, Kim YJ, Lee KH, Danchaivijitr P, Ferreira CG, Cheng Y, Sendur MAN, Chang GC, Wang CC, Prabhash K, Shinno Y, Stroyakovskiy D, Paz-Ares L, Rodriguez-Cid JR, Martin C, Campelo MRG, Hayashi H, Nguyen D, Tomasini P, Gottfried M, Dooms C, Passaro A, Schuler M, Gelatti ACZ, Owen S, Perdrizet K, Ou SI, Curtin JC, Zhang J, Gormley M, Sun T, Panchal A, Ennis M, Fennema E, Daksh M, Sethi S, Bauml JM, and Lee SH. Amivantamab plus lazertinib versus osimertinib in first-line EGFR-mutant advanced non-small-cell lung cancer with biomarkers of high-risk disease: a secondary analysis from MARIPOSA. *Ann Oncol* 2024; Epub ahead of print. PMID: 38942080. Full Text

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BACKGROUND: Amivantamab-lazertinib significantly prolonged progression-free survival (PFS) versus osimertinib in patients with epidermal growth factor receptor (EGFR)-mutant advanced non-small-cell lung cancer [NSCLC; hazard ratio (HR) 0.70; P < 0.001], including those with a history of brain metastases (HR 0.69). Patients with TP53 co-mutations, detectable circulating tumor DNA (ctDNA), baseline liver metastases, and those without ctDNA clearance on treatment have poor prognoses. We evaluated outcomes in these high-risk subgroups. PATIENTS AND METHODS: This analysis included patients with treatment-naive, EGFR-mutant advanced NSCLC randomized to amivantamab-lazertinib (n = 429) or osimertinib (n = 429) in MARIPOSA. Pathogenic alterations were identified by next-generation sequencing (NGS) of baseline blood ctDNA with Guardant360 CDx. Ex19del and L858R ctDNA in blood was analyzed at baseline and cycle 3 day 1 (C3D1) with Biodesix droplet digital polymerase chain reaction (ddPCR). RESULTS: Baseline ctDNA for NGS of pathogenic alterations was available for 636 patients (amivantamab-lazertinib, n = 320; osimertinib, n = 316). Amivantamab-lazertinib improved median PFS (mPFS) versus osimertinib for patients with TP53 co-mutations {18.2 versus 12.9 months; HR 0.65 [95% confidence interval (CI) 0.48-0.87]; P = 0.003} and for patients with wild-type TP53 [22.1 versus 19.9 months; HR 0.75 (95% CI 0.52-1.07)]. In patients with EGFR-mutant, ddPCR-detectable baseline ctDNA, amivantamab-lazertinib significantly prolonged mPFS versus osimertinib [20.3 versus 14.8 months; HR 0.68 (95% CI 0.53-0.86); P = 0.002]. Amivantamab-lazertinib significantly improved mPFS versus osimertinib in patients without ctDNA clearance at C3D1 [16.5 versus 9.1 months; HR 0.49 (95% CI 0.27-0.87); P = 0.015] and with clearance [24.0 versus 16.5 months; HR 0.64 (95% CI 0.48-0.87); P = 0.004]. Amivantamab-lazertinib significantly prolonged mPFS versus osimertinib among randomized patients with [18.2 versus 11.0 months; HR 0.58 (95% CI 0.37-0.91); P = 0.017] and without baseline liver metastases [24.0 versus 18.3 months; HR 0.74 (95% CI 0.60-0.91); P = 0.004]. CONCLUSIONS: Amivantamab-lazertinib effectively overcomes the effect of high-risk features and represents a promising new standard of care for patients with EGFR-mutant advanced NSCLC.

Hematology-Oncology

Golivi Y, Kumari S, **Farran B**, Alam A, Peela S, and Nagaraju GP. Small molecular inhibitors: Therapeutic strategies for pancreatic cancer. *Drug Discov Today* 2024; 29(7):104053. PMID: 38849028. Request Article

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Pancreatic cancer (PC), a disease with high heterogeneity and a dense stromal microenvironment, presents significant challenges and a bleak prognosis. Recent breakthroughs have illuminated the crucial interplay among RAS, epidermal growth factor receptor (EGFR), and hedgehog pathways in PC progression. Small molecular inhibitors have emerged as a potential solution with their advantages of oral administration and the ability to target intracellular and extracellular sites effectively. However, despite the US FDA approving over 100 small-molecule targeted antitumor drugs, challenges such as low response rates and drug resistance persist. This review delves into the possibility of using small molecules to treat persistent or spreading PC, highlighting the challenges and the urgent need for a diverse selection of inhibitors to develop more effective treatment strategies.

Hematology-Oncology

Hamid O, Lewis KD, **Weise A**, McKean M, Papadopoulos KP, Crown J, Kim TM, Lee DH, Thomas SS, Mehnert J, Kaczmar J, Lakhani NJ, Kim KB, Middleton MR, Rabinowits G, Spira AI, Yushak M, Mehmi I, Fang F, Chen S, Mani J, Jankovic V, Wang F, Fiaschi N, Brennan L, Paccaly A, Masinde S, Salvati M, Fury MG, Kroog G, Lowy I, and Gullo G. Phase I Study of Fianlimab, a Human Lymphocyte Activation Gene-3 (LAG-3) Monoclonal Antibody, in Combination With Cemiplimab in Advanced Melanoma. *J Clin Oncol* 2024; Jco2302172. Epub ahead of print.:. PMID: 38900987. Full Text

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PURPOSE: Coblockade of lymphocyte activation gene-3 (LAG-3) and PD-1 receptors could provide significant clinical benefit for patients with advanced melanoma. Fianlimab and cemiplimab are high-affinity, human, hinge-stabilized IgG4 monoclonal antibodies, targeting LAG-3 and PD-1, respectively. We report results from a first-in-human phase-I study of fianlimab and cemiplimab safety and efficacy in various malignancies including advanced melanoma. METHODS: Patients with advanced melanoma were eligible for enrollment into four cohorts: three for patients without and one for patients with previous anti-PD-1 therapy in the advanced disease setting. Patients were treated with fianlimab 1,600 mg and cemiplimab 350 mg intravenously once every 3 weeks for up to 51 weeks, with an optional additional 51 weeks if clinically indicated. The primary end point was objective response rate (ORR) per RECIST 1.1

criteria. RESULTS: ORRs were 63% for patients with anti-PD-1-naïve melanoma (cohort-6; n = 40; median follow-up 20.8 months), 63% for patients with systemic treatment-naïve melanoma (cohort-15; n = 40; 11.5 months), and 56% for patients with previous neo/adjuvant treatment melanoma (cohort-16; n = 18, 9.7 months). At a median follow-up of 12.6 months for the combined cohorts (6 + 15 + 16), the ORR was 61.2% and the median progression-free survival (mPFS) 13.3 months (95% CI, 7.5 to not estimated [NE]). In patients (n = 13) with previous anti-PD-1 adjuvant therapy, ORR was 61.5% and mPFS 12 months (95% CI, 1.4 to NE). ORR in patients with previous anti-PD-1 therapy for advanced disease (n = 15) was 13.3% and mPFS 1.5 months (95% CI, 1.3 to 7.7). Treatment-emergent and treatment-related adverse events ≥grade 3 (G3) were observed in 44% and 22% of patients, respectively. Except for increased incidence of adrenal insufficiency (12%-G1-4, 4%-G3-4), no new safety signals were recorded. CONCLUSION: The current results show a promising benefit-risk profile of fianlimab/cemiplimab combination for patients with advanced melanoma, including those with previous anti-PD-1 therapy in the adjuvant, but not advanced, setting.

Hematology-Oncology

Heath EI, Thakur A, Chen W, **Hwang C**, Paller CJ, Cackowski FC, Boerner JL, Heilbrun L, Smith MP, Schalk DL, Schienschang A, Whitaker SA, Polend A, Smith D, Vaishampayan UN, Dickow B, and Lum LG. Race-related Differences in Sipuleucel-T Response Among Men with Metastatic Castrate-Resistant Prostate Cancer. *Cancer Res Commun* 2024; Epub ahead of print. PMID: 38856749. Full Text

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PURPOSE: Sipuleucel-T is an autologous cellular immunotherapy that targets prostatic acid phosphatase (PAP) and is available for treatment of men with asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer (mCRPC). In this single-arm, two-cohort, multicenter clinical study, potential racial differences in immune responses to sipuleucel-T in men with mCRPC were explored. PATIENTS AND METHODS: Patients' blood samples were obtained to assess serum cytokines, humoral responses, and cellular immunity markers pre- and post-treatment. Baseline cumulative product parameters (total nucleated and CD54+ cell counts, and CD54 upregulation) were evaluated. IgM titers against the immunogen PA2024, the target antigen PAP, prostate-specific membrane antigen (PSMA) and prostate-specific antigen (PSA) were quantified by ELISA. Cytotoxic T lymphocyte activity was determined by ELISpots, and cytokine and chemokine concentrations by Luminex. RESULTS: Twenty-nine African Americans (AA) and 28 non-African Americans (non-AA) with mCRPC received sipuleucel-T. Baseline total nucleated cell count, CD54+ cell count, CD54 expression, and cumulative product parameters were higher in non-AA. Although PSA baseline levels were higher in AA, there were no racial differences in IgM antibody and IFN-□ ELISpots responses against PA2024, PAP, PSA and PSMA pre- and post-treatment. Expression of co-stimulatory receptor ICOS on CD4+ and CD8+ T cells, and the levels of Th1 cytokine granulocyte-macrophage colony-stimulating factor and chemokines CCL4 and CCL5, were significantly higher in AA pre- and/or post-treatment. Despite no difference in the overall survival, PSA changes from baseline were significantly different between the two races. CONCLUSIONS: The data suggest that immune correlates in blood differ in AA and non-AA with mCRPC pre- and post-sipuleucel-T.

Hematology-Oncology

Jain T, Estrada-Merly N, Salas MQ, Kim S, DeVos JD, Chen M, Fang X, Kumar R, Andrade-Campos M, Elmariah H, Agrawal V, Aljurf M, Bacher U, Badar T, Badawy SM, Ballen KK, Beitinjaneh A, Bhatt VR, Bredeson CN, DeFilipp Z, Dholaria B, Farhadfar N, **Farhan S**, Gandhi A, Ganguly S, Gergis U, Grunwald MR, Hamad N, Hamilton BK, Inamoto Y, Iqbal M, Jamy O, Juckett M, Kharfan-Dabaja MA, Krem MM, Lad DP, Liesveld JL, Al Malki MM, Malone AK, Murthy HS, Ortí G, Patel SS, Pawarode A, Perales MA, van der Poel MWM, Ringden O, Rizzieri DA, Rovo A, Savani BN, Savoie ML, Seo S, Solh MM, Ustun C, Verdonck LF, Wingard JR, Wirk B, Bejanyan N, Jones RJ, Nishihori T, Oran B, Nakamura R, Scott BL, Saber W, and Gupta V. Donor Types and Outcomes of Transplantation in Myelofibrosis: A CIBMTR Study. *Blood Adv* 2024; Epub ahead of print. PMID: 38916866. Full Text

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We aim to evaluate impact of donor types on outcomes of hematopoietic cell transplantation (HCT) in myelofibrosis, using CIBMTR registry data for HCTs done between 2013 and 2019. In all 1597 undergoing HCT for myelofibrosis, the use of haploidentical donors increased from 3% in 2013 to 19% in 2019. In study eligible, 1032 patients who received peripheral blood grafts for chronic phase myelofibrosis, 38% recipients of haploidentical-HCT were of non-White/Caucasian ethnicity. Matched sibling donor (MSD)-HCTs were independently associated with superior overall survival (OS) in the first 3 months [reference MSD, haploidentical HR 5.80 (95% CI 2.52-13.35), matched unrelated HR 4.50 (95% CI 2.24-9.03), and mismatched unrelated HR 5.13 (95% CI 1.44-18.31), P<0.001]. This difference in OS aligns with lower graft failure with MSD [haploidentical HR 6.11 (95%CI 2.98-12.54), matched unrelated HR 2.33 (95%CI 1.20-4.51), mismatched unrelated HR 1.82 (95%CI 0.58-5.72). There was no significant difference in OS among haploidentical, matched unrelated, and mismatched unrelated donor HCTs in the first 3 months. Donor type was not associated with differences in OS beyond 3 months post-HCT, relapse, disease-free survival or OS among patients who underwent HCT within 24 months of diagnosis. Patients who experienced graft failure had more advanced disease and commonly used nonmyeloablative conditioning. While MSDs remain a superior donor option due to improved engraftment, there is no significant difference in HCT outcomes from haploidentical and matched unrelated donors. These results establish haploidentical-HCT with posttransplantation cyclophosphamide as a viable option in myelofibrosis, especially for ethnic minorities underrepresented in the donor registries.

Hematology-Oncology

Patel S, Tareen K, Patel C, and Rosinski A. Herbal and Non-Herbal Dietary Supplements for Psychiatric Indications: Considerations in Liver Transplantation. *Curr Psychiatry Rep* 2024; Epub ahead of print. PMID: 38941032. Full Text

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PURPOSE OF REVIEW: Traditional, complementary, and integrative medicine (TCIM) modalities are widely employed. However, TCIM, specifically herbal and non-herbal dietary supplements, can pose challenges in the context of organ transplantation. In this review, we discuss common supplements used for psychiatric purposes and highlight important considerations for candidates and recipients of liver transplants. RECENT FINDINGS: Ashwagandha, kava kava, green tea extract, skullcap, turmeric, and valerian have known idiosyncratic hepatotoxic potential and may complicate the liver transplantation course. Multiple supplements reportedly carry a lower risk of hepatotoxicity, though evidence for widespread use in those at risk for or with hepatic impairment is limited. Psychiatrists caring for candidates and recipients of liver transplants must recognize that patients may find supplements helpful in alleviating psychiatric symptoms, despite an overall limited evidence base. Evaluating benefit versus

risk ratios and reviewing drug-drug interactions is essential to promote transplant candidacy and mitigate the possibility of native or graft liver dysfunction.

Hematology-Oncology

Peters S, **Gadgeel SM**, Mok T, Nadal E, Kilickap S, Swalduz A, Cadranel J, Sugawara S, Chiu CH, Yu CJ, Moskovitz M, Tanaka T, Nersesian R, Shagan SM, Maclennan M, Mathisen M, Bhagawati-Prasad V, Diarra C, Assaf ZJ, Archer V, and Dziadziuszko R. Entrectinib in ROS1-positive advanced non-small cell lung cancer: the phase 2/3 BFAST trial. *Nat Med* 2024; Epub ahead of print. PMID: 38898120. Full Text

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Although comprehensive biomarker testing is recommended for all patients with advanced/metastatic non-small cell lung cancer (NSCLC) before initiation of first-line treatment, tissue availability can limit testing. Genomic testing in liquid biopsies can be utilized to overcome the inherent limitations of tissue sampling and identify the most appropriate biomarker-informed treatment option for patients. The Blood First Assay Screening Trial is a global, open-label, multicohort trial that evaluates the efficacy and safety of multiple therapies in patients with advanced/metastatic NSCLC and targetable alterations identified by liquid biopsy. We present data from Cohort D (ROS1-positive). Patients ≥18 years of age with stage IIIB/IV, ROS1-positive NSCLC detected by liquid biopsies received entrectinib 600 mg daily. At data cutoff (November 2021), 55 patients were enrolled and 54 had measurable disease. Cohort D met its primary endpoint: the confirmed objective response rate (ORR) by investigator was 81.5%, which was consistent with the ORR from the integrated analysis of entrectinib (investigator-assessed ORR, 73.4%; data cutoff May 2019, ≥12 months of follow-up). The safety profile of entrectinib was consistent with previous reports. These results demonstrate consistency with those from the integrated analysis of entrectinib in patients with ROS1-positive NSCLC identified by tissue-based testing, and support the clinical value of liquid biopsies to inform clinical decision-making. The integration of liquid biopsies into clinical practice provides patients with a less invasive diagnostic method than tissue-based testing and has faster turnaround times that may expedite the reaching of clinical decisions in the advanced/metastatic NSCLC setting. ClinicalTrials.gov registration: NCT03178552 .

Hospital Medicine

Adzemovic T, Govindan S, Zheutlin A, Horowitz J, Heath M, Kuhn L, Nabeel M, Kalra SK, Dhillon D, **Kaatz S**, Swaminathan L, Harba N, and Chopra V. Awareness of Peripheral IV Catheters Among Nurses, Physicians, and Trainees: A Prospective Cohort Study. *Am J Infect Control* 2024; Epub ahead of print. PMID: 38844143. Full Text

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BACKGROUND: Peripheral intravenous catheters (PIVs) are the most frequently used invasive device in hospitalized patients. These devices are not benign and may put patients at risk of serious complications. However, clinician awareness of their presence is variable and poorly understood. METHODS: We conducted a prospective, multi-center, observational point prevalence study to assess awareness of PIV presence among clinicians caring for hospitalized patients in four hospitals between 05/2018 and 02/2019 located in Michigan, United States of America. We first assessed patients for presence of a PIV then interviewed their providers. Differences in awareness by provider type was assessed via chi-square tests; $p< 0.05$ was considered statistically significant. Analyses were performed on Stata MP v16 (College Station, TX). RESULTS: A total of 1,385 patients and 4,003 providers were interviewed. Nurses had the greatest awareness of overall PIV presence, 98.6%, while attendings were correct 88.1% of the time. Nurses were more likely to correctly assess PIV presence and exact location than physicians (67.7% vs. < 30% for all others). Awareness of PIV presence did not significantly vary among providers in patients with multiple vascular access device(s), on contact precautions, or those receiving active infusions. CONCLUSIONS: Given the ubiquity of PIVs and known complications, variable awareness of vascular devices is problematic. Methods to increase awareness to ensure appropriate care and removal appear necessary.

Hospital Medicine

Ahmed O, **Singh H**, **Bai S**, **Maraj D**, **Qureshi MA**, **Hawes E**, **Alamelumangapuram C**, and **Othman H**. Delayed Presentation of a Post-infarction Ventricular Septal Rupture. *J Investig Med High Impact Case Rep* 2024; 12:23247096241262514. PMID: 38904301. Full Text

Henry Ford Allegiance Health, Jackson, MI, USA.

Ventricular septal rupture, a formidable complication of acute myocardial infarction (AMI), is linked to significant morbidity and mortality. The clinical manifestation typically involves pronounced hemodynamic compromise necessitating prompt surgical intervention. This report outlines the case of a 60-year-old male presenting with acute heart failure 3 weeks post a presumed AMI. On evaluation, a substantial ventricular septal defect with left-to-right shunt was observed. The patient, although hemodynamically stable with mild symptoms, underwent surgical closure of the defect and coronary artery bypass graft for multivessel coronary artery disease. This case contributes to the literature on the delayed presentation of post-myocardial infarction (MI) ventricular septal rupture, a scenario deviating from the anticipated severe hemodynamic instability given the timing of the MI and the extent of the septal defect.

Hospital Medicine

Schaefer JK, Errickson J, Kong X, Ali MA, DeCamillo D, Edupuganti S, Haymart B, **Kaatz S**, Kline-Rogers E, Kozlowski JH, **Krol GD**, Sood SL, Froehlich JB, and Barnes GD. Outcomes of direct oral anticoagulants with aspirin vs warfarin with aspirin: a registry-based cohort study. *Res Pract Thromb Haemost* 2024; 8(4). PMID: Not assigned. Full Text

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Background: For patients anticoagulated with direct oral anticoagulants (DOACs) or warfarin and on aspirin (ASA) for nonvalvular atrial fibrillation and/or venous thromboembolism, it is unclear if bleeding outcomes differ. Objectives: To assess bleeding rates for ASA with DOACs vs warfarin and one another. Methods: Registry-based cohort study of patients followed by a 6-center quality improvement collaborative in Michigan using data from 2009 to 2022. The study included adults on ASA with warfarin or DOACs for atrial fibrillation and/or venous thromboembolism without a recent myocardial infarction or heart valve replacement. Results: After propensity matching by anticoagulant class, we compared 2 groups of 1467 patients followed for a median of 18.0 months. Any bleeding and nonmajor bleeding was increased with DOACs + ASA compared with warfarin + ASA (32.2 vs 27.8 and 27.1 vs 22.9 events/100 patient-years; relative risks [RRs], 1.1 and 1.2; 95% CIs, 1.1-1.2 and 1.1-1.3, respectively). After matching by drug, patients on apixaban + ASA vs warfarin + ASA had more bleeding (31.2 vs 27.8 events/100 patient-years; RR, 1.1; 95% CI, 1.0-1.2) and nonmajor bleeding but less major bleeding (3.8 vs 4.7 events/100 patient-years; RR, 0.8; 95% CI, 0.6-1.0) and emergency room visits for bleeding. Patients on rivaroxaban + ASA vs warfarin + ASA had more bleeding (39.3 vs 26.3 events/100 patient-years, RR, 1.5; 95% CI, 1.3-1.6), nonmajor bleeding, and thrombosis. Patients on apixaban + ASA vs rivaroxaban + ASA had significantly less bleeding (22.5 vs 39.3/100 patient-years; RR, 0.6; 95% CI, 0.5-0.7), nonmajor bleeding, major bleeding (2.1 vs 5.5 events/100 patient-years; RR, 0.4; 95% CI, 0.2-0.6), emergency room visits for bleeding, and thrombotic events. Conclusion: Patients on DOAC + ASA without a recent myocardial infarction or heart valve replacement had more nonmajor bleeding but otherwise similar outcomes compared with warfarin + ASA. Patients treated with rivaroxaban + ASA experienced more adverse clinical events compared with warfarin + ASA or apixaban + ASA.

Hypertension and Vascular Research

Srinivas B, Alluri K, **Rhaleb NE**, Belmadani S, and Matrougui K. Role of plasmacytoid dendritic cells in vascular dysfunction in mice with renovascular hypertension. *Heliyon* 2024; 10(11):e31799. PMID: 38882290. Full Text

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Endothelial dysfunction and inflammation are clinically significant risk factors for cardiovascular diseases in hypertension. Although immune cells play a role in hypertension, the impact of plasmacytoid dendritic cells in established renovascular hypertension-induced cardiovascular complications is not fully understood. We investigated plasmacytoid dendritic cells' contribution to arterial endothelial dysfunction and inflammation in renovascular hypertension. A two-kidney one-clip (2K1C) model for four weeks in both male and female mice was used to induce renovascular hypertension. We treated mice with or without anti-PDCA-1 antibodies for one week to deplete the plasmacytoid dendritic cells. Renovascular hypertension causes cardiac hypertrophy, lung edema, and microvascular endothelial dysfunction associated with inflammation induction in mice. Moreover, renovascular hypertension affects the profile of immune cells, including dendritic cells and macrophages, with variations between male and female mice. Interestingly, the depletion of plasmacytoid dendritic cells significantly reduces blood pressure, cardiac hypertrophy, lung edema, inflammation, and oxidative stress and improves microvascular endothelial function via the endoplasmic reticulum (ER) stress, autophagy, and mTOR-dependent mechanisms.

Plasmacytoid dendritic cells significantly contribute to the development of cardiovascular complications in renovascular hypertension by modulating immune cells, inflammation, oxidative stress, and ER stress.

Infectious Diseases

Kraft CS, Sims M, Silverman M, Louie TJ, Feuerstadt P, Huang ES, Khanna S, Berenson CS, Wang EEL, Cohen SH, Korman L, Lee C, Kelly CR, Odio A, Cook PP, Lashner B, **Ramesh M**, Kumar P, De A, Memisoglu A, Lombardi DA, Hasson BR, McGovern BH, von Moltke L, and Pardi DS. Integrated Safety and Efficacy Analyses of Phase 3 Trials of a Microbiome Therapeutic for Recurrent CDI. *Infect Dis Ther* 2024; Epub ahead of print. PMID: 38941068. Full Text

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INTRODUCTION: Recurrent Clostridioides difficile infection (rCDI) often occurs after standard-of-care antibiotics. VOWST oral spores (VOS, previously SER-109), an FDA-approved orally administered microbiome therapeutic, is indicated to prevent rCDI following antibiotics for rCDI. OBJECTIVE, DESIGN, AND PATIENTS: To evaluate safety and efficacy of VOS from two phase 3 trials, (randomized, placebo-controlled [ECOSPOR III: NCT03183128] and open-label, single arm [ECOSPOR IV: NCT03183141]) of 349 adults with rCDI and prevalent comorbidities. METHODS: VOS or placebo [ECOSPOR III only] (4 capsules once daily for 3 days). Integrated analysis of treatment-emergent adverse events (TEAEs) collected through week 8; serious TEAEs and TEAEs of special interest collected through week 24; and rates of rCDI (toxin-positive diarrhea requiring treatment) evaluated through weeks 8 and 24. RESULTS: TEAEs were mostly mild or moderate and gastrointestinal. Most common treatment-related TEAEs were flatulence, abdominal pain and distension, fatigue, and diarrhea. There were 11 deaths (3.2%) and 48 patients (13.8%) with serious TEAEs, none treatment-related. The rCDI rate through week 8 was 9.5% (95% CI 6.6-13.0) and remained low through 24 weeks (15.2%; 95% CI 11.6-19.4). Safety and rCDI rates were consistent across subgroups including age, renal impairment/failure, diabetes, and immunocompromise/immunosuppression. CONCLUSIONS: VOS was well tolerated and rates of rCDI remained low through week 24 including in those with comorbidities. These data support the potential benefit of VOS following antibiotics to prevent recurrence in high-risk patients. TRIAL REGISTRATION: ClinicalTrials.gov identifier, NCT03183128 and NCT03183141.

Infectious Diseases

Singh H, Kaushal J, Garcia A, and **Kak V**. Clostridium perfringens Empyema: Anaerobic Invasion in an Uncommon Location. *Cureus* 2024; 16(5):e60082. PMID: 38860109. Request Article

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Clostridium perfringens bacteremia arises due to skin inoculation from the external environment or translocation from the gastrointestinal tract. In the event of bacteremia, it tends to colonize in anaerobic environments due to its obligatory anaerobic nature. Its inoculation in the lung, albeit rare, can occur if an anaerobic nidus is created. In the presented case, the patient developed C. perfringens bacteremia andempyema in the area of lung necrosis caused by acute pulmonary embolism. He did not have any history of chest trauma, and the source of bacteremia was deemed to be via gut translocation. The patient was noted to have multiple gastric ulcers on endoscopy and jejunal wall thickening, which likely led to the bacterial translocation into the bloodstream. He underwent video-assisted thoracoscopic surgery-assisted decortication and intravenous antibiotics, eventually leading to clinical improvement. To identify the source of Clostridium in the absence of penetrating trauma, a thorough gastrointestinal evaluation, including a colonoscopy, is warranted to identify the pathology leading to the gastrointestinal translocation.

Infectious Diseases

Weston G, Giri A, Komarow L, Ge L, Baum KR, Abbenante E, Gallagher JC, Jacob JT, Kaye KS, Kim AC, Huskins WC, **Zervos M**, **Herc E**, Patel R, Van Duin D, and Doi Y. Clinical outcomes in patients infected with ertapenem-only-resistant Enterobacterales versus multi-carbapenem-resistant Enterobacterales. *J Antimicrob Chemother* 2024; Epub ahead of print. PMID: 38863337. Full Text

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BACKGROUND: Use of anti-carbapenem-resistant Enterobacterales (anti-CRE) agents such as ceftazidime/avibactam has been associated with improved clinical outcome in cohorts that primarily include patients infected with CRE that are resistant to meropenem (MCRE). OBJECTIVES: To clarify whether patients with CRE resistant to ertapenem but susceptible to meropenem (ertapenem-only-resistant Enterobacterales; EORE) benefit from therapy with anti-CRE agents. METHODS: Patients treated for CRE infection in hospitals in the USA between 2016 and 2019 and enrolled in the CRACKLE-2

study were included. The primary outcome was the desirability of outcome ranking (DOOR) assessed at 30 days after index cultures. RESULTS: The EORE group included 213 patients and the MCRE group included 643. The demographics were similar between the groups except for the patients' race and origin before admission. The MCRE group received anti-CRE agents for definitive therapy significantly more frequently compared with the EORE group (30% versus 5% for ceftazidime/avibactam). We did not observe a significant difference between the groups in the adjusted DOOR probability of a more desirable outcome for a randomly selected patient in the EORE group compared with the MCRE group (52.5%; 95% CI, 48.3%-56.7%). The MCRE group had a similar proportion of patients who died at 30 days (26% versus 21%) and who were discharged to home (29% versus 40%), compared with the EORE group. CONCLUSIONS: Patients with clinical EORE infection rarely received anti-CRE agents, but attained similar outcomes compared with patients with MCRE infection. The findings support current IDSA treatment guidance for meropenem- or imipenem-based therapy for treatment of EORE infections.

Internal Medicine
Abusuliman M, **Jamali T**, and **Elatrache M**. Esophageal Obstruction After Bleeding Within an Esophageal Duplication Cyst. *Gastrointest Endosc* 2024; Epub ahead of print. PMID: 38879043. Full Text

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Internal Medicine
Abusuliman M, **Jamali T**, and **Elatrache M**. Heterotopic Pancreatic Tissue Containing a Mucinous Cystic Neoplasm Within the Duodenum With Fish-Mouth Appearance on Endoscopy. *Gastrointest Endosc* 2024; Epub ahead of print. PMID: 38876264. Full Text

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Internal Medicine
Ahmed O, **Singh H**, **Bai S**, **Maraj D**, **Qureshi MA**, **Hawes E**, **Alamelumangapuram C**, and **Othman H**. Delayed Presentation of a Post-infarction Ventricular Septal Rupture. *J Investig Med High Impact Case Rep* 2024; 12:23247096241262514. PMID: 38904301. Full Text

Henry Ford Allegiance Health, Jackson, MI, USA.

Ventricular septal rupture, a formidable complication of acute myocardial infarction (AMI), is linked to significant morbidity and mortality. The clinical manifestation typically involves pronounced hemodynamic compromise necessitating prompt surgical intervention. This report outlines the case of a 60-year-old male presenting with acute heart failure 3 weeks post a presumed AMI. On evaluation, a substantial ventricular septal defect with left-to-right shunt was observed. The patient, although hemodynamically stable with mild symptoms, underwent surgical closure of the defect and coronary artery bypass graft for multivessel coronary artery disease. This case contributes to the literature on the delayed presentation of post-myocardial infarction (MI) ventricular septal rupture, a scenario deviating from the anticipated severe hemodynamic instability given the timing of the MI and the extent of the septal defect.

Internal Medicine
Chaudhary AJ, **Joyce KM**, **Haq K**, Qureshi MH, and **Donthireddy V**. Non-alcoholic Wernicke's Encephalopathy Masquerading As CNS Relapse of Acute Myeloid Leukemia. *Cureus* 2024; 16(5):e61184. PMID: 38933646. Request Article

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While Wernicke's encephalopathy (WE) is mostly caused by thiamine deficiency secondary to chronic alcohol use, other conditions that may affect one's nutritional status, such as bariatric surgery, hyperemesis gravidarum, chronic gastrointestinal disease, HIV/AIDS, and certain malignancies, may also lead to this outcome. We are discussing one such case, WE, in a young man with acute myeloid leukemia (AML) who underwent chemotherapy. The patient presented with blurred vision, paresthesia, weakness, and vomiting. Although he denied alcohol abuse, his symptoms, physical exam findings, and MRI results were consistent with WE. Treatment with thiamine resulted in a significant improvement in his visual disturbances and mental status. The authors highlight the importance of recognizing WE in non-alcoholic patients, particularly those undergoing prolonged hospitalization and chemotherapy, as nutritional deficiencies can develop. They recommend thiamine supplementation for patients receiving chemotherapy and those with poor oral intake. The case underscores the need for high clinical suspicion and early intervention in atypical cases of WE.

Internal Medicine
Chaudhary AJ, **Khan MZ**, Sohail A, Zaidi SMH, Denha E, and **Venkat D**. Acute onset nitrofurantoin-induced autoimmune hepatitis after urinary tract infection treatment. *Clin Case Rep* 2024; 12(6):e9050. PMID: 38868111. Full Text

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KEY CLINICAL MESSAGE: This case signifies the importance of recognizing DIAIH within the context of antibiotic therapy, especially in older adults and even shortly after common drug exposures for treating UTI. ABSTRACT: Various drugs can induce immune-mediated liver damage and in rare instances may lead to autoimmune hepatitis. Here we report an 84-year-old woman who developed autoimmune hepatitis less than 3 weeks after treatment for urinary tract infection with the antibiotic nitrofurantoin. She presented with jaundice, right upper quadrant abdominal pain, nausea, and vomiting. In the absence of a history of an autoimmune disorder or elevated liver enzymes in the past; elevated liver enzymes after a short course of Nitrofurantoin and the presence of smooth muscle antibodies strongly suggested autoimmune hepatitis, which was confirmed through biopsy sample analysis. The patient scored 7 points on the Naranjo adverse reaction probability scale. The patient's rapid recovery within 1 month of prednisone therapy supports the association of liver damage with nitrofurantoin use.

Internal Medicine
Cherabuddi MR, **Goodman B**, **Ayyad A**, **Almajali DA**, **Nadeem O**, **Bradley P**, **Russell C**, and **Ouellette D**. Association of Area Deprivation Index with Adherence to Proposed Regimen in Patients with Sarcoidosis in Detroit, Michigan. *Sarcoidosis Vasc Diffuse Lung Dis* 2024; 41(2):e2024031. PMID: 38940707. Full Text

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BACKGROUND AND AIM: Social predictors affect severity of sarcoidosis, with Black patients, older individuals, those with lower income, and those without insurance having greater severity. This study aimed to explore potential disparities affecting access to care in sarcoidosis patients with a primary focus on metrics such as area deprivation index (ADI) and its association with adherence to the proposed regimen. METHODS: A retrospective chart review study of all patients seen in pulmonary clinics at a large urban tertiary care center over 2 years with sarcoidosis patients identified with International Classification of Diseases diagnosis code D86. Data collected included age, race, sex, ADI, insurance, online patient portal usage, chest x-rays, pulmonary function tests, missed visits, hospitalizations, positive biopsy, communication and visits around bronchoscopy. Categorical variables were described using frequency and percentage. Numerical variables were described using median, mean and standard deviation.

Statistical analysis included chi-square test, two-sample T-test and Wilcoxon rank sum test. Multivariate logistic regression analysis was performed to model independent association with 12 month no-show occurrence as a metric of adherence to the proposed regimen. RESULTS: Among sarcoidosis patients (N = 788), univariate models showed the presence of active online patient portal use among younger patients (58.6 years with portal vs. 65.1 years without portal, $p < 0.001$), those with lower ADI (73 with portal vs. 92 without portal, $p < 0.001$) and with commercial insurance (48.5% with portal vs. 20.7% without portal, $p < 0.001$); more x-rays (45.6% with x-rays vs. 36.6% without x-rays, $p = 0.018$) and hospitalizations (50.3% with hospitalizations vs. 36.2% without hospitalizations, $p < 0.001$) in Medicare patients. Sarcoidosis patients with positive biopsies on file from 2013-2023 were more likely to be male (44.19% with positive biopsy vs. 33.91% without positive biopsy, $p = 0.006$), White (36.29% with positive biopsy vs. 22.9% without positive biopsy, $p < 0.001$) or other races (3.23% with positive biopsy vs. 2.25% without positive biopsy, $p < 0.001$), younger (55.8 years with positive biopsy vs. 61.7 years without positive biopsy, $p < 0.001$) and belonged to lower national ADI ranks (73 with positive biopsy vs. 80 without biopsy, $p = 0.041$). A multivariate analysis was done with those variables found to be significant in the univariate analyses, which revealed that higher ADI national was associated with failure to adhere to the proposed regimen. CONCLUSIONS: We identified intricate patterns of sociodemographic variables affecting access to care in sarcoidosis patients, especially higher ADI national associated with failure to adhere to the proposed regimen, raising concerns for potential healthcare barriers. Understanding these barriers is vital for equitable high-quality care, assisting in timely and efficient management of the patient's disease.

Internal Medicine

Ellauzi R, Erdem S, Salam MF, Kumar A, **Aggarwal V**, **Koenig G**, **Aronow HD**, and **Basir MB**. Mechanical Circulatory Support Devices in Patients with High-Risk Pulmonary Embolism. *J Clin Med* 2024; 13(11). PMID: 38892871. Full Text

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Pulmonary embolism (PE) is a common acute cardiovascular condition. Within this review, we discuss the incidence, pathophysiology, and treatment options for patients with high-risk and massive pulmonary embolisms. In particular, we focus on the role of mechanical circulatory support devices and their possible therapeutic benefits in patients who are unresponsive to standard therapeutic options. Moreover, attention is given to device selection criteria, weaning protocols, and complication mitigation strategies. Finally, we underscore the necessity for more comprehensive studies to corroborate the benefits and safety of MCS devices in PE management.

Internal Medicine

Kleinaki M, Vey JA, Awounvo S, **Ishak A**, Arnaouti M, Ryu HS, and Nikas IP. The Diagnostic Accuracy of Claudin-4 Immunochemistry in Differentiating Metastatic Carcinomas From Mesothelial Processes in Serous Effusion Cytology: A Systematic Review and Meta-analysis. *Arch Pathol Lab Med* 2024; Epub ahead of print. PMID: 38871358. Full Text

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CONTEXT.—: Distinguishing metastatic carcinomas from mesotheliomas or reactive mesothelial cells in pleural, peritoneal, and pericardial effusions is a common diagnostic problem cytopathologists encounter. OBJECTIVE.—: To perform the first meta-analysis on the pooled diagnostic accuracy of claudin-4

immunochemistry in serous effusion cytopathology. DESIGN.—: This report followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines for diagnostic test accuracy studies. Three databases (PubMed, Scopus, and the Cochrane Library) were searched until October 9, 2023, followed by study selection using specific inclusion and exclusion criteria and data extraction. The study quality assessment was performed by using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool. Statistical analysis was performed by using R to calculate the pooled sensitivity and specificity of claudin-4 immunochemistry. In addition, the diagnostic odds ratio was measured, representing the odds ratio of a positive result indicating a carcinoma rather than a mesothelial process in serous effusion cytology. RESULTS.—: Fourteen observational studies, published between 2011 and 2023, fulfilled the selection criteria and were included. All 14 studies used the 3E2C1 clone. Claudin-4 immunochemistry showed a high diagnostic accuracy in serous effusion cytology. The pooled sensitivity and specificity were 98.02% (95% CI, 93.96%-99.37%) and 99.72% (95% CI, 97.36%-99.97%), respectively. Lastly, the pooled diagnostic odds ratio was 1660.5 (95% CI, 760.0-3627.8) and no evidence of statistical heterogeneity between the included studies was found ($I2 = 0\%$, $\tau 2 = 0$). CONCLUSIONS.—: Claudin-4 may be used as a single pan-carcinoma immunochemical biomarker in the differential diagnosis between metastatic carcinomas and mesotheliomas or reactive mesothelial cells in serous effusion cytology.

Internal Medicine

Lockhart E, Turner D, Guastaferro K, Szalacha LA, Alzate HT, Marhefka S, **Pittiglio B**, **Dekker M**, **Yeh HH**, **Zelenak L**, **Toney J**, **Manogue S**, and **Ahmedani BK**. Increasing pre-exposure prophylaxis (PrEP) in primary care: A study protocol for a multi-level intervention using the multiphase optimization strategy (MOST) framework. *Contemp Clin Trials* 2024; 143:107599. PMID: 38848935. Full Text

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BACKGROUND: In the United States, over 1.2 million people are living with HIV. This disease disproportionately affects men who have sex with men (MSM), people of color, youth and young adults, and transgender individuals. Pre-exposure prophylaxis (PrEP) is an effective HIV prevention method. Barriers exist for both primary care providers (PCPs) to prescribe PrEP and prevent patients from initiating PrEP. METHODS: This study, MOST: PrEP, follows the multiphase optimization strategy

(MOST) framework. The purpose is to identify a multi-level intervention among patients and PCPs to increase PrEP prescriptions in primary care. First, feedback will be obtained from providers and patients via focus groups, then, suggestions related to the context-specific (provider and individual level) factors of intervention component delivery will be incorporated. Subsequently, a rigorous experiment will be conducted using a 2(4) factorial design focusing on priority populations for PrEP initiation. Provider components include computer-based simulation training and a best practice alert. Patient components include a tailored PrEP educational video and HIV risk assessment. Finally, the facilitators and barriers to implementing the intervention components will be qualitatively examined. CONCLUSION: In this protocol paper, we describe the one of the first known multilevel MOST optimization trial in healthcare. Intervention components are to be delivered to patients and providers in a large healthcare system, based in an HIV Ending the Epidemic priority jurisdiction. If effective, this multi-level approach could be disseminated to providers and patients in other large healthcare systems to make a significant impact on HIV prevention.

Internal Medicine

Miller J, **Cook B**, **Gandolfo C**, Mills NL, Mahler S, Levy P, **Parikh S**, **Krupp S**, **Nour K**, **Klausner H**, **Gindi R**, **Lewandowski A**, **Hudson M**, **Perrotta G**, **Zweig B**, **Lanfear D**, **Kim H**, Dangoulian S, **Tang A**, **Todter E**, **Khan A**, Keerie C, **Bole S**, **Nasseredine H**, **Oudeif A**, **Abou Asala E**, **Mohammed M**, **Kazem A**, **Malette K**, **Singh-Kucukarslan G**, Xu N, Wittenberg S, **Morton T**, **Gunaga S**, **Affas Z**, **Tabbaa K**, Desai P, **Alsaadi A**, **Mahmood S**, **Schock A**, **Konowitz N**, **Fuchs J**, **Joyce K**, Shamoun L, Babel J, Broome A, **Digiacinto G**, **Shaheen E**, **Darnell G**, **Muller G**, **Heath G**, **Bills G**, **Vieder J**, **Rockoff S**, **Kim B**, **Colucci A**, **Plemmons E**, and **McCord J**. Rapid Acute Coronary Syndrome Evaluation Over One Hour With High-Sensitivity Cardiac Troponin I: A United States-Based Stepped-Wedge, Randomized Trial. *Ann Emerg Med* 2024; Epub ahead of print. PMID: 38888531. Full Text

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STUDY OBJECTIVE: The real-world effectiveness and safety of a 0/1-hour accelerated protocol using high-sensitivity cardiac troponin (hs-cTn) to exclude myocardial infarction (MI) compared to routine care in the United States is uncertain. The objective was to compare a 0/1-hour accelerated protocol for evaluation of MI to a 0/3-hour standard care protocol. METHODS: The RACE-IT trial was a stepped-wedge, randomized trial across 9 emergency departments (EDs) that enrolled 32,609 patients evaluated for possible MI from July 2020 through April 2021. Patients undergoing high-sensitivity cardiac troponin I testing with concentrations less than or equal to 99th percentile were included. Patients who had MI excluded by the 0/1-hour protocol could be discharged from the ED. Patients in the standard care protocol had 0- and 3-hour troponin testing and application of a modified HEART score to be eligible for discharge. The primary endpoint was the proportion of patients discharged from the ED without 30-day death or MI. RESULTS: There were 13,505 and 19,104 patients evaluated in the standard care and accelerated protocol groups, respectively, of whom 19,152 (58.7%) were discharged directly from the ED. There was no significant difference in safe discharges between standard care and the accelerated protocol (59.5% vs 57.8%; adjusted odds ratio (aOR)=1.05, 95% confidence interval [CI] 0.95 to 1.16). At 30 days, there were 90 deaths or MIs with 38 (0.4%) in the standard care group and 52 (0.4%) in the accelerated protocol group (aOR=0.84, 95% CI 0.43 to 1.68). CONCLUSION: A 0/1-hour accelerated protocol using high-sensitivity cardiac troponin I did not lead to more safe ED discharges compared with standard care.

Internal Medicine

Nimri F, **Ichkhanian Y**, Shinn B, Kowalski TE, Loren DE, Kumar A, Schlachterman A, Tantau A, Arevalo M, **Taha A**, **Shamaa O**, Viales MC, Khashab MA, **Simmer S**, **Singla S**, **Piraka C**, and **Zuchelli TE**. Comprehensive analysis of adverse events associated with transmural use of LAMS in patients with liver cirrhosis: International multicenter study. *Endosc Int Open* 2024; 12(6):E740-e749. PMID: 38847015. Full Text

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Background and study aims Endoscopic ultrasound (EUS)-guided transmural (TM) deployment of lumen-apposing metal stents (LAMS) is considered relatively safe in non-cirrhotic patients and is cautiously offered to cirrhotic patients. Patients and methods This was a retrospective, multicenter, international matched case-control study to study the safety of EUS-guided TM deployment of LAMS in cirrhotic patients. Results Forty-three cirrhotic patients with model for end-stage liver disease score 12.5 ± 5, with 23 having ascites and 16 with varices underwent EUS-guided TM LAMS deployment, including 19 for pancreatic fluid collection (PFC) drainage, 13 gallbladder drainage, six for endoscopic ultrasound-directed transgastric endoscopic retrograde cholangiopancreatography (ERCP), three for EDGI, one for endoscopic ultrasound-directed transenteric ERCP, and one postsurgical collection drainage. Technical failure occurred in one LAMS for PFC drainage. Clinical failure was encountered in another PFC. Nine adverse events (AEs) occurred. The most common AE was LAMS migration (3), followed by non-bleeding mucosal erosion (2), delayed bleeding (2), sepsis (1), and anesthesia-related complication (pulseless electrical activity) (1). Most AEs were graded as mild (6), followed by severe (2), and moderate (1); the majority were managed conservatively. On univariable comparison, risk of AE was higher when using a 20 × 10 mm LAMS and the absence of through-the-LAMS plastic stent(s). Conditional logistic regression of matched case-control patients did not show any association between potential predicting factors and occurrence of AEs. Conclusions Our study demonstrated that mainly in patients with Child-Pugh scores A and B cirrhosis and despite the presence of mild-to-moderate ascites in over half of cases, the majority of AEs were mild and could be managed conservatively. Further studies are warranted to verify the safety of LAMS in cirrhotic patients.

Internal Medicine

Schaefer JK, Errickson J, Kong X, Ali MA, DeCamillo D, Edupuganti S, Haymart B, **Kaatz S**, Kline-Rogers E, Kozlowski JH, **Krol GD**, Sood SL, Froehlich JB, and Barnes GD. Outcomes of direct oral anticoagulants with aspirin vs warfarin with aspirin: a registry-based cohort study. *Res Pract Thromb Haemost* 2024; 8(4). PMID: Not assigned. Full Text

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Background: For patients anticoagulated with direct oral anticoagulants (DOACs) or warfarin and on aspirin (ASA) for nonvalvular atrial fibrillation and/or venous thromboembolism, it is unclear if bleeding outcomes differ. Objectives: To assess bleeding rates for ASA with DOACs vs warfarin and one another. Methods: Registry-based cohort study of patients followed by a 6-center quality improvement collaborative in Michigan using data from 2009 to 2022. The study included adults on ASA with warfarin or DOACs for atrial fibrillation and/or venous thromboembolism without a recent myocardial infarction or heart valve replacement. Results: After propensity matching by anticoagulant class, we compared 2 groups of 1467 patients followed for a median of 18.0 months. Any bleeding and nonmajor bleeding was increased with DOACs + ASA compared with warfarin + ASA (32.2 vs 27.8 and 27.1 vs 22.9 events/100

patient-years; relative risks [RRs], 1.1 and 1.2; 95% CIs, 1.1-1.2 and 1.1-1.3, respectively). After matching by drug, patients on apixaban + ASA vs warfarin + ASA had more bleeding (31.2 vs 27.8 events/100 patient-years; RR, 1.1; 95% CI, 1.0-1.2) and nonmajor bleeding but less major bleeding (3.8 vs 4.7 events/100 patient-years; RR, 0.8; 95% CI, 0.6-1.0) and emergency room visits for bleeding. Patients on rivaroxaban + ASA vs warfarin + ASA had more bleeding (39.3 vs 26.3 events/100 patient-years, RR, 1.5; 95% CI, 1.3-1.6), nonmajor bleeding, and thrombosis. Patients on apixaban + ASA vs rivaroxaban + ASA had significantly less bleeding (22.5 vs 39.3/100 patient-years; RR, 0.6; 95% CI, 0.5-0.7), nonmajor bleeding, major bleeding (2.1 vs 5.5 events/100 patient-years; RR, 0.4; 95% CI, 0.2-0.6), emergency room visits for bleeding, and thrombotic events. Conclusion: Patients on DOAC + ASA without a recent myocardial infarction or heart valve replacement had more nonmajor bleeding but otherwise similar outcomes compared with warfarin + ASA. Patients treated with rivaroxaban + ASA experienced more adverse clinical events compared with warfarin + ASA or apixaban + ASA.

Internal Medicine
Singh H, Kaushal J, Garcia A, and **Kak V**. Clostridium perfringens Empyema: Anaerobic Invasion in an Uncommon Location. *Cureus* 2024; 16(5):e60082. PMID: 38860109. Request Article

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Clostridium perfringens bacteremia arises due to skin inoculation from the external environment or translocation from the gastrointestinal tract. In the event of bacteremia, it tends to colonize in anaerobic environments due to its obligatory anaerobic nature. Its inoculation in the lung, albeit rare, can occur if an anaerobic nidus is created. In the presented case, the patient developed C. perfringens bacteremia andempyema in the area of lung necrosis caused by acute pulmonary embolism. He did not have any history of chest trauma, and the source of bacteremia was deemed to be via gut translocation. The patient was noted to have multiple gastric ulcers on endoscopy and jejunal wall thickening, which likely led to the bacterial translocation into the bloodstream. He underwent video-assisted thoracoscopic surgery-assisted decortication and intravenous antibiotics, eventually leading to clinical improvement. To identify the source of Clostridium in the absence of penetrating trauma, a thorough gastrointestinal evaluation, including a colonoscopy, is warranted to identify the pathology leading to the gastrointestinal translocation.

Internal Medicine
Sohail A, Shehadah A, **Chaudhary A**, Naseem K, Iqbal A, Khan A, and Singh S. Impact of index admission cholecystectomy vs interval cholecystectomy on readmission rate in acute cholangitis: National Readmission Database survey. *World J Gastrointest Endosc* 2024; 16(6):350-360. PMID: 38946855. Full Text

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BACKGROUND: Elective cholecystectomy (CCY) is recommended for patients with gallstone-related acute cholangitis (AC) following endoscopic decompression to prevent recurrent biliary events. However, the optimal timing and implications of CCY remain unclear. AIM: To examine the impact of same-admission CCY compared to interval CCY on patients with gallstone-related AC using the National Readmission Database (NRD). METHODS: We queried the NRD to identify all gallstone-related AC

hospitalizations in adult patients with and without the same admission CCY between 2016 and 2020. Our primary outcome was all-cause 30-d readmission rates, and secondary outcomes included in-hospital mortality, length of stay (LOS), and hospitalization cost. RESULTS: Among the 124964 gallstone-related AC hospitalizations, only 14.67% underwent the same admission CCY. The all-cause 30-d readmissions in the same admission CCY group were almost half that of the non-CCY group (5.56% vs 11.50%). Patients in the same admission CCY group had a longer mean LOS and higher hospitalization costs attributable to surgery. Although the most common reason for readmission was sepsis in both groups, the second most common reason was AC in the interval CCY group. CONCLUSION: Our study suggests that patients with gallstone-related AC who do not undergo the same admission CCY have twice the risk of readmission compared to those who undergo CCY during the same admission. These readmissions can potentially be prevented by performing same-admission CCY in appropriate patients, which may reduce subsequent hospitalization costs secondary to readmissions.

Nephrology

Clifton E, Winder GS, Lentine KL, Zimbrean PC, Yadav A, Rubman S, Kalil R, Kumar V, **Prashar R**, Gan G, Deng Y, Joyce M, Holmes R, Laflen J, Bakhai D, Liapakis A, and Doshi MD. Psychosocial Evaluation of Living Kidney Donors: A Survey of Current Practices in the United States. *Transplantation* 2024; Epub ahead of print. PMID: 38867351. Full Text

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BACKGROUND: Best practices in psychosocial evaluation and care of living donor candidates and donors are not well established. METHODS: We surveyed 195 living kidney donor (LKD) transplant centers in United States from October 2021 to April 2022 querying (1) composition of psychosocial teams, (2) evaluation processes including clinical tools and domains assessed, (3) selection criteria, and (4) psychosocial follow-up post-donation. RESULTS: We received 161 responses from 104 programs, representing 53% of active LKD programs and 67% of LKD transplant volume in 2019. Most respondents (63%) were social workers/independent living donor advocates. Over 90% of respondents indicated donor candidates with known mental health or substance use disorders were initially evaluated by the psychosocial team. Validated psychometric or transplant-specific tools were rarely utilized but domains assessed were consistent. Active suicidality, self-harm, and psychosis were considered absolute contraindications in >90% of programs. Active depression was absolute contraindication in 50% of programs; active anxiety disorder was excluded 27%. Conditions not contraindicated to donation include those in remission: anxiety (56%), depression (53%), and posttraumatic stress disorder (41%). There was acceptance of donor candidates using alcohol, tobacco, or cannabis recreationally, but not if pattern met criteria for active use disorder. Seventy-one percent of programs conducted post-donation psychosocial assessment and use local resources to support donors. CONCLUSIONS: There was variation in acceptance of donor candidates with mental health or substance use disorders. Although most programs conducted psychosocial screening post-donation, support is not standardized and unclear if adequate. Future studies are needed for consensus building among transplant centers to form guidelines for donor evaluation, acceptance, and support.

Neurology

Elrefaey A, **Mohamedelkhair A**, **Fahmy L**, Affan M, **Schultz LR**, **Cerghet M**, and **Memon AB**. The clinical, diagnostic and treatment spectrum of seropositive and seronegative autoimmune encephalitis: Single-center cohort study of 51 cases and review of the literature. *Clin Exp Neuroimmunol* 2024. PMID: Not assigned. Full Text

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Objective: Autoimmune encephalitis (AE) comprises a spectrum of inflammatory neurological syndromes characterized by immune responses to neuronal autoantigens, leading to diverse clinical manifestations, particularly behavioral and cognitive decline. Methods: This single-center retrospective study included 51 patients diagnosed with AE from 2013 to 2019 in a southeast Michigan tertiary care hospital. Patients were then divided into two groups, seropositive AE (AE+) and seronegative AE (AE−), based on antibody detection in the serum, cerebrospinal fluid or both when available. The study compares AE+ and AE− subtypes across clinical, diagnostic, and therapeutic parameters. Results: A total of 34 patients were classified as AE+, and 17 as AE−. Demographic analysis showed no significant differences in age, sex or race between the two groups. Clinical presentations varied widely, encompassing psychiatric symptoms, movement disorders, seizures and confusion; 24% patients had a prior malignancy. Laboratory assessments found diverse autoantibodies in AE+ patients' serum. Radiological and electrophysiological assessments showed no significant differences between the groups. AE− patients had higher rates of confusion compared with AE+ patients (59% vs. 18%, P = 0.004). Conclusions: This study focuses on the complexities associated with diagnosing AE, emphasizing the challenges posed by the heterogeneity of symptoms and often negative antibody test results. Rapid identification of AE, regardless of seropositivity or seronegativity, emerges as a critical factor for clinicians, facilitating the prompt initiation of immunotherapy and/or tumor removal if needed. These insights contribute to a better understanding of the landscape of this condition, offering clinicians the tools to refine their diagnostic and treatment strategies. Ultimately, the study aimed to enhance the management of AE, empowering healthcare professionals to make accurate and timely interventions for patients.

Neurology

LeWitt PA, Hong L, and Moehle MS. Anticholinergic drugs for parkinsonism and other movement disorders. *J Neural Transm (Vienna)* 2024; Epub ahead of print. PMID: 38904792. Full Text

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Anticholinergic (AC) drugs, a medication class that acts by blocking nicotinic and muscarinic acetylcholine receptors, were first utilized for therapeutic purposes in the mid-19th century. Initial applications were as symptomatic therapy for Parkinson disease (PD), a practice continuing to the present. Initially, the AC drugs used were naturally-occurring plant compounds. Synthetic AC drugs were developed in the late 1940s and predominated in neurological therapeutics. Until the advent of pharmaceuticals acting upon striatal dopaminergic motor pathways, AC drugs provided the only effective means for lessening tremors and other clinical problems of the PD patient. However, because dopaminergic compounds are so effective at meeting the needs of the typical PD patient, AC medications are far less utilized by clinicians today. In recent years, there has been only a few investigations of AC drugs as neurological treatments. This review will revisit the clinical landscape of AC pharmacology and application for movement disorders along with recent research in search of improving therapeutics with AC drugs.

Neurosurgery

Ahluwalia MS, Ozair A, Drappatz J, Ye X, Peng S, Lee M, Rath S, Dhruv H, Hao Y, Berens ME, **Walbert T**, Holdhoff M, Lesser GJ, Cloughesy TF, Sloan AE, Takebe N, Couce M, Peereboom DM, Nabors B, Wen PY, Grossman SA, and **Rogers LR**. Evaluating the Base Excision Repair Inhibitor TRC102 and Temozolomide for patients with Recurrent Glioblastoma in the Phase 2 Adult Brain Tumor Consortium Trial BERT. *Clin Cancer Res* 2024; Epub ahead of print. PMID: 38836759. Full Text

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PURPOSE: Patients with glioblastoma (GBM) have a dismal prognosis. While DNA alkylating agent temozolomide (TMZ) is mainstay of chemotherapy, therapeutic resistance develops rapidly in patients. Base excision repair inhibitor TRC102 (methoxyamine) reverses TMZ resistance in preclinical glioma models. We sought to investigate efficacy and safety of oral TRC102+TMZ for recurrent GBM (rGBM). PATIENTS AND METHODS: A pre-registered (NCT02395692), non-randomized, multicenter, phase 2 clinical trial (BERT) was planned and conducted through the Adult Brain Tumor Consortium (ABTC-1402). Arm 1 included bevacizumab-naïve GBM patients at first recurrence, with primary endpoint of response rates. If sufficient activity was identified, a second arm was planned in bevacizumab-refractory patients. Secondary endpoints were overall survival (OS), progression-free survival (PFS), PFS at six months (PFS-6), and toxicity. RESULTS: Arm 1 enrolled 19 patients with median of two treatment cycles. Objective responses were not observed, hence, arm 2 did not open. Median OS was 11.1 months (95%CI 8.2-17.9). Median PFS was 1.9 months (95%CI 1.8-3.7). PFS-6 was 10.5% (95%CI 1.3-33.1%). Most toxicities were Grade 1-2, with two Grade 3 lymphopenias and one Grade 4 thrombocytopenia. Two patients with PFS ≥17 months and OS >32 months were deemed 'extended survivors'. RNA sequencing of tumor tissue, obtained at diagnosis, demonstrated significantly enriched signatures of DNA damage response (DDR), chromosomal instability (CIN70, CIN25), and cellular proliferation (PCNA25) in 'extended survivors'. CONCLUSIONS: These findings confirm safety and feasibility of TRC102+TMZ for rGBM patients. They also warrant further evaluation of combination therapy in biomarker-enriched trials enrolling GBM patients with baseline hyperactivated DDR pathways.

Neurosurgery

Jaber QAH, Shentaif AH, Almajidi M, Ahmad I, Patel H, Azad A, Alnasser SM, Alatawi HA, Menaa F, Alfaifi SYM, Rahman MM, **Ali MM**, and Rao SJA. Synthesis, Structure, and In Vitro Pharmacological Evaluation of some New Pyrimidine-2-Sulfonamide Derivatives and Their Molecular Docking Studies on Human Estrogen Receptor Alpha and CDK2/Cyclin Proteins. *Russ J Bioorg Chem* 2023; 49(SUPPL 1):S106-S118. PMID: Not assigned. Full Text

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In this approach, novel pyrimidine-2-sulfonamide derivatives based on the 2H-chromen-2-one moiety were synthesized and evaluated as anticancer and antibacterial agents. Molecular docking studies have been conducted to investigate the interactions of these compounds with human estrogen receptor alpha (ER alpha) and 4CDK2/Cyclin proteins. The studies have shown that these derivatives can bind to (ER alpha and 4CDK2/Cyclin) proteins with high affinity, suggesting that they may have potential as anti-cancer agents. The cytotoxicity of these compounds was investigated in vitro against MCF-7 and HCT-116 cancer cell lines, with encouraging results being obtained for some of the tested derivatives. In addition, antibacterial studies revealed that some of the synthesized derivatives exhibited effectiveness against tested microorganisms compared to the well-established antibacterial drug Ciprofloxacin. Further, molecular interaction studies revealed that the synthesized molecules have a significant binding affinity toward human estrogen receptor Alpha and CDK2/cyclin A proteins.

Neurosurgery
Kapural L, Melton J, Kim B, Mehta P, Sigdel A, Bautista A, Petersen EA, Slavin KV, Eidt J, Wu J, Elshihabi S, **Schwalb JM**, Garrett HE, Jr., Veizi E, Barolat G, Rajani RR, Rhee PC, Guirguis M, and Mekhail N. Primary 3-Month Outcomes of a Double-Blind Randomized Prospective Study (The QUEST Study) Assessing Effectiveness and Safety of Novel High-Frequency Electric Nerve Block System for Treatment of Post-Amputation Pain. *J Pain Res* 2024; 17:2001-2014. PMID: 38860215. Full Text

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PURPOSE: This multicenter, randomized, double-blinded, active sham-controlled pivotal study was designed to assess the efficacy and safety of high-frequency nerve block treatment for chronic post-amputation and phantom limb pain. PATIENTS AND METHODS: QUEST enrolled 180 unilateral lower-limb amputees with severe post-amputation pain, 170 of whom were implanted with the Altius device, were randomized 1:1 to active-sham or treatment groups and reached the primary endpoint. Responders were those subjects who received ≥50% pain relief 30 min after treatment in ≥50% of their self-initiated treatment sessions within the 3-month randomized period. Differences between the active treatment and sham control groups as well as numerous secondary outcomes were determined. RESULTS: At 30-min, (primary outcome), 24.7% of the treatment group were responders compared to 7.1% of the control group (p=0.002). At 120-minutes following treatment, responder rates were 46.8% in the Treatment group and 22.2% in the Control group (p=0.001). Improvement in Brief Pain Inventory interference score of 2.3 ± 0.29 was significantly greater in treatment group than the 1.3 ± 0.26-point change in the Control group (p = 0.01). Opioid usage, although not significantly different, trended towards a greater reduction in the treatment group than in the control group. The incidence of adverse events did not differ significantly between the treatment and control groups. CONCLUSION: The primary outcomes of the study were met, and the majority of Treatment patients experienced a substantial improvement in PAP (regardless of meeting the study definition of a responder). The significant in PAP was associated with significantly improved QOL metrics, and a trend towards reduced opioid utilization compared to Control. These data indicate that Altius treatment represents a significant therapeutic advancement for lower-limb amputees suffering from chronic PAP.

Neurosurgery

Møller MW, Andersen MS, Halle B, Pedersen CB, Boldt HB, Tan Q, Jurmeister PS, **Herrgott GA**, **Castro AV**, Petersen JK, and Poulsen FR. Genome-Wide DNA Methylation Profiling as a Prognostic Marker in Pituitary Adenomas-A Pilot Study. *Cancers (Basel)* 2024; 16(12). PMID: 38927917. Full Text

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BACKGROUND: The prediction of the regrowth potential of pituitary adenomas after surgery is challenging. The genome-wide DNA methylation profiling of pituitary adenomas may separate adenomas into distinct methylation classes corresponding to histology-based subtypes. Specific genes and differentially methylated probes involving regrowth have been proposed, but no study has linked this epigenetic variance with regrowth potential and the clinical heterogeneity of nonfunctioning pituitary adenomas. This study aimed to investigate whether DNA methylation profiling can be useful as a clinical prognostic marker. METHODS: A DNA methylation analysis by Illumina's MethylationEPIC array was performed on 54 pituitary macroadenomas from patients who underwent transsphenoidal surgery during 2007-2017. Twelve patients were excluded due to an incomplete postoperative follow-up, degenerated biobank-stored tissue, or low DNA methylation quality. For the quantitative measurement of the tumor regrowth rate, we conducted a 3D volumetric analysis of tumor remnant volume via annual magnetic resonance imaging. A linear mixed effects model was used to examine whether different DNA methylation clusters had different regrowth patterns. RESULTS: The DNA methylation profiling of 42 tissue samples showed robust DNA methylation clusters, comparable with previous findings. The subgroup of 33 nonfunctioning pituitary adenomas of an SF1-lineage showed five subclusters with an approximately unbiased score of 86%. There were no overall statistically significant differences when comparing hazard

ratios for regrowth of 100%, 50%, or 0%. Despite this, plots of correlated survival estimates suggested higher regrowth rates for some clusters. The mixed effects model of accumulated regrowth similarly showed tendencies toward an association between specific DNA methylation clusters and regrowth potential. CONCLUSION: The DNA methylation profiling of nonfunctioning pituitary adenomas may potentially identify adenomas with increased growth and recurrence potential. Larger validation studies are needed to confirm the findings from this explorative pilot study.

Obstetrics, Gynecology and Women's Health Services
Ayyash MK, McLaren R, Jr., **Shaman M**, and Al-Kouatly HB. Trends in Preeclampsia Risk Factors in the US From 2010 to 2021. *JAMA* 2024; Epub ahead of print. PMID: 38857021. Full Text

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This population-based retrospective study uses data from the National Vital Statistics System to evaluate trends in risk factors for preeclampsia in the US between 2010 and 2021.
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Obstetrics, Gynecology and Women's Health Services
Bhatnagar AR, **Ghanem AI**, **Alkamachi B**, **Allo G**, **Lin CH**, **Hijaz M**, and **Elshaikh MA**. The prognostic impact of substantial lymphovascular space invasion in women with node negative FIGO stage I uterine carcinoma. *Gynecol Oncol* 2024; 188:44-51. PMID: 38936280. Full Text

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OBJECTIVE: Substantial lymphovascular space invasion (LVSI) is an important predictor of lymph node (LN) involvement in women with endometrial carcinoma. We studied the prognostic significance of substantial LVSI in patients with 2009-FIGO stage-I uterine endometrioid adenocarcinoma (EC) who all had pathologic negative nodal evaluation (PNNE). METHODS: Pathologic specimens were retrieved and LVSI was quantified (focal or substantial) in women with stage-I EC who had a hysterectomy and PNNE. In addition to multivariate analysis (MVA), recurrence-free (RFS), disease-specific (DSS), and overall (OS) survival was compared between women with focal vs. substantial LVSI. RESULTS: 1052 patients were identified with a median follow-up of 9.7 years. 358 women (34%) received adjuvant radiotherapy. 907 patients (86.2%) had no LVSI, 87 (8.3%) had focal, and 58 (5.5%) had substantial LVSI. Five-year RFS was 93.3% (95% CI: 91.5-95.1), 76.8% (95% CI: 67.2-87.7) and 79.1% (95% CI: 67.6-95.3) for no, focal, and substantial LVSI($p < 0.0001$). There was no statistically significant difference in 5-year RFS, DSS, OS, and in the patterns of initial recurrence between women with focal vs substantial LVSI. On MVA with propensity score matching, substantial LVSI was not independently associated with any survival endpoint compared to focal LVSI, albeit both were detrimental when compared to no LVSI.
Age ≥ 60 years and higher grade were predictors of worse RFS, DSS, and OS. Additionally, comorbidity burden was an independent predictor for OS. CONCLUSIONS: Our results suggest that substantial LVSI does not predict worse survival endpoints or different recurrence patterns in women with stage-I EC with PNNE when compared to focal LVSI.

Orthopedics/Bone and Joint Center

Cantu CA, **Myhand M**, **Hazime AA**, **Yedulla NR**, and **Day CS**. Patient-Reported Outcomes Can Serve as a Functional Substitute for Grip Strength. *J Wrist Surg* 2023. PMID: Not assigned. Full Text

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Background Grip strength has traditionally been seen as an objective measurement of hand function, while the Patient-Reported Outcomes Measurement Information System Upper Extremity (PROMIS UE) has emerged recently as a common patient-reported outcome metric for similar purposes. The primary objective of this study was to determine if a correlation exists between grip strength, PROMIS UE, and Quick Disabilities of the Arm, Shoulder, and Hand (QuickDASH) scores in hand and upper extremity clinic patients. Methods PROMIS UE, Pain Interference (PI), and Depression (D), as well as QuickDASH were prospectively administered to patients from July 16 to September 3, 2020. A grip strength ratio (GSR), calculated by dividing the grip strength of the injured hand by that of the noninjured hand, was recorded for each individual to control for personal differences in grip strength. Data were analyzed using Spearman's correlation coefficients with the significance level at $p < 0.05$. Results Fifty patients participated in this study. The median GSR was 0.55. QuickDASH demonstrated strong correlations with both PROMIS UE and PI ($r (48) = -0.81$, $p < 0.05$; $r (48) = 0.86$, $p < 0.05$). GSR correlated moderately with PROMIS UE ($r (48) = 0.63$, $p < 0.05$). Finally, GSR and QuickDASH also exhibited moderate correlation with each other ($r (48) = -0.62$, $p < 0.05$). Conclusion PROMIS UE and QuickDASH are shown to correlate moderately with GSR. This suggests the PROMIS UE forms as an effective measure of hand/wrist function in hand clinic patients and may be substituted for grip strength measurements.

Orthopedics/Bone and Joint Center

Parikh SN, Nemunaitis J, Wall EJ, **Cabatu C**, Gupta R, and Veerkamp MW. Midterm Outcomes of Isolated Medial Patellofemoral Ligament Reconstruction for Patellar Instability in Ehlers-Danlos Syndrome. *Orthop J Sports Med* 2024; 12(6):23259671241241096. PMID: 38845609. Full Text

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BACKGROUND: Patellar instability is frequently encountered in patients with Ehlers-Danlos syndrome (EDS). The clinical outcomes of isolated medial patellofemoral ligament reconstruction (MPFLR) for patellar instability in patients with EDS are unknown. PURPOSE: To evaluate midterm clinical outcomes of isolated MPFLR for patellar instability in patients with EDS and factors affecting these outcomes. STUDY DESIGN: Case series; Level of evidence, 4. METHODS: In a retrospective study, 31 patients (n = 47 knees) with EDS and patellar instability who underwent isolated MPFLR for recurrent patellar instability between 2008 and 2017 and had a minimum 2-year follow-up were identified. Preoperative radiographic images were measured for anatomic risk factors. Clinical outcomes-including postoperative complications-were evaluated. Factors associated with MPFLR failure were identified. Postoperative patient-reported outcomes (PROs)-including the pediatric version of the International Knee Documentation Committee, the Kujala score, the Hospital for Special Surgery Pediatric Functional Activity Brief Scale, the Banff Patellofemoral Instability Instrument 2.0, and the Knee injury and Osteoarthritis Outcome Score-were collected, and factors affecting PRO scores were analyzed. RESULTS: The mean age of the cohort was 14.9 ± 2 years. At a mean follow-up of 7.2 years, 18 of 47 (38.3%) knees required reoperations, of which 9 of 47 (19.1%) knees required revision stabilization for recurrent patellar instability. Also, 7 of 31 knees (22.6%) with autografts failed compared with 2 of 16 (12.5%) with allografts (P = .69). For autografts, 6 of 17 (35.3%) failures occurred with gracilis, but 0 of 13 (0%) occurred with semitendinosus (P = .02). Compared with patients without failures, patients with failed primary MPFLR were significantly younger (P = .0005) and were able to touch the palm to the floor with their knees extended (P = .03). For radiographic parameters, the patellar height and tilt were significantly higher in the failure group. The postoperative PROs were suboptimal at a mean follow-up of 5.2 years. All but 1 patient were satisfied with the final outcome. CONCLUSION: At the midterm follow-up, 38.3% of patients with EDS required further surgery after isolated MPFLR for patellar instability; half of these revisions

(19.1%) were to address recurrent instability. Recurrent instability after isolated MPFLR was more likely in younger patients and those who could touch the palm to the floor with their knees extended. Postoperative PROs were inferior; nonetheless, patient satisfaction was high.

Orthopedics/Bone and Joint Center

Singh A, Mantebea H, Badar F, Batool S, Tetmeyer A, Abdelmessih G, Sebastian T, Newton M, **Baker K**, Salem S, and Xia Y. Assessment of post-trauma microstructural alterations in the rabbit knee cartilage and subchondral bone. *J Anat* 2024; Epub ahead of print. PMID: 38924533. Full Text

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Early diagnosis of post-traumatic osteoarthritis (PTOA) is critical for designing better treatments before the degradation becomes irreversible. We utilized multimodal high-resolution imaging to investigate early-stage deterioration in articular cartilage and the subchondral bone plate from a sub-critical impact to the knee joint, which initiates PTOA. The knee joints of 12 adult rabbits were mechanically impacted once on the femoral articular surface to initiate deterioration. At 2- and 14-week post-impact surgery, cartilage-bone blocks were harvested from the impact region in the animals (N = 6 each). These blocks were assessed for deterioration using polarized light microscopy (PLM), microcomputed tomography (μCT), and biochemical analysis. Statistically significant changes were noted in the impact tissues across the calcified zone (CZ) at 14 weeks post-impact: the optical retardation values in the CZ of impact cartilage had a drop of 29.0% at 14 weeks, while the calcium concentration in the CZ of impact cartilage also had a significant drop at 14 weeks. A significant reduction of 6.3% in bone mineral density (BMD) was noted in the subchondral bone plate of the impact samples at 14 weeks. At 2 weeks post-impact, only minor, non-significant changes were measured. Furthermore, the impact knees after 14 weeks had greater structural changes compared with the 2-week impact knees, indicating progressive degradation over time. The findings of this study facilitated a connection between mineralization alterations and the early deterioration of knee cartilage after a mechanical injury. In a broader context, these findings can be beneficial in improving clinical strategies to manage joint injuries.

Otolaryngology – Head and Neck Surgery

Salmon MK, **Eide JG**, Kshirsagar RS, Palmer JN, Adappa ND, and Kohanski MA. Bleeding risk from nonsteroidal anti-inflammatory drugs after functional endoscopic sinus surgery: Analysis of the TriNetX database. *World J Otorhinolaryngol Head Neck* 2023. PMID: Not assigned. Full Text

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Objectives: Postoperative pain medications and aspirin before undergoing functional endoscopic sinus surgery (FESS) are managed carefully due to concern for bleeding. Little is known regarding the increase in the risk of bleeding for patients unable to stop aspirin as trials are limited in this area. We compared outcomes for patients undergoing FESS who were managed postoperatively with nonsteroidal anti-inflammatory drugs (NSAIDs) versus opioids. We also determined the epistaxis rate for patients on aspirin at the time of surgery compared to those who were not on aspirin. Data Source: Retrospective analysis of patients undergoing FESS using the TriNetX database. Methods: Patients were propensity-matched, and the odds of bleeding complications between the patients prescribed postoperative NSAIDs were compared to those prescribed opioids. We also compared postoperative odds of bleeding in patients unable to halt aspirin use at the time of surgery to those who were not on aspirin before surgery. Results: A total of 51,361 patients received opioids after FESS compared to 1923 patients who received NSAIDs. After propensity matching, 1918 patients were in each group and odds of epistaxis were similar between

the NSAID group and the opioid group (odds ratio [OR]: 1.32, 95% confidence interval (CI): 0.90–1.94); 7.67% of the NSAID group required rescue opioids. Patients on aspirin who were unable to hold aspirin at surgery showed bleeding rates of 14.67% compared to 9.00% in propensity-matched controls who were not on aspirin (OR: 1.74, 95%CI: 1.20–2.51). Conclusions: NSAID use appears to be a safe alternative to opioids for patients without pre-existing risk factors for bleeding. Patients who remained on aspirin in the week before FESS had an increased risk of postoperative epistaxis.

Pathology and Laboratory Medicine
Abou Daher L, **Heppell O**, **Lopez-Plaza I**, and **Guerra-Londono CE**. Perioperative Blood Transfusions and Cancer Progression: A Narrative Review. *Curr Oncol Rep* 2024; Epub ahead of print. PMID: 38847973. Full Text

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PURPOSE OF REVIEW: To examine the most recent evidence about known controversies on the effect of perioperative transfusion on cancer progression. RECENT FINDINGS: Laboratory evidence suggests that transfusion-related immunomodulation can be modified by blood management and storage practices, but it is likely of less intensity than the effect of the surgical stress response. Clinical evidence has questioned the independent effect of blood transfusion on cancer progression for some cancers but supported it for others. Despite major changes in surgery and anesthesia, cancer surgery remains a major player in perioperative blood product utilization. Prospective data is still required to strengthen or refute existing associations. Transfusion-related immunomodulation in cancer surgery is well-documented, but the extent to which it affects cancer progression is unclear. Associations between transfusion and cancer progression are disease-specific. Increasing evidence shows autologous blood transfusion may be safe in cancer surgery.

Pathology and Laboratory Medicine
Bhatnagar AR, **Ghanem AI**, **Alkamachi B**, **Allo G**, **Lin CH**, **Hijaz M**, and **Elshaikh MA**. The prognostic impact of substantial lymphovascular space invasion in women with node negative FIGO stage I uterine carcinoma. *Gynecol Oncol* 2024; 188:44-51. PMID: 38936280. Full Text

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OBJECTIVE: Substantial lymphovascular space invasion (LVSI) is an important predictor of lymph node (LN) involvement in women with endometrial carcinoma. We studied the prognostic significance of substantial LVSI in patients with 2009-FIGO stage-I uterine endometrioid adenocarcinoma (EC) who all had pathologic negative nodal evaluation (PNNE). METHODS: Pathologic specimens were retrieved and LVSI was quantified (focal or substantial) in women with stage-I EC who had a hysterectomy and PNNE. In addition to multivariate analysis (MVA), recurrence-free (RFS), disease-specific (DSS), and overall (OS) survival was compared between women with focal vs. substantial LVSI. RESULTS: 1052 patients were identified with a median follow-up of 9.7 years. 358 women (34%) received adjuvant radiotherapy. 907 patients (86.2%) had no LVSI, 87 (8.3%) had focal, and 58 (5.5%) had substantial LVSI. Five-year RFS was 93.3% (95% CI: 91.5-95.1), 76.8% (95% CI: 67.2-87.7) and 79.1% (95% CI: 67.6-95.3) for no,

focal, and substantial LVSI(p < 0.0001). There was no statistically significant difference in 5-year RFS, DSS, OS, and in the patterns of initial recurrence between women with focal vs substantial LVSI. On MVA with propensity score matching, substantial LVSI was not independently associated with any survival endpoint compared to focal LVSI, albeit both were detrimental when compared to no LVSI.
Age ≥ 60 years and higher grade were predictors of worse RFS, DSS, and OS. Additionally, comorbidity burden was an independent predictor for OS. CONCLUSIONS: Our results suggest that substantial LVSI does not predict worse survival endpoints or different recurrence patterns in women with stage-I EC with PNNE when compared to focal LVSI.

Pathology and Laboratory Medicine
Kaur A, Rojek AE, Symes E, Nawas MT, Patel AA, Patel JL, Sojitra P, Aqil B, Sukhanova M, McNerney ME, Wu LP, Akmatbekov A, Segal J, Tjota MY, Gurbuxani S, Cheng JX, Yeon SY, Ravisankar HV, Fitzpatrick C, Lager A, Drazer MW, Saygin C, Wanjari P, Katsonis P, Lichtarge O, Churpek JE, **Ghosh SB**, Patel AB, Menon MP, Arber DA, Wang P, and Venkataraman G. Real world predictors of response and 24-month survival in high-grade TP53-mutated myeloid neoplasms. *Blood Cancer J* 2024; 14(1):99. PMID: 38890297. Full Text

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Current therapies for high-grade TP53-mutated myeloid neoplasms (≥10% blasts) do not offer a meaningful survival benefit except allogeneic stem cell transplantation in the minority who achieve a complete response to first line therapy (CR1). To identify reliable pre-therapy predictors of complete response to first-line therapy (CR1) and outcomes, we assembled a cohort of 242 individuals with TP53-mutated myeloid neoplasms and ≥10% blasts with well-annotated clinical, molecular and pathology data. Key outcomes examined were CR1 & 24-month survival (OS24). In this elderly cohort (median age 68.2 years) with 74.0% receiving frontline non-intensive regimens (hypomethylating agents +/- venetoclax), the overall cohort CR1 rate was 25.6% (50/195). We additionally identified several pre-therapy factors predictive of inferior CR1 including male gender (P = 0.026), ≥2 autosomal monosomies (P < 0.001), -17/17p (P = 0.011), multi-hit TP53 allelic state (P < 0.001) and CUX1 co-alterations (P = 0.010). In univariable analysis of the entire cohort, inferior OS24 was predicated by ≥2 monosomies (P = 0.004), TP53 VAF > 25% (P = 0.002), TP53 splice junction mutations (P = 0.007) and antecedent treated myeloid neoplasm (P = 0.001). In addition, mutations/deletions in CUX1, U2AF1, EZH2, TET2, CBL, or KRAS ('EPI6' signature) predicted inferior OS24 (HR = 2.0 [1.5-2.8]; P < 0.0001). In a subgroup analysis of HMA +/-Ven treated individuals (N = 144), TP53 VAF and monosomies did not impact OS24. A risk score for HMA +/-Ven treated individuals incorporating three pre-therapy predictors including TP53 splice junction mutations, EPI6 and antecedent treated myeloid neoplasm stratified 3 prognostic distinct groups: intermediate, intermediate-poor, and poor with significantly different median (12.8, 6.0, 4.3 months) and 24-month (20.9%, 5.7%, 0.5%) survival (P < 0.0001). For the first time, in a seemingly monolithic high-risk cohort, our data identifies several baseline factors that predict response and 24-month survival.

Pathology and Laboratory Medicine
Lkhagvaa K, Tsogbadrakh B, Gochoosuren G, Badamdorj O, and **Stark A**. The effect of outcome-based education on clinical performance and perception of pediatric care of the third-year nursing students in Mongolia. *PLoS One* 2024; 19(6):e0305298. PMID: 38861566. Full Text

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BACKGROUND: Mongolian government has set improvement of clinical proficiency of nursing students as one of its priorities. Nursing professionals have the sentinel role in providing healthcare services in rural areas. Outcome-based education (OBE) offers a promising pedagogical approach to actively mentally engage students to strengthen their clinical proficiencies. We implemented a pilot project with the objective of comparing students' clinical performance under OBE with our traditional didactic techniques. METHODS: The researchers implemented a non-equivalent two-armed quasi-experimental post-test-only' design approach study. The intervention arm (n = 34) received OBE pediatric training, while the control arm (n = 32) received the traditional pedagogical pediatric nursing training. Each arm of the study completed 16 hours of theory, 32 hours of clinical skills practice and 32 hours of seminars in pediatric nursing care. Data were collected using a five-section instrument, Demographic, Competency Inventory, Nursing Students' Satisfaction, Course Experience, and Objective Structured Clinical Examination. Performance and knowledge proficiencies were evaluated by applying the two-sided independent T-test. The distributions of categorical variables were assessed by Fisher's exact test or chi-squared test of significance. RESULTS: The intervention arm had higher mean score value in the competency inventory ([Formula: see text] = 238.70, SD = ± 23.07) compared to the control arm ([Formula: see text] = 222.11, SD = ± 39.94) (P = 0.04); similarly, the mean value for nursing students' satisfaction was higher for the intervention arm ([Formula: see text] = 117.87, SD = ± 15.94) compared to the control group ([Formula: see text] = 109.76, SD = ± 16.94) (P = 0.049). Additionally, the difference in the mean value for course experience questionnaire between the intervention arm ([Formula: see text] = 125.33, SD = ± 19.30) and the control arm ([Formula: see text] = 110.41, SD = ± 11.28) was statistically significant (P = 0.0001). Finally, the intervention arm had a higher mean value ([Formula: see text] = 85.40, SD = ± 6.11) for objective structural clinical examination compared to the control arm ([Formula: see text] = 81.56, SD = ± 7.01) (P = 0.023). CONCLUSION: OBE pedagogical approach offers promising benefits to improving nursing students' clinical competencies; additionally, the OBE approach seems to increase students' satisfactions with their clinical curriculum.

Pathology and Laboratory Medicine

Miller J, **Cook B**, **Gandolfo C**, Mills NL, Mahler S, Levy P, **Parikh S**, **Krupp S**, **Nour K**, **Klausner H**, **Gindi R**, **Lewandowski A**, **Hudson M**, **Perrotta G**, **Zweig B**, **Lanfear D**, **Kim H**, Dangoulian S, **Tang A**, **Todter E**, **Khan A**, Keerie C, **Bole S**, **Nasseredine H**, **Oudeif A**, **Abou Asala E**, **Mohammed M**, **Kazem A**, **Malette K**, **Singh-Kucukarslan G**, Xu N, Wittenberg S, **Morton T**, **Gunaga S**, **Affas Z**, **Tabbaa K**, Desai P, **Alsaadi A**, **Mahmood S**, **Schock A**, **Konowitz N**, **Fuchs J**, **Joyce K**, Shamoun L, Babel J, Broome A, **Digiacinto G**, **Shaheen E**, **Darnell G**, **Muller G**, **Heath G**, **Bills G**, **Vieder J**, **Rockoff S**, **Kim B**, **Colucci A**, **Plemmons E**, and **McCord J**. Rapid Acute Coronary Syndrome Evaluation Over One Hour With High-Sensitivity Cardiac Troponin I: A United States-Based Stepped-Wedge, Randomized Trial. *Ann Emerg Med* 2024; Epub ahead of print. PMID: 38888531. Full Text

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STUDY OBJECTIVE: The real-world effectiveness and safety of a 0/1-hour accelerated protocol using high-sensitivity cardiac troponin (hs-cTn) to exclude myocardial infarction (MI) compared to routine care in the United States is uncertain. The objective was to compare a 0/1-hour accelerated protocol for evaluation of MI to a 0/3-hour standard care protocol. METHODS: The RACE-IT trial was a stepped-wedge, randomized trial across 9 emergency departments (EDs) that enrolled 32,609 patients evaluated for possible MI from July 2020 through April 2021. Patients undergoing high-sensitivity cardiac troponin I testing with concentrations less than or equal to 99th percentile were included. Patients who had MI excluded by the 0/1-hour protocol could be discharged from the ED. Patients in the standard care protocol had 0- and 3-hour troponin testing and application of a modified HEART score to be eligible for discharge. The primary endpoint was the proportion of patients discharged from the ED without 30-day death or MI. RESULTS: There were 13,505 and 19,104 patients evaluated in the standard care and accelerated protocol groups, respectively, of whom 19,152 (58.7%) were discharged directly from the ED. There was no significant difference in safe discharges between standard care and the accelerated protocol (59.5% vs 57.8%; adjusted odds ratio (aOR)=1.05, 95% confidence interval [CI] 0.95 to 1.16). At 30 days, there were 90 deaths or MIs with 38 (0.4%) in the standard care group and 52 (0.4%) in the accelerated protocol group (aOR=0.84, 95% CI 0.43 to 1.68). CONCLUSION: A 0/1-hour accelerated protocol using high-sensitivity cardiac troponin I did not lead to more safe ED discharges compared with standard care.

Pathology and Laboratory Medicine

Palathingal Bava E, Sanfrancesco JM, Alkashash A, **Favazza L**, **Aldilami A**, Williamson SR, Cheng L, Idrees MT, and **Al-Obaidy KI**. Acquired cystic disease associated renal cell carcinoma: A clinicopathologic and molecular study of 31 tumors. *Hum Pathol* 2024; 149:48-54. PMID: 38862094. Full Text

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Acquired cystic disease associated renal cell carcinomas (ACD-RCC) are rare and their molecular and histopathological characteristics are still being explored. We therefore investigated the clinicopathologic and molecular characteristics of 31 tumors. The patients were predominantly male (n = 30), with tumors mainly left-sided (n = 17), unifocal (n = 19), and unilateral (n = 29) and a mean tumor size of 25 mm (range, 3-65 mm). Microscopically, several histologic patterns were present, including pure classic sieve-like (n = 4), and varied proportions of mixed classic sieve-like with papillary (n = 23), tubulocystic (n = 9), compact tubular (n = 4) and solid (n = 1) patterns. Calcium-oxalate crystals were seen in all tumors. Molecular analysis of 9 tumors using next generation sequencing showed alterations in SMARCB1 in 3 tumors (1 with frameshift deletion and 2 with copy number loss in chromosome 22 involving SMARCB1 region), however, INI1 stain was retained in all. Nonrecurrent genetic alterations in SETD2, NF1, NOTCH4, BRCA2 and CANT1 genes were also seen. Additionally, MTOR p.Pro351Ser was identified in one tumor. Copy number analysis showed gains in chromosome 16 (n = 5), 17 (n = 2) and 8 (n = 2) as well as loss in chromosome 22 (n = 2). In summary, ACD-RCC is a recognized subtype of kidney tumors,

with several histological architectural patterns. Our molecular data identifies genetic alterations in chromatin modifying genes (SMARCB1 and SETD2), which may suggest a role of such genes in ACD-RCC development.

Pathology and Laboratory Medicine

Sriramulu S, **Thoidingjam S**, Chen WM, **Hassan O**, **Siddiqui F**, **Brown SL**, **Movsas B**, Green MD, Davis AJ, Speers C, **Walker E**, and **Nyati S**. BUB1 regulates non-homologous end joining pathway to mediate radioresistance in triple-negative breast cancer. *J Exp Clin Cancer Res* 2024; 43(1):163. PMID: 38863037. Full Text

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BACKGROUND: Triple-negative breast cancer (TNBC) is a highly aggressive form of breast cancer subtype often treated with radiotherapy (RT). Due to its intrinsic heterogeneity and lack of effective targets, it is crucial to identify novel molecular targets that would increase RT efficacy. Here we demonstrate the role of BUB1 (cell cycle Ser/Thr kinase) in TNBC radioresistance and offer a novel strategy to improve TNBC treatment. METHODS: Gene expression analysis was performed to look at genes upregulated in TNBC patient samples compared to other subtypes. Cell proliferation and clonogenic survivals assays determined the IC(50) of BUB1 inhibitor (BAY1816032) and radiation enhancement ratio (rER) with pharmacologic and genomic BUB1 inhibition. Mammary fat pad xenografts experiments were performed in CB17/SCID. The mechanism through which BUB1 inhibitor sensitizes TNBC cells to radiotherapy was delineated by γ-H2AX foci assays, BLRR, Immunoblotting, qPCR, CHX chase, and cell fractionation assays. RESULTS: BUB1 is overexpressed in BC and its expression is considerably elevated in TNBC with poor survival outcomes. Pharmacological or genomic ablation of BUB1 sensitized multiple TNBC cell lines to cell killing by radiation, although breast epithelial cells showed no radiosensitization with BUB1 inhibition. Kinase function of BUB1 is mainly accountable for this radiosensitization phenotype. BUB1 ablation also led to radiosensitization in TNBC tumor xenografts with significantly increased tumor growth delay and overall survival. Mechanistically, BUB1 ablation inhibited the repair of radiation-induced DNA double strand breaks (DSBs). BUB1 ablation stabilized phospho-DNAPKcs (S2056) following RT such that half-lives could not be estimated. In contrast, RT alone caused BUB1 stabilization, but pre-treatment with BUB1 inhibitor prevented stabilization (t(1/2), ~8 h). Nuclear and chromatin-enriched fractionations illustrated an increase in recruitment of phospho- and total-DNAPK, and KAP1 to chromatin indicating that BUB1 is indispensable in the activation and recruitment of non-homologous end joining (NHEJ) proteins to DSBs. Additionally, BUB1 staining of TNBC tissue microarrays demonstrated significant correlation of BUB1 protein expression with tumor grade. CONCLUSIONS: BUB1 ablation sensitizes TNBC cell lines and xenografts to RT and BUB1 mediated radiosensitization may occur through NHEJ. Together, these results highlight BUB1 as a novel molecular target for radiosensitization in women with TNBC.

Pharmacy
Smith ZR, Palm NM, Smith SE, Dixit D, Keats K, Ciapala SR, Tran T, Sikora A, and Heavner MS. Critical care pharmacist perspectives on optimal practice models and prioritization of professional activities: A cross-sectional survey. *Am J Health Syst Pharm* 2024; Epub ahead of print. PMID: 38861312. Full Text

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DISCLAIMER: In an effort to expedite the publication of articles, AJHP is posting manuscripts online as soon as possible after acceptance. Accepted manuscripts have been peer-reviewed and copyedited, but are posted online before technical formatting and author proofing. These manuscripts are not the final version of record and will be replaced with the final article (formatted per AJHP style and proofed by the authors) at a later time. PURPOSE: Critical care pharmacists (CCPs) are essential members of the multidisciplinary critical care team. Professional activities of the CCP are outlined in a 2020 position paper on critical care pharmacy services. This study looks to characterize CCP perspectives for priorities in optimizing pharmacy practice models and professional activities. METHODS: This was a cross-sectional survey conducted from July 24 to September 20, 2023. A 41-question survey instrument was developed to assess 7 domains: demographics, CCP resource utilization, patient care, quality improvement, research and scholarship, training and education, and professional development. This voluntary survey was sent to members of the American College of Clinical Pharmacy's Critical Care Practice and Research Network. The survey was open for a total of 6 weeks. RESULTS: There was a response rate of 20.7% (332 of 1,605 invitees), with 66.6% of respondents (n = 221) completing at least 90% of the survey questions. Most respondents were clinical specialists (58.2%) and/or practiced at an academic medical center (58.5%). Direct patient care, quality improvement and medication safety, and teaching and precepting were identified as the CCP activities of highest importance to CCPs. The CCP-to-patient ratios considered ideal were 1:11-15 (selected by 49.8% of respondents) and 1:16-20 (33.9% of respondents). The ideal percentage of time dedicated to direct patient care activities, as identified by survey respondents, was 50% (interquartile range, 40-50). CONCLUSION: These findings highlight the professional activities viewed as having the highest priority by CCPs. Future research is needed to define optimal CCP practice models for the delivery of patient care in real-world settings.

Pharmacy
Veve MP, and Patel N. Reply to Lau et al Re: "Antipseudomonal Antibiotics in Diabetic Foot Infections: A Practical Perspective From a Community Hospital". *Open Forum Infect Dis* 2024; 11(6):ofae259. PMID: 38933741. Full Text

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Public Health Sciences
Afshan TS, **Kulkarni A**, Smith JM, Tesson E, Blackshere T, **Joseph C**, **Zoratti EM**, Rivera-Spoljaric K, Hartert T, Gern JE, and Singh AM. Research protocol and recruitment redesign of a study of pregnant women and their infants during the COVID-19 pandemic: Childhood Allergy and the NeOnatal Environment (CANOE). *J Allergy Clin Immunol Glob* 2024; 3(3):100270. PMID: 38881739. Full Text

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BACKGROUND: Recruitment for research studies is a challenging endeavor that was further complicated by the coronavirus disease 2019 pandemic. We launched a new multicenter birth cohort, Childhood Allergy and the NeOnatal Environment (CANOE), supported by the National Institutes of Health in January 2020 across 4 sites. Although the pandemic temporarily halted clinical research, we restructured the study and instituted novel recruitment methods that we hypothesized would enable brisk enrollment when research activities resumed. OBJECTIVE: We sought to develop protocol modifications and recruitment methods that promote successful recruitment of diverse populations in clinical research despite a global pandemic. METHODS: Even though study activities were suspended, we modified recruitment strategies to limit in-person contact, shifting toward alternative HIPAA-compliant methods such as clinician referrals, institutional social media, and telemedicine screening and consent procedures. Protocol changes included reducing the frequency of in-person visits, leveraging clinical care visits to collect biospecimens, expanded self-collection of samples at home, and making study materials available online. RESULTS: Remote methods, including targeted social media posts, mailed letters, and email, combined with in-clinic recruitment with modifications for social distancing led to successful recruitment at all sites. Rates of consent have been similar across recruitment sites, with the highest rates of enrollment of mother-infant dyads realized by sites that implemented multiple recruitment strategies. CONCLUSIONS: Study procedures that prioritize health and safety measures such as social distancing, study participant convenience, and use diverse recruitment strategies enable successful enrollment of pregnant women and their newborns into clinical research while adhering to public health restrictions during a global pandemic.

Public Health Sciences

Begley KM, Leis AM, Petrie JG, Truscon R, Johnson E, **Lamerato LE**, Wei M, Monto AS, and Martin ET. Epidemiology of RSV in Adults and Children with Medically-Attended Acute Respiratory Illness over Three Seasons. *Clin Infect Dis* 2024; Epub ahead of print. PMID: 38836601. Full Text

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BACKGROUND: Data on the true prevalence of RSV among medically-attended acute respiratory illnesses (MAARI) has been limited by the lack of regular clinical testing of mild to moderate illnesses. Here we present a prospective evaluation of the epidemiology of RSV-associated MAARI across age groups and multimorbidity status over three seasons, which is informative in light of the recommendations for shared decision-making for vaccination in older adults. METHODS: Ambulatory patients ≥6 months of age meeting a common MAARI case definition were prospectively enrolled in the Michigan Ford Influenza Vaccine Effectiveness (MFIVE) study, a subsite of the US Influenza Vaccine Effectiveness Network. All participants were tested by nasal-throat swab for RSV and influenza, including subtype, independently from clinician-directed testing. Participant illness characteristics and calculated Multimorbidity-Weighted Index (MWI) were collected by in-person survey and electronic medical record review. RESULTS: Over three surveillance seasons (fall 2017 to spring 2020), 9.9% (n=441) of 4,442 participants had RSV detected. RSV-associated MAARI was more prevalent than influenza for participants 6 months-4 years of age. Adults with RSV-MAARI had higher median MWI scores overall compared to influenza-MAARI and controls with neither virus (1.62, 0.40, and 0.64, respectively). CONCLUSIONS: RSV is a significant, underrecognized cause of MAARI in both children and adults presenting for ambulatory care. Multimorbidity is an important contributor to RSV-associated MAARI in outpatient adults, providing information to support shared clinical decision-making for vaccination.

Public Health Sciences

Bhatnagar AR, **Ghanem AI**, **Alkamachi B**, **Allo G**, **Lin CH**, **Hijaz M**, and **Elshaikh MA**. The prognostic impact of substantial lymphovascular space invasion in women with node negative FIGO stage I uterine carcinoma. *Gynecol Oncol* 2024; 188:44-51. PMID: 38936280. Full Text

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OBJECTIVE: Substantial lymphovascular space invasion (LVSI) is an important predictor of lymph node (LN) involvement in women with endometrial carcinoma. We studied the prognostic significance of substantial LVSI in patients with 2009-FIGO stage-I uterine endometrioid adenocarcinoma (EC) who all had pathologic negative nodal evaluation (PNNE). METHODS: Pathologic specimens were retrieved and LVSI was quantified (focal or substantial) in women with stage-I EC who had a hysterectomy and PNNE. In addition to multivariate analysis (MVA), recurrence-free (RFS), disease-specific (DSS), and overall (OS) survival was compared between women with focal vs. substantial LVSI. RESULTS: 1052 patients were identified with a median follow-up of 9.7 years. 358 women (34%) received adjuvant radiotherapy. 907 patients (86.2%) had no LVSI, 87 (8.3%) had focal, and 58 (5.5%) had substantial LVSI. Five-year RFS was 93.3% (95% CI: 91.5-95.1), 76.8% (95% CI: 67.2-87.7) and 79.1% (95% CI: 67.6-95.3) for no, focal, and substantial LVSI($p < 0.0001$). There was no statistically significant difference in 5-year RFS, DSS, OS, and in the patterns of initial recurrence between women with focal vs substantial LVSI. On MVA with propensity score matching, substantial LVSI was not independently associated with any survival endpoint compared to focal LVSI, albeit both were detrimental when compared to no LVSI.
Age ≥ 60 years and higher grade were predictors of worse RFS, DSS, and OS. Additionally, comorbidity burden was an independent predictor for OS. CONCLUSIONS: Our results suggest that substantial LVSI does not predict worse survival endpoints or different recurrence patterns in women with stage-I EC with PNNE when compared to focal LVSI.

Public Health Sciences

Biagini JM, Martin LJ, He H, Bacharier LB, Gebretsadik T, Hartert TV, Jackson DJ, **Kim H**, Miller RL, Rivera-Spoljaric K, Schauberger EM, Singh AM, Visness CM, **Wegienka G**, **Ownby DR**, Gold DR, Martinez FD, Johnson CC, Wright AL, Gern JE, and Khurana Hershey GK. Performance of the Pediatric Asthma Risk Score across Diverse Populations. *NEJM Evid* 2023; 2(10):EVIDoa2300026. PMID: 38320177. Full Text

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BACKGROUND: Methods to determine whether a toddler is likely to develop asthma are of value to parents and clinical trialists testing primary prevention strategies. The Pediatric Asthma Risk Score (PARS) is a 14-point score of six factors designed to predict asthma in early life. PARS was developed and validated in relatively homogenous populations, so its generalizability is unknown. METHODS: We computed PARS using the six factors of self-declared race (parent-reported as “Black” or “not Black”), parental asthma, eczema, any wheezing, wheezing without a cold, and polysensitization in 5634 children from birth to 3 years of age. The primary outcome of our analysis was the ability of PARS to predict asthma development at 5 to 10 years of age using the area under the receiver operating curve in each cohort and across all cohorts with varying ethnicity, sex, cohort type, birth decades, missing PARS factors, and polysensitization definition. We also performed a meta-analysis across all the cohorts. Finally, we compared PARS predictive ability with the binary Asthma Predictive Index (API). RESULTS: Across 10 cohorts, the area under the receiver operating curve for PARS was 0.76. PARS performance did not differ by ethnicity, sex, cohort type, enrollment decade, missing PARS factors, or polysensitization definition (all P>0.05). The weights of each factor in the meta-analysis were similar to the original PARS weights. PARS and API equally identified children at high risk for developing asthma or not; API missed 31% of children at moderate asthma risk. CONCLUSIONS: PARS provided robust estimates of asthma risk in children from a wide range of ethnicities, backgrounds, and susceptibility. (Funded by the National Institute of Allergy and Infectious Diseases and others.)

Public Health Sciences

Chung JR, Shirk P, Gaglani M, Mutnal MB, Nowalk MP, Moehling Geffel K, House SL, Curley T, Wernli KJ, Kiniry EL, Martin ET, **Vaughn IA**, Murugan V, Lim ES, Saade E, Faryar K, Williams OL, Walter EB, Price AM, Barnes JR, DaSilva J, Kondor R, Ellington S, and Flannery B. Late-Season Influenza Vaccine Effectiveness Against Medically Attended Outpatient Illness, United States, December 2022-April 2023. *Influenza Other Respir Viruses* 2024; 18(6):e13342. PMID: 38923314. Full Text

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BACKGROUND: The 2022-23 US influenza season peaked early in fall 2022. METHODS: Late-season influenza vaccine effectiveness (VE) against outpatient, laboratory-confirmed influenza was calculated among participants of the US Influenza VE Network using a test-negative design. RESULTS: Of 2561 participants enrolled from December 12, 2022 to April 30, 2023, 91 laboratory-confirmed influenza cases primarily had A(H1N1)pdm09 (6B.1A.5a.2a.1) or A(H3N2) (3C.2a1b.2a.2b). Overall, VE was 30% (95%

confidence interval -9%, 54%); low late-season activity precluded estimation for most subgroups. CONCLUSIONS: 2022-23 late-season outpatient influenza VE was not statistically significant. Genomic characterization may improve the identification of influenza viruses that circulate postinfluenza peak.

Public Health Sciences
Elrefaey A, **Mohamedelkhair A**, **Fahmy L**, Affan M, **Schultz LR**, **Cerghet M**, and **Memon AB**. The clinical, diagnostic and treatment spectrum of seropositive and seronegative autoimmune encephalitis: Single-center cohort study of 51 cases and review of the literature. *Clin Exp Neuroimmunol* 2024. PMID: Not assigned. Full Text

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Objective: Autoimmune encephalitis (AE) comprises a spectrum of inflammatory neurological syndromes characterized by immune responses to neuronal autoantigens, leading to diverse clinical manifestations, particularly behavioral and cognitive decline. Methods: This single-center retrospective study included 51 patients diagnosed with AE from 2013 to 2019 in a southeast Michigan tertiary care hospital. Patients were then divided into two groups, seropositive AE (AE+) and seronegative AE (AE−), based on antibody detection in the serum, cerebrospinal fluid or both when available. The study compares AE+ and AE− subtypes across clinical, diagnostic, and therapeutic parameters. Results: A total of 34 patients were classified as AE+, and 17 as AE−. Demographic analysis showed no significant differences in age, sex or race between the two groups. Clinical presentations varied widely, encompassing psychiatric symptoms, movement disorders, seizures and confusion; 24% patients had a prior malignancy. Laboratory assessments found diverse autoantibodies in AE+ patients' serum. Radiological and electrophysiological assessments showed no significant differences between the groups. AE− patients had higher rates of confusion compared with AE+ patients (59% vs. 18%, P = 0.004). Conclusions: This study focuses on the complexities associated with diagnosing AE, emphasizing the challenges posed by the heterogeneity of symptoms and often negative antibody test results. Rapid identification of AE, regardless of seropositivity or seronegativity, emerges as a critical factor for clinicians, facilitating the prompt initiation of immunotherapy and/or tumor removal if needed. These insights contribute to a better understanding of the landscape of this condition, offering clinicians the tools to refine their diagnostic and treatment strategies. Ultimately, the study aimed to enhance the management of AE, empowering healthcare professionals to make accurate and timely interventions for patients.

Public Health Sciences
Hutchings H, **Wang A**, Grady S, **Popoff A**, **Zhang Q**, and **Okereke I**. Influence of Air Quality on Lung Cancer in People Who Have Never Smoked. *J Thorac Cardiovasc Surg* 2024; Epub ahead of print. PMID: 38936598. Full Text

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OBJECTIVE: Lung cancer is the leading cause of cancer-related death. The percentage of people who have never smoked with lung cancer has risen recently, but alternative risk factors require further study. Our goal was to determine the impact of air quality on incidence of lung cancer in people who have smoked or never smoked. METHODS: The Cancer Registry from a large urban medical center was queried to include every new diagnosis of lung cancer from 2013 to 2021. Air quality and pollution data for the county were obtained from the United States Environmental Protection Agency from 1980 to 2018. Patient demographics, location of residence, smoking history and tumor stage were recorded. Bivariate comparison analyses were conducted in R. RESULTS: A total of 2,223 new cases of lung cancer were identified. Mean age was 69.2 years. There was a nonsmoking rate of 8.1 percent. A total of 37 percent of patients identified as a racial minority. People who have never smoked were more likely to be diagnosed at an advanced stage. When analyzing geographic distribution, incidence of lung cancer among people who have never smoked was more closely associated with highly polluted areas. People who have never

smoked with lung cancer had significantly higher exposure levels of multiple pollutants. CONCLUSIONS: Newly diagnosed lung cancer appears to be more related to poor air quality among people who have never smoked than people who have smoked. Future studies are needed to examine the associations of specific pollutants with lung cancer incidence.

Public Health Sciences
Hutchings H, **Zhang Q**, Grady SC, Cox J, **Popoff A**, **Wilson CP**, Zhu S, and **Okereke I**. Lung Cancer and Air Quality in a Large Urban County in the United States. *Cancers (Basel)* 2024; 16(11). PMID: 38893265. Full Text

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Lung cancer is the leading cancer-related killer in the United States. The incidence varies geographically and may be affected by environmental pollutants. Our goal was to determine associations within time series for specific air pollutants and lung cancer cases over a 33-year period in Wayne County, Michigan, controlling for population change. Lung cancer data for Wayne County were queried from the Michigan Cancer Registry from 1985 to 2018. Air pollutant data were obtained from the United States Environmental Protection Agency from 1980 to 2018. Autoregressive distributed lag (ARDL) models were estimated to investigate time lags in years between specific air pollution levels and lung cancer development. A total of 58,866 cases of lung cancer were identified. The mean age was 67.8 years. Females accounted for 53 percent of all cases in 2018 compared to 44 percent in 1985. Three major clusters of lung cancer incidence were detected with the most intense clusters in downtown Detroit and the heavily industrialized downriver area. Sulfur dioxide (SO(2)) had the strongest statistically significant relationship with lung cancer, showing both short- and long-term effects (lag range, 1-15 years). Particulate matter (PM(2.5)) (lag range, 1-3 years) and nitrogen dioxide (NO(2)) (lag range, 2-4 years) had more immediate effects on lung cancer development compared to carbon monoxide (CO) (lag range, 5-6 years), hazardous air pollutants (HAPs) (lag range, 9 years) and lead (Pb) (lag range, 10-12 years), which had more long-term effects on lung cancer development. Areas with poor air quality may benefit from targeted interventions for lung cancer screening and reductions in environmental pollution.

Public Health Sciences
Hutchings HE, Grady SC, **Zhang Q**, **Schwarze E**, **Popoff A**, Khanipov K, and **Okereke IC**. Regional trends in diagnosis of advanced lung cancer in Michigan over 33 years. *J Thorac Dis* 2024; 16(5):2936-2947. PMID: 38883653. Full Text

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BACKGROUND: Lung cancer is the most common cancer killer worldwide. Nearly 80 percent of lung cancers are diagnosed at advanced stages. Lack of access to medical care and undwerutilized lung cancer screening are key reasons for advanced diagnoses. We sought to understand the regional differences in presentation of lung cancer across Michigan. Utilizing a comprehensive cancer registry over 33 years, our goal was to examine associations between sociodemographic patient factors and diagnoses at advanced stages. METHODS: The Michigan Cancer Registry was queried from 1985 to 2018 to include all new diagnoses of non-small cell lung cancer (NSCLC) using International Classification of Diseases for Oncology (ICD-O) version 3 codes. NSCLC was categorized as early, regional and distant disease. Advanced disease was considered to be any disease that was regional or distant. NSCLC rates were calculated and mapped at the zip code level using the 2010 population as the denominator and spatial empirical Bayes methodology. Regional hospital service areas were constructed

using travel time to treatment from the patient's zip code centroid. Logistic regression models were estimated to investigate the significance of rural vs. urban and travel time on level of disease at presentation. Kaplan-Meier and multivariate survival analysis was performed to evaluate the association between distance from the nearest medical center and length of survival controlling for known risk factors for lung cancer. RESULTS: From 1985 to 2018, there were 141,977 patients in Michigan diagnosed with NSCLC. In 1985, men were 2.2 times more likely than women to be diagnosed but by 2018 women and men developed disease at equal rates. Mean age was 67.8 years. Among all patients with known stage of disease, 72.5% of patients were diagnosed with advanced disease. Regional and distant NSCLC rates were both higher in the northern parts of the state. Longer drive times in rural regions also significantly increased the likelihood of advanced NSCLC diagnoses, in particular regional lung cancer. Patients with longer drive times also experienced overall worse survival after controlling for other factors. CONCLUSIONS: Regional disparities exist in Michigan for diagnoses of NSCLC at advanced stages. Factors such as lack of screening in urban regions and distances to treating institutions in rural areas likely contribute to the increased likelihood of advanced NSCLC. Future interventions should target the specific needs of residents to detect disease at earlier stages and improve overall outcomes.

Public Health Sciences

Ioerger P, Mills K, Wagoner SF, Lawrence A, Alapati R, Nallani R, Hamill CS, **Adjei Boakye E**, and Sykes KJ. Inequities Associated With Advanced Stage at Presentation of Head and Neck Cancer: A Systematic Review. *JAMA Otolaryngol Head Neck Surg* 2024; Epub ahead of print. PMID: 38935363. Full Text

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IMPORTANCE: Social determinants of health (SDoH) are defined by a wide range of factors (eg, built environment, economic stability, education level, discrimination, racism, access to health care). Advanced stage at presentation or delayed diagnosis heavily influences health outcomes in patients with head and neck cancer (HNC). While the drivers of advanced-stage presentation come from a multitude of sources, SDoH plays an outsized role. OBJECTIVE: To systematically review the published literature to identify which SDoH are established as risk factors for delayed diagnosis or advanced stage at presentation among patients with HNC. EVIDENCE REVIEW: In this systematic review, a literature search of PubMed, Web of Science, and Embase was conducted on February 27, 2023, using keywords related to advanced stage at presentation and delayed diagnosis of HNC between 2013 and 2023. Quality assessment was evaluated through the Newcastle-Ottawa Scale. Articles were included if they focused on US-based populations and factors associated with advanced stage at presentation or delayed diagnosis of HNC. FINDINGS: Overall, 50 articles were included for full-text extraction, of which 30 (60%) were database studies. Race was the most commonly reported variable (46 studies [92%]), with Black race (43 studies [93%]) being the most studied racial group showing an increased risk of delay in diagnosis of HNC. Other commonly studied variables that were associated with advanced stage at presentation included sex and gender (41 studies [82%]), insurance status (25 studies [50%]), geographic region (5 studies [10%]), and socioeconomic status (20 studies [40%]). Male sex, lack of insurance, rurality, and low socioeconomic status were all identified as risk factors for advanced stage at presentation. CONCLUSIONS AND RELEVANCE: This systematic review provides a comprehensive list of factors that were associated with advanced HNC stage at presentation. Future studies should focus on evaluating interventions aimed at addressing the SDoH in communities experiencing disparities to provide a net positive effect on HNC care.

Public Health Sciences

Kaur N, **Patel K**, **Lu M**, **Dababneh Y**, **Jomaa D**, **Nagirimadugu A**, **Oruganti P**, and **Yee K**. Enhancing Community-Based Specialty Access Through Virtual Care. *NEJM Catal Innov Care Deliv* 2024; 5(6):1-1. PMID: Not assigned. Full Text

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In December 2020, the authors set out to improve access to tertiary care at Henry Ford Health by creating a network of virtual care clinics to overcome the challenges of home-based virtual care, including broadband access or the need for physical examination. These clinics provided connectivity to the tertiary specialist, vital sign assessment, physical examination, and facilitation of diagnostic testing at a location convenient to the patient. Each clinic was staffed by an on-site team including medical assistants and a single advanced practice provider; the tertiary specialists were present only virtually. For example, a patient with complex Crohn's disease requiring surgery and parenteral nutrition is best served by a tertiary specialist and multidisciplinary team. These patients require frequent, thorough follow-up visits, including blood pressure checks to assess hydration, catheter site checks, and physical examination to assess healing after surgery, in addition to medical management of Crohn's disease by a tertiary specialist. Each of these parameters is clinically paramount and not optimally assessed during a home-based video visit. In this clinical scenario, the medical assistant telepresented the patient to the off-site specialist, checked vital signs, and showed the specialist the catheter and surgical site. The clinical consultation took place in the local clinic facility, with the support of the on-site team. Laboratory testing and imaging studies were coordinated through community settings, and tertiary site-based surgical, health psychology, and nutritional teams also followed up with this patient via virtual care clinic visits. By providing these clinical services closer to the patient's home through a clinical facility, numerous objectives were achieved: (1) patients received thorough clinical assessment and care plans; (2) patients were less likely to use the hospital or ED; (3) patients were more likely to remain in the workforce; and (4) community health care was off-loaded, reducing burnout and improving workforce retention. This approach combines virtual care with a cooperative care delivery model, where the aim is not to shift patient care from one provider to another, but to expand access for patients and to create both new and clinically appropriate care for each care participant, with the aim that improved access will lead to enhanced care outcomes and more efficient care utilization. Telemedicine endeavors have increased dramatically in the past few years, and to the best of the authors' knowledge, no other health system or hospital has expanded specialty services into rural communities in this collaborative manner. The novel approach to health care delivery outlined herein provides a model to improve access to specialty care and patient outcomes, and could be replicated in other regions. Collaboration across institutions, cooperation among leaders and physicians, and commitment to serve communities are the keys to success.

Public Health Sciences

Miller J, **Cook B**, **Gandolfo C**, Mills NL, Mahler S, Levy P, **Parikh S**, **Krupp S**, **Nour K**, **Klausner H**, **Gindi R**, **Lewandowski A**, **Hudson M**, **Perrotta G**, **Zweig B**, **Lanfear D**, **Kim H**, Dangoulian S, **Tang A**, **Todter E**, **Khan A**, Keerie C, **Bole S**, **Nasseredine H**, **Oudeif A**, **Abou Asala E**, **Mohammed M**, **Kazem A**, **Malette K**, **Singh-Kucukarslan G**, Xu N, Wittenberg S, **Morton T**, **Gunaga S**, **Affas Z**, **Tabbaa K**, Desai P, **Alsaadi A**, **Mahmood S**, **Schock A**, **Konowitz N**, **Fuchs J**, **Joyce K**, Shamoun L, Babel J, Broome A, **Digiacinto G**, **Shaheen E**, **Darnell G**, **Muller G**, **Heath G**, **Bills G**, **Vieder J**, **Rockoff S**, **Kim B**, **Colucci A**, **Plemmons E**, and **McCord J**. Rapid Acute Coronary Syndrome Evaluation Over One Hour With High-Sensitivity Cardiac Troponin I: A United States-Based Stepped-Wedge, Randomized Trial. *Ann Emerg Med* 2024; Epub ahead of print. PMID: 38888531. Full Text

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STUDY OBJECTIVE: The real-world effectiveness and safety of a 0/1-hour accelerated protocol using high-sensitivity cardiac troponin (hs-cTn) to exclude myocardial infarction (MI) compared to routine care in the United States is uncertain. The objective was to compare a 0/1-hour accelerated protocol for evaluation of MI to a 0/3-hour standard care protocol. METHODS: The RACE-IT trial was a stepped-wedge, randomized trial across 9 emergency departments (EDs) that enrolled 32,609 patients evaluated for possible MI from July 2020 through April 2021. Patients undergoing high-sensitivity cardiac troponin I testing with concentrations less than or equal to 99th percentile were included. Patients who had MI excluded by the 0/1-hour protocol could be discharged from the ED. Patients in the standard care protocol had 0- and 3-hour troponin testing and application of a modified HEART score to be eligible for discharge. The primary endpoint was the proportion of patients discharged from the ED without 30-day death or MI. RESULTS: There were 13,505 and 19,104 patients evaluated in the standard care and accelerated protocol groups, respectively, of whom 19,152 (58.7%) were discharged directly from the ED. There was no significant difference in safe discharges between standard care and the accelerated protocol (59.5% vs 57.8%; adjusted odds ratio (aOR)=1.05, 95% confidence interval [CI] 0.95 to 1.16). At 30 days, there were 90 deaths or MIs with 38 (0.4%) in the standard care group and 52 (0.4%) in the accelerated protocol group (aOR=0.84, 95% CI 0.43 to 1.68). CONCLUSION: A 0/1-hour accelerated protocol using high-sensitivity cardiac troponin I did not lead to more safe ED discharges compared with standard care.

Public Health Sciences

Nechuta S, Chen WY, Goerge A, **Boopathy D**, and Sanderson M. The role of breast cancer-related arm lymphedema in physical functioning and physical activity participation among long-term African American breast cancer survivors. *Support Care Cancer* 2024; 32(7):446. PMID: 38900224. Full Text

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PURPOSE: Breast cancer-related arm lymphedema (BCRL) is a common chronic and debilitating condition that involves accumulation of lymphatic fluid in the arm or hand. Limited data are available on BCRL in African American women. Lack of physical activity (PA) and poor physical functioning (PF) are both associated with increased morbidity and mortality among breast cancer survivors. We examined the association of BCRL with PA and PF among African American breast cancer survivors. METHODS: 323 African American women who previously participated in a case-only study in three states (TN, GA, SC) completed a survivorship-focused questionnaire (mean: 4.2 years post-diagnosis) in 2015-2016. Validated measures were used to determine BCRL, PF, and PA. Adjusted binary logistic regression models estimated ORs and 95% CIs for the association of BCRL and meeting PA guidelines (≥ 150 min/week), while multinomial logistic regression was used for PF and PA (minutes/week) categorized based on tertiles. RESULTS: Approximately 32% reported BCRL since diagnosis; 25.4% reported BCRL in the last 12-months. About 26% and 50% reported that BCRL interfered with exercise and ability to do daily activities, respectively. The mean PF among those with BCRL was 51.0(SD:29.0) vs. 68.5(SD:30.1) among those without BCRL. BCRL was associated with lower PF (adjusted-OR for tertile 2: 2.12(95% CI:1.03-4.36) and adjusted-OR for tertile 1: 2.93(95% CI:1.44-5.96)). CONCLUSIONS: BCRL was associated with lower PF among long-term African American breast cancer survivors.

Continued monitoring by health care professionals and increased education and behavioral interventions to support PA and improved PF among survivors living with BCRL are warranted.

Public Health Sciences

Nel NH, Haddad EN, Kerver JM, **Cassidy-Bushrow AE**, and Comstock SS. Maternal Body Mass Index Associates with Prenatal Characteristics and Fecal Microbial Communities. *Nutrients* 2024; 16(12). PMID: 38931236. Full Text

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The maternal microbiome plays a vital role in shaping pregnancy outcomes, but there remains a substantial gap in understanding its precise relationships to maternal health, particularly in relation to potential effects of body mass index (BMI) on gut microbial diversity. The aim of this observational study was to assess maternal characteristics in association with pre-pregnancy BMI and to further assess microbial diversity in association with specific maternal characteristics. Eighty-four pregnant women were recruited during their third trimester of pregnancy from various prenatal clinics across the state of Michigan. The participants completed an enrollment questionnaire including self-reported pre-pregnancy BMI; stool samples were collected to assess the fecal microbial community composition. Pre-pregnancy obesity (BMI 30+) was associated (univariably) with antibiotic use before pregnancy, ever smoked, lower education level, and being unmarried. The gut microbiota alpha diversity was significantly different for pregnant women by pre-pregnancy BMI category (normal, overweight, obese). The beta diversity was unique for the gut microbiotas of pregnant women within each BMI category, by education level, and by marital status. Multivariable models revealed that pre-pregnancy BMI, maternal education, marital status, and maternal age were associated with the microbial diversity of the gut microbiota during pregnancy. These results give new insight into the relationship between a woman's microbiome during pregnancy and their prenatal health, along with an understanding of the relationships between socioeconomic factors and microbial diversity.

Public Health Sciences

Newman LA, **Chen Y**, Martini R, Demaria S, Formenti S, Elemento O, and Davis MB. Tumor-Associated Lymphocytes and Breast Cancer Survival in Black and White Women. *JAMA Surg* 2024; 159(6):712-714. PMID: 38446467. Full Text

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This case series evaluates whether differences in immune filtration are associated with breast cancer risk in Black vs White women.

Public Health Sciences

Ryan PH, Zanobetti A, Coull BA, Andrews H, Bacharier LB, Bailey D, Beamer PI, Blossom J, Brokamp C, Datta S, Hartert T, Khurana Hershey GK, Jackson DJ, **Johnson CC**, **Joseph C**, Kahn J, Lothrop N, Louisias M, Luttmann-Gibson H, Martinez FD, Mendonça E, Miller RL, Ownby D, Ramratnam S, Seroogy CM, Visness CM, Wright AL, **Zoratti EM**, Gern JE, and Gold DR. The Legacy of Redlining: Increasing Childhood Asthma Disparities Through Neighborhood Poverty. *Am J Respir Crit Care Med* 2024; Epub ahead of print. PMID: 38869320. Full Text

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RATIONALE: Identifying the root causes of racial disparities in childhood asthma is critical for health equity. OBJECTIVES: To determine if the 1930's racist policy of redlining led to present-day disparities in childhood asthma by increasing community-level poverty and decreasing neighborhood socioeconomic position (SEP). METHODS: We categorized census tracts at birth of participants from the Children's Respiratory and Environmental Workgroup birth cohort consortium into A, B, C, or D categories as defined by the Home Owners Loan Corporation (HOLC), with D being the highest perceived risk. Surrogates of present-day neighborhood-level SEP were determined for each tract including the percentage of low-income households, the CDC's social vulnerability index (SVI), and other tract-level variables. We performed causal mediation analysis, which, under the assumption of no unmeasured confounding, estimates the direct and mediated pathways by which redlining may cause asthma disparities through census tract-level mediators adjusting for individual-level covariates. MEASUREMENTS AND MAIN RESULTS: Of 4,849 children, the cumulative incidence of asthma through age 11 was 26.6% and 13.2% resided in census tracts with a HOLC grade of D. In mediation analyses, residing in grade D tracts (aOR = 1.03 [95%CI 1.01,1.05]) was significantly associated with childhood asthma, with 79% of this increased risk mediated by percentage of low-income households; results were similar for SVI and other tract-level variables. CONCLUSIONS: The historical structural racist policy of redlining led to present-day asthma disparities in part through decreased neighborhood SEP. Policies aimed at reversing the effects of structural racism should be considered to create more just, equitable, and healthy communities.

Public Health Sciences

Santarossa S, Baber M, **Hussein J**, Oley C, Slangerup K, **Murphy D**, and **Kippen KE**. Using action research and a community-academic partnership to understand clinical trial participation: a patient-centered perspective. *Res Involv Engagem* 2024; 10(1):61. PMID: 38872195. Full Text

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BACKGROUND: Clinical trials that are patient-centered appear to be more successful (e.g., clinical outcomes, improved communication, mutual empowerment, changed attitudes), thus, action research may be a field of importance. The current study explores the Formation and Execution of Activities phases of a community-academic partnership (CAP). METHODS: Members consisted of industry stakeholders, a healthcare/academic institution, and patients/families with lived experiences as cancer survivors and/or caregivers. Retrospectively, CAP members described the facilitating and/or hindering factors present in the partnership development. A document review process was used. Field notes from three CAP meetings, which focused on understanding clinical trial participation, were analyzed using a thematic approach. RESULTS: Seven facilitating and three hindering factors were present. Interpersonal (vs. operational) processes were referenced as influential facilitating factors more often. Themes that emerged included 'trials as a treatment option', 'leaving a legacy', and 'timing is critical.' CONCLUSION: This study provides a patient-centered perspective on barriers/challenges of clinical trial participation and how to improve future perceptions.
Clinical trials are more successful when patients are engaged, and their perspectives have been considered in the study design. Community-academic partnerships (CAPs) are one way to ensure patients are more engaged in the research process by creating a collaboration where all parties involved play an equitable role. We provide an example of a CAP with an industry stakeholder, a healthcare/academic institution, and patients as well as families with lived experiences as cancer survivors and/or caregivers. Described here two phases of the CAP: the Formation and the Execution of Activities phases. The Formation phase covers the collaboration process and development of the CAP. In our study, to better understand this phase, CAP members described what did and did not go well during the partnership development. We found more aspects went well than did not and that processes related to the quality of the relationship and communication among CAP members were important. The Execution of Activities phase focuses on how the CAP is working towards an agreed upon outcome. In our study, to better understand this phase, we reviewed notes taken at previous CAP meetings that focused on exploring participation in clinical trials as a treatment option. We found that when it comes to participation in clinical trials, patients and/or caregivers with lived experiences with cancer, felt that timing of this treatment option was important and that reasons for participation included wanting to leave a legacy. In this paper we describe some challenges of clinical trial participation, identified by patients and caregivers, and discuss how to improve views of clinical trial participation in the future.
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Public Health Sciences

Schuster ALR, Crossnohere NL, **Boakye EA**, Angove R, Baldwin B, Barreto EA, Chen RC, Gillespie TW, Hamilton B, McCleary NJ, Karmo M, Kaufmann T, Lee W, Mehta V, Meyer L, Mittal K, Owens L, Peterson R, Pusic A, Rainey AM, Richardson A, Shapiro L, Sibbitt B, Smith C, Vargo M, Vickers A, Brundage M, and Snyder C. A Framework to Promote Implementation of Patient-Reported Outcomes in Institutions Caring for Vulnerable and Underserved Cancer Populations. *Patient* 2024; Epub ahead of print. PMID: 38909128. Request Article

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Public Health Sciences

Wise LA, Coleman CM, Schildroth S, Geller RJ, Lovett SM, Claus Henn B, Calafat AM, Botelho JC, Marsh EE, Noel N, **Wegienka GR**, Bethea TN, Harmon QE, Baird DD, and Wesselink AK. Associations of per- and polyfluoroalkyl substances with uterine leiomyomata incidence and growth: a prospective ultrasound study. *J Expo Sci Environ Epidemiol* 2024; Epub ahead of print. PMID: 38914782. Request Article

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BACKGROUND: Per- and polyfluoroalkyl substances (PFAS) are endocrine-disrupting chemicals used in commercial and consumer products. OBJECTIVE: We evaluated PFAS exposure in relation to incidence and growth of uterine leiomyomata (UL), hormone-dependent neoplasms that are associated with severe gynecologic morbidity. METHODS: We studied 1158 participants in the Study of Environment, Lifestyle, and Fibroids, a Detroit-based prospective cohort study of Black females aged 23-35 years at enrollment (2010-2012). At enrollment and four subsequent visits during 10 years of follow-up, participants attended in-person clinic visits, completed questionnaires, provided non-fasting blood samples, and underwent ultrasound for UL detection. We quantified 7 PFAS in baseline plasma samples using mass spectrometry. We used Cox regression and probit Bayesian kernel machine regression to estimate individual and joint

effects of PFAS on UL incidence. We fit linear mixed models to estimate effects of individual PFAS on UL growth. We stratified by parity, an important route of PFAS elimination and determinant of UL. RESULTS: In individual PFAS analyses, we observed inverse associations for perfluorodecanoate (PFDA; ≥0.3 vs. <0.2 ng/ml: hazard ratio [HR] = 0.74; 95% confidence interval [CI]: 0.54-1.00) and perfluoroundecanoate (detected vs. non-detected: HR = 0.78; 95% CI: 0.61-1.01) and a weak positive association for perfluorohexane sulfonate (≥1 vs. <0.6 ng/ml: HR = 1.17; 95% CI: 0.85-1.61), while perfluorooctane sulfonate, perfluorooctanoate, perfluorononanoate (PFNA), and 2-N-methyl-perfluorooctane sulfonamido acetate (MeFOSAA) showed little association with UL incidence. The PFAS mixture was inversely associated with UL incidence, a finding driven by MeFOSAA and PFDA; however, PFNA was positively associated with UL incidence. The inverse association for PFDA and positive association for PFNA were stronger among nulliparous participants. Most PFAS showed slight inverse associations with UL growth. IMPACT STATEMENT: In this prospective ultrasound study of 1158 Black females aged 23-35 years at enrollment, we conducted a mixtures analysis to account for co-pollutant confounding and interaction. MeFOSAA and PFDA concentrations were inversely associated with UL incidence, while PFNA concentrations were positively associated with UL incidence. Concentrations of most PFAS were associated with decreased UL growth. This study contributes data to the sparse literature on PFAS exposure and UL development.

Pulmonary and Critical Care Medicine

Cherabuddi MR, **Goodman B**, **Ayyad A**, **Almajali DA**, **Nadeem O**, **Bradley P**, **Russell C**, and **Ouellette D**. Association of Area Deprivation Index with Adherence to Proposed Regimen in Patients with Sarcoidosis in Detroit, Michigan. *Sarcoidosis Vasc Diffuse Lung Dis* 2024; 41(2):e2024031. PMID: 38940707. Full Text

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BACKGROUND AND AIM: Social predictors affect severity of sarcoidosis, with Black patients, older individuals, those with lower income, and those without insurance having greater severity. This study aimed to explore potential disparities affecting access to care in sarcoidosis patients with a primary focus on metrics such as area deprivation index (ADI) and its association with adherence to the proposed regimen. METHODS: A retrospective chart review study of all patients seen in pulmonary clinics at a large urban tertiary care center over 2 years with sarcoidosis patients identified with International Classification of Diseases diagnosis code D86. Data collected included age, race, sex, ADI, insurance, online patient portal usage, chest x-rays, pulmonary function tests, missed visits, hospitalizations, positive biopsy, communication and visits around bronchoscopy. Categorical variables were described using frequency and percentage. Numerical variables were described using median, mean and standard deviation. Statistical analysis included chi-square test, two-sample T-test and Wilcoxon rank sum test. Multivariate logistic regression analysis was performed to model independent association with 12 month no-show occurrence as a metric of adherence to the proposed regimen. RESULTS: Among sarcoidosis patients (N = 788), univariate models showed the presence of active online patient portal use among younger patients (58.6 years with portal vs. 65.1 years without portal, $p < 0.001$), those with lower ADI (73 with portal vs. 92 without portal, $p < 0.001$) and with commercial insurance (48.5% with portal vs. 20.7% without portal, $p < 0.001$); more x-rays (45.6% with x-rays vs. 36.6% without x-rays, $p = 0.018$) and hospitalizations (50.3% with hospitalizations vs. 36.2% without hospitalizations, $p < 0.001$) in Medicare patients. Sarcoidosis patients with positive biopsies on file from 2013-2023 were more likely to be male (44.19% with positive biopsy vs. 33.91% without positive biopsy, $p = 0.006$), White (36.29% with positive biopsy vs. 22.9% without positive biopsy, $p < 0.001$) or other races (3.23% with positive biopsy vs. 2.25% without positive biopsy, $p < 0.001$), younger (55.8 years with positive biopsy vs. 61.7 years without positive biopsy, $p < 0.001$) and belonged to lower national ADI ranks (73 with positive biopsy vs. 80 without biopsy, $p = 0.041$). A multivariate analysis was done with those variables found to be significant in the univariate analyses, which revealed that higher ADI national was associated with failure to adhere to the proposed regimen. CONCLUSIONS: We identified intricate patterns of sociodemographic variables affecting access to care in sarcoidosis patients, especially higher ADI national associated with failure to adhere to the proposed regimen, raising concerns for potential healthcare barriers. Understanding these

barriers is vital for equitable high-quality care, assisting in timely and efficient management of the patient's disease.

Radiation Oncology

Bhatnagar AR, **Ghanem AI**, **Alkamachi B**, **Allo G**, **Lin CH**, **Hijaz M**, and **Elshaikh MA**. The prognostic impact of substantial lymphovascular space invasion in women with node negative FIGO stage I uterine carcinoma. *Gynecol Oncol* 2024; 188:44-51. PMID: 38936280. Full Text

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OBJECTIVE: Substantial lymphovascular space invasion (LVSI) is an important predictor of lymph node (LN) involvement in women with endometrial carcinoma. We studied the prognostic significance of substantial LVSI in patients with 2009-FIGO stage-I uterine endometrioid adenocarcinoma (EC) who all had pathologic negative nodal evaluation (PNNE). METHODS: Pathologic specimens were retrieved and LVSI was quantified (focal or substantial) in women with stage-I EC who had a hysterectomy and PNNE. In addition to multivariate analysis (MVA), recurrence-free (RFS), disease-specific (DSS), and overall (OS) survival was compared between women with focal vs. substantial LVSI. RESULTS: 1052 patients were identified with a median follow-up of 9.7 years. 358 women (34%) received adjuvant radiotherapy. 907 patients (86.2%) had no LVSI, 87 (8.3%) had focal, and 58 (5.5%) had substantial LVSI. Five-year RFS was 93.3% (95% CI: 91.5-95.1), 76.8% (95% CI: 67.2-87.7) and 79.1% (95% CI: 67.6-95.3) for no, focal, and substantial LVSI($p < 0.0001$). There was no statistically significant difference in 5-year RFS, DSS, OS, and in the patterns of initial recurrence between women with focal vs substantial LVSI. On MVA with propensity score matching, substantial LVSI was not independently associated with any survival endpoint compared to focal LVSI, albeit both were detrimental when compared to no LVSI.
Age ≥ 60 years and higher grade were predictors of worse RFS, DSS, and OS. Additionally, comorbidity burden was an independent predictor for OS. CONCLUSIONS: Our results suggest that substantial LVSI does not predict worse survival endpoints or different recurrence patterns in women with stage-I EC with PNNE when compared to focal LVSI.

Radiation Oncology

Sriramulu S, **Thoidingjam S**, Chen WM, **Hassan O**, **Siddiqui F**, **Brown SL**, **Movsas B**, Green MD, Davis AJ, Speers C, **Walker E**, and **Nyati S**. BUB1 regulates non-homologous end joining pathway to mediate radioresistance in triple-negative breast cancer. *J Exp Clin Cancer Res* 2024; 43(1):163. PMID: 38863037. Full Text

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BACKGROUND: Triple-negative breast cancer (TNBC) is a highly aggressive form of breast cancer subtype often treated with radiotherapy (RT). Due to its intrinsic heterogeneity and lack of effective targets, it is crucial to identify novel molecular targets that would increase RT efficacy. Here we demonstrate the role of BUB1 (cell cycle Ser/Thr kinase) in TNBC radioresistance and offer a novel strategy to improve TNBC treatment. METHODS: Gene expression analysis was performed to look at genes upregulated in TNBC patient samples compared to other subtypes. Cell proliferation and clonogenic survivals assays determined the IC(50) of BUB1 inhibitor (BAY1816032) and radiation enhancement ratio (rER) with pharmacologic and genomic BUB1 inhibition. Mammary fat pad xenografts experiments were performed in CB17/SCID. The mechanism through which BUB1 inhibitor sensitizes TNBC cells to radiotherapy was delineated by γ-H2AX foci assays, BLRR, Immunoblotting, qPCR, CHX chase, and cell fractionation assays. RESULTS: BUB1 is overexpressed in BC and its expression is considerably elevated in TNBC with poor survival outcomes. Pharmacological or genomic ablation of BUB1 sensitized multiple TNBC cell lines to cell killing by radiation, although breast epithelial cells showed no radiosensitization with BUB1 inhibition. Kinase function of BUB1 is mainly accountable for this radiosensitization phenotype. BUB1 ablation also led to radiosensitization in TNBC tumor xenografts with significantly increased tumor growth delay and overall survival. Mechanistically, BUB1 ablation inhibited the repair of radiation-induced DNA double strand breaks (DSBs). BUB1 ablation stabilized phospho-DNAPKcs (S2056) following RT such that half-lives could not be estimated. In contrast, RT alone caused BUB1 stabilization, but pre-treatment with BUB1 inhibitor prevented stabilization (t(1/2), ~8 h). Nuclear and chromatin-enriched fractionations illustrated an increase in recruitment of phospho- and total-DNAPK, and KAP1 to chromatin indicating that BUB1 is indispensable in the activation and recruitment of non-homologous end joining (NHEJ) proteins to DSBs. Additionally, BUB1 staining of TNBC tissue microarrays demonstrated significant correlation of BUB1 protein expression with tumor grade. CONCLUSIONS: BUB1 ablation sensitizes TNBC cell lines and xenografts to RT and BUB1 mediated radiosensitization may occur through NHEJ. Together, these results highlight BUB1 as a novel molecular target for radiosensitization in women with TNBC.

Radiation Oncology

Sriramulu S, **Thoidingjam S**, **Siddiqui F**, **Brown SL**, **Movsas B**, **Walker E**, and **Nyati S**. BUB1 Inhibition Sensitizes TNBC Cell Lines to Chemotherapy and Radiotherapy. *Biomolecules* 2024; 14(6). PMID: 38927028. Full Text

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BUB1 is overexpressed in most human solid cancers, including breast cancer. Higher BUB1 levels are associated with a poor prognosis, especially in patients with triple-negative breast cancer (TNBC). Women with TNBC often develop resistance to chemotherapy and radiotherapy, which are still the mainstay of treatment for TNBC. Our previous studies demonstrated that a BUB1 kinase inhibitor (BAY1816032) reduced tumor cell proliferation and significantly enhanced radiotherapy efficacy in TNBC. In this study, we evaluated the effectiveness of BAY1816032 with a PARP inhibitor (olaparib), platinum agent (cisplatin), and microtubule poison (paclitaxel) alone or in combination with radiotherapy using cytotoxicity and clonogenic survival assays. BUB1 inhibitors sensitized BRCA1/2 wild-type SUM159 and MDA-MB-231 cells to olaparib, cisplatin, and paclitaxel synergistically (combination index; CI < 1). BAY1816032 significantly increased the radiation sensitization of SUM159 and MDA-MB-231 by olaparib, cisplatin, or paclitaxel at non-toxic concentrations (doses well below the IC(50) concentrations). Importantly, the small molecular inhibitor of BUB1 synergistically (CI < 1) sensitized the BRCA mutant TNBC cell line HCC1937 to olaparib. Furthermore, the BUB1 inhibitor significantly increased the radiation enhancement ratio (rER) in HCC1937 cells (rER 1.34) compared to either agent alone (BUB1i rER 1.19; PARPi rER 1.04). The data presented here are significant as they provide proof that inhibition of BUB1

kinase activity sensitizes TNBC cell lines to a PARP inhibitor and radiation, irrespective of BRCA1/2 mutation status. Due to the ability of the BUB1 inhibitor to sensitize TNBC to different classes of drugs (platinum, PARPi, microtubule depolarization inhibitors), this work strongly supports the role of BUB1 as a novel molecular target to improve chemoradiation efficacy in TNBC and provides a rationale for the clinical evaluation of BAY1816032 as a chemosensitizer and chemoradiosensitizer in TNBC.

Research Administration

Gupta RC, **Singh-Gupta V**, **Szekely KJ**, **Zhang K**, **Lanfear DE**, and **Sabbah HN**. Dysregulation of cardiac mitochondrial aldehyde dehydrogenase 2: Studies in dogs with chronic heart failure. *J Mol Cell Cardiol Plus* 2024; 8. PMID: 38938550. Full Text

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Mitochondrial (MITO) dysfunction occurs in the failing heart and contributes to worsening of heart failure (HF). Reduced aldehyde dehydrogenase 2 (ALDH2) in left ventricular (LV) myocardium of diabetic hearts has been implicated in MITO dysfunction through accumulation of toxic aldehydes including and elevated levels of 4-hydroxy-2-nonenal (4HNE). This study examined whether dysregulation of MITO ALDH2 (mALDH2) occurs in mitochondria of the failing LV and is associated with increased levels of 4HNE. LV tissue from 7 HF and 7 normal (NL) dogs was obtained. Protein quantification of total mitochondrial ALDH2 (t-mALDH2), phosphorylated mALDH2 (p-mALDH2), total MITO protein kinase c epsilon (t-mPKCε), phosphorylated mPKCε (p-mPKCε) was performed by Western blotting, and total mALDH2 enzymatic activity was measured. Protein adducts of 4HNE-MITO and 4HNE-mALDH2 were also measured in MITO fraction by Western Blotting. Protein level of t-mALDH2 was decreased in HF compared with NL dogs (0.63 ± 0.07 vs 1.17 ± 0.08, $p < 0.05$) as did mALDH2 enzymatic activity (51.39 ± 3 vs. 107.66 ± 4 nmol NADH/min/mg, $p < 0.05$). Phosphorylated-mALDH2 and p-mPKCε were unchanged. 4HNE-MITO proteins adduct levels increased in HF compared with NL (2.45 ± 0.08 vs 1.30 ± 0.03 du, $p < 0.05$) as did adduct levels of 4HNE-mALDH2 (1.60 ± 0.20 vs 0.39 ± 0.08, $p < 0.05$). In isolated failing cardiomyocytes (CM) exposure to 4HNE decreased mALDH2 activity, increased ROS and 4HNE-ALDH2 adducts, and worsened MITO function. Stimulation of mALDH2 activity with ALDA-1 in isolated HF CMs compared to NL CMs improved ADP-stimulated respiration and maximal ATP synthesis to a greater extant (+47 % and +89 %, respectively). Down-regulation of mALDH2 protein levels and activity occurs in HF and contributes to MITO dysfunction and is likely caused by accumulation of 4HNE-mALDH2 adduct. Increasing mALDH2 activity (via ALDA-1) improved MITO function in failing CMs.

Research Administration

Miller J, **Cook B**, **Gandolfo C**, Mills NL, Mahler S, Levy P, **Parikh S**, **Krupp S**, **Nour K**, **Klausner H**, **Gindi R**, **Lewandowski A**, **Hudson M**, **Perrotta G**, **Zweig B**, **Lanfear D**, **Kim H**, Dangoulian S, **Tang A**, **Todter E**, **Khan A**, Keerie C, **Bole S**, **Nasseredine H**, **Oudeif A**, **Abou Asala E**, **Mohammed M**, **Kazem A**, **Malette K**, **Singh-Kucukarslan G**, Xu N, Wittenberg S, **Morton T**, **Gunaga S**, **Affas Z**, **Tabbaa K**, Desai P, **Alsaadi A**, **Mahmood S**, **Schock A**, **Konowitz N**, **Fuchs J**, **Joyce K**, Shamoun L, Babel J, Broome A, **Digiacinto G**, **Shaheen E**, **Darnell G**, **Muller G**, **Heath G**, **Bills G**, **Vieder J**, **Rockoff S**, **Kim B**, **Colucci A**, **Plemmons E**, and **McCord J**. Rapid Acute Coronary Syndrome Evaluation Over One Hour With High-Sensitivity Cardiac Troponin I: A United States-Based Stepped-Wedge, Randomized Trial. *Ann Emerg Med* 2024; Epub ahead of print. PMID: 38888531. Full Text

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STUDY OBJECTIVE: The real-world effectiveness and safety of a 0/1-hour accelerated protocol using high-sensitivity cardiac troponin (hs-cTn) to exclude myocardial infarction (MI) compared to routine care in the United States is uncertain. The objective was to compare a 0/1-hour accelerated protocol for evaluation of MI to a 0/3-hour standard care protocol. METHODS: The RACE-IT trial was a stepped-wedge, randomized trial across 9 emergency departments (EDs) that enrolled 32,609 patients evaluated for possible MI from July 2020 through April 2021. Patients undergoing high-sensitivity cardiac troponin I testing with concentrations less than or equal to 99th percentile were included. Patients who had MI excluded by the 0/1-hour protocol could be discharged from the ED. Patients in the standard care protocol had 0- and 3-hour troponin testing and application of a modified HEART score to be eligible for discharge. The primary endpoint was the proportion of patients discharged from the ED without 30-day death or MI. RESULTS: There were 13,505 and 19,104 patients evaluated in the standard care and accelerated protocol groups, respectively, of whom 19,152 (58.7%) were discharged directly from the ED. There was no significant difference in safe discharges between standard care and the accelerated protocol (59.5% vs 57.8%; adjusted odds ratio (aOR)=1.05, 95% confidence interval [CI] 0.95 to 1.16). At 30 days, there were 90 deaths or MIs with 38 (0.4%) in the standard care group and 52 (0.4%) in the accelerated protocol group (aOR=0.84, 95% CI 0.43 to 1.68). CONCLUSION: A 0/1-hour accelerated protocol using high-sensitivity cardiac troponin I did not lead to more safe ED discharges compared with standard care.

Surgery

Chamseddine H, Chahrour M, Aboul Hosn M, and **Kabbani L**. In Patients with Heart Failure Undergoing Carotid Endarterectomy, Locoregional Anesthesia is Not Associated with Decreased Mortality, Stroke, or Myocardial Infarction Compared to General Anesthesia. *Ann Vasc Surg* 2024; 106:189-195. PMID: 38821474. Full Text

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BACKGROUND: While existing literature reports no benefit of locoregional anesthesia (LRA) over general anesthesia (GA) in patients undergoing carotid endarterectomy (CEA), the effect of LRA on patients with congestive heart failure (CHF) has not been explored. This study aims to assess whether the choice of anesthesia plays a role in influencing outcomes within this population. METHODS: Using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) files between 2005 and 2022 and the procedural targeted ACS-NSQIP database for CEA between 2011-2022, all patients receiving CEA were identified, and the subset of patients with CHF was included. Patient characteristics and 30-day outcomes were compared using $\chi(2)$ or Fischer's exact test as appropriate for categorical variables and the independent t-test or Mann-Whitney U test as appropriate for continuous variables. Mortality, stroke, myocardial infarction (MI), and major adverse cardiac events (MACE) were compared between patients receiving GA and LRA using univariate analysis. RESULTS: A total of 3,040 patients (2,733 undergoing GA, 307 undergoing LRA) with a diagnosis of CHF undergoing CEA were identified. No difference in mortality (GA 3.1% vs. LRA 4.6%, P = 0.162), MI (GA 3.0% vs. LRA 2.3%, P = 0.478), stroke (2.4% vs. 2.6%, P = 0.805) or MACE (GA 7.4% vs. LRA 8.1%, P = 0.654) was observed. LRA patients had a significantly lower hospital stay compared to GA patients (1 day [interquartile range (IQR) 1-3] vs. 2 days [IQR 1-4], P < 0.001). Shunt was more commonly used in patients receiving GA (32.9% vs. 12.5%, P < 0.001) compared to LRA. CONCLUSIONS: While utilizing LRA compared to GA during CEA in patients with CHF is associated with a shorter hospital stay and less intraoperative shunting, the choice of anesthesia did not impact the outcomes of mortality, MI or stroke. Further research is needed to determine the effect of LRA on the outcomes of CEA among patients with different stages of heart failure.

Surgery

Chamseddine H, Chahrour M, **Shepard A**, **Nypaver T**, **Weaver M**, **Kavousi Y**, **Onofrey K**, Hosn MA, and **Kabbani L**. Locoregional Anesthesia Is Associated with Decreased Cardiac Complications in Symptomatic Heart Failure Patients Undergoing Carotid Endarterectomy. *J Vasc Surg* 2024; Epub ahead of print. PMID: 38851468. Full Text

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OBJECTIVE: While current literature reports no advantage for locoregional anesthesia (LRA) over general anesthesia (GA) in patients undergoing carotid endarterectomy (CEA), there remains a gap in understanding the impact of LRA on individuals with congestive heart failure (CHF). This study aims to assess whether the choice of anesthesia influences the rates of perioperative complications within this patient population. METHODS: Using the Vascular Quality Initiative (VQI) carotid endarterectomy module, all patients undergoing CEA between 2013-2023 were identified. The subset of patients with CHF was included, and patients were divided based on the type of anesthesia received. Patient characteristics and outcomes were compared using $\chi(2)$ or Fischer's exact test as appropriate for categorical variables and the independent t-test or Mann-Whitney U test as appropriate for continuous variables. A sensitivity analysis was performed based on the symptomatic status of CHF, and the association between anesthesia modality and post-operative outcomes was studied using multivariable logistic regression analysis. The primary outcomes of this study included perioperative stroke, MI, acute heart failure (HF), and the combination of MI and acute HF defined as major cardiac complications. RESULTS: A total of 21,292 patients (19,730 receiving GA, 1,562 receiving LRA) with a diagnosis of CHF undergoing CEA were identified. On multivariable logistic regression analysis, LRA was independently associated with lower MI (OR 0.35, 95% CI 0.13-0.96), acute HF (OR 0.27, 95% CI 0.09-0.87), major cardiac complications (OR 0.30, 95% CI 0.13-0.67), hemodynamic instability (OR 0.64, 95% CI 0.53-0.78), cranial nerve injury (OR 0.40, 95% CI 0.19-0.81), shunt use (OR 0.25, 95% CI 0.20-0.31), and neuromonitoring device use (OR 0.20, 95% CI 0.17-0.24) compared to GA in symptomatic CHF patients. No difference in MI, acute HF, and major cardiac complications was seen in asymptomatic CHF patients. CONCLUSION: CEA can be safely performed in patients with CHF. Utilizing LRA is associated with a decreased incidence of perioperative cardiac complications in patients with symptomatic heart failure undergoing CEA.

Surgery

Dobesh K, Natour AK, **Kabbani L**, **Rteil A**, **Lee A**, **Nypaver TJ**, **Weaver M**, and **Shepard AD**. PATIENTS WITH ACUTE LOWER LIMB ISCHEMIA CONTINUE TO HAVE SIGNIFICANT MORBIDITY AND MORTALITY. *Ann Vasc Surg* 2024; Epub ahead of print. PMID: 38848889. Full Text

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BACKGROUND: The treatment of acute lower limb ischemia (ALLI) has evolved over the last several decades with the availability of several new treatment modalities. This study was undertaken to evaluate the contemporary presentation and outcomes of ALLI patients. METHODS: We retrospectively analyzed data from a prospectively collected database of all patients who presented to our tertiary referral hospital with acute ischemia of the lower extremity between May 2016 and October 2020. The cause of death was obtained from the Michigan State Death Registry. RESULTS: During the study period, 233 patients (251 lower limbs) were evaluated for ALLI. Seventy-three percent had thrombotic occlusion 24% had embolic occlusion, and 3% due to a low-flow state. Rutherford classification of ischemia severity was 7%, 49%, 40%, and 4% for Rutherford grade I, IIA, IIB, and III, respectively. Five percent underwent primary

amputations, and 6% received medical therapy only. The mean length of stay was 11 ± 9 days. Nineteen percent of patients were readmitted within 30 days of discharge. At 30 days postoperatively, mortality was 9% and limb loss was 19%. On multivariate analysis, one or no vessel runoff to the foot post-operatively was associated with higher 30-day limb loss. Patients with no run-off vessels post-operatively had significantly higher 30-day mortality. Cardiovascular complications accounted for most deaths (48%). At 1-year postoperatively, mortality and limb loss reached 17% and 34%, respectively. CONCLUSION: Despite advances in treatment modalities and cardiovascular care, patients presenting with ALLI continue to have high mortality, limb loss, and readmission rates at 30 days.

Surgery
Hutchings H, **Behinaein P**, and **Okereke I**. Well-being Through the Synergy of Community Engagement, Health Equity, and Advocacy. *Thorac Surg Clin* 2024; 34(3):281-290. PMID: 38944455. Full Text

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Facets of well-being for cardiothoracic surgeons include interconnectivity, or a sense of belonging within a community, and social relatedness. Striving for health equity achieves a sense of belonging and meaning to one's work. In "Elevating Health Equity: The Synergy of Community Engagement and Advocacy," the imperative for mentorship and diversification within health care is expounded, establishing a multitiered blueprint for equity. Integral to this framework is the nurturing of a heterogeneous health care workforce, ameliorating racial and gender disparities in patient care. This article puts forth an intricate, empirically substantiated roadmap toward a more empathic and efficacious health care system.

Surgery
Hutchings H, **Wang A**, Grady S, **Popoff A**, **Zhang Q**, and **Okereke I**. Influence of Air Quality on Lung Cancer in People Who Have Never Smoked. *J Thorac Cardiovasc Surg* 2024; Epub ahead of print. PMID: 38936598. Full Text

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OBJECTIVE: Lung cancer is the leading cause of cancer-related death. The percentage of people who have never smoked with lung cancer has risen recently, but alternative risk factors require further study. Our goal was to determine the impact of air quality on incidence of lung cancer in people who have smoked or never smoked. METHODS: The Cancer Registry from a large urban medical center was queried to include every new diagnosis of lung cancer from 2013 to 2021. Air quality and pollution data for the county were obtained from the United States Environmental Protection Agency from 1980 to 2018. Patient demographics, location of residence, smoking history and tumor stage were recorded. Bivariate comparison analyses were conducted in R. RESULTS: A total of 2,223 new cases of lung cancer were identified. Mean age was 69.2 years. There was a nonsmoking rate of 8.1 percent. A total of 37 percent of patients identified as a racial minority. People who have never smoked were more likely to be diagnosed at an advanced stage. When analyzing geographic distribution, incidence of lung cancer among people who have never smoked was more closely associated with highly polluted areas. People who have never smoked with lung cancer had significantly higher exposure levels of multiple pollutants. CONCLUSIONS: Newly diagnosed lung cancer appears to be more related to poor air quality among people who have never smoked than people who have smoked. Future studies are needed to examine the associations of specific pollutants with lung cancer incidence.

Surgery

Hutchings H, **Zhang Q**, Grady SC, Cox J, **Popoff A**, **Wilson CP**, Zhu S, and **Okereke I**. Lung Cancer and Air Quality in a Large Urban County in the United States. *Cancers (Basel)* 2024; 16(11). PMID: 38893265. Full Text

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Lung cancer is the leading cancer-related killer in the United States. The incidence varies geographically and may be affected by environmental pollutants. Our goal was to determine associations within time series for specific air pollutants and lung cancer cases over a 33-year period in Wayne County, Michigan, controlling for population change. Lung cancer data for Wayne County were queried from the Michigan Cancer Registry from 1985 to 2018. Air pollutant data were obtained from the United States Environmental Protection Agency from 1980 to 2018. Autoregressive distributed lag (ARDL) models were estimated to investigate time lags in years between specific air pollution levels and lung cancer development. A total of 58,866 cases of lung cancer were identified. The mean age was 67.8 years. Females accounted for 53 percent of all cases in 2018 compared to 44 percent in 1985. Three major clusters of lung cancer incidence were detected with the most intense clusters in downtown Detroit and the heavily industrialized downriver area. Sulfur dioxide (SO(2)) had the strongest statistically significant relationship with lung cancer, showing both short- and long-term effects (lag range, 1-15 years). Particulate matter (PM(2.5)) (lag range, 1-3 years) and nitrogen dioxide (NO(2)) (lag range, 2-4 years) had more immediate effects on lung cancer development compared to carbon monoxide (CO) (lag range, 5-6 years), hazardous air pollutants (HAPs) (lag range, 9 years) and lead (Pb) (lag range, 10-12 years), which had more long-term effects on lung cancer development. Areas with poor air quality may benefit from targeted interventions for lung cancer screening and reductions in environmental pollution.

Surgery

Hutchings HE, Grady SC, **Zhang Q**, **Schwarze E**, **Popoff A**, Khanipov K, and **Okereke IC**. Regional trends in diagnosis of advanced lung cancer in Michigan over 33 years. *J Thorac Dis* 2024; 16(5):2936-2947. PMID: 38883653. Full Text

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BACKGROUND: Lung cancer is the most common cancer killer worldwide. Nearly 80 percent of lung cancers are diagnosed at advanced stages. Lack of access to medical care and undwerutilized lung cancer screening are key reasons for advanced diagnoses. We sought to understand the regional differences in presentation of lung cancer across Michigan. Utilizing a comprehensive cancer registry over 33 years, our goal was to examine associations between sociodemographic patient factors and diagnoses at advanced stages. METHODS: The Michigan Cancer Registry was queried from 1985 to 2018 to include all new diagnoses of non-small cell lung cancer (NSCLC) using International Classification of Diseases for Oncology (ICD-O) version 3 codes. NSCLC was categorized as early, regional and distant disease. Advanced disease was considered to be any disease that was regional or distant. NSCLC rates were calculated and mapped at the zip code level using the 2010 population as the denominator and spatial empirical Bayes methodology. Regional hospital service areas were constructed using travel time to treatment from the patient's zip code centroid. Logistic regression models were estimated to investigate the significance of rural vs. urban and travel time on level of disease at presentation. Kaplan-Meier and multivariate survival analysis was performed to evaluate the association between distance from the nearest medical center and length of survival controlling for known risk factors for lung cancer. RESULTS: From 1985 to 2018, there were 141,977 patients in Michigan diagnosed with

NSCLC. In 1985, men were 2.2 times more likely than women to be diagnosed but by 2018 women and men developed disease at equal rates. Mean age was 67.8 years. Among all patients with known stage of disease, 72.5% of patients were diagnosed with advanced disease. Regional and distant NSCLC rates were both higher in the northern parts of the state. Longer drive times in rural regions also significantly increased the likelihood of advanced NSCLC diagnoses, in particular regional lung cancer. Patients with longer drive times also experienced overall worse survival after controlling for other factors. CONCLUSIONS: Regional disparities exist in Michigan for diagnoses of NSCLC at advanced stages. Factors such as lack of screening in urban regions and distances to treating institutions in rural areas likely contribute to the increased likelihood of advanced NSCLC. Future interventions should target the specific needs of residents to detect disease at earlier stages and improve overall outcomes.

Surgery

Murray MF, **Pearl ES**, **Zelenak L**, **Hamann A**, **Sehgal M**, **Braciszewski JM**, **Carlin AM**, and **Miller-Matero LR**. COVID-19-Related Increases in Depressive and Anxious Symptoms Are Associated with Maladaptive Eating Among Patients up to 4 years Post-bariatric Surgery. *Obes Surg* 2024; Epub ahead of print. PMID: 38839635. Full Text

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INTRODUCTION: Depressive and anxious symptoms and maladaptive eating behaviors fluctuate with stressful events for patients seeking bariatric surgery. These associations are less clear for patients postoperatively. Using the COVID-19 pandemic as a frame, we examined associations between changes in depressive and anxious symptoms and maladaptive eating behaviors between up to four years postoperatively. METHODS: Participants (N = 703) who underwent surgery between 2018 and 2021 completed web-based questionnaires between 2021 and 2022. Demographic and surgical data were obtained from electronic health records. Participants reported whether depressive and anxious symptoms increased or were stable/decreased during the COVID-19 pandemic, and completed eating behavior measures. RESULTS: Many participants reported increased depressive (27.5%) and anxious (33.7%) symptoms during the COVID-19 pandemic. Compared to those who reported stable or decreased symptoms, these participants were as follows: (1) more likely to endorse presence of binge, loss-of-control, graze, and night eating; (2) reported higher emotional eating in response to anger and frustration, depression, and anxiety; and (3) reported higher driven and compulsive eating behaviors. Frequency of binge, loss-of-control, graze, and night eating episodes did not differ between groups (e.g., increased vs. stable/decreased anxious symptoms) among participants who endorsed any episodes. CONCLUSION: A large portion of the sample reported increased depressive and anxious symptoms during the COVID-19 pandemic, and these increases were associated with maladaptive eating behaviors. Depressive and anxious symptoms and eating behaviors should be assessed postoperatively as significant stressors may be associated with increased distress and maladaptive eating behaviors that can affect postoperative outcomes. Postoperative interventions may be useful at simultaneously targeting these concerns.

Surgery

Pender S, **Lu AK**, and **Hans SS**. Squamous cell carcinoma arising in a below-knee stump of a patient with chronic lymphocytic leukemia. *J Vasc Surg Cases Innov Tech* 2024; 10(4). PMID: Not assigned. Full Text

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We report a case of localized squamous cell carcinoma arising in the ulceration at the site of a below-knee amputation in a patient with chronic lymphocytic leukemia on treatment with ibrutinib. The patient

underwent local excision of the skin and soft tissue with histopathology showing a small focus of well-differentiated squamous cell carcinoma in the specimen. This case highlights the importance of clinical evaluation and histopathological review for underlying malignancy in the setting of amputation stump ulceration.

Urology

Ditonno F, Franco A, Veccia A, Bologna E, Wang L, **Abdollah F**, **Finati M**, Simone G, Tuderti G, Helstrom E, Correa A, O DEC, Ferro M, Porpiglia F, Amparore D, Tufano A, Perdonà S, Bhanvadia R, Margulis V, Brönimann A, Singla N, Puri D, Derweesh IH, Mendiola DF, Gonzalgo ML, Ben-David R, Mehrazin R, Moon SC, Rais-Bahrami S, Yong C, Moghaddam FS, Ghoreifi A, Sundaram CP, Wu Z, Djaladat H, Antonelli A, and Autorino R. Robotic distal ureterectomy for high-risk distal ureteral urothelial carcinoma: a retrospective multicenter comparative analysis (ROBUUST 2.0 collaborative group). *Minerva Urol Nephrol* 2024; 76(3):331-339. PMID: 38920013. Request Article

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BACKGROUND: The role of kidney-sparing surgery in patients with high-risk upper urinary tract urothelial carcinoma is controversial. The present study aimed to assess oncological and functional outcomes of robot-assisted distal ureterectomy in patients with high-risk distal ureteral tumors. METHODS: The ROBUUST 2.0 multicenter international (2015-2022) dataset was used for this retrospective cohort analysis. High-risk patients with distal ureteral tumors were divided based on type of surgery: robot-assisted distal ureterectomy or robot-assisted nephroureterectomy. A survival analysis was performed for local recurrence-free survival, distant metastasis-free survival, and overall survival. After adjusting for clinical features of the high-risk prognostic group, Cox proportional hazard model was plotted to evaluate significant predictors of time-to-event outcomes. RESULTS: Overall, 477 patients were retrieved, of which 58 received robot-assisted distal ureterectomy and 419 robot-assisted nephroureterectomy, respectively, with a mean (±SD) follow-up of 29.6 months (±2.6). The two groups were comparable in terms of baseline features. At survival analysis, no significant difference was observed in terms of recurrence-free survival (P=0.6), metastasis-free survival (P=0.5) and overall survival (P=0.7) between robot-assisted distal ureterectomy and robot-assisted nephroureterectomy. At Cox regression analysis, type of surgery was never a significant predictor of worse oncological outcomes. At last follow-up patients undergoing robot-assisted distal ureterectomy had significantly better postoperative renal function. CONCLUSIONS: Comparable outcomes in terms of recurrence-free survival, metastasis-free survival, and overall survival between robot-assisted distal ureterectomy and robot-assisted nephroureterectomy patients, and better

postoperative renal function preservation in the former group were observed. Kidney-sparing surgery should be considered as a potential option for selected patients with high-risk distal ureteral UTUC.

Urology
Etta PD, **Majdalany SE**, **Raza JS**, and **Atiemo HO**. Management of Vaginal Prolapse After Orthotopic Bladder. *Curr Bladder Dysfunct Rep* 2023. PMID: Not assigned. Full Text

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Purpose of review: Pelvic organ prolapse is a well-understood clinical condition in many women that can lead to pelvic discomfort, sexual dysfunction, and voiding difficulty. Iatrogenic pelvic organ prolapse is a known complication of radical cystectomy with urinary diversion in women. The prevention, diagnosis, and management of this complication are not well described in literature and practice, creating a gap in the surgical care of women with bladder cancer. We sought to further investigate this phenomenon. Recent findings: While many causes of post-cystectomy pelvic organ prolapse are the same as those in the general female population, it is imperative to describe the normal anatomy and physiology of the female pelvis that, when disrupted during radical cystectomy, can increase the risk of this phenomenon. The clinical evaluation of post-cystectomy pelvic organ prolapse requires pelvic examinations and few diagnostic studies. Summary: Traditional management of pelvic organ prolapse may be challenging after radical cystectomy; thus, it is important for surgeons to have knowledge of the existing techniques for prevention and correction of this distressing sequala. In this manuscript, we present the evidence-based literature regarding this subject matter and describe the techniques at our institution to prevent and treat this condition. Robust prospective studies are needed to better understand the prevention and management of pelvic organ prolapse after radical cystectomy in women.

Urology
Kachroo N. EDITORIAL COMMENTS. *J Urol* 2023; 210(3):528-528. PMID: Not assigned. Full Text

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Urology
Suleyman G, **McCormick ME**, **McLenon N**, **Chami E**, **Pollak E**, and **Dabaja AA**. Urinary catheter alleviation navigator protocol (UCANP): Update to the hospital-wide implementation at a single tertiary health care center. *Am J Infect Control* 2024; Epub ahead of print. PMID: 38876167. Full Text

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BACKGROUND: Catheter-associated urinary tract infections (CAUTIs) are commonly reported healthcare-associated infections. It was demonstrated that the urinary catheter alleviation navigator protocol (UCANP) pilot resulted in a reduction of catheter utilization and catheter days. METHODS: Quality improvement initiative that was implemented at a single urban, tertiary health care center, focusing on early discontinuation of indwelling urinary catheters (IUC) and avoidance of reinsertion. Protocol was expanded hospital-wide September 2020-April 2022. We compared IUC utilization, IUC standardized utilization ratio (SUR) and CAUTI standardized infection ratio (SIR) in the pre-intervention period (March 2020-August 2020) to the post-intervention period (May 2022-October 2022). RESULTS: Pre-implementation, 2 patients with IUC removal were placed on UCANP. Post-implementation, 835 (45%) patients with IUC removal participated in the protocol. Number of patients requiring IUC reinsertion did not differ among the 2 groups. IUC utilization was significantly decreased from 0.28 to 0.24 with 14%

reduction (p=0.025). SUR decreased by 11% from 0.778 to 0.693 (p=0.007) and SIR by 84% from 0.311 to 0.049 (p=0.009). CONCLUSION: Our protocol significantly reduced IUC utilization and SUR after hospital-wide implementation. UCANP is a safe and effective strategy that can potentially decrease unnecessary IUCs in patients with transient urinary retention.

Administration
Alvi RBR, **Mann Y**, **Brar S**, **Brar I**, and **Suleyman G**. Characterization of Mpox in Southeast Michigan. *Open Forum Infect Dis* 2023; 10:S1165-S1166. Full Text

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Background. More than 30,000 cases of mpox have been identified in the United States. Data suggest that about 40% of affected persons are co-infected with HIV. Although most cases are self-limiting, patients with low CD4 counts are at increased risk of developing severe clinical manifestations and dying. Methods. Retrospective case-control study comparing mpox cases among people with HIV (PWH) and HIV-uninfected persons from July to Dec 2022, at Henry Ford Health in Southeast Michigan. Demographic data, clinical characteristics, treatment, and outcomes were evaluated. Results. 54 patients were diagnosed with mpox. Overall, 42 (78%) were MSM or bisexual men, 36 (67%) Black, and 34 (63%) PWH; median age was 34.5 years (Table 1). The majority (63%) had prior sexually transmitted infections (STIs), which were more common in PWH (82% vs 30%, p< 0.001). About one-third had multiple sexual partners; more than half engaged in insertive or receptive anal intercourse. 32 (94%) of PWH were on ART, 26 (76%) had CD4 counts >200 and 19 (60%) had undetectable viral load; mean CD4 count was 602 and viral load 7942. Of the HIV-uninfected persons, 5 (25%) were on PrEP. Receipt of mpox vaccine was uncommon in either group. All patients presented with rash that was disseminated in 35%. Fever/chills, lymphadenopathy, headache, proctitis and pharyngitis were the most common manifestations and did not differ among the two groups. Concomitant STIs were present in 22 (48%) of 46 persons tested; syphilis co-infection was more prevalent among PWH (35% vs 25%, p< 0.006). Hospitalization and receipt of tecovirimat were similar between the two groups; no patients died. Demographics, Risk Factors, Clinical Manifestations and Outcomes of Mpox Patients Conclusion. Overall, there were no significant differences in clinical manifestations or outcomes between PWH and HIV-uninfected persons with mpox except for syphilis co-infection. Most of our PWH cohort was on ART and virally suppressed with high CD4 count. Hence, efforts should focus on rapid treatment of PWH with effective ART to achieve virological suppression and immunological recovery to minimize clinical complications and severe outcomes associated with opportunistic pathogens. Vaccinating all high-risk individuals, early mpox recognition and testing, and screening for additional STIs should be prioritized.

Administration
Failla AJ, and **Suleyman G**. Risk Factors and Outcomes Associated with Daptomycin-nonsusceptible Enterococcus Bloodstream Infections. *Open Forum Infect Dis* 2023; 10:S417. Full Text

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Background. Enterococcus spp. are a common cause of nosocomial bloodstream infections (BSIs) with increasing resistance to currently available antibiotics and high mortality. Although the emergence of daptomycinnonsusceptible Enterococcus (DNSE) has been reported, risk factors and outcomes associated with acquisition of daptomycin (DAP) resistance are not well characterized. Methods. Retrospective cohort study of patients with enterococcal BSIs at Henry Ford Health in Southeast Michigan from 2014 to 2022. Cases included patients with DNSE; patients with persistent daptomycin (DAP)-susceptible Enterococcus (DSE) bacteremia (> 2 days of positive blood cultures) were used as controls. Outcomes included 30-day readmission and mortality. Results. 24 cases and 24 controls were included; median age was 67 years (IQR 59-72), 28 (58.3%) were male and 26 (54%) white. All patients were exposed to antibiotics within 90 days with no difference in DAP use between the two groups (8% vs 21%, p=0.220). The majority (90%) had prior hospitalization within the year, 44% were immune suppressed and 42% had end-stage renal disease. Hepatitis C virus (HCV) (17% vs 0, 0.037) and prior VRE (42% vs 21%, p < 0.001) were more prevalent among cases. Indwelling urinary catheter (IUC) use was more common in cases (83% vs 54%, p=0.029), but there was no difference in central venous catheter use (75% vs 58%, p=0.221). Most common source of infection was intra-abdominal in both groups (54% vs 75%, p=0.188). Although not statistically significant, need for intensive care unit admission was higher (75% vs 50%, p=0.074) and length of stay was longer (54 vs 32 days, p=0.063) in

cases compared to controls; treatment duration was significantly longer in controls (23 vs 16 days, p=0.04). There was no significant difference in readmission (12.5% vs 25%, p=0.267) or mortality (58% vs 46%, p=0.386) between the two groups. (Table Presented) DNSE patient demographics, risk factors and outcomes Conclusion. DNSE is an emerging pathogen associated with HCV, prior VRE and IUC use in our cohort; however, prior daptomycin exposure was not a significant risk factor for DNSE. Despite the high mortality, there was no difference in outcome between the two groups. Mechanism of DNSE in patients without prior DAP exposure should be explored to prevent potential spread of resistance.

Administration

Gubler J, **Ruby A**, **Chami E**, Weaver J, and **Suleyman G**. Management of a New Delhi metallo-β-lactamase (NDM)-producing Escherichia coli Outbreak and Large-Scale Exposure Event Associated with Endoscopes. *Am J Infect Control* 2024; 52(6):S33. Full Text

Background: Between July 2021-March 2023, 9 cases of genetically similar New Delhi metallo-β-lactamase (NDM)-producing Escherichia coli (E. coli) were identified in our healthcare facility. Upon investigation, it was discovered that these patients had procedures in the same procedural area using the same five endoscopes. These endoscopes were also used in thousands of other procedures. Methods: A multi-prong approach was taken to evaluate the situation and determine if other patients may have been exposed and prevent further transmission. This approach included establishing a case definition to determine exposure period, offering screening to 1097 exposed patients, auditing the affected procedural and reprocessing areas, evaluating the maintenance of the implicated endoscopes, and having these endoscopes evaluated by an external third-party vendor. Results: An incredible amount of resources and time were required to manage this event. Seventy-seven individuals participated in the planning, implementation, and management of this outbreak. A total of 205 patients sought testing and 115 called with questions. During live observations, it was discovered that the cleaning process of rooms between cases was inconsistent and varied by staff member due to lack of formal education or competency on room cleaning and turn-over. This area also lacked the necessary housekeeping support due to staffing. Investigation into the endoscopes revealed a lengthy history of repair and minimal preventative maintenance (e.g., borescope inspections). The external assessment of the endoscopes revealed significant internal damage within the channels, and all grew multiple organisms. Conclusions: Through proper planning, communication, and having a clearly outlined process for patient screening, we were able to manage this exposure event relatively smoothly. This also helped minimize fear and backlash on social media and in the news media. This presentation will outline the steps taken to manage an exposure event involving nearly 1100 patients and provide lessons learned to help other Infection Preventionists prepare for future outbreaks.

Administration

Hanna ZW, **Alangaden GJ**, **Zervos M**, and **Suleyman G**. Evaluation of Risk Factors and Outcomes Associated with Daptomycin-nonsusceptible Staphylococcus aureus Bacteremia. *Open Forum Infect Dis* 2023; 10:S144. Full Text

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Background. Staphylococcus aureus (SA) is a major cause of hospital-associated infections in the US with high morbidity and mortality. With SA developing resistance to many first-line antibiotics, daptomycin (DAP) has become a critical agent for SA therapy. However, increasing use of DAP has resulted in emergence of DAP-nonsusceptible (DNS) SA strains. We aim to elucidate risk factors associated with DNS SA and compare outcomes between patients with DAP-susceptible (DS) and DNS SA bacteremia (SAB). Methods. Retrospective cohort analysis was performed on patients with DNS (cases) and DS (controls) SAB admitted to Henry Ford Health between 9/2005 and 3/2023. Patients with persistent (>7 days of positive blood cultures) DS SAB were used as controls. Demographic, risk factors, clinical characteristics, and outcomes were evaluated. Primary outcomes were 30-day relapse or progression, readmission and mortality; secondary endpoint was 90-day mortality. Results. A total of 122 patients included 59 (48%) cases and 63 (52%) controls. The majority were male (56.6%) with median age of 59. The study population had a high burden of comorbidities as outlined in the Table; central venous catheter use was significantly more common among cases (p=0.049). History of MRSA infection (p< 0.001) and

prior hospitalization (p< 0.001) within 1-year, and antibiotic (p=0.017) use, particularly vancomycin (p=0.011), within 90 days were associated with DNS SA. Primary source of infection and infectious complications were not significantly different among cases and controls. There was no significant difference in outcomes between the two groups. Although not statistically significant, 90-mortality was higher in the DNS group (p=0.075). Conclusion. Our study highlights risk factors for DNS SA, including recent vancomycin use, and prior hospitalization and MRSA infection within 1 year. While there was no significant difference in outcomes between DNS and DS SAB, overall mortality was high. These findings highlight the need for continued surveillance of DNS SA and careful consideration of risk factors when selecting antimicrobial agents for complicated SA infections. Further studies are needed to identify potential mechanisms of vancomycin cross-resistance in DNS SA. (Table Presented).

Administration

Joshi S, **Alvi RBR**, **Shanahan C**, **Ruby A**, **Chami E**, and **Suleyman G**. Clinical Characteristics and Outcomes in Patients with Healthcare Facility-Onset Clostridiodes difficile Infections. *Open Forum Infect Dis* 2023; 10:S386-S387. Full Text

S. Joshi, Henry Ford Hospital, Detroit, MI, United States

Background. Healthcare facility-onset (HCFO) Clostridiodes difficile infection (CDI) is the most common hospital-acquired infection. Although risk factors associated with CDI have been described, characterization and outcome of HFCO-CDI are limited. Methods. This was a retrospective observational study comparing disease severity among adult patients with HCFO-CDI from January 1, 2020, to December 31, 2022, at an 877-bed tertiary care hospital in Detroit. Patients were identified using National Healthcare Safety Network (NHSN) definition. CDI was classified as nonsevere, severe, or fulminant. Severe disease was defined as having white blood cell (WBC) count ≥ 15,000 cells/mm3 or acute kidney injury (AKI) defined as increase in creatinine of ≥ 0.3mg/dL within 48 hours of diagnosis. Fulminant disease included patients with ileus or toxic megacolon, or need for colectomy, intensive care unit or vasopressors. Risk factors, treatment and outcomes were evaluated. Results. 98 patients were diagnosed with HFCO CDI during the study period (Table 1); 37 (38%) were non-severe, 47 (38%) severe and 14 (24%) fulminant. Median age was 66 years, 50% were female and 45% white. Almost half were immune suppressed; 5% had prior CDI. Most patients (88%) were exposed to antibiotics (abx) prior to CDI with no difference between the groups (p=0.427); 61% received cephalosporins. Cirrhosis was more common among patients with fulminant disease (p=0.048) and receipt of chemotherapy was associated with severe and/or fulminant disease cases (p=0.049). AKI (p< 0.001), fever (p=0.030), and WBC >25,000 or < 2,000 cells/mm3 (p< 0.001) were more prevalent among patients with fulminant CDI; combination or alternative therapy was more common among fulminant cases (p< 0.001). Most were eligible, but only 6% received bezlotoxumab (BZX). Although outcomes were not significantly different between the groups, length of stay was longer and refractory disease and recurrence were more common in severe/fulminant CDI. Conclusion. In our HCFO-CDI cohort, most patients were exposed to abx, and cirrhosis and chemotherapy were associated with more severe CDI. Efforts should focus on appropriate abx utilization and increasing use of BZX to reduce burden of CDI and risk of recurrence and readmission.

Administration

Kaur J, Gurdziel K, Wasinski B, Vakeesan N, Raza SH, Liu W, **Zervos M**, and **Suleyman G**. Genomic Epidemiology of SARS-CoV-2 in Metropolitan Detroit. *Open Forum Infect Dis* 2023; 10:S979. Full Text

J. Kaur, Henry Ford Health, Detroit, MI, United States

Background. The COVID-19 pandemic, resulting from the rapidly evolving SARS-CoV-2 virus, has drastically impacted health systems and economies worldwide. Genomic sequencing is critical for the surveillance of SARS-CoV-2 to monitor the rapidly evolving virus and identify new strains. Methods. 583 isolates from Henry Ford Health were retrospectively profiled across 3 years (117 isolates in 2020; 39 in 2021; 427 in 2022). DNA was extracted using Kingfisher viral isolation kit; RT-PCR screening was used to identify isolates with cycle threshold < 32 for whole genome sequencing (WGS). Libraries were generated using QIAseq DIRECT SARS-CoV-2 Kit, followed by Illumina sequencing (MiSeq or NovaSeq 6000; 300

cycles). Lineage analysis of the SARS-CoV-2 consensus genome sequences generated from samtools variant analysis pipeline was determined using Nextclade and Pangolin software. Results. Sequences were classified into 11 unique clades across 108 lineages by Nextclade and Pangolin, respectively. Almost three-fourths of the sequenced isolates were from 2022. 117 (20%) genomes were from the early pandemic (2020) and were clustered into 8 clades: 19A, 19B, 20A, 20B, 20C, 21 J (Delta) and 21L (Omicron). Most of the 2022 genomes (72%) were in clade 20C from lineage B.1, identified during the outbreak in Europe. 15 (13%) genomes had clade 19A (lineage B) and 1 had 19B (lineage A.3), identified early in the pandemic in Wuhan, China. Of the 39 (7%) genomes from 2021, the majority (82%) clustered into clade Delta 21J that originated in India. Only 2 (5%) of the genomes from 2021 had Alpha variant of concern (21I) from the lineage B1.1.7, which were suspected to be more transmissible. Of the 427 (73%) genomes from 2022, 393 (92%) had variants within Omicron variant of concern (21L), with 79 different lineages; 1 was Omicron variant 21K from the lineage BA1.1. Other clades observed in the 2022 batch were 19A (6%), 20A (0.2%), 20B (0.2%), 20C (0.2%) and 21M (1%). Conclusion. Our genomic surveillance data suggest that SARS-CoV-2 infections at the local level mirrored global outbreaks. This underscores the importance of robust genomic surveillance efforts to inform public health planning and practice.

Administration

Parke DM, **Kenney RM**, **Bogojevich J**, **El-Khoury C**, **Joshi S**, **Brar S**, **MacDonald L**, **Salib C**, **MacDonald N**, **Veve M**, and **Suleyman G**. Barriers to Improving Outcomes among People Experiencing Homelessness and People Who Inject Drugs Hospitalized for Complicated Infections. *Open Forum Infect Dis* 2023; 10:S864-S865. Full Text

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Background. People experiencing homelessness (PEH) and people who inject drugs (PWID) experience health disparities and worse outcomes. Challenges include suboptimal medication use, loss to follow-up, and non-compliance due to social determinant of health (SDOH) barriers, including lack of stable housing and transportation, limited financial resources, substance use, and addiction. Methods. This quality improvement project aimed to address SDOH barriers among hospitalized PEH and/or PWID requiring ≥ 2 weeks of antibiotics to improve antibiotic compliance and outcomes in Detroit from 6/2022-4/2023. Interventions included antibiotic education, addiction medicine and pharmacy discharge medication cost inquiry consults when indicated, ensuring oral antibiotics were in hand at discharge, strengthening discharge planning between inpatient and ambulatory case managers (ACM), and referrals to community-based organizations to address SDOHneeds. Results. 34 patients were included (8 PEH, 11 PWID, 15 both); 3 who died in the hospital were excluded. Multiple individual and structural barriers and challenges to improving adherence and outcomes were identified (Table 1). Loss to follow-up was a significant challenge among this cohort, primarily due to patients self-discharging (29%) and being unreachable (52%). 10 (37%) patients were offered SDOH services (Table 2). Patients also had significant behavioral health/substance use disorder needs and utilized healthcare at a very high rate, with 29% having an ED revisit and 44% being readmitted within 30 days after discharge. Several structural and SDOH barriers existed, including limited staff capacity and limited placement options after discharge, resulting in suboptimal treatment delivery. Conclusion. AddressingSDOHbarriers for PEHand PWIDis challenging but vital to improving outcomes. Qualitative research should be conducted to understand these barriers. Having an interdisciplinary team comprising of infectious diseases, pharmacy, addictionmedicine, casemanagement and population health is critical to address patient needs holistically. Strengthening internal processes and building additional communitybased partnerships will be essential to better meet patient needs after discharge. (Table Presented).

Administration

Shanahan C, **Ruby A**, **Chami E**, and **Suleyman G**. Implementing an electronic best practice advisory to reinforce Clostridioides difficile testing. *Am J Infect Control* 2024; 52(6):S48. Full Text

Background: The National Healthcare Safety Network (NHSN) defines a hospital-onset Clostridioides difficile (C. diff) infection as one identified after the third hospital day of a patient's admission. Conversely, a community-onset C. diff infection is identified during the first three hospital days of patient admission.

Our facility identified that in a subset of our hospital-onset C. diff infections, unformed stools were documented in the first three days of patient admission. A best practice advisory (BPA) was developed to reinforce our nurse-driven protocol for C. diff testing and increase adherence to this protocol. Methods: The electronic medical record system was utilized to build a BPA that would fire if nursing documented an unformed stool during the first three hospital days of a patient's admission. When this BPA fired, it linked to the C. diff test and isolation order to facilitate easier ordering. For our 800+ bed facility, we evaluated the percentage of hospital-onset C. diff infections with unformed stools during the first three hospital days of admission during a 24 month pre-intervention period and a 24 month post-intervention period. Additionally, we quantified the total C. diff community-onset infections identified during the pre-intervention and post-intervention periods. Results: The percentage of hospital-onset C. diff infections with unformed stools during the first three hospital days of admission decreased from 41% (n=117) during the pre-intervention period to 32% (n=126) during the post-intervention period. Additionally, the number of community-onset C. diff infections identified increased from 291 during the pre-intervention period to 527 in the post-intervention period. Conclusions: Implementation of a BPA has decreased the percentage of hospital-onset C. diff infections with unformed stools during the first three hospital days of admission and increased early C. diff testing in our facility. Through utilizing this BPA, our C. diff testing protocol is continually reinforced which will promote adherence to testing guidelines.

Administration

Wu B, Hu D, **Yang M**, Witonsky J, **Hochstadt S**, Elhawary JR, Eng C, **Debbs J**, Chang C, **Cabral W**, Huntsman S, Ziv E, Burchard EG, and **Williams KL**. Decoding the Transcriptional Response to Severe Exacerbations Among African-american Individuals With Asthma. *Am J Respir Crit Care Med* 2024; 209. Full Text

B. Wu, Center for Individualized and Genomic Medicine Research (CIGMA), Department of Internal Medicine, Henry Ford Health, Detroit, MI, United States

Rationale: Asthma exacerbations are characterized by worsening symptoms and airway obstruction; they can result in severe outcomes, such as emergency visits (ED) and in-patient hospitalization (IP). The molecular immune responses involved in exacerbations remain poorly understood. Therefore, our aim was to identify genes associated with severe exacerbations. Methods: Our study population included African-American individuals from the Study of Asthma Phenotypes and Pharmacogenomic Interactions by Race-Ethnicity (SAPPHIRE). We analyzed the gene expression (RNA-seq) results from 429 healthy controls, 29 individuals with uncontrolled asthma (asthma control test score ≤19 but no history of asthma-related ED/IP), and 15 individuals peri-exacerbation (asthma-related ED/IP ±30 days of assessment). We assessed for differential gene expression, performed a weighted gene correlation network analysis, and modeled via cubic spline regression. Results: We identified 118 and 678 genes upregulated among individuals with uncontrolled asthma and severe exacerbations, respectively. 29 genes were significantly increased in both groups. Network analysis revealed three modules that were positively and significantly associated with severe exacerbations. Of the 678 genes upregulated among individuals with severe exacerbations, 559 (82%) were covered by these three modules. Functional analysis revealed that the semaphorin-plexin signaling pathway, the type-I interferon signaling pathway, and neutrophil degranulation were the top terms in each module. In addition, spline modeling of expression surrounding the timing of events revealed 55 genes with a hill pattern; these genes included NFIL3, a transcription factor controlling IgE production. Conclusions: Our study identified a number of genes associated with severe asthma exacerbations among African Americans, providing new potential biomarkers to predict impending events, as well as targets for treatment and measuring therapeutic response.

Anesthesiology

Bava EP, **Epelman M**, **Yeldo N**, **Uribe-Marquez S**, and **Lopez-Plaza I**. Use of Plasmapheresis in Heparin Induced Thrombocytopenia in Patients Undergoing Urgent Cardiac Surgery. *Am J Clin Pathol* 2023; 160:S115-S116. Full Text

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Behavioral Health Services/Psychiatry/Neuropsychology
Magidson J, Bradley V, Kleinman M, Anvari M, Hines A, Belcher A, Greenblatt A, Abidogun T, Dean D, Seitz-Brown C, Wagner M, Bennett M, and **Felton J**. Peer recovery specialist-delivered, behavioral activation intervention to improve retention in methadone treatment: results from an open-label, type 1 hybrid effectiveness-implementation pilot trial. *Implement Sci* 2023; 18:2. Full Text

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Cardiology/Cardiovascular Research
Alexandrou M, Rempakos A, Al-Ogaili A, Mutlu D, Choi J, Poommipanit P, **Alaswad K**, **Basir B**, Davies R, Benton S, Jaffer F, Chandwaney R, Azzalini L, ElGuindy A, Rafeh NA, Goktekin O, Gorgulu S, Khatri J, Aygul N, Cincin A, Rangan B, Mastrodemos O, Allana S, Sandoval Y, Burke MN, and Brilakis E. Balloon-Assisted Subintimal Entry in Chronic Total Occlusion Percutaneous Coronary Interventions. *J Am Coll Cardiol* 2023; 82(17):B161-B161. Full Text

[Alexandrou, Michaella; Rempakos, Athanasios; Mutlu, Deniz] Minneapolis Heart Inst Fdn, Minneapolis, MN USA. [Al-Ogaili, Ahmed] Minneapolis Heart Inst, Minneapolis, MN USA. [Choi, James] Baylor Univ, Med Ctr, Dallas, TX USA. [Poommipanit, Paul] Univ Hosp, Cleveland, OH USA. [Alaswad, Khaldoon; Basir, Babar] Henry Ford Hosp, Detroit, MI USA. [Davies, Rhian] Wellspan York Hosp, York, PA USA. [Benton, Stewart] Wellspan Hlth, York, PA USA. [Jaffer, Farouc] Massachusetts Gen Hosp, Boston, MA USA. [Chandwaney, Raj] Oklahoma Heart Inst, Tulsa, OK USA. [Azzalini, Lorenzo] Univ Washington, Seattle, WA USA. [ElGuindy, Ahmed] Magdi Yacoub Heart Fdn, Cairo, Egypt. [Rafeh, Nidal Abi] North Oaks Hlth Syst, Hammond, LA USA. [Goktekin, Omer] Mem Bahcelievler Hosp, Istanbul, Turkiye. [Gorgulu, Sevket] Biruni Univ, Sch Med, Istanbul, Turkiye. [Khatri, Jaikirshan] Cleveland Clin, Cleveland, OH USA. [Aygul, Nazif] Selcuk Univ, Konya, Turkiye. [Cincin, Altug] Medpar Med, Istanbul, Turkiye. [Mastrodemos, Olga] Minneapolis Heart Inst, Minneapolis, MN USA. [Mastrodemos, Olga] Abbott NW Hosp, Minneapolis Heart Inst Fdn, Minneapolis, MN USA. [Allana, Salman] UT SouthWestern Med Ctr, Minneapolis, MN USA. [Sandoval, Yader; Burke, M. Nicholas] Abbott NW Hosp, Minneapolis Heart Inst, Minneapolis, MN USA. Foundation; Baylor University Medical Center; Baylor University; University Hospitals of Cleveland; Henry Ford Health System; Henry Ford Hospital; Harvard University; Massachusetts General Hospital; University of Washington; University of Washington Seattle; Biruni University; Cleveland Clinic Foundation; Selcuk University; Minneapolis Heart Institute Foundation; Minneapolis Heart Institute Foundation; University of Texas System; University of Texas Southwestern Medical Center Dallas; Minneapolis Heart Institute Foundation

Cardiology/Cardiovascular Research
Almajed MR, **Mahmood S**, **Obri M**, **Gonzalez PE**, **Wang DD**, **Lee J**, **Frisoli T**, **Basir M**, **Alaswad K**, **O'Neill B**, **O'Neill W**, and **Villablanca P**. MANTA vascular closure device bleeding and vascular complications in association with cardiovascular risk factors: a large single centre experience. *Eur Heart J* 2023; 44:1. Full Text

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Cardiology/Cardiovascular Research
Basir B. CERAMICS Trial: Best Practices for Mechanical Circulatory Support Escalation and Management in Acute MI-Cardiogenic Shock. *Interv Cardiol* 2024; 19:18-19. Full Text

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The National Cardiogenic Shock Initiative (NCSI) was assembled to assess the impact of early mechanical circulatory support (MCS) in patients with acute MI (AMI) and cardiogenic shock (CS) treated with percutaneous coronary intervention (PCI). Before establishment of the NCSI in 2016, there was significant variability in the use of MCS in AMI-CS. There were no standardised practices, and outcomes associated with the use of MCS in AMI-CS were variable. In addition, experience in the use of large-bore MCS placement, management and approval was only beginning to grow. There were also limited data on the association of right heart failure, intensive care unit (ICU) management of MCS, MCS weaning and escalation. The NCSI addressed these needs by providing a uniform shock protocol to help healthcare systems obtain predictable outcomes and a set of standardised best practices based on foundational principles. The initiative offers a number of protocols to improve patient survival by encouraging the early use of Impella pre-PCI during optimal PCI techniques of the target artery or other large-bore vessels and avoiding escalating vasopressor and inotrope doses, which are associated with poorer outcomes. The initiative enables devices to be weaned based on invasive haemodynamics with right-sided heart catheterisation and offers hub-and-spoke models of care for the transfer of patients. Overall, the NCSI has consistently demonstrated survival in AMI-CS of over 70%.1 Over the past few years, the NCSI has continued to collect data to improve its best practice protocols on the mechanical support management of these patients with AMI. This has included data from the Cardiogenic Shock Working Group on the use of invasive haemodynamics in guiding therapy, a practice that has been shown to improve survival in AMI-CS.2 Conversely, a delay in treatment and delivery of MCS is associated with higher mortality in AMI-CS.3 This finding is consistent with evidence that CS should be treated acutely and with minimum delay to reverse the CS state. The Impella device can also help predict right-sided heart failure. Evidence obtained by the NCSI has shown that of the 92% of patients with right ventricular (RV) catheterisation, those who had RV failure (RVF) had an absolute mortality of approximately 14% more than those without RVF.4 However, despite these favourable outcomes, the NCSI found that the use of RV haemodynamic support devices for treatment escalation is <20% in practice.4 Similarly, instead of escalating treatment to mechanical support devices, patients in AMI-CS are often maintained on increasing doses of vasopressors and inotropes, which are associated with increased mortality independent of underlying cardiac power output.5,6 NCSI analysis found that the cause of death for the majority of patients is due to ongoing CS (58%) and multiorgan failure (18%), but only 19% of patients in CS receive escalation of treatment appropriate for worsening CS.2,3 The NCSI also found that there was a considerable variation in ICU-level care and the ability of sites to escalate MCS.2 Unless sites have the appropriate tools and devices, they are unable to effectively treat patients in CS with haemodynamic support and improve clinical outcomes. Taking all the learnings from the NSCI, Dr Basir and his team designed the study Can Escalation Reduce Acute Myocardial Infarction in Cardiogenic Shock (CERAMICS). Twenty sites were selected, all with rapid MCS escalation capabilities, including Impella, RV MCS and ECPella support devices. Data were collected on the survival of all AMI-CS patients, including those not treated with Impella. The sites participating in the trial used the same definitions as per the NCSI protocol, namely Society for Cardiovascular Angiography and Interventions (SCAI) SHOCK classes C, D and E. AMI was defined as ischaemic symptoms with ECG and/or biomarker evidence of ST-elevation MI (STEMI) or non-STEMI. CS was defined as at least two of the following: hypotension (systolic blood pressure [SBP] <90 mmHg or the use of inotropes o vasopressors to maintain SBP); signs of end organ hypoperfusion, including cool extremities, oliguria/anuria, elevated lactate concentrations, altered mentation; and hypodynamic evidence of hypoperfusion, represented by a cardiac index <2.2 l/min/m2 or cardiac power output <0.6 W. The NCSI protocol was adhered to, which includes escalation of treatment with quick implantation of the Impella CP, followed by revascularisation and right heart catheterisation for monitoring to rapidly reduce the use of inotropes. Escalation could occur at any time, but ideally as early as possible and preferably in the cardiac cath lab. Key triggers for escalation with an unloading strategy were guided by haemodynamics and aimed at achieving survival >80% (Table 1). The implementation of shock protocols alongside a team-based approach is associated with improved patient outcomes. Dr Basir closed his presentation by confirming that the foundations, strategy and principles of the NSCI will be studied further in the CERAMICS study, as well as in the RECOVER IV randomised controlled trial for AMI-CS patients.

Bharadwaj A, Truesdell A, Lemor A, Thompson J, Abu-Much A, Zhang YR, Schonning M, Redfors B, Cohen D, Witzke C, Matthews R, Dixon S, Lansky A, and **O'Neill W**. Defining High-Risk Percutaneous

Coronary Intervention: Characteristics of Patients Undergoing Contemporary Percutaneous Coronary Intervention With Axial-Flow Mechanical Support. *J Am Coll Cardiol* 2023; 82(17):B83-B84. Full Text

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Cardiology/Cardiovascular Research
Bonnet G, Rommel KP, Falah B, Lansky A, Zhang YR, Schonning M, Redfors B, Burkhoff D, Cohen D, Patel R, **Basir B**, **O'Neill W**, and Granada J. Relationship Between Preprocedural Blood Pressure and Outcomes in Patients Undergoing Impella-Supported High-Risk PCI: Insights From the cVAD PROTECT III Study. *J Am Coll Cardiol* 2023; 82(17):B56-B57. Full Text

[Bonnet, Guillaume; Falah, Batla; Zhang, Yiran] Cardiovasc Res Fdn, New York, NY USA. [Rommel, Karl-Philipp] Heart Ctr Leipzig, Leipzig, Germany. [Lansky, Alexandra] Yale Sch Med, New Haven, CT USA. [Schonning, Michael; Redfors, Bjorn; Burkhoff, Daniel; O'Neill, William] Cardiovasc Res Fdn, New York, NY USA. [Cohen, David] St Francis Hosp, New York, NY USA. [Patel, Rajan] Ochsner Clin Fdn, New Orleans, LA USA. [Basir, Babar] Henry Ford Hosp, Detroit, MI 48202 USA. [O'Neill, William] Henry Ford Hlth Syst, Orchard Lake, MI USA. Yale University; Cardiovascular Research Foundation (CRF); Ochsner Health System; Henry Ford Health System; Henry Ford Hospital; Henry Ford Health System

Cardiology/Cardiovascular Research
Fadel R, **Almajed MR**, **Parsons A**, **Kalsi J**, **Shadid AM**, **Maki M**, **Jones C**, **Williams C**, **Aronow H**, **Tanaka D**, **Nemeh H**, **Fuller B**, **Alqarqaz M**, **Koenig G**, **Villablanca P**, **Frisoli T**, **O'Neill B**, **Khandelwal A**, **Cowger J**, **Grafton G**, **Kim H**, **O'Neill W**, **Alaswad K**, and **Basir B**. TCT-302 Feasibility and Outcomes of a Cardiology-Based Extracorporeal Membrane Oxygenation Service. *J Am Coll Cardiol* 2023; 82(17):B120. Full Text

Background: There has been a significant increase in the use of veno-arterial extracorporeal membrane oxygenation (VA-ECMO). ECMO programs have typically been led by cardiothoracic surgery teams, and there is little evidence on alternative care models. Methods: We performed a retrospective analysis of patients treated with peripheral VA-ECMO at a tertiary care center from 2018 to 2022. The primary outcome was death while on ECMO or within 24 hours of decannulation. Results: A total of 244 patients were included in the analysis (median age 61 years; 28.7% female). Interventional cardiologists performed 91.8% of cannulations, and 84.4% of patients were managed primarily by a cardiology service comprising interventional cardiologists, cardiac intensivists, or advanced heart failure cardiologists. The most common indications for ECMO were acute myocardial infarction (34.8%), decompensated heart failure (30.3%), and refractory VT/VF (10.2%). ECMO was utilized for peri-procedural arrest in 26.6% of patients. The median (IQR) pre-ECMO SAVE score was 0.0 (–4.0 to 3.0), and median (IQR) SOFA score was 13.0 (10.0 to 16.0). Forty-six percent of patients survived through decannulation; the majority of patients were decannulated percutaneously in the cardiac catheterization laboratory. There was no difference in survival following cannulation by a cardiac surgeon vs cardiologist (50% vs 45%; P = 0.90). Complications included arterial injury (3.7%), compartment syndrome (4.1%), cannulation site infection (1.2%), stroke (14.8%), AKI (52.5%), dialysis (22.5%), access site bleeding (16%), and need for blood transfusion (83.2%). Positive independent predictors of death while on ECMO or within 24 hours of decannulation included elevated initial serum lactate (OR per mmol/L increase: 1.13; 95% CI: 1.04-1.23; P < 0.01) and SOFA score (OR per 1 unit increase: 1.27; 95% CI: 1.15-1.40; P < 0.01), while SAVE score (OR per 1 unit increase: 0.92; 95% CI: 0.86-0.99; P = 0.03) and 8-hour lactate clearance (OR per % decrease: 0.98; 95% CI: 0.97-0.99; P < 0.01) were negative predictors of this outcome. Conclusion: The

use of a cardiology-based ECMO service is feasible. As ECMO services and indications expand, the use of cardiology-based ECMO care may be practical for select centers. Categories: CORONARY: Hemodynamic Support and Cardiogenic Shock

Cardiology/Cardiovascular Research
Hargens TA, Richardson LA, **Brawner CA**, Perry D, Verrill DE, and **Kerrigan DJ**. Regional Differences In Salary For Clinical Exercise Physiologists: The CEPA 2020 Clinical Practice Survey. *Med Sci Sports Exerc* 2023; 55(9):134-135. Full Text.

[Hargens, Trent A.] James Madison Univ, Harrisonburg, VA 22807 USA. [Richardson, Laura A.] Univ Michigan, Ann Arbor, MI 48109 USA. [Brawner, Clinton A.; Kerrigan, Dennis J.] Henry Ford Hosp, Detroit, MI 48202 USA. [Perry, Diane] Michigan Med, Ann Arbor, MI USA. [Verrill, David E.] Univ North Carolina Charlottee, Charlotte, NC USA. Michigan; Henry Ford Health System; Henry Ford Hospital

Cardiology/Cardiovascular Research
Jakob P, Falah B, Abu-Much A, Lansky A, **Basir MB**, Schonning M, Zhou Z, Batchelor W, Grines C, **O'Neill W**, and Barbar S. Characteristics and outcomes of elderly patients undergoing protected percutaneous coronary intervention with impella mechanical circulatory support. *Eur Heart J* 2023; 44:2. Full Text

[Jakob, P.; Barbar, Stahli] Univ Heart Ctr, Zurich, Switzerland. [Falah, B.; Abu-Much, A.; Schonning, M.; Zhou, Z.] Cardiovasc Res Fdn, New York, NY USA. [Lansky, A.] Yale Sch Med, New Haven, CT USA. [Basir, M. B.; O'neill, W.] Henry Ford Hosp, Detroit, MI USA. [Batchelor, W.] Inova Heart & Vasc Inst, Fairfax, VA USA. [Grines, C.] Northside Hosp, Atlanta, GA USA. Health System; Henry Ford Hospital; Inova Fairfax Hospital

Cardiology/Cardiovascular Research
Jomaa D, **Ichkhanian Y**, **Gupta K**, **Chaudhary AJ**, and **Jafri SM**. PREDICTIVE ROLE OF TRICUSPID REGURGITATION SEVERITY AMONG PERI-LIVER TRANSPLANT PATIENTS: RESULTS FROM A LARGE TERTIARY CARE CENTER. *Hepatology* 2023; 78:S338-S339. Full Text

[Jomaa, Diana; Ichkhanian, Yervant; Gupta, Kartik; Chaudhary, Ammad Javaid] Henry Ford Hosp, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Hospital

Cardiology/Cardiovascular Research
Karacsonyi J, Rempakos A, Alexandrou M, Allana S, Kostantinis S, Simsek B, Al-Ogaili A, **Alaswad K**, Karmpaliotis D, Kirtane A, McEntegart M, Jaffer F, Choi J, Poommipanit P, Elbarouni B, Gorgulu S, ElGuindy A, Rafeh NA, Goktekin O, and Azzalini L. TCT-451 Use of CrossBoss in Chronic Total Occlusion Percutaneous Coronary Intervention. *Journal of the American College of Cardiology (JACC)* 2023; 82(17):B181-B182. Full Text

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North Oaks Health System, Hammond, Louisiana, USA
Memorial Bahcelievler Hospital, Istanbul, Turkey
University of Washington, Seattle, Washington, USA

Cardiology/Cardiovascular Research
Mont L, Daubert J, Kutyifa V, Zareba W, Ando K, Wold N, Yong P, and **Schuger C**. Has the use of concomitant cardiac medications improved over time in primary prevention ICD patients? Insights from the APPRAISE ATP study. *Eur Heart J* 2023; 44:2. Full Text.

[Mont, L.] Univ Barcelona, Barcelona, Spain. [Daubert, J.] Duke Univ, Med Ctr, Durham, NC USA. [Kutyifa, V.; Zareba, W.] Univ Rochester, Med Ctr, Rochester, NY USA. [Ando, K.] Kokura Mem Hosp, Fukuoka, Japan. [Wold, N.; Yong, P.] Boston Sci, St Paul, MN USA. [Schuger, C.] Henry Ford Hosp, Detroit, MI USA. Kokura Memorial Hospital; Boston Scientific; Henry Ford Health System; Henry Ford Hospital

Cardiology/Cardiovascular Research
Mont L, Daubert J, Zareba W, Kutyifa V, Ando K, Wold N, Yong P, and **Schuger C**. Changes in study enrollment of patients with non-ischemic cardiomyopathy receiving an ICD for primary prevention: Insights from the APPRAISE ATP study. *Eur Heart J* 2023; 44:2. Full Text

[Mont, L.] Univ Barcelona, Barcelona, Spain. [Daubert, J.] Duke Univ, Med Ctr, Durham, NC USA. [Zareba, W.; Kutyifa, V.] Univ Rochester, Med Ctr, Rochester, NY USA. [Ando, K.] Kokura Mem Hosp, Fukuoka, Japan. [Wold, N.; Yong, P.] Boston Sci, St Paul, MN USA. [Schuger, C.] Henry Ford Hosp, Detroit, MI USA. Kokura Memorial Hospital; Boston Scientific; Henry Ford Health System; Henry Ford Hospital

Cardiology/Cardiovascular Research
O'Neill W. Is Unloading the Left Ventricle the Key to Improving Survival in Anterior Wall Acute MI? *Interv Cardiol* 2024; 19:11-12. Full Text

W. O'Neill, Henry Ford Hospital, Detroit, MI, United States

The concept of myocardial salvage has been described since the 1970s. Acute MI is survivable but its impact is time dependent because the 'wavefront' of tissue necrosis begins to spread from a small area of infarct after 40 minutes of coronary occlusion, plateauing at around 96 hours.1 Dr O'Neill commented on the difficulty researchers faced at the time to accurately measure infarct size in human patients to prove that a therapy could potentially reduce infarct, and recognised that a method to directly or indirectly measure infarct size was needed. In a 1981 study that used systolic time intervals to estimate left ventricular (LV) viability, it was found that patients who had preserved LV systolic function following MI had superior 5-year survival.2 These findings supported the notion that patients who survived acute MI with a large infarct scar had poor long-term prognosis and led to a scientific pursuit of therapies to decrease infarct size. Dr O'Neill shared his experience in his first randomised trial for streptokinase, conducted in 1983, that compared the intracoronary administration of streptokinase versus dextrose placebo within 6 hours from the onset of symptoms of acute MI in 40 patients.3 Although streptokinase achieved re-establishment of flow in 60% of patients, compared with 10% of patients in the control group, there was no statistically significant improvement in LV function measured by LV ejection fraction (EF).3 Following this, a study conducted in 2005 examined advanced imaging techniques as a means to determine the size of infarction. That study demonstrated the time dependency of salvage in patients with anterior infarction.4 For patients who presented within 2 hours of symptom onset, infarct size remained relatively small and rapid reopening of the artery could effectively decrease infarct size. However, this window of opportunity to salvage the myocardium rapidly diminished after 3 hours, after which there was limited scope for improvement in infarct size.4 In the US, the median time from symptom onset to presentation is 4.0 (IQR 1.6-16.0) hours.5 With the recommended door-to-balloon (DTB) time of 90 minutes, the total time from onset to reperfusion can be between 3.0 and 17.5 hours from symptom onset.6 This may be one of the reasons why, even though DTB time has improved markedly in the US over the past 20 years, it has had minimum impact on long-term survival. Therefore, in Dr O'Neill's opinion, the biggest challenge is to treat patients within the time frame in which reperfusion can make a difference. Given the practical difficulties in achieving this, an alternative strategy is to devise time-independent methods to decrease infarct size and improve myocardial function and salvage. In hearts

with small infarcts, the apex may remain hypokinetic but the rest of the myocardium has the potential to positively remodel and recover. However, in hearts with large infarcts, both the apex and anterior wall become akinetic, with sequelae of adverse remodelling and ventricular dilation, leaving only a small potential for myocardial recovery.7 Therefore, the goal should be to decrease the infarct size enough so that the ventricle can positively remodel following the insult. Dr O'Neill discussed data from the CRISP-AMI randomised trial that showed that among patients with acute anterior ST-elevation MI (STEMI) without shock, intra-aortic balloon counter-pulsation plus primary percutaneous coronary intervention (PCI) compared with PCI alone did not result in reduced infarct size.8 In contrast, the AMIHOT I + II trials showed that among patients with anterior STEMI undergoing PCI within 6 hours of symptom onset, the infusion of supersaturated oxygen into the left anterior descending artery infarct territory resulted in a significant reduction in infarct size.9,10 Dr O'Neill presented the STEMI-DTU pilot study, a multicentre prospective randomised safety and feasibility trial.9 In all, 50 patients were enrolled and randomised 1 : 1 to LV unloading with the Impella CP followed by immediate reperfusion (UR-IR arm) versus delayed reperfusion after 30 minutes of unloading (UR-DR arm). Forty-one patients were assessed by cardiac MRI (CMR) at 3-5 days and 30 days after PCI; 39 were analysed for the final analysis (Figure 1). In order to assess the impact of the initial infarct size on heart recovery, the pilot study subjects were divided according to their infarct size measured by CMR 3-5 days after PCI into two groups: those with an infarct size measuring ≤25% LV mass and those with infarct size >25% LV mass. Results from the 30-day CMR and 90-day echocardiogram showed that the group with smaller initial infarct size experienced a greater increase in LVEF. For those with an initial infarct size >25% LV mass, LVEF remained flat at 30 and 90 days. These individuals also exhibited a significant increase in LV end-systolic and end-systolic volumes, indicating that the ventricle began to adversely remodel and dilate.11 Dr O'Neill also shared the echocardiogram-based wall motion analysis of the STEMI-DTU pilot cohort. The wall motion analysis showed that in patients with a larger infarct size (>25% LV mass), all three sections of the myocardium (basal, mid-cavity and apical) had significant proportions of hypokinesis and akinesis at 3-5 days. In the group with smaller (≤25% LV mass) infarct size, all three sections showed a significant proportion of hypokinesis, but a smaller proportion of akinesis and a larger proportion of normal wall motion compared with the group with larger infarct size. At 90 days, the group with smaller infarct size showed recovery to fully normal basal and nearly normal mid-cavity, with approximately 25% of patients with a hypokinetic or akinetic apex. In the group with large infarct size, the wall motion in the basal and mid-cavity at 90 days was largely hypokinetic, and the wall motion of the apex did not improve; 80% remained akinetic. These data show that if the anterior wall was akinetic in the period 3-5 days after injury, it was unlikely to be recoverable. The aim is that patients are discharged from hospital with infarct sizes ≤25% of their LV mass. Current STEMI-DTU roll-in experience shows that twothirds of patients enrolled are achieving infarct size ≤25%. Although not part of the original assessment, the study team will continue to monitor this. Dr O'Neill summarised his presentation by reiterating that early revascularisation is the most potent intervention possible for improvement in survival outcomes, but unfortunately most patients do not present quickly enough to benefit from revascularisation. Multiple strategies have failed to limit infarct size, although intracoronary adenosine and supersaturated oxygen are potential therapeutic treatments. Dr O'Neill believes that unloading in the setting of STEMI offers enormous promise and feels optimistic about the findings that will come from the STEMI-DTU pivotal study.

Cardiology/Cardiovascular Research

Panoulas V, Escaned J, Hill J, Baker E, Butler K, Mealing S, Bilazarian S, Almedychy A, Goetzenich A, Klesius AA, Unterkofler J, Tsintzos S, and **O'Neill W**. Predictive value of residual SYNTAX score for clinical outcomes after High-Risk Percutaneous Coronary Intervention (HR-PCI): Evidence from pooled analysis of prospective studies. *Eur Heart J* 2023; 44:1. Full Text

[Panoulas, V.] Royal Brompton & Harefield NHS Fdn Trust, Harefield Hosp, London, England. [Escaned, J.] Hosp Clin San Carlos, Madrid, Spain. [Hill, J.] Royal Brompton & Harefield Hosp, London, England. [Baker, E.; Butler, K.; Mealing, S.] Univ York, York Hlth Econ Consortium, York, N Yorkshire, England. [Bilazarian, S.; Almedychy, A.] Abiomed Inc, Danvers, MA USA. [Goetzenich, A.; Klesius, A. A.; Unterkofler, J.; Tsintzos, S.] Abiomed Europe GmbH, Aachen, Germany. [O'neill, W.] Henry Ford Hosp, Detroit, MI USA. Hospital Clinico San Carlos; Royal Brompton Hospital; Royal Brompton & Harefield NHS Foundation Trust; Harefield Hospital; University of York - UK; Henry Ford Health System; Henry Ford Hospital

Cardiology/Cardiovascular Research
Sabbah H, **Gupta RC**, **Singh-Gupta V**, **Castle K**, and **Lanfear DE**. Mitochondrial function is abnormal in circulating blood monocytes of patients with chronic heart failure. *Eur Heart J* 2023; 44:1. Full Text

[Sabbah, H.; Gupta, R. C.; Singh-Gupta, V.; Castle, K.; Lanfear, D. E.] Henry Ford Hosp, Detroit, MI USA.

Cardiology/Cardiovascular Research
Sabbah H, **Singh-Gupta V**, **Gupta RC**, **Castle K**, **Zhang K**, and **Xu J**. Treatment of cardiomyocytes isolated from left ventricular myocardium of dogs with chronic heart failure with ALDA-1, an activator of aldehyde dehydrogenase-2, improves mitochondrial function. *Eur Heart J* 2023; 44:1. Full Text

[Sabbah, H.; Singh-Gupta, V.; Gupta, R. C.; Castle, K.; Zhang, K.; Xu, J.] Henry Ford Hosp, Detroit, MI 48202 USA.

Cardiology/Cardiovascular Research
Shah T, Lemor A, Thompson J, Protty M, Mamas M, Kinnaird T, Bharadwaj A, Truesdell A, Zhang YR, Hussain Y, Falah B, Cohen D, Redfors B, Baron S, Witzke C, Dixon S, Lansky A, **Basir B**, and **O'Neill W**. Performance of Existing Risk Models in Impella-Supported High- Risk Percutaneous Coronary Intervention. *J Am Coll Cardiol* 2023; 82(17):B85-B85. Full Text

[Shah, Tayyab] Hosp Univ Penn, Philadelphia, PA USA. [Lemor, Alejandro] UMMC, Jackson, MS USA. [Thompson, Julia] Cardiovasc Res Fdn, Brooklyn, NY USA. [Protty, Majd] Cardiff Univ, Cardiff, Wales. [Mamas, Mamas] Royal Stoke Hosp, Stoke On Trent, Staffs, England. [Kinnaird, Tim] UHW, Cardiff, Wales. [Bharadwaj, Aditya] Loma Linda Univ, Loma Linda, CA USA. [Truesdell, Alexander] Virginia Heart Inova Heart & Vasc Inst, Mclean, VA USA. [Zhang, Yiran; Falah, Batla] CRF, New York, NY USA. [Hussain, Yasin; Lansky, Alexandra] Yale Sch Med, New Haven, CT USA. [Cohen, David] St Francis Hosp, New York, NY USA. [Redfors, Bjorn] Cardiovasc Res Fdn, New York, NY USA. [Baron, Suzanne] Massachusetts Gen Hosp, Winchester, MA USA. [Witzke, Christian] Jefferson Hlth, Philadelphia, PA USA. [Dixon, Simon] William Beaumont Univ Hosp, Royal Oak, MI USA. [Basir, Babar] Henry Ford Hosp, Detroit, MI USA. [O'Neill, William] Henry Ford Hlth Syst, Orchard Lake, MI USA. Cardiovascular Research Foundation (CRF); Cardiff University; Royal Stoke University Hospital; Loma Linda University; Yale University; Cardiovascular Research Foundation (CRF); Harvard University; Massachusetts General Hospital; Henry Ford Health System; Henry Ford Hospital; Henry Ford Health System

Center for Health Policy and Health Services Research
Avalos LA, Daida YG, Vazquez-Benitez G, **Loree AM**, Negriff S, Rossom RC, Lipkind HS, Goodman SH, **Zabel CN**, Martinez YT, Ehresmann K, Seburg EM, and Palmsten K. Antidepressant and psychotherapy initiation among patients with new episodes of depression during pregnancy. *Pharmacoepidemiol Drug Saf* 2023; 32:528-528. Full Text

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Center for Health Policy and Health Services Research
Gonzalez H, **Gordon SC**, Daida YG, Schmidt MA, **Zhou YR**, **Wu T**, **Rupp L**, **Trudeau S**, and Lu M. SUSTAINED VIROLOGICAL RESPONSE REDUCES RISK OF PORTAL VEIN THROMBOSIS IN HEPATITIS C PATIENTS WITH CIRRHOSIS. *Hepatology* 2023; 78:S710-S711. Full Text

[Gonzalez, Humberto; Gordon, Stuart C.; Zhou, Yueren; Wu, Trueman; Rupp, Lora; Trudeau, Sheri] Henry Ford Hlth, Detroit, MI USA. [Gordon, Stuart C.] Wayne State Univ, Sch Med, Detroit, MI USA. [Daida, Yihe G.] Kaiser Permanente Hawail, Honolulu, HI USA. [Schmidt, Mark A.] Kaiser Permanente Northwest, Washington, DC USA. [Lu, Mei] 156 Pocatello Rd, Middletown, NY USA.

Center for Individualized and Genomic Medicine Research

Wu B, Hu D, **Yang M**, Witonsky J, **Hochstadt S**, Elhawary JR, Eng C, **Debbs J**, Chang C, **Cabral W**, Huntsman S, Ziv E, Burchard EG, and **Williams KL**. Decoding the Transcriptional Response to Severe Exacerbations Among African-american Individuals With Asthma. *Am J Respir Crit Care Med* 2024; 209. Full Text

B. Wu, Center for Individualized and Genomic Medicine Research (CIGMA), Department of Internal Medicine, Henry Ford Health, Detroit, MI, United States

Rationale: Asthma exacerbations are characterized by worsening symptoms and airway obstruction; they can result in severe outcomes, such as emergency visits (ED) and in-patient hospitalization (IP). The molecular immune responses involved in exacerbations remain poorly understood. Therefore, our aim was to identify genes associated with severe exacerbations. Methods: Our study population included African-American individuals from the Study of Asthma Phenotypes and Pharmacogenomic Interactions by Race-Ethnicity (SAPPHIRE). We analyzed the gene expression (RNA-seq) results from 429 healthy controls, 29 individuals with uncontrolled asthma (asthma control test score ≤19 but no history of asthma-related ED/IP), and 15 individuals peri-exacerbation (asthma-related ED/IP ±30 days of assessment). We assessed for differential gene expression, performed a weighted gene correlation network analysis, and modeled via cubic spline regression. Results: We identified 118 and 678 genes upregulated among individuals with uncontrolled asthma and severe exacerbations, respectively. 29 genes were significantly increased in both groups. Network analysis revealed three modules that were positively and significantly associated with severe exacerbations. Of the 678 genes upregulated among individuals with severe exacerbations, 559 (82%) were covered by these three modules. Functional analysis revealed that the semaphorin-plexin signaling pathway, the type-I interferon signaling pathway, and neutrophil degranulation were the top terms in each module. In addition, spline modeling of expression surrounding the timing of events revealed 55 genes with a hill pattern; these genes included NFIL3, a transcription factor controlling IgE production. Conclusions: Our study identified a number of genes associated with severe asthma exacerbations among African Americans, providing new potential biomarkers to predict impending events, as well as targets for treatment and measuring therapeutic response.

Clinical Quality and Safety

Gubler J, **Ruby A**, **Chami E**, Weaver J, and **Suleyman G**. Management of a New Delhi metallo-β-lactamase (NDM)-producing Escherichia coli Outbreak and Large-Scale Exposure Event Associated with Endoscopes. *Am J Infect Control* 2024; 52(6):S33. Full Text

Background: Between July 2021-March 2023, 9 cases of genetically similar New Delhi metallo-β-lactamase (NDM)-producing Escherichia coli (E. coli) were identified in our healthcare facility. Upon investigation, it was discovered that these patients had procedures in the same procedural area using the same five endoscopes. These endoscopes were also used in thousands of other procedures. Methods: A multi-prong approach was taken to evaluate the situation and determine if other patients may have been exposed and prevent further transmission. This approach included establishing a case definition to determine exposure period, offering screening to 1097 exposed patients, auditing the affected procedural and reprocessing areas, evaluating the maintenance of the implicated endoscopes, and having these endoscopes evaluated by an external third-party vendor. Results: An incredible amount of resources and time were required to manage this event. Seventy-seven individuals participated in the planning, implementation, and management of this outbreak. A total of 205 patients sought testing and 115 called with questions. During live observations, it was discovered that the cleaning process of rooms between cases was inconsistent and varied by staff member due to lack of formal education or competency on room cleaning and turn-over. This area also lacked the necessary housekeeping support due to staffing. Investigation into the endoscopes revealed a lengthy history of repair and minimal preventative

maintenance (e.g., borescope inspections). The external assessment of the endoscopes revealed significant internal damage within the channels, and all grew multiple organisms. Conclusions: Through proper planning, communication, and having a clearly outlined process for patient screening, we were able to manage this exposure event relatively smoothly. This also helped minimize fear and backlash on social media and in the news media. This presentation will outline the steps taken to manage an exposure event involving nearly 1100 patients and provide lessons learned to help other Infection Preventionists prepare for future outbreaks.

Clinical Quality and Safety

Joshi S, **Alvi RBR**, **Shanahan C**, **Ruby A**, **Chami E**, and **Suleyman G**. Clinical Characteristics and Outcomes in Patients with Healthcare Facility-Onset Clostridiodes difficile Infections. *Open Forum Infect Dis* 2023; 10:S386-S387. Full Text

S. Joshi, Henry Ford Hospital, Detroit, MI, United States

Background. Healthcare facility-onset (HCFO) Clostridiodes difficile infection (CDI) is the most common hospital-acquired infection. Although risk factors associated with CDI have been described, characterization and outcome of HFCO-CDI are limited. Methods. This was a retrospective observational study comparing disease severity among adult patients with HCFO-CDI from January 1, 2020, to December 31, 2022, at an 877-bed tertiary care hospital in Detroit. Patients were identified using National Healthcare Safety Network (NHSN) definition. CDI was classified as nonsevere, severe, or fulminant. Severe disease was defined as having white blood cell (WBC) count ≥ 15,000 cells/mm3 or acute kidney injury (AKI) defined as increase in creatinine of ≥ 0.3mg/dL within 48 hours of diagnosis. Fulminant disease included patients with ileus or toxic megacolon, or need for colectomy, intensive care unit or vasopressors. Risk factors, treatment and outcomes were evaluated. Results. 98 patients were diagnosed with HFCO CDI during the study period (Table 1); 37 (38%) were non-severe, 47 (38%) severe and 14 (24%) fulminant. Median age was 66 years, 50% were female and 45% white. Almost half were immune suppressed; 5% had prior CDI. Most patients (88%) were exposed to antibiotics (abx) prior to CDI with no difference between the groups (p=0.427); 61% received cephalosporins. Cirrhosis was more common among patients with fulminant disease (p=0.048) and receipt of chemotherapy was associated with severe and/or fulminant disease cases (p=0.049). AKI (p< 0.001), fever (p=0.030), and WBC >25,000 or < 2,000 cells/mm3 (p< 0.001) were more prevalent among patients with fulminant CDI; combination or alternative therapy was more common among fulminant cases (p< 0.001). Most were eligible, but only 6% received bezlotoxumab (BZX). Although outcomes were not significantly different between the groups, length of stay was longer and refractory disease and recurrence were more common in severe/fulminant CDI. Conclusion. In our HCFO-CDI cohort, most patients were exposed to abx, and cirrhosis and chemotherapy were associated with more severe CDI. Efforts should focus on appropriate abx utilization and increasing use of BZX to reduce burden of CDI and risk of recurrence and readmission.

Clinical Quality and Safety

Shanahan C, **Ruby A**, **Chami E**, and **Suleyman G**. Implementing an electronic best practice advisory to reinforce Clostridioides difficile testing. *Am J Infect Control* 2024; 52(6):S48. Full Text

Background: The National Healthcare Safety Network (NHSN) defines a hospital-onset Clostridioides difficile (C. diff) infection as one identified after the third hospital day of a patient's admission. Conversely, a community-onset C. diff infection is identified during the first three hospital days of patient admission. Our facility identified that in a subset of our hospital-onset C. diff infections, unformed stools were documented in the first three days of patient admission. A best practice advisory (BPA) was developed to reinforce our nurse-driven protocol for C. diff testing and increase adherence to this protocol. Methods: The electronic medical record system was utilized to build a BPA that would fire if nursing documented an unformed stool during the first three hospital days of a patient's admission. When this BPA fired, it linked to the C. diff test and isolation order to facilitate easier ordering. For our 800+ bed facility, we evaluated the percentage of hospital-onset C. diff infections with unformed stools during the first three hospital days of admission during a 24 month pre-intervention period and a 24 month post-intervention period. Additionally, we quantified the total C. diff community-onset infections identified during the pre-

intervention and post-intervention periods. Results: The percentage of hospital-onset C. diff infections with unformed stools during the first three hospital days of admission decreased from 41% (n=117) during the pre-intervention period to 32% (n=126) during the post-intervention period. Additionally, the number of community-onset C. diff infections identified increased from 291 during the pre-intervention period to 527 in the post-intervention period. Conclusions: Implementation of a BPA has decreased the percentage of hospital-onset C. diff infections with unformed stools during the first three hospital days of admission and increased early C. diff testing in our facility. Through utilizing this BPA, our C. diff testing protocol is continually reinforced which will promote adherence to testing guidelines.

Clinical Quality and Safety

Wells A, **Edmondson A**, **Mahal R**, and **Prascius S**. What Could Go Wrong? Utilizing a Failure Mode and Effects Analysis to Identify Endoscope Reprocessing Process Improvement Opportunities. *Am J Infect Control* 2024; 52(6):S3. Full Text

Background: When implemented correctly, endoscope reprocessing using high level disinfection (HLD) renders a reusable endoscope safe for the next patient. However, the amount and complexity of the steps of the HLD process make this challenging. An endoscopy department within a 191-bed acute care hospital with an average of 30 procedures per day had history of highly compliant HLD audits performed by the infection prevention team. However, due to staffing changes and increasing staff expectations, errors in the HLD process led to two patient exposures. Though mitigated swiftly, an improvement process was sought to prevent future patient exposures. Methods: The quality department chose to facilitate a Failure Mode and Effects Analysis (FMEA) to determine what other steps could fail next. Quality department leadership composed a multidisciplinary team to review the 70+ steps in channeled endoscope reprocessing to identify failure modes. First, the infection prevention/quality manager categorized the steps. Next, endoscopy nursing leadership, an endoscope reprocessing technician, surgical services leadership, and quality/risk management delineated the possible failure modes, causes, and effects for each step. The team scored the likelihood of each failure occurring and its severity, each on a scale of 1 to 4, to find areas in need of action plans. The likelihood and severity scores were multiplied to identify highest areas of risk. Results: Four steps of the HLD process had a risk score of eight or higher, and the group chose to focus on these for process improvement plans. These steps included portions of the manual endoscope cleaning process, new employee training and competency, and automated endoscope reprocessor parameter verification. Specific action plans will be created for these highest risk elements. Conclusions: There are often several opportunities for improvement of complex processes such as HLD. Quality improvement tools such as the FMEA can assist infection prevention programs with prioritizing competing opportunities.

Clinical Quality and Safety

Wells A, **Prascius S**, and **Assenova T**. Two Years of Zero Harm: A Multi-Faceted Approach for Achieving Two Years Without a Catheter-Associated Urinary Tract Infection (CAUTI). *Am J Infect Control* 2024; 52(6):S44. Full Text

Background: After experiencing five catheter-associated urinary tract infections (CAUTI) in 2019 (standardized infection ratio [SIR] 0.69) and six in 2020 (SIR 0.6), a 191-bed acute care hospital was determined to find a sustainable way to reduce the number of infections. Methods: Many interventions were introduced to reduce the number of CAUTIs, consisting of education, alternative device implementation, and electronic medical record (EMR) tools. Registered nurses (RN) and nurse assistants (NA) were reeducated on the importance of aseptic urine specimen collection and indwelling urinary catheter (IUC) maintenance bundles at annual skills fairs. The infection prevention (IP) and nursing team explored alternative external male urine collection devices such as condom catheters and moisture-wicking urinary pouches. The IP team performed audits with nursing unit leaders on IUC maintenance bundle compliance and reported the data monthly to unit staff and leadership. Additionally, inappropriate urine cultures decreased through the implementation of a urine culture hard stop in the EMR to ensure urine specimens were ordered and sent only if truly indicated. Results: After implementation of these interventions, the hospital had one reportable CAUTI in 2021. In 2022 and 2023, zero were reported. The standardized infection ratio (SIR) declined from 0.69 in 2019 to 0 in 2022 and 2023. Conclusions: The IP and nursing department credits the sustenance of zero harm to the culture of high reliability created by

the above interventions. Team members providing direct patient care are aware of the expectations related to CAUTI prevention. The facility plans to continue diligent daily review of IUCs, prevent placement of IUCs if another viable option exists, educate team members on IUC maintenance expectations, and ensure all urine cultures ordered when the IUC has been in place for three or more days are reviewed by an infectious disease physician for appropriateness.

Dermatology

Dimitrion P, **Toor J**, **Ge J**, **Wang Q**, Allen CE, **Zhou L**, and **Mi QS**. HDAC3 Is Required for Pathognomonic Features of Langerhans Cell Histiocytes. *Blood* 2023; 142:676. Full Text

Langerhans cell histiocytosis (LCH) is a pediatric inflammatory myeloid neoplasm that develops due to dysregulated myeloid cell development. BRAFV600E is the most common disease-causing mutation and constitutively activates the mitogen-activated protein kinase (MAPK) pathway in myeloid lineage precursors leading to the key pathognomonic features of LCH cells. Enhanced myelopoiesis and reduced CCR7 expression promote accumulation of LCH cells in tissues by simultaneously increasing the production of pathological DCs and preventing tissue egress. Furthermore, LCH cells acquire an oncogene induced senescence-associated secretory phenotype (SASP) that depends on mammalian target of rapamycin (mTOR), which is hallmarked by increased expression of anti-apoptotic proteins, inflammatory cytokines, and matrix metalloproteinases enhancing survival of LCH cells and promoting recruitment of inflammatory immune cells forming characteristic granulomatous lesions. These pathognomonic features result in the accumulation of LCH cells in any organ causing a wide range of clinical symptoms. Frontline therapy for LCH involves combination chemotherapy and steroidal anti-inflammatories, or MAPK inhibitors, which have significant toxicity and fail to eliminate disease causing precursors. New therapeutic approaches are urgently needed. Here, using multiple genetic mouse models, we show that normal epidermal Langerhans cells (LCs) depend on HDAC3 for their development, differentiation, and survival. Integrative RNA and chromatin-immunoprecipitation-sequencing show loss of HDAC3 abrogates the expression of master regulators of myeloid development and function including Csf1r, Spi1, Id2 and Runx3. LCH cells are also known to rely on Csf1r and Pu.1 for their development and homeostasis, thus we hypothesized that LCH cells similarly rely on HDAC3 for their development and survival. CD11c Cre LSL-BRAFV600E (BRAFV600E CD11c) mice develop severe multifocal LCH with pronounced lesion development in their livers and lungs, hepatosplenomegaly, and a reduced lifespan due to the accumulation of pathological dendritic cells (DCs). We generated BRAFV600E CD11c HDAC3 fl/fl (BRAFV600E HD3KO) mice, which produce pathological DCs that simultaneously express BRAFV600E and harbor a conditional deletion in the deacetylase domain of HDAC3. Compared to BRAFV600E CD11c mice, BRAFV600E HD3KO mice exhibited significantly less hepatosplenomegaly, reduced lesional burden (Panel A), attenuated disease progression, and improved survival indicating reduced LCH disease burden. Compared to BRAFV600E CD11c flow cytometry showed BRAFV600E HD3KO had reduced numbers of LCH cells in lungs and livers linking improved disease outcomes to abrogation of pathological DCs. Flow cytometric analysis of circulating myeloid cells further found reduced frequency of circulating DCs and DC progenitors, indicating that a lack of HDAC3 activity prevents the development of pathological DCs (Panel B). LCH-like cells can be generated in vitro by culturing BRAFV600E CD11c bone marrow with granulocyte-monocyte colony-stimulating factor (GM-CSF), providing a valuable drug screening tool. Treating LCH-like cells with RGFP966, an HDAC3-specific inhibitor, increased apoptosis indicated by annexin-V and DAPI staining, reduced expression of Bcl-2, increased CCR7 expression, and decreased S6 phosphorylation (an indication of decreased mTOR activity), showing that pharmacological inhibition of HDAC3 may prove therapeutically efficacious by abrogating pathognomonic features of LCH cells. Together, our findings identify HDAC3 as a critical epigenetic regulator for both healthy and pathological LCs. We further show, HDAC3 is required for multiple pathognomonic features of LCH cells and could be a promising drug target. Furthermore, if HDAC3 is required for the development of pathological DC and DC progenitors, HDAC3 blockade would address a great need in treatment of patients with LCH.

Dermatology

Gold LS, Lebwohl MG, Brown PM, Rubenstein DS, Tabolt G, Jett JE, and Piscitelli SC. Tapinarof Cream 1% Once Daily for Plaque Psoriasis in Two Pivotal Phase 3 Trials: Minimal Systemic Exposure is Consistent With Adverse Event Profile. *J Am Acad Dermatol* 2023; 89(3):AB229-AB229. Full Text

[Gold, Linda Stein] Henry Ford Hlth Syst, Detroit, MI USA. [Lebwohl, Mark G.] Icahn Sch Med Mt Sinai, New York, NY USA. [Brown, Philip M.; Rubenstein, David S.; Tabolt, Glenn; Jett, John E.; Piscitelli, Stephen C.] Dermavant Sci Inc, Morrisville, NC USA. at Mount Sinai

Dermatology
Ko D, **Artz C**, and **Kohen L**. Virtual dermoscopy course series in the improvement of resident education. *J Am Acad Dermatol* 2023; 89(3):AB248-AB248. Full Text

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Dermatology
Merola JF, Ogdie A, Gottlieb AB, **Gold LS**, Flower A, Jardon S, Deignan C, and Lebwohl M. Impact of Psoriasis in Special Areas on Patient Quality-of-Life Outcomes: Findings From the UPLIFT Survey in the United States. *J Am Acad Dermatol* 2023; 89(3):AB176-AB176. Full Text

[Merola, Joseph F.] Harvard Univ, Brigham & Womens Hosp, Sch Med, Cambridge, MA USA. [Ogdie, Alexis] Univ Penn, Philadelphia, PA USA. [Gottlieb, Alice B.; Lebwohl, Mark] Icahn Sch Med Mt Sinai, New York, NY USA. [Gold, Linda Stein] Henry Ford Hlth Syst, West Bloomfield, MI USA. [Flower, Andrea; Jardon, Shauna; Deignan, Cynthia] Amgen Inc, Thousand Oaks, CA USA. Pennsylvania; Icahn School of Medicine at Mount Sinai; Henry Ford Health System; Amgen

Dermatology
van der Zee HH, Szepietowski JC, Sayed C, Guillem P, **Hamzavi IH**, Goldberg S, Field C, Ortmann CE, Lobach I, Wozniak MB, Llobet-Martinez A, Ravichandran S, Bachhuber T, and Bechara FG. Impact of secukinumab on the need for rescue surgical intervention in patients with moderate to severe hidradenitis suppurativa: Post-hoc analysis of week 16 data from sunshine and sunrise trials. *Exp Dermatol* 2023; 32:30-31. Full Text

[van der Zee, Hessel H.; Szepietowski, Jacek C.; Sayed, Christopher; Guillem, Philippe; Hamzavi, Iltefat H.; Bechara, Falk G.] European Hidradenitis Suppurativa Fdn, Dessau, Germany. [van der Zee, Hessel H.] Erasmus MC, Dept Dermatol, Rotterdam, Netherlands. [Szepietowski, Jacek C.] Wroclaw Med Univ, Dept Dermatol Venereol & Allergol, Wroclaw, Poland. [Sayed, Christopher] Univ N Carolina, Sch Med, Dept Dermatol, Chapel Hill, NC 27515 USA. [Guillem, Philippe] Clin Val dOuest, Dept Surg, Ecully, France. ResoVerneuil, Paris, France. Soc Natl Francaise Coloproctol SNFCP, Grp Rech Proctol, Paris, France. [Hamzavi, Iltefat H.] Henry Ford Hosp, Dept Dermatol, Multicultural Dermatol Ctr, Detroit, MI 48202 USA. [Goldberg, Stephanie] Mary Washington Healthcare, Fredericksburg, VA USA. [Field, Clarice; Wozniak, Magdalena B.] Novartis Ireland Ltd, Dublin, Ireland. [Ortmann, Christine-Elke; Lobach, Iryna; Llobet-Martinez, Angela; Bachhuber, Teresa] Novartis Pharma AG, Basel, Switzerland. [Ravichandran, Shoba] Novartis Pharmaceut, E Hanover, NJ USA. [Bechara, Falk G.] Ruhr Univ Bochum, Dept Dermatol Venereol & Allergol, Bochum, Germany. University of North Carolina School of Medicine; University of North Carolina; University of North Carolina Chapel Hill; Henry Ford Health System; Henry Ford Hospital; Novartis; Novartis; Novartis; Ruhr University Bochum

Diagnostic Radiology
Ahmed M, **Azam M**, **Haque M**, **Rehman N**, **Chohan S**, **Husain A**, and **Jafri SM**. Transplant Hepatology Fellowship: Shifts in Sex and Ethnic Representation From 2013-2022. *Am J Gastroenterol* 2023; 118(10):S1284-S1285. Full Text

[Ahmed, Muhammad; Rehman, Narmeen; Chohan, Sikander; Husain, Arqam] Wayne State Univ, Sch Med, Detroit, MI USA. [Azam, Manha] Michigan State Univ, Coll Osteopath Med, Detroit, MI USA. [Haque, Mahfujul] Michigan State Univ, Coll Human Med, E Lansing, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. University College of Osteopathic Medicine; Michigan State University; Michigan State University College of Human Medicine; Henry Ford Health System; Henry Ford Hospital

Diagnostic Radiology

Akbari H, Bakas S, Garcia J, Kazerooni AF, Sako C, Villanueva-Meyer J, Baid U, Mamourian E, Brem S, Lustig RA, Nasrallah MP, O'Rourke DM, Calabrese E, Rudie J, Chang S, Rauschecker A, LaMontagne P, Marcus DS, Balana C, Capellades J, Puig J, Barnholtz-Sloan J, Badve C, Sloan A, Waite K, Colen R, Choi YS, Ahn SS, Dicker AP, Flanders AE, Shi W, **Griffith B**, **Poisson LM**, **Rogers LR**, Booth TC, Jain R, Chakravarti A, Palmer J, Cepeda S, Wiestler B, Di Stefano AL, Alexander K, Melhem ER, Woodworth GF, Kamel PI, Tiwari P, Aboian M, Mohan S, and Davatzikos C. ROBUSTNESS OF PROGNOSTIC STRATIFICATION IN DE NOVO GLIOBLASTOMA PATIENTS ACROSS 22 GEOGRAPHICALLY DISTINCT INSTITUTIONS: INSIGHTS FROM THE RESPOND CONSORTIUM. *Neuro Oncol* 2023; 25:v187. Full Text

H. Akbari, University of Pennsylvania, Philadelphia, United States

PURPOSE: Glioblastoma is the most prevalent primary malignant brain tumor in adults, with a median overall survival (OS) of approximately 15 months and only limited advancements in prognostication and survival prediction. This study aims to evaluate an AI-based prognostic stratification model for OS prediction trained on the ReSPOND consortium data and to validate its performance on an independent dataset. METHODS: The AI model was trained on a cohort of 2,293 glioblastoma patients from 22 institutions across three continents. For validation, an independent cohort of 78 treatment-naïve patients was used from three institutions. Preoperative structural MRI scans were utilized for feature extraction. Automated segmentation defined three tumor sub-compartments: enhancing, necrotic, and peritumoral T2-FLAIR abnormality. The AI predictor incorporated variables such as patient age, normalized tumor sub-compartment volume, spatial distribution characteristics, and morphologic descriptors. The overall survival predictor index provided a continuous value between 0 and 1 for patient stratification that higher values indicating longer predicted OS. Generalizability was assessed using Leave-One-Cohort-Out-Cross-Validation (LOCOCV) for training data, and the model was subsequently applied to the validation cohort. RESULTS: Survival analysis demonstrated a concordance index of 0.64 for LOCOCV training data and 0.59 for the independent validation data, indicating effective prognostic stratification of patients. CONCLUSION: Multi-parametric AI assisted image analysis extracts prognostic biomarkers, which correlate with OS in glioblastoma patients. The generalizability of this method was validated using the extensive centralized glioblastoma imaging dataset registry from the ReSPOND consortium and an independent dataset, demonstrating its generalizability across diverse patient populations and acquisition settings. This model holds promise for robust prognostic stratification and prediction in de novo glioblastoma patients.

Diagnostic Radiology

Gongala S, Garcia J, Korakavi N, Patil N, Akbari H, Tippareddy C, Sloan A, Barnholtz-Sloan J, Bakas S, Kazerooni AF, Sako C, Baid U, Brem S, Lustig RA, Capellades J, Nasrallah M, O'Rourke DM, La Montagne P, Marcus DS, Balana C, Puig J, Waite K, Colen R, Choi YS, Lee SK, Dicker AP, Flanders AE, Shi W, **Griffith B**, **Poisson LM**, **Rogers LR**, Booth TC, Jain R, Chakravarti A, Palmer J, Mohan S, Tiwari P, Aboian M, Ahn SS, Davatzikos C, and Badve C. SEX-SPECIFIC DIFFERENCES IN GLIOBLASTOMA IN THE RESPOND CONSORTIUM. *Neuro Oncol* 2023; 25:v118. Full Text

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AIM: The goal of this study was to understand sex-specific differences in the molecular, clinical and radiological tumor parameters and survival outcomes of Glioblastoma (GBM) patients within the international GBM dataset, known as the ReSPOND (Radiomic Signatures for PrecisiON Diagnostics) consortium. METHODS: Sex-based differences were retrospectively studied in 1922 GBM patients from the ReSPOND consortium which includes information from over 14 institutions across 3 continents. The parameters include age, Methylguanine-DNA Methyltransferase (MGMT) promoter methylation status, isocitrate dehydrogenase 1 (IDH1) mutation status, Karnofsky performance status (KPS), extent of resection (EOR), tumor epicenter, volumes, laterality and spatial extent. Non-parametric tests, log-rank test and cox-proportional hazard analysis were performed to understand sex-based differences in tumor parameters, survival rates and hazard ratios. Spatial atlases were generated to understand radiological

parameters such as tumor spatial extent. RESULTS: GBM in was diagnosed at a median age of 62.6 years in females compared to 61 years in males (p = 0.001). Additionally, 44% females compared to 37% males (p = 0.04) had methylated MGMT and 79% females compared to 73% males (p = 0.004) had IDH1 wildtype. The tumor volumes were smaller in females (necrotic core, edema, and enhancing tumor) compared to males. Females exhibited a higher prevalence of right hemisphere (39.6%) and right temporal lobe tumors (19.7%), while males showed a higher prevalence of left hemisphere (40.3%) left temporal lobe tumors (23.7%). No significant sex-based differences in OS and PFS was observed in overall sample, although longer PFS was observed in elderly (above 60 years) female patients. CONCLUSION: This is a first international large cohort study looking at sex-based differences in GBM patients using the ReSPOND consortium data. Several sex-specific differences in the distribution of various tumor phenotypes were noted, however sex was not a contributing factor in OS and PFS.

Diagnostic Radiology
Obri M, **Dawod S**, Qasawa A, Fahoury A, **Stephan J**, **Kamran W**, and **Jafri SM**. A Rare Presentation of Drug-Induced Pancreatitis After Cyclophosphamide Infusion. *Am J Gastroenterol* 2023; 118(10):S1538-S1538. Full Text

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Emergency Medicine
Ahmed M, **Azam M**, **Haque M**, **Rehman N**, **Chohan S**, **Husain A**, and **Jafri SM**. Transplant Hepatology Fellowship: Shifts in Sex and Ethnic Representation From 2013-2022. *Am J Gastroenterol* 2023; 118(10):S1284-S1285. Full Text

[Ahmed, Muhammad; Rehman, Narmeen; Chohan, Sikander; Husain, Arqam] Wayne State Univ, Sch Med, Detroit, MI USA. [Azam, Manha] Michigan State Univ, Coll Osteopath Med, Detroit, MI USA. [Haque, Mahfujul] Michigan State Univ, Coll Human Med, E Lansing, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. University College of Osteopathic Medicine; Michigan State University; Michigan State University College of Human Medicine; Henry Ford Health System; Henry Ford Hospital

Emergency Medicine
Allen B, Millard M, Ashburn N, Snavely A, **Nowak R**, Mumma B, Madsen T, Wilkerson RG, Christenson R, Stopyra J, Mahler S, and Stop CP. Performance of the High-STEACS Early Rule-Out Pathway for High Sensitivity Cardiac Troponin T at 30-days in a US population. *Eur Heart J* 2023; 44:1. Full Text

[Allen, B.] Univ Florida, Gainesville, FL USA. [Millard, M.; Ashburn, N.; Snavely, A.; Stopyra, J.; Mahler, S.] Wake Forest Univ, Emergency Med, Winston Salem, NC 27101 USA. [Nowak, R.] Henry Ford Hosp, Emergency Med, Detroit, MI 48202 USA. [Mumma, B.] Univ Calif Davis, Emergency Med, Davis, CA 95616 USA. [Madsen, T.] Univ Utah, Emergency Med, Salt Lake City, UT USA. [Wilkerson, R. G.; Christenson, R.] Univ Maryland, Pathol, Baltimore, MD 21201 USA. University; Henry Ford Health System; Henry Ford Hospital; University of California System; University of California Davis; Utah System of Higher Education; University of Utah; University System of Maryland; University of Maryland Baltimore

Emergency Medicine
Brochu JM, **Kenney RM**, **Herbin S**, **Gunaga S**, and **Veve M**. Risk Factors for Unplanned Healthcare Encounters in Patients Discharged from the Emergency Department with Extended-spectrum β-lactamase Urinary Tract Infections. *Open Forum Infect Dis* 2023; 10:S1259-S1260. Full Text

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Background. The management of extended spectrum β-lactamase (ESBL) urinary tract infections (UTIs) in the emergency department (ED) has not been well documented in literature. The purpose of this study

was to describe treatment and outcomes of patients with ESBL UTIs in the ED, which can inform best practices for antimicrobial stewardship. Methods. This IRB approved, retrospective cohort analysis included patients who were discharged from the ED with an ESBL UTI between January 2020 and November 2022. The primary outcome of interest was any unplanned healthcare encounter related to the UTI within 30 days of the index ED visit, which included phone/ virtual visits, clinic visits, ED visits, and hospitalizations. Patients ≥18 years of age treated for symptomatic UTI with a monomicrobial urine culture were included, while those with altered mental status, history of renal transplant, abnormal urinary tract, or were on active antibiotic therapy prior to the ED visit were excluded. Patient characteristics, initial and definitive antibiotic therapy, culture results including pathogen and susceptibilities were described. Logistic regression analysis was used to identify any exposures that were independently associated with unplanned healthcare encounters related to the UTI. Results. 162 patients were included; 103 (64%) had an unplanned healthcare encounter. Patient characteristics are depicted in Table 1. Complicated lower UTI was most frequent occuring in 71 patients (44%). Susceptibility data revealed that nitrofurantoin was effective in 121 (75%) patients, aminoglycosides in 117 (72%) patients, TMP/SMX in 66 (41%) patients, and quinolones in 62 (38%) patients. 76 (74%) patients with unplanned encounters received an inactive empiric prescription: β-lactams being prescribed to 52 (51%) patients with cephalexin used for 49/52 (94%). Of the 81 patients with lower UTI, 20 (25%) initially received a prescription for nitrofurantoin. Factors associated with an unplanned healthcare encounter are described in Table 2. Abbreviations: Un-Adj OR = unadjusted odds ratio; Adj OD = adjusted odds ratio Conclusion. Patients discharged from the ED with an ESBL UTI were at higher risk for unplanned healthcare encounters if they had CKD or were initially prescribed an oral β-lactam. Prescribing first line therapy with nitrofurantoin for lower UTI is a potential area for improvement.

Emergency Medicine

McIntosh J, **Moonka D**, and **Jayaprakash N**. When the Critical Illness Dominoes Fall, Unforeseen Events Post BRTO. *Am J Respir Crit Care Med* 2024; 209. Full Text

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Introduction: Gastric variceal bleeding is a complication of cirrhosis with portal hypertension (PHT) associated with significant morbidity and mortality. Management of suspected variceal bleeding includes resuscitation, medical therapy, endoscopic intervention and early consideration for advanced procedures such as TIPS, BRTO, surgery or liver transplant. Herein, we describe a rare adverse event following BRTO. Case: A 39 year old male with alcoholic cirrhosis and PHT, gastric varices (GV) and Gastroesophageal varices (GOV), presented to emergency department (ED) with hematemesis. He was intubated and transfused per massive transfusion protocol for large volume hematemesis. A Minnesota tube was placed emergently. Medical therapy was initiated including IV pantoprazole, octreotide, ceftriaxone. An endoscopy within 24 hours revealed a large GOV without stigmata of recent bleeding and GV with stigmata of recent bleeding. The GOV were banded and the GV identified as the source of hematemesis. To address the GV, he was taken to Interventional radiology (IR) for a Balloon-occluded Retrograde Transvenous Obliteration (BRTO) procedure. 12 hours later the patient developed abdominal distension, lactic acidosis and sudden rise in norepinephrine requirements refractory to fluid resuscitation. CT abdomen with contrast showed diffuse hypo enhancement and thickening of the bowel favored to be related to mesenteric ischemia secondary to mesenteric venous hypertension (MVH). As a solution, a TIPS procedure was performed to reduce MVH. MICU course was complicated by ARDS, Renal failure required SLED, multiple transfusion of blood products for correction of coagulopathy. Discussion: A BRTO is an advanced procedure for intervention of GV as the source For GV as the source of the variceal bleeding in decompensated liver cirrhosis, advanced options such as BRTO are available as secondary prevention for further bleeding. This case highlights an adverse event associated with BRTO that has not been commonly reported. Intensivists, while not performing advanced procedures for these patients, must have heightened awareness of all complications and adverse events related to BRTO, because early recognition can result in expedited care to decrease severity of morbidity or mortality.

Emergency Medicine

Munroe E, Nielsen D, Heath M, Horowitz JK, McLaughlin ES, Creutz E, Bernstein SJ, Digiovine B, Bozyk PD, **Jayaprakash N**, Taylor SP, Flanders SA, and Prescott HC. Variation in Initial Fluid Resuscitation

Volume and Type in Patients With Sepsis Across Michigan Hospitals. *Am J Respir Crit Care Med* 2024; 209. Full Text

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RATIONALE: The Surviving Sepsis Campaign guidelines suggest a 30ml/kg initial intravenous (IV) fluid bolus for patients with sepsis-induced hypoperfusion and suggest using balanced crystalloids over normal saline. Studies have raised concerns about compliance with these fluid guidelines, but it has been difficult to determine the scope of the problem given challenges inherent to accurately identifying eligible patients retrospectively in electronic health records. In this study, we evaluated variation in IV fluid volume and type in patients with sepsis across Michigan hospitals, where we have detailed, chart-abstracted data that allows us to assess fluid practices in eligible patients. Methods: This is a retrospective cohort study of patients hospitalized with communityacquired sepsis at 65 hospitals in the Michigan Hospital Medicine Safety Consortium (HMS), a Collaborative Quality Initiative sponsored by Blue Cross Blue Shield of Michigan. Data from a random sample of adult sepsis hospitalizations (11/2020-7/2023) were entered into the HMS-Sepsis registry by trained abstractors. Sepsis (infection and ≥1 organ dysfunction) was determined using both diagnosis codes and chart review. We sought to determine how commonly eligible patients with sepsis met fluid guideline measures. Patients were eligible for the 30ml/kg measure if they had hypoperfusion (lactate ≥4 mmol/L, systolic blood pressure <90mmHg, or treatment with vasopressors) within 3 hours of hospital arrival and none of the following contraindications to fluid: end-stage renal disease, moderate-severe aortic stenosis, or heart failure with ejection fraction ≤39%. Patients were eligible for the balanced fluid measure if they received > 3 liters IV fluid within 48 hours and passed if ≥75% of fluid delivered was balanced. Results: Of 18,204 patients in the HMS-Sepsis registry, 5,439 (29.9%) were eligible for a 30ml/kg fluid bolus. Of these, 3,221 (59.2%) received 30ml/kg of fluid by ideal body weight within 6 hours of hospital arrival (range across hospitals with ≥10 observations each: 24.2% - 81.9%). (Figure 1A). Among the sub-set of patients treated with vasopressors, 364/579 (62.9%) received 30ml/kg IV fluids within 2 hours of vasopressor initiation (range across hospitals with ≥10 observations each: 16.7% - 100%). For fluid type, 10,070/18,204 (55.3%) patients were eligible for the balanced fluid measure. Of these, 1,395/10,070 (13.9%) received ≥75% balanced fluids (range across hospitals with ≥10 observations each: 0% - 75.5%) (Figure 1B). Conclusion: Rates of compliance with an initial 30ml/kg bolus and use of balanced fluids in eligible patients is low and widely variable across hospitals, presenting an opportunity for quality improvement.

Emergency Medicine

Plemmons J, **Saleh M**, **Johnson P**, and **Kirk N**. QAPI 124 - Effect of Education and Performance Feedback to Eliminate Central Line Associated Blood Stream Infections on an Internal Medicine Unit...Association for Professionals in Infection Control and Epidemiology (APIC) 51st Annual Conference and Exposition, June 3-5, 2024, San Antonio, Texas. *Am J Infect Control* 2024; 52(6):S61-S61. Full Text

Henry Ford Hospital, Henry Ford Health
Henry Ford Health

Gastroenterology

Agha YH, and **Schairer J**. Delayed Micro-Perforation Following Endoscopic Stricturotomy: A Rare Complication Managed Medically. *Am J Gastroenterol* 2023; 118(12):S14. Full Text

Y.H. Agha, Henry Ford Health, Detroit, MI, United States

Background: Small bowel and colon strictures affect approximately one-third of patients with Crohn's disease (CD). While surgery is the most definitive treatment, 28 % of patients develop postoperative complications such as bleeding, bowel leaks, and recurrent anastomotic strictures. Endoscopic balloon dilation (EBD) is a less invasive alternative that can temporarily postpone surgery but necessitates repeated treatments to maintain luminal patency. Endoscopic stricturotomy (ES) is an emerging technique that has been increasingly employed as a definite treatment for CD strictures, offering prolonged luminal patency compared to EBD and a lower risk of perforation. Methods: A 55-year-old Caucasian male with a history of ileocolonic CD had a total colectomy and ileal pouch anal anastomosis

30 years ago. Subsequently, he developed CD of the J-pouch with recurrent pouch inlet and neo-terminal ileal strictures managed with serial balloon dilations. ES was offered as an alternative to EBD. During the procedure, four consecutive chronic fibrotic strictures were seen in the neo-terminal ileum. Results: ES was accomplished by radial incisions connected by parallel incisions. The patient felt well during recovery and was discharged home. He presented to the emergency department 3 days after his procedure with abdominal pain. Computed tomography of the abdomen and pelvis (CTAP) showed multiple air-fluid collections, the largest measuring 7.5 cm in diameter in the right lower quadrant adjacent to small bowel loops, concerning for ES-induced micro-perforation. The colorectal surgery and infectious disease teams were consulted. The patient was managed medically with intravenous fluids, antibiotics, and strict bowel rest. During his 5-day hospitalization, he improved significantly and tolerated a regular diet without the need for any surgical intervention. Follow-up imaging showed stable abscesses. He was discharged home and completed 4 weeks of Ertapenem. CTAP was repeated and showed resolving abscesses. Nine months later, he remains well and has not required any further ES or EBD. Discussion: ES has gained significant attention over the recent years due to its comparable efficacy to EBD with a lower risk of perforation, approximately 1%, in contrast to the substantially higher 4-5% risk associated with EBD. Conclusions: One key advantage of ES lies in its ability to precisely control the depth and length of the incisions made during the procedure. In contrast, EBD exerts a blunt radial force that is transmitted across the entire circumference of the stricture and may overly dilate weaker stricture segments, heightening perforation risk. In our presented case, thermal injury emerged as a potential primary mechanism of delayed micro-perforation. Excessive energy use during repeated attempts to create an incision in severely inflamed or fibrotic strictures leads to heat dissipation into tissue. Treating multiple strictures concurrently also prolongs heat exposure. Fortunately, the micro-perforation was effectively managed with antibiotics, obviating the need for surgical intervention-an ultimate goal of ES.

Gastroenterology

Ahmed M, **Azam M**, **Haque M**, **Rehman N**, **Chohan S**, **Husain A**, and **Jafri SM**. Transplant Hepatology Fellowship: Shifts in Sex and Ethnic Representation From 2013-2022. *Am J Gastroenterol* 2023; 118(10):S1284-S1285. Full Text

[Ahmed, Muhammad; Rehman, Narmeen; Chohan, Sikander; Husain, Arqam] Wayne State Univ, Sch Med, Detroit, MI USA. [Azam, Manha] Michigan State Univ, Coll Osteopath Med, Detroit, MI USA. [Haque, Mahfujul] Michigan State Univ, Coll Human Med, E Lansing, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. University College of Osteopathic Medicine; Michigan State University; Michigan State University College of Human Medicine; Henry Ford Health System; Henry Ford Hospital

Gastroenterology

Ali SA, and **Jafri SM**. Unmasking the Complexity: A Case Report of Severe Refeeding Syndrome in a Post-Liver Transplant Patient With Pharyngeal Squamous Cell Carcinoma. *Am J Gastroenterol* 2023; 118(10):S2314-S2314. Full Text

[Ali, Suhaib Alhaj; Jafri, Syed-Mohammed] Henry Ford Hosp, Detroit, MI USA.

Gastroenterology

Ali SA, and **Jafri SM**. From Rarity to Recognition: A Case Report of Cronkhite-Canada Syndrome. *Am J Gastroenterol* 2023; 118(10):S1973-S1973. Full Text

[Ali, Suhaib Alhaj] Henry Ford Hosp, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Hospital

Gastroenterology

Alluri S, and **Jafri SM**. An Educational Initiative to Train Michigan Residents on Identification and Treatment of Hepatitis C. *Am J Gastroenterol* 2023; 118(10):S1065-S1065. Full Text

[Alluri, Spandana; Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA.

Gastroenterology
Beydoun H, and **Jafri SM**. Portal Hypertension Associated With Neuroendocrine Tumors. *Am J Gastroenterol* 2023; 118(10):S2344-S2344. Full Text

[Beydoun, Haya] Wayne State Univ, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA.

Gastroenterology
Buti M, Heo J, Tanaka Y, Andreone P, Atsukawa M, Cabezas J, Chak E, Coffin CS, Fujiwara K, Gankina N, **Gordon SC**, Janczewska E, Komori A, Lampertico P, McPherson S, Morozov V, Niu JQ, Plesniak R, Poulin S, Ryan P, Sagalova O, Sheng GP, Voloshina N, Xie Q, Yim HJ, Dixon S, Paff M, Felton L, Lee M, Greene T, Lakshminarayanan D, Plein H, Youssef A, Elston R, Kendrick SFW, and Theodore D. PEGYLATED INTERFERON REDUCES RELAPSES FOLLOWING BEPIROVIRSEN TREATMENT IN PARTICIPANTS WITH CHRONIC HEPATITIS B VIRUS INFECTION ON NUCLEOS(T) IDE ANALOGUES: END OF STUDY RESULTS FROM THE PHASE 2b B-TOGETHER STUDY. *Hepatology* 2023; 78:S49-S53. Full Text

[Buti, Maria] Hosp Valle De Hebron, Barcelona, Spain. [Buti, Maria] Ciberehd Inst Carlos III, Barcelona, Spain. [Heo, Jeong] Pusan Natl Univ, Coll Med, Dept Internal Med, Busan, South Korea. [Heo, Jeong] Pusan Natl Univ Hosp, Biomed Res Inst, Busan, South Korea. [Tanaka, Yasuhito] Kumamoto Univ Hosp, Kumamoto, Japan. [Andreone, Pietro] Aou Modena, Unita Operat Complessa Med Interna, Modena, Italy. [Andreone, Pietro] Univ Modena & Reggio Emilia, Modena, Italy. [Atsukawa, Masanori] Nippon Med Coll Hosp, Tokyo, Japan. [Cabezas, Joaquin] Marques De Valdecilla Univ Hosp, Gastroenterl & Hepatol Dept, Clin & Translat Res Digest Dis Valdecilla Res Ins, Santander, Spain. [Chak, Erik] Univ Calif Davis, Sacramento, CA USA. [Coffin, Carla S.] Univ Calgary, Cumming Sch Med, Calgary, AB, Canada. [Fujiwara, Kei] Nagoya City Univ Hosp, Nagoya, Aichi, Japan. [Gankina, Natalia] Krasnojarsk Reg Ctr AIDS Prevent, Krasnoyarsk, Russia. [Gordon, Stuart C.] Henry Ford Hlth, Detroit, MI USA. [Gordon, Stuart C.] Wayne State Univ, Sch Med, Detroit, MI USA. [Janczewska, Ewa] ID Clin, Myslowice, Poland. [Komori, Atsumasa] Natl Hosp Org Nagasaki Med Ctr, Nagasaki, Japan. [Lampertico, Pietro] Fdn Irccs Ca Granda Osped Maggiore Policlin, Div Gastroenterol & Hepatol, Milan, Italy. [Lampertico, Pietro] Univ Milan, CRC AM & A Migliavacca Ctr Liver Dis, Dept Pathophysiol & Transplantat, Milan, Italy. [McPherson, Stuart] Freeman Rd Hosp, Hepatol, Newcastle Upon Tyne, Tyne & Wear, England. [Morozov, Viacheslav] Hepatol Med Co, Moscow, Russia. [Niu, Junqi] First Hosp Jilin Univ, Changchun, Peoples R China. [Plesniak, Robert] Univ Rzeszow, Ctr Med Lancucie Sp Zoo, Lancut, Poland. [Poulin, Sebastien] Clin Med Urbaine Quartier Latin, Montreal, PQ, Canada. [Ryan, Pablo] Hosp Univ Infanta Leonor, Madrid, Spain. [Sagalova, Olga] South Ural State Med Univ, Chelyabinsk, Russia. [Sheng, Guoping] Shulan Hangzhou Hosp, Hangzhou, Peoples R China. [Voloshina, Natalya] Med Ctr Healthy Family, Novosibirsk, Russia. [Xie, Qing] Shanghai Jiao Tong Univ, Ruijin Hosp, Shanghai, Peoples R China. [Yim, Hyung Joon] Korea Univ Ansan Hosp, Ansan, South Korea. [Dixon, Susan; Felton, Leigh; Plein, Helene] GSK, London, England. [Paff, Melanie; Lee, Maximilian; Greene, Thomas; Lakshminarayanan, Divya; Youssef, Amir] GSK, Collegeville, PA USA. [Elston, Robert; Kendrick, Stuart F. W.] GSK, Stevenage, Herts, England. [Theodore, Dickens] GSK, Durham, NC USA. Biomedica en Red; CIBEREHD; Pusan National University; Pusan National University; Pusan National University Hospital; Kumamoto University; Universita di Modena e Reggio Emilia; Nippon Medical School; Hospital Universitario Marques de Valdecilla (HUMV); University of California System; University of California Davis; University of Calgary; Nagoya City University; Henry Ford Health System; Wayne State University; IRCCS Ca Granda Ospedale Maggiore Policlinico; University of Milan; Newcastle Freeman Hospital; Newcastle University - UK; Jilin University; University of Rzeszow; Hospital Universitario Infanta Leonor; South Ural State Medical University; Shanghai Jiao Tong University; Korea University; Korea University Medicine (KU Medicine); GlaxoSmithKline; GlaxoSmithKline; GlaxoSmithKline; GlaxoSmithKline

Gastroenterology
Chaudhary A, **Denha E**, **Khan MZ**, **Rehman S**, Zaidi SMH, El Alayli A, Gharaibeh EZ, and Farooq U. Unraveling the Unusual: Autoimmune Hepatitis After a 5-day Course of Nitrofurantoin for Uncomplicated UTI. *Am J Gastroenterol* 2023; 118(10):S2311-S2311. Full Text

[Chaudhary, Ammad; Denha, Eric; Khan, Muhammad Zarrar; Rehman, Sheema] Henry Ford Hosp, Detroit, MI USA. [Zaidi, Syed Murtaza Haider] King Edward Med Univ, Lahore, Punjab, Pakistan. [El Alayli, Abdallah; Gharaibeh, Eyad Z.] St Louis Univ, St Louis, MO USA. [Farooq, Umer] Rochester Gen Hosp, Rochester, NY USA. Rochester General Hospital

Gastroenterology
Chaudhary A, **Fahad H**, **Francis A**, **Samad M**, **Rehman S**, **Baldwin H**, **Rana F**, Farooq U, El Alayli A, and **Jafri SM**. Unveiling the Influence of Age and Race on COVID-19 Incidence in Liver and Kidney Transplant Population. *Am J Gastroenterol* 2023; 118(10):S1074-S1074. Full Text

[Chaudhary, Ammad; Fahad, Hamna; Rehman, Sheema] Henry Ford Hosp, Detroit, MI 48202 USA. [Francis, Ashley; Baldwin, Hope; Rana, Fariba] Wayne State Univ, Detroit, MI USA. [Samad, Momin] Henry Ford Hosp, Rochester Hills, MI USA. [Farooq, Umer] Rochester Gen Hosp, Rochester, NY 14621 USA. [El Alayli, Abdallah] St Louis Univ, St Louis, MO 63103 USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Health System; Rochester General Hospital; Saint Louis University; Henry Ford Health System; Henry Ford Hospital

Gastroenterology
Chaudhary A, **Fahad H**, **Samad M**, **Rehman S**, Francis A, Baldwin H, Rana F, Farooq U, **Ichkhanian Y**, and **Jafri SM**. Revolutionary Defense: Evusheld Triumphs in Combating Post Covid-ILD Among Liver and Kidney Transplant Recipients. *Am J Gastroenterol* 2023; 118(10):S1075-S1075. Full Text

[Chaudhary, Ammad; Fahad, Hamna; Rehman, Sheema; Ichkhanian, Yervant] Henry Ford Hosp, Detroit, MI 48202 USA. [Samad, Momin] Henry Ford Hosp, Rochester Hills, MI USA. [Francis, Ashley; Baldwin, Hope; Rana, Fariba] Wayne State Univ, Detroit, MI USA. [Farooq, Umer] Univ Rochester, Rochester, NY USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. Wayne State University; University of Rochester; Henry Ford Health System; Henry Ford Hospital

Gastroenterology
Chaudhary A, **Khan MZ**, **Fahad H**, **Muszkat Y**, and **Jafri SM**. TPN and Pregnancy: A Series of Successful Conceptions. *Am J Gastroenterol* 2023; 118(10):S2517-S2517. Full Text

[Chaudhary, Ammad; Khan, Muhammad Zarrar; Fahad, Hamna; Muszkat, Yakir] Henry Ford Hosp, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Hospital

Gastroenterology
Chaudhary AJ, **Fahad H**, **Samad M**, **Rehman S**, **Baldwin H**, **Francis A**, **Rana F**, **Ichkhanian Y**, **Jomaa D**, **Gupta K**, and **Jafri SM**. EVUSHELD IN LIVER AND KIDNEY TRANSPLANT PATIENTS , WAS IT WORTH IT? *Hepatology* 2023; 78:S310-S311. Full Text

A.J. Chaudhary, Henry Ford Hospital, Detroit, MI, United States

Background: Immunosuppression in patients with solid organ transplant has raised significant concerns regarding outcomes of COVID-19 infection. Pre-exposure use of monoclonal antibodies, specific to certain viral strains as an adjunct to vaccination has been proposed to enhance the immune response following the vaccine. In this study, we aimed to assess the efficacy of the emergency use of Evusheld in this sub-population. Methods: This was a retrospective chart review study conducted at a tertiary care center during the time period of 2022 , 2023 during which adult patients (age >18 y old) with liver, kidney or simultaneous Liver- Kidney transplant who received Evusheld were included. Patients' demographics, disease characteristics, and outcomes were recorded in de-identified datasheets. The primary outcome was incidence of COVID-19 positive PCR test. Secondary outcomes included: progression to Interstitial lung disease (ILD), rate of hospitalization. The Wilcoxon rank sum test, Pearson's Chi-squared test, Fisher's exact test and Wilcoxon rank sum exact test were used for univariate analyses. Results: Among 1149 who received solid organ transplant, 273 (23.7%) patients were diagnosed with COVID-19 from the advent of the pandemic, to February 2023. Patients infected with COVID-19 were more likely to be younger (mean age 61.6 ± 10.9 y versus 63.4 ± 11.5 y, p =0.007), of white race (25.6% versus black 15.2

% and others 14.7 %, p= 0.014). In the total population 26% (296) received Evusheld. Among those who received Evusheld the incidence of covid was 13% (37/296) compared to 28% (236/853) in the patients who did not receive the Evusheld, p< 0.01. Data for post covid ILD was available in only 43.7% (118) patients. Among those with data available, prevalence of post covid ILD was 0%(0/22) and 8.1% (8/96) among those who did and did not receive evusheld respectively, p-value 0.045. Among those with data available, 16.1% (5/31) patients were hospitalized after getting Evusheld as compared to 20.7% (46/176) in patients who did not receive evusheld, p =0.689. Conclusion: Our data shows that Evusheild may have reduced incidence of COVID-19 and provided significant protection against post infectious ILD. It also showed that incidence of COVID-19 in post-transplant patients may be much higher than previously reported. Currently, the FDA has halted all use of Evusheild due to the combined frequency of non-susceptible SARSCoV- 2 variants nationally being more than 90%. However, they do recommend keeping the unexpired batches safe for future, in case new variants show susceptibility.

Gastroenterology
Chowdhury TF, and **Jafri SM**. Small for Size Syndrome Following Living Donor Liver Transplantation. *Am J Gastroenterol* 2023; 118(10):S2372-S2372. Full Text

[Chowdhury, Tabassum F.] Wayne State Univ, Troy, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA.

Gastroenterology
Chowdhury TF, and **Jafri SM**. Two Unique Complications of Lumen-Apposing Metal Stent Placement for Biliary Strictures Following Liver Transplant. *Am J Gastroenterol* 2023; 118(10):S1516-S1517. Full Text

[Chowdhury, Tabassum F.] Wayne State Univ, Troy, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA.

Gastroenterology
Clark K, **Varma A**, and **Jafri SM**. A Case of Rare IgG4-Related Disease. *Am J Gastroenterol* 2023; 118(10):S2565-S2565. Full Text

[Clark, Katie] Wayne State Univ, Sch Med, Detroit, MI USA. [Varma, Adarsh] Henry Ford Hlth, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. System; Henry Ford Hospital

Gastroenterology
Cobty K, and **Jafri SM**. A Unique Case of Biliary Necrosis and Arterial Complications Following Two Orthotopic Liver Transplants. *Am J Gastroenterol* 2023; 118(10):S2270-S2270. Full Text

[Cobty, Kevin] Wayne State Univ Sch Med, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA.

Gastroenterology
Cobty K, **Suresh S**, and **Jafri SM**. Schwann Cell Hamartoma in the Gastrointestinal Tract: A Rare Case Identified on Screening Colonoscopy. *Am J Gastroenterol* 2023; 118(10):S1613-S1613. Full Text

[Cobty, Kevin] Wayne State Univ, Sch Med, Detroit, MI USA. [Suresh, Suraj] Henry Ford Hosp, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Health System; Henry Ford Hospital

Gastroenterology
Currier EE, **Sarowar A**, and **Jafri SM**. HIGHER PLATELETS LEVELS IN POSTOPERATIVE ORTHOTOPIC LIVER TRANSPLANT PATIENTS ASSOCIATED WITH HIGHER RATES OF COMPLICATIONS. *Hepatology* 2023; 78:S315. Full Text

E.E. Currier, Wayne State University, United States

Background: Prior research into the relationship between liver transplant outcomes and platelet levels is limited, but research has shown that peri-operative thrombocytopenia is linked to decreased outcomes and thrombocytopenia on postoperative day 5 have been linked to higher 90-day mortality. However, there is little known about the effect of immediate postoperative thrombocytopenia on long-term morbidity and mortality. The aim of this research was to investigate the relationship between platelet levels immediately posttransplant and one-year postoperative morbidity, including re-hospitalization, rejection, surgical complications, and graft failure, and mortality. Methods: A retrospective chart review was conducted at a diverse, urban transplant center and included 828 adults who underwent orthotopic liver transplant between 2012 and 2022. Data from medical charts including platelet levels, postoperative and surgical complications, platelet infusion history, acute and chronic rejection, graft failure, and death from time of transplant one-year postoperatively was recorded and analyzed. Immediate postoperative platelets levels were defined as platelets levels available closest to transplant surgery end time. To analyze postoperative survival, participants were separated into cohorts based on immediate postop platelet levels (uL): <60,000, 61-90,000, 91-130,000, and >130,000. Results: Average preoperative platelets levels were 99,000 uL (SD =62,000) and average postoperative levels were 77,000 uL (SD = 50,000). Average time from surgery end to measurement of immediate postoperative platelet levels was 37.5 minutes. Contrary to data published thus far, this study showed that higher immediate post-operative platelet levels were found to be associated with a higher chance of readmission (p = 0.046) and acute rejection (p= 0.007). In fact, for every one unit increase in platelets, there was a 0.2% increased risk of readmission and 0.5% increased risk of acute rejection. Overall survival rate was found to be 82.8% and there was no significant difference found between post-op platelet levels and survival rates at one-year (p =0.628). Furthermore, no significant difference was found between postoperative levels and chronic rejection, surgical complications, and graft failure at one year postoperatively. Conclusion: Overall, this study shows that post-operative thrombocytopenia might not be as detrimental to long-term outcomes as previously thought and shows that increased platelets may pose a slight increased risk of complications.

Gastroenterology
Desai PA, **Gordon S**, and **Jafri SM**. A Rare Case of Recurrent Pylephlebitis Secondary to Diverticulitis. *Am J Gastroenterol* 2023; 118(10):S2369-S2370. Full Text

[Desai, Pranally A.; Gordon, Stuart; Jafri, Syed-Mohammed] Henry Ford Hosp, Detroit, MI USA.

Gastroenterology
Dunn W, Alkhouri N, Kundu R, Robert S, Nadeem R, Dunn N, Wong VWS, Verma N, Yip TCF, Loomba R, Abdelmalek MF, Diaz LA, Devuni D, Castera L, Noureddin M, **Jafri SM**, Arab JP, Charlton MR, Wong GLHC, Yang L, Duseja AK, Chen V, Singal AK, Harrison SA, Al Yassin A, and Hino K. MACHINE LEARNING ADVANCED FIBROSIS IN NASH (ALADDIN) WITH WEB-BASED CALCULATION FOR PROBABILITY PREDICTION. *Hepatology* 2023; 78:S829-S835. Full Text

W. Dunn, University of Kansas Medical Center, United States

Background: Nonalcoholic Fatty Liver Disease (NAFLD) prevalence poses a significant challenge, with fibrosis stage acting as a crucial prognostic indicator. Advanced fibrosis/cirrhosis (F3-4) cases often face swift disease progression. Non-Invasive Tests (NITs) for hepatologist referral or biopsy have limited accuracy. We propose a machine learning (ML) model offering a probabilistic prediction adaptable for both community and referral centers, where prevalence varies from 3.7 - 50%. Preliminary two-center data from the multi-center consortium inform this model. Methods: We collected retrospective data on patients diagnosed with NAFLD, Nonalcoholic Steatohepatitis (NASH), or cryptogenic cirrhosis; patients with other liver diseases were excluded. The primary outcome was advanced fibrosis (F3) or cirrhosis (F4). Data was divided into derivation (training) and validation (testing) cohorts. We employed Random Forest for ML, considering other models such as ElasticNet and Grant Boosting Machines. Results: The study incorporated 986 patients, with 269 having advanced fibrosis or cirrhosis. The mean FIB-4 was 1.76 (SD 1.52). The proposed ALADDIN score presented a 1 - Out-of-Bag (OOB) error rate of 78.3%, suggesting a strong fit to the training data. In the validation cohort, ALADDIN score demonstrated an AUC of 0.794 (95% CI 0.750 - 0.837), surpassing FIB-4 0.747 (0.697 - 0.798), p= 0.0039. With a 65%

probability threshold, ALADDIN showed a PPV and NPV of 79%, against FIB-4's 65% PPV and 80% NPV at a 2.66 threshold. The Net Reclassification Improvement (NRI) of 0.379 and Integrated Discrimination Improvement (IDI) of 0.068 accentuate ALADDIN Score's enhanced reclassification and discrimination capacities over FIB-4. Figure 1 displayed ROC comparison of ALADDIN and FIB-4, and the top 20 variables. Conclusion: Preliminary data underscores the ALADDIN score's potential in outperforming the conventional FIB-4 score in a tertiary referral center setting. Patients with an ALADDIN score >65% might require liver biopsy, 15% - 65% may need additional noninvasive testing, and < 15% can be monitored in primary care. The ALADDIN score facilitates tailor-made care based on specific cirrhosis probability. With further data, the model can be calibrated for community settings. This is the first ML model with an online calculator for public use, enabling personalized care. The model is accessible at https://globalalchep.shinyapps.io/ALADDIN/.

Gastroenterology
Faisal MS, **Ashraf T**, **Harris K**, **Khan MZ**, **Chaudhary A**, **Watson A**, **Dang DY**, **Pompa R**, **Elatrache M**, **Piraka C**, **Singla S**, and **Zuchelli T**. Cystic Duct Stenting vs Other Treatment Modalities for Management of Acute Cholecystitis in Patients With Decompensated Cirrhosis. *Am J Gastroenterol* 2023; 118(10):S957-S957. Full Text

[Faisal, Muhammad Salman; Ashraf, Taha; Harris, Kevin; Khan, Muhammad Zarrar; Chaudhary, Ammad; Watson, Andrew; Dang, Duyen; Pompa, Robert; Elatrache, Mazen; Piraka, Cyrus; Singla, Sumit; Zuchelli, Tobias] Henry Ford Hlth Syst, Detroit, MI USA.

Gastroenterology
Faisal MS, **Shamaa O**, **Dang DY**, **Watson A**, **Elatrache M**, **Pompa R**, **Zuchelli T**, **Piraka C**, and **Singla S**. Safety and Efficacy of Biliary Radiofrequency Ablation in Management of Ampullary Lesions. *Am J Gastroenterol* 2023; 118(10):S2218-S2219. Full Text

[Faisal, Muhammad Salman; Shamaa, Omar] Henry Ford Hlth Syst, Detroit, MI USA. [Dang, Duyen; Watson, Andrew; Elatrache, Mazen; Pompa, Robert; Zuchelli, Tobias; Piraka, Cyrus; Singla, Sumit] Henry Ford Hosp, Detroit, MI 48202 USA. Henry Ford Hospital

Gastroenterology
Francis A, **Farooqui S**, **Suresh S**, and **Jafri SM**. VACCINATION, MONOCLONAL ANTIBODY AND MYCOPHENOLATE EFFECTS ON CLINICAL OUTCOMES IN LIVER VERSUS KIDNEY TRANSPLANT RECIPIENTS WITH COVID-19 INFECTION. *Hepatology* 2023; 78:S352-S353. Full Text

A. Francis, Wayne State University, School of Medicine, United States

Background: We aim to evaluate how vaccination, monoclonal antibody (MAB) treatment, and mycophenolate use correlate to outcomes for liver and renal transplant (LRT) recipients infected with SARS-CoV-2. Methods: A retrospective study of LRT recipients diagnosed with COVID-19 between 3/2020 to 1/2022 was performed. We recorded data on patient demographics, immunosuppressants, vaccine dose numbers, MAB treatment, hospitalization, length of stay (LOS, days), mechanical ventilation (MV) use, as well as 3- and 6-month mortality. Results: Of 255 LRT recipients diagnosed with COVID-19, 68 (26%) liver, 177 (69%) renal, and 10 (4%) dual LRT patients were identified. When comparing liver transplant to renal transplant patients, there was no significant difference in hospitalization and mortality. Overall, no significant correlation was found between number of vaccine doses (up to 3) and hospitalization rates (p = 0.948), LOS (p = 0.688), 3- month mortality (p =0.549), or 6-month mortality (p= 0.595). 65 (25%) patients were treated with MABs; these had fewer hospitalizations (37% vs 68% p< 0.001) and a trend towards reduced mortality at 3 months (11% vs 18% p =0.177) and 6 months (11% vs 20% p= 0.092). However, when comparing 12 liver transplant to 51 renal transplant recipients treated with MABs, there was no significant difference in hospitalization or mortality at 3 or 6 months. Mycophenolate use in 199 patients was associated with increased hospitalization (62% vs 55% p= 0.383), MV (24% vs 10% p= 0.135), and mortality at 3 and 6 months respectively when compared to non-users (18% vs 9% p =0.099 and 20% vs 11% p = 0.123). Of 78 liver transplant patients, 53 (68%) were on mycophenolate. Similarly, within this group, mycophenolate use was associated with increased hospitalization rates (58%

vs 44% p= 0.231), and mortality at 3 and 6 months respectively when compared to non-users (19% vs 0% p =0.020 and 11% vs 0% p = 0.014, respectively). Of 187 renal transplant patients, 152 (81%) were on mycophenolate. Within this group, there was no difference in hospitalization rates among users and non-users (62% vs 62%). When comparing 47 liver to 146 renal transplant patients on mycophenolate (excluding dual LRT patients), there was no significant difference in hospitalization (p = 0.672) or mortality at 3 months (p =0.595) or 6 months (p = 0.530). Conclusion: Our data demonstrates that MAB treatment significantly reduces hospitalizations and 3- and 6-month mortality, irrespective of the type of transplant. Mycophenolate was associated with increased hospitalizations and mortality rates, with common trends seen in liver transplant patients alone. Our data further suggests that a 3- vaccine series was inadequate to predict improvements in clinical outcomes for LRT recipients, suggesting further study of a fourth mRNA vaccine dose and the use of tixagevimab/cilgavimab.

Gastroenterology
Francis A, **Farooqui S**, **Suresh S**, and **Jafri SM**. Understanding Clinical Outcomes Associated With Mycophenolate Use Among Liver and Renal Transplant Recipients Infected With SARS-CoV2. *Am J Gastroenterol* 2023; 118(10):S1205-S1205. Full Text

[Francis, Ashley; Farooqui, Sara] Wayne State Univ, Sch Med, Detroit, MI USA. [Suresh, Suraj] Henry Ford Hosp, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Health System; Henry Ford Hospital

Gastroenterology
Gonzalez H, **Gordon SC**, Daida YG, Schmidt MA, **Zhou YR**, **Wu T**, **Rupp L**, **Trudeau S**, and Lu M. SUSTAINED VIROLOGICAL RESPONSE REDUCES RISK OF PORTAL VEIN THROMBOSIS IN HEPATITIS C PATIENTS WITH CIRRHOSIS. *Hepatology* 2023; 78:S710-S711. Full Text

[Gonzalez, Humberto; Gordon, Stuart C.; Zhou, Yueren; Wu, Trueman; Rupp, Lora; Trudeau, Sheri] Henry Ford Hlth, Detroit, MI USA. [Gordon, Stuart C.] Wayne State Univ, Sch Med, Detroit, MI USA. [Daida, Yihe G.] Kaiser Permanente Hawail, Honolulu, HI USA. [Schmidt, Mark A.] Kaiser Permanente Northwest, Washington, DC USA. [Lu, Mei] 156 Pocatello Rd, Middletown, NY USA.

Gastroenterology
Guivatchian E, and **Jafri SM**. Drug-Induced Collagenous Colitis Secondary to Capecitabine. *Am J Gastroenterol* 2023; 118(10):S2141-S2141. Full Text

[Guivatchian, Elnaz] Wayne State Univ Sch Med, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA.

Gastroenterology
Guivatchian E, and **Jafri SM**. Cutaneous Sensitivity as a Unique Presentation of Liver Cirrhosis. *Am J Gastroenterol* 2023; 118(10):S2356-S2356. Full Text

[Guivatchian, Elnaz] Wayne State Univ, Sch Med, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA.

Gastroenterology
Hadi M, **Youssef RM**, Dourra M, **Obri M**, **Beidoun M**, and **Jafri SM**. A Late Diagnosis of Caroli Syndrome. *Am J Gastroenterol* 2023; 118(10):S1520-S1520. Full Text

[Hadi, Moustafa] Michigan State Univ, Coll Human Med, Detroit, MI USA. [Youssef, Rami M.; Obri, Mark; Jafri, Syed-Mohammed] Henry Ford Hosp, Detroit, MI 48202 USA. [Dourra, Mohsen] Corewell Hlth, Woodhaven, MI USA. [Beidoun, Mohamad] Henry Ford Hosp, Livonia, MI USA. Medicine; Henry Ford Health System; Henry Ford Hospital; Henry Ford Health System

Gastroenterology
Haq KS, Solanki D, Ugonabo O, Memon A, Iqbal U, Rajwana YR, Khan ZH, Ogude D, Varghese T, Solanki S, Khan MA, Chakinala RC, **Jafri SM**, and Gbadehan E. Rectal and Anal Ulceration: Analysis of Demographic Trends, Comorbidity Measures, and Outcomes from the National Inpatient Sample Database. *Am J Gastroenterol* 2023; 118(10):S174-S174. Full Text

[Haq, Khwaja S.; Ogude, Derick; Varghese, Teresa; Gbadehan, Emmanuel] Wellstar Spalding Reg Med Ctr, Griffin, GA USA. [Solanki, Dhanshree] Rutgers State Univ, New Brunswick, NJ USA. [Ugonabo, Onyinye] Marshall Univ, Joan C Edwards Sch Med, Huntington, WV USA. [Memon, Adil] Louisiana State Univ, Shreveport, LA USA. [Iqbal, Unzela] Trinitas Reg Med Ctr, Elizabeth, NJ USA. [Rajwana, Yasir R.] Stanford Healthcare, Stanford, CA USA. [Khan, Zarak H.] East Carolina Univ, Greenville, NC USA. [Solanki, Shantanu; Khan, Muhammad Ali] MD Anderson Canc Ctr, Houston, TX USA. [Chakinala, Raja Chandra] Guthrie Robert Packer Hosp, Sayre, PA USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. University; Louisiana State University System; Louisiana State University Shreveport; University of North Carolina; East Carolina University; University of Texas System; UTMD Anderson Cancer Center; Henry Ford Health System; Henry Ford Hospital

Gastroenterology
Harris KB, **Nimri FM**, and **Salgia RJ**. LONG-TERM OUTCOMES OF RUPTURED HEPATOCELLULAR CARCINOMA. *Hepatology* 2023; 78:S1860-S1861. Full Text

K.B. Harris, Henry Ford Health, United States

Background: It is estimated that spontaneous rupture of hepatocellular carcinoma (HCC) occurs in 2-5% of patients with HCC. Long-term outcomes in patients with ruptured HCC are not well described. Ruptured HCC requires a stepwise approach with control of bleeding followed by treatment for HCC. The spectrum of treatment options has expanded over the years for HCC. This study describes a single-center tertiary referral center experience with treating patients longitudinally with ruptured HCC. Methods: Between 2014 to 2022, our center experienced 7 cases of initial HCC presentation with a spontaneously ruptured hepatocellular carcinoma. Results: The average age of patients with ruptured HCC was 60 years old. Six of the patients (85.7%) were male and one patient (14.1%) was female. Six of the seven patients had underlying cirrhosis with 50% due to HCV, 33% due to alcohol and 16% due to a combination of HCV and alcohol. Three (42.9%) of the patients had Barcelona Clinic Liver Cancer (BCLC) stage B disease at presentation and four (57.1%) of the patients had BCLC stage C disease. None of the patients who presented with ruptured HCC were in an HCC screening protocol. Five (71.4%) of the patients had solitary hepatomas while two (28.6%) of the patients had multiple hepatomas at diagnosis. Both patients with multiple hepatomas had bilobar involvement. The median AFP level at presentation was 23.6 ng/mL (range 5.2 ng/mL to>30000 ng/mL). Two (28.6%) of the patients at presentation were on aspirin and one (14.1%) was on a direct-acting oral anticoagulant (DOAC). Five of our patients were initially treated with bland embolization and two were initially treated with TACE. The patients received various subsequent treatments including bland embolization, TACE, TARE, SBRT and systemic therapies. None of our patients received surgical management or liver transplantation. The median overall survival from date of rupture was 817 days (range 381 d to 2796 d). Conclusion: Our series highlights the wide spectrum of outcomes for patients with ruptured HCC. With improved treatment options, patient survival has increased. In this study, all patients survived at least one year and the longest survival was over 7 years. Noting the improved consideration by UNOS to patients with distant HCC rupture being considered for liver transplantation, continued attention to this group of patients can improve their outcomes.

Gastroenterology
Ibrahim A, **Chaudhary A**, Sarowar A, Baldwin H, Khan MZ, and **Jafri SM**. Unveiling the Risk: Factors Affecting Clostridioides difficile Infection Incidence Within 1 Year of Liver Transplantation. *Am J Gastroenterol* 2023; 118(10):S1115-S1115. Full Text

[Ibrahim, Ahmed; Chaudhary, Ammad; Khan, Muhammad Zarrar] Henry Ford Hosp, Detroit, MI USA. [Sarowar, Arif; Baldwin, Hope] Wayne State Univ, Sch Med, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Health System; Henry Ford Hospital

Gastroenterology
Ibrahim AM, **Chaudhary AJ**, **Baldwin H**, **Sarowar A**, **Khan MZ**, and **Jafri SM**. EVALUATION OF THE EFFECT OF THE COVID-19 PANDEMIC ON THE RATE OF CLOSTRIDIUM DIFFICILE INFECTION FOLLOWING LIVER TRANSPLANTATION. *Hepatology* 2023; 78:S309-S310. Full Text

[Ibrahim, Ahmed Mostafa; Chaudhary, Ammad Javaid; Khan, Muhammad Zarrar] Henry Ford Hosp, Detroit, MI USA. [Baldwin, Hope; Sarowar, Arif] Wayne State Univ, Sch Med, Wayne, NJ USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Health System; Henry Ford Hospital

Gastroenterology
Ichkhanian Y, **Veracruz N**, **Al-Haddad M**, Albunni H, Schlachterman A, Gouda Z, Canakis A, Kim R, D'Souza L, Khashab M, **Nimri F**, **Ashraf T**, **Faisal MS**, **Jomaa D**, **Dababneh Y**, **Rehman S**, **Rizwan A**, **Singla S**, **Alsheik E**, **Ginnebaugh B**, **McFarlin K**, **Piraka C**, and **Zuchelli T**. Management of Patients After Failed Gastric Peroral Endoscopic Myotomy: A Multi-Center Study. *Am J Gastroenterol* 2023; 118(10):S1410-S1411. Full Text

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Gastroenterology
Jamali T, **Alvelo-Rivera M**, and **Elatrache M**. A Rare Case of Esophageal Obstruction After Rupture of an Esophageal Duplication Cyst. *Am J Gastroenterol* 2023; 118(10):S2187-S2188. Full Text

[Jamali, Taher] Henry Ford Hlth, Farmington Hills, MI USA. [Alvelo-Rivera, Miguel] Henry Ford Hlth, Detroit, MI USA. [Elatrache, Mazen] Henry Ford Hosp, Detroit, MI USA. System; Henry Ford Hospital

Gastroenterology
Jamali T, **Elatrache M**, **Zuchelli T**, and **Singla S**. A Unique Case of a Migrated Plastic Stents Resulting in Delayed Pancreatitis Following EDGE Procedure. *Am J Gastroenterol* 2023; 118(10):S2188-S2188. Full Text

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Gastroenterology
Jamali T, **Nassif G**, **Kwon D**, and **Pompa R**. A Rare Case of Solid Pseudopapillary Tumor of the Pancreas in a Male Patient. *Am J Gastroenterol* 2023; 118(10):S1437-S1437. Full Text

[Jamali, Taher] Henry Ford Hlth, Farmington Hills, MI USA. [Nassif, Georges; Kwon, David] Henry Ford Hlth, Detroit, MI USA. [Pompa, Robert] Henry Ford Hosp, Detroit, MI USA. System; Henry Ford Hospital

Gastroenterology
Jamali T, **Pimentel J**, **Perry K**, Tocco J, **Tejwani S**, **Mayerhoff R**, and **Pompa R**. First Reported Case of Endoscopic En Bloc Resection of Esophageal Liposarcoma. *Am J Gastroenterol* 2023; 118(10):S2186-S2187. Full Text

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Gastroenterology
Jamali T, and **Salgia R**. Late Presentation of Recurrent Solid Pseudopapillary Pancreatic Neoplasm With Liver Metastasis During Pregnancy. *Am J Gastroenterol* 2023; 118(10):S2277-S2277. Full Text

[Jamali, Taher] Henry Ford Hlth, Farmington Hills, MI USA. [Salgia, Reena] Henry Ford Hlth, Detroit, MI USA.

Gastroenterology
Jomaa D, **Dababneh Y**, **Nagirimadugu A**, **Oruganti P**, **Lu M**, **Melkonian C**, and **Kaur N**. Bridging Healthcare Disparities in Patients With Inflammatory Bowel Disease (IBD) in Underserved Communities: Results From a Telemedicine Intervention at a Large Tertiary Care Center. *Am J Gastroenterol* 2023; 118(12):S18. Full Text

D. Jomaa, Henry Ford Health, Detroit, MI, United States

Background: The prevalence of IBD in the United States is greater than 3 million and rising, while the access to IBD specialists in rural areas remains limited. Urban areas associated with large healthcare systems have 263 specialists per 100,000 residents, whereas rural areas have only 30 specialists per residents. The specific aims of this study are to identify the impact access to specialty care has on frequency of IBD flares, emergency department (ED) visits, and hospitalizations. Methods: We conducted a retrospective chart review of adult patients (>18 years) with the diagnosis of IBD who reside in Michigan. Patients were divided into either pre or post periods, where preperiod was defined as before the initiation of telehealth services between 1/1/2018-12/31/2019, and post-period was defined as after the advent of telehealth, between 10/1/2021-10/31/2022, including both video visits as well as the Henry Ford Specialty Center, which offers IBD specialty care virtually. Patient's demographic information, IBD encounters, ED visits, hospitalizations were collected at the end of each study period. The outcomes of interest were the number of IBD-related outpatient encounters, ED visits, and hospitalizations in each period. Results: A total of 5520 IBD encounters were observed in both time periods from 4941 individual patients. Among the total 4941patients, 2992 patients were in the pre-period cohort, and 1949 patients were in the post-period cohort including 721 patients who were seen in both period cohorts. Patients' IBD encounters were significantly reduced in the post-period compared to those in the preperiod (RR=0.73, 95% CI 0.69-0.76 and p-value< 0.001). There was also a significant decrease in ED visits (RR=0.53, 95% CI 0.50-0.56) and hospitalizations in the post-period (RR=0.35, 95% CI 0.33- 0.37). In addition, we looked at the geospatial distribution in patients and found that there was a wider distribution of patients seeking care for their IBD in neighboring and rural counties in the postperiod compared to the pre-period. Conclusions: The IBD Center at Henry Ford Health serves more than 3,000 patients annually and an estimated 15% travel more than 60 miles for their care. Given the need to provide specialty care throughout Michigan, Henry Ford Health is offering telehealth services within a standard clinic to overcome the barriers of telehealth in IBD care. Our study shows that this effort has bridged access to medical care and increased distribution of patients in Michigan receiving specialty care for IBD. It also significantly reduced IBD flares, hospitalization, and ED visits for these patients.

Gastroenterology
Jomaa D, **Ichkhanian Y**, **Dababneh Y**, **Brown P**, **Dang D**, **Gonzalez H**, **Venkat D**, and **Zuchelli T**. A NATIONAL SURVEY ON THE RISING ROLE OF ENDOSCOPIC BARIATRIC PROCEDURES FOR THE MANAGEMENT OF NONALCOHOLIC STEATOHEPATITIS. *Hepatology* 2023; 78:S1230-S1231. Full Text

D. Jomaa, Henry Ford Hospital, United States

Background: Weigh loss is the cornerstone of halting disease progression in patients with nonalcoholic fatty liver disease (NAFLD) and preventing nonalcoholic steatohepatitis (NASH). Patients who fail to lose

weight through conservative modalities are often offered the option of bariatric surgeries, but most patients are either high-risk surgical candidates or prefer non-surgical modalities. Endoscopic Sleeve Gastrectomy (ESG) was introduced as a minimally invasive bariatric procedure that provides patients with acceptable weight loss and improvement in their metabolic disease that contributes to NAFLD and NASH. In the study, we aimed to conduct a national survey to evaluate practicing gastroenterologist's perception on the role of ESG for managing NASH. Methods: We conducted a descriptive study through a national survey of 15 questions. The survey was built through an online cloud-based software, and a link was emailed to a total of 493 U.S. GI fellowship programs. The email recipients were asked to forward the survey link to additional faculty members. There was no monetary compensation for filling out the survey. The survey was anonymous, and no physician or patient identifier was shared. Total estimated time for completing the survey was 4 minutes. Results: A total of 54 responses were obtained during the time period 01-09-2021 and 2-12-2021, with estimated completion rate of 50%. Survey questions were summarized in Table 1. The majority of participants, 72%, were from tertiary care academic center, mostly commonly located in the Midwest, (39%). About half (48%) of the institutions had an established multidisciplinary team to manage patients with NASH who failed to lose weight following conservative modalities, with 65% having an advanced endoscopist trained in bariatric endoscopy in the team. Providers were most commonly, advanced endoscopists (40%), hepatologists (26%), general gastroenterologists, (18%), and gastroenterology fellows (11%). More than half of the participants (62%) encountered NASH patients sometimes with BMI > 40 kg/m2 who failed the current standard of care noninvasive weight loss measures, and refused surgical bariatric procedures, or deemed not to be a surgical candidate. Providers reported that endoscopic bariatric options, most commonly ESG (80%), are sometimes discussed with the patients in 46% of the times. Barriers for referral for endoscopic bariatric procedures in NASH patients were overwhelmingly due to lack of insurance coverage in 86% of the times while 32% of the participants thought that there was still not enough literature. Advanced endoscopists reported that they are unable to obtain insurance coverage for managing NASH patients in 78% of the time. Conclusion: NASH is projected to be the leading cause of cirrhosis, and the utilization of novel management modalities such as ESG are overwhelmingly impacted by the health insurance reimbursement policies.

Gastroenterology
Jomaa D, **Ichkhanian Y**, **Gupta K**, **Chaudhary AJ**, and **Jafri SM**. PREDICTIVE ROLE OF TRICUSPID REGURGITATION SEVERITY AMONG PERI-LIVER TRANSPLANT PATIENTS: RESULTS FROM A LARGE TERTIARY CARE CENTER. *Hepatology* 2023; 78:S338-S339. Full Text

[Jomaa, Diana; Ichkhanian, Yervant; Gupta, Kartik; Chaudhary, Ammad Javaid] Henry Ford Hosp, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Hospital

Gastroenterology
Jomaa D, **Jamali T**, **Manivannan A**, **Zahedi S**, **Peleman A**, **Pillai S**, **Zalawadia A**, and **Fain C**. A Syndrome of Diarrhea, Anasarca, and Nail Dystrophy: A Curious Case of Cronkhite-Canada Syndrome. *Am J Gastroenterol* 2023; 118(10):S1990-S1991. Full Text

[Jomaa, Diana; Jamali, Taher; Zahedi, Sulmaz; Peleman, Andrew; Pillai, Shreejith; Zalawadia, Ashish; Fain, Christopher] Henry Ford Hosp, Detroit, MI USA. [Manivannan, Ahila] Henry Ford Hlth, Detroit, MI USA.

Gastroenterology
Kabir K, Kapten BS, Thet AM, and **Schairer J**. Misdiagnosis and MSM: A Systematic Review Assessing the Diagnosis of IBD and Sexually Transmitted Infectious Colitis in Gay Men. *Am J Gastroenterol* 2023; 118(10):S775-S775. Full Text

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Gastroenterology
Khan MZ, **Obri M**, **Chaudhary A**, **Elatrache M**, **Singla S**, **Watson A**, and **Zuchelli T**. Transcolonic Drainage of Walled-Off Pancreatic Necrosis: A Case Report. *Am J Gastroenterol* 2023; 118(10):S2245-S2245. Full Text

[Khan, Muhammad Zarrar] Henry Ford Med Ctr, Detroit, MI USA. [Obri, Mark; Chaudhary, Ammad; Elatrache, Mazen; Singla, Sumit; Watson, Andrew; Zuchelli, Tobias] Henry Ford Hosp, Detroit, MI USA.

Gastroenterology
Manivannan A, **Davis W**, **Betcher S**, and **Pompa R**. Management of a Necrotic Pancreatic Pseudocyst - Avoiding the Dreaded Pseudoaneurysm Bleed. *Am J Gastroenterol* 2023; 118(10):S2182-S2183. Full Text

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Gastroenterology
Manivannan A, Liapakis AM, Diehl AM, Verna E, Kumar V, **Salgia RJ**, **Wu T**, Lu M, Parikh ND, and **Jesse M**. INTERACTIONS BETWEEN RACE/ETHNICITY AND GENDER IN LIVER TRANSPLANTS: DO ACUITY CIRCLES MATTER? *Hepatology* 2023; 78:S277. Full Text

A. Manivannan, Henry Ford Health, New Haven, CT, United States

Background: Despite continued efforts, there are welldocumented disparities in liver transplantation (LT) from listing through post-transplant. National policies on allocation of deceased donor liver transplants (DDLT) aim to provide consistent and equitable access. However, the impacts of Acuity Circles (AC) and interactions between race and gender on delisting due to deterioration/death or receipt of DDLT have been minimally explored. Methods: Using data from the United Network for Organ Sharing (UNOS), we studied listed adults for DDLT from April 3, 2017, to October 4, 2022, a 60-month period (30 mo pre- and post-AC). Fine-Gray subdistribution hazard model was used to study AC impact on LT while delisting due to deterioration/ death was used as a competing risk. The model focused on AC indicator by race by gender interactions, as well as AC by hepatocellular carcinoma (HCC) diagnosis interactions. Results: 59,592 patients (30,202 pre-AC, 29,390 post-AC) were studied. No 3- way (AC X race X gender) interaction was detected, indicating effect of race and gender on LT was consistent pre- and post-AC periods. However, there were significant gender by race or AC by HCC interactions (Table 1): patients with HCC had greater chance for LT than non-HCC, though post-AC this effect was reduced. AC increased LT 25% in patients without HCC. Across gender, White, Black, and Hispanic men were more likely to receive transplant compared to their female counterparts. Within gender, Black and Hispanic women were less likely to receive transplant than White women, with no significant differences between White and Asian women. For men, there were no statistical difference in likelihood for transplant between White versus Black or Hispanic men, but Asian men had a lower likelihood for LT than White men. Additional significant predictors outlined in Table 1. Conclusion: Accounting for listing characteristics, AC did not significantly impact interactions between gender and race on receipt of LT. However, AC may have improved access to LT amongst those without HCC but may have diminished access amongst those with HCC post-AC. Regardless of AC, there were important gender-race interactions requiring closer examination, particularly where Black and Hispanic women appear disproportionately negatively impacted. The same patterns were not noted across male racial categories, suggesting future research and interventions should target those at greatest risk. (Table Presented).

Gastroenterology
Manivannan A, **Nagirimadugu A**, and **Kaur N**. Ulcerative Colitis in a Neovagina - An Unexpected Complication From M<spacing diaeresis>ullerian Agenesis. *Am J Gastroenterol* 2023; 118(10):S2116-S2116. Full Text

[Manivannan, Ahila; Nagirimadugu, Ankita; Kaur, Nirmal] Henry Ford Hlth, Detroit, MI USA.

Gastroenterology
McIntosh J, **Moonka D**, and **Jayaprakash N**. When the Critical Illness Dominoes Fall, Unforeseen Events Post BRTO. *Am J Respir Crit Care Med* 2024; 209. Full Text

J. Mcintosh, Pulmonary and Critical Care, Henry Ford Health, Detroit, MI, United States

Introduction: Gastric variceal bleeding is a complication of cirrhosis with portal hypertension (PHT) associated with significant morbidity and mortality. Management of suspected variceal bleeding includes resuscitation, medical therapy, endoscopic intervention and early consideration for advanced procedures such as TIPS, BRTO, surgery or liver transplant. Herein, we describe a rare adverse event following BRTO. Case: A 39 year old male with alcoholic cirrhosis and PHT, gastric varices (GV) and Gastroesophageal varices (GOV), presented to emergency department (ED) with hematemesis. He was intubated and transfused per massive transfusion protocol for large volume hematemesis. A Minnesota tube was placed emergently. Medical therapy was initiated including IV pantoprazole, octreotide, ceftriaxone. An endoscopy within 24 hours revealed a large GOV without stigmata of recent bleeding and GV with stigmata of recent bleeding. The GOV were banded and the GV identified as the source of hematemesis. To address the GV, he was taken to Interventional radiology (IR) for a Balloon-occluded Retrograde Transvenous Obliteration (BRTO) procedure. 12 hours later the patient developed abdominal distension, lactic acidosis and sudden rise in norepinephrine requirements refractory to fluid resuscitation. CT abdomen with contrast showed diffuse hypo enhancement and thickening of the bowel favored to be related to mesenteric ischemia secondary to mesenteric venous hypertension (MVH). As a solution, a TIPS procedure was performed to reduce MVH. MICU course was complicated by ARDS, Renal failure required SLED, multiple transfusion of blood products for correction of coagulopathy. Discussion: A BRTO is an advanced procedure for intervention of GV as the source For GV as the source of the variceal bleeding in decompensated liver cirrhosis, advanced options such as BRTO are available as secondary prevention for further bleeding. This case highlights an adverse event associated with BRTO that has not been commonly reported. Intensivists, while not performing advanced procedures for these patients, must have heightened awareness of all complications and adverse events related to BRTO, because early recognition can result in expedited care to decrease severity of morbidity or mortality.

Gastroenterology
Miyake K, **Al-Juburi S**, **Young K**, **Chau LC**, **Kitajima T**, **Wickramaratne N**, **Nassar A**, **Yoshida A**, **Moonka D**, **Venkat D**, **Abouljoud MS**, and **Nagai S**. HIGHER INTRA-OPERATIVE PEAK LACTATE VALUE MAY BE ASSOCIATED WITH PROLONGED HEMODIALYSIS REQUIREMENT AFTER LIVER TRANSPLANT ALONE IN PATIENTS WITH PRE- TRANSPLANT KIDNEY DYSFUNCTION. *Hepatology* 2023; 78:S314-S315. Full Text

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Gastroenterology
Mo J, **Agha YH**, and **Jafri SM**. An Unusual Cause of Achalasia Following Liver Transplantation. *Am J Gastroenterol* 2023; 118(10):S1845-S1845. Full Text

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Gastroenterology
Mueller A, and **Jafri SM**. RESPONSE TO URSODIOL THERAPY IN REDUCING ALKALINE PHOSPHATASE TO NORMAL LEVELS IN PRIMARY BILIARY CHOLANGITIS IN A DIVERSE COMMUNITY PRACTICE. *Hepatology* 2023; 78:S2071-S2072. Full Text

A. Mueller, Wayne State University, School of Medicine, United States

Background: Primary biliary cholangitis (PBC) is an autoimmune cholestatic liver disease that can lead to advanced fibrosis and cirrhosis. First-line treatment is ursodiol (UDCA), which decreases hepatic synthesis of cholesterol and desaturates biliary cholesterol. The objective is to assess the effectiveness of UDCA on lowering alkaline phosphatase (ALP) levels in patients diagnosed with PBC. Methods: A retrospective review was conducted at a diverse urban academic center to obtain UDCA dosage and ALP values at the start of UDCA therapy and at 6 and 12 month periods to correlate with long term survival. Covariants such as Fibroscan results and liver transplant status were analyzed followed by chi-squared tests and linear regression analysis. Results: 122 newly-presenting PBC patients were treated only with UDCA. Mean age was 61.6 years old (range 26-90). 73% (n =89) of the patients were females. The mean liver stiffness by Fibroscan evaluation was 9.7 kPa with standard deviation (SD) of 6.65 (n = 47). Results were tiered based on low (<130), medium (130-200) and high (> 200) ALP levels. At baseline, the percentage of patients in low, medium, and high ALP groups were 11%, 36%, and 53%, respectively. After 12 months of treatment, the percentage of patients in low, medium, and high ALP groups were 42%, 33%, and 21%, respectively. Treatment regimen was defined as low dose (<10mg/kg/day, 31%), medium dose (10-15mg/ kg/day, 51%) and high dose (> 15mg/kg/day, 18%). The mean UDCA dose was 11.7 mg/kg/day (SD 4.44) upon initiation of therapy. Baseline ALP levels in low, medium and high dose UDCA groups was 47%, 53%, and 59%, respectively. ALP > 200 at 12 months in low, medium and high dose UDCA groups was 21%, 18%, and 18%, respectively. Overall 20.9% of patients had ALP >200 after 12 months. 56.5% of patients had ALP >130 at 12 months. The chi-square test showed no significant association between categorical UDCA dose and categorical ALP at 6 and 12 months. Linear regression analysis showed no significant UDCA dose effect on change in ALP from baseline to 6 and 12 months. The 3 and 5 year survival following diagnosis was 96% (n = 117) and 95% (n = 116), respectively. Survival at 3 and 5 years was 100% in those with 12 month ALP < 130, 97.6% and 95.1% in those with 12 month ALP 130-200, and 95.7% in those with 12 month ALP > 200, respectively. In patients with ALP >200 at baseline, 44.4% had a Fibroscan value < 8kpa vs 18.5% had a Fibroscan value > 14 kpa. In patients with ALP > 200 at 12 months, 21.7% had a Fibroscan value < 8kpA vs 0% had a Fibroscan value > 14kpa. Conclusion: Initiating UDCA decreased the number of patients with ALP >200 at 6 and 12 months compared to baseline. UDCA therapy aids survival but failed to reduce ALP levels <200 in 20% of patients. Additional therapies should be considered for these patients.

Gastroenterology
Nimri FM, **Dawod S**, **Nimri R**, **Albusoul L**, **Shadid A**, **Maki M**, **Dababneh Y**, **Russell S**, and **Kutait A**. The Calm Before the Scope: A Look at Sedation Methods for Patients with History of Atrial Fibrillation Undergoing Screening Colonoscopy. *Am J Gastroenterol* 2023; 118(10):S560-S561. Full Text

[Nimri, Faisal M.; Dawod, Sanad; Albusoul, Linda; Shadid, Al Muthanna; Maki, Mohamed; Dababneh, Yara; Russell, Sarah; Kutait, Anas] Henry Ford Hosp, Detroit, MI USA. [Nimri, Rund] Jordan Univ Sci & Technol, Irbid, Jordan. Science & Technology

Gastroenterology
Obri M, **Ali SA**, **Alluri S**, **Samad M**, **Almajed MR**, **Ichkhanian Y**, and **Jafri SM**. SIMILAR REJECTION AND RETRANSPLANT RATES BUT DECREASED SURVIVAL AMONG AFRICAN AMERICAN PATIENTS FOLLOWING LIVER TRANSPLANTATION. *Hepatology* 2023; 78:S1320-S1321. Full Text

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Background: There are known disparities in medicine in regards to sex and race. Investigation is important to evaluate these disparities and to aim to correct them, offering the best outcome for a diverse range of patients. The study aims to compare liver transplant outcomes based off of the race of the patient. Methods: A retrospective study was conducted at a single tertiary liver transplant center and was comprised of patients who underwent liver transplant from 2009 to 2019. The primary outcome was the rate of survival among different races. Secondary outcomes measured included the rate of rejection and re-transplant among different races in addition to the rate of survival among different sexes and donor types. Results: This study included 450 patients with race distribution of 83.6% white patients (n =376), 10.4% black patients (n=47), and 6.0% patients classified as 'Other' races (n=27). The primary outcome was the rate of survival compared amongst the three groups at 1 year, 3 years, and last known follow-up.

Differences in survival rate among the three groups at 1 year was not statistically significant. At 3 years, the survival rate for white patients was 88.6%, black patients was 74.5%, and other patients was 92.6%; the chi-square statistics was 8.2 (p=0.016) which is statistically significant at p <0.05. At the last known follow-up, survival rate for white patients was 82.2%, black patients was 66.0%, and other patients was 88.9%; the chi-square statistic was 8.3 (p =0.016) which is significant. Re-transplant rates did not significantly differ between races with re-transplant rates among white, black, and other patients at 4.3%, 1.2%, and 3.7% respectively. Rejection rates did not significantly differ between races with white, black, and other patients at 24.5%, 31.9%, and 18.5% respectively. Comparisons of survival among patients with difference sexes did not demonstrate a statistically significant difference. Conclusion: Correlation exists between different patients races and survival among liver transplant patients. Patients who are black have a statistically lower survival rate (66.0%) compared to those who are white (82.2%) or other (88.9%). Further investigation with larger population sizes including epidemiological studies and subgroup analyses is necessary to delineate the disparities which influence these outcomes. Published literature suggests that access to care, socioeconomic status, and racial biases are factors that influence healthcare access and affect outcomes.

Gastroenterology
Obri M, **Davis W**, **Faisal MS**, and **Watson A**. An Unusual Late Presentation of Caroli Syndrome. *Am J Gastroenterol* 2023; 118(10):S1538-S1539. Full Text

[Obri, Mark; Davis, William; Faisal, Muhammad Salman; Watson, Andrew] Henry Ford Hosp, Detroit, MI USA.

Gastroenterology
Obri M, **Davis W**, **Khan MZ**, **Fahad H**, **Curran J**, and **Pompa R**. A Case of Metastatic Seminoma Mimicking a Primary Pancreatic Tumor. *Am J Gastroenterol* 2023; 118(10):S1539-S1540. Full Text

[Obri, Mark; Davis, William; Khan, Muhammad Zarrar; Fahad, Hamna; Curran, John; Pompa, Robert] Henry Ford Hosp, Detroit, MI USA.

Gastroenterology
Obri M, **Dawod S**, Qasawa A, Fahoury A, **Stephan J**, **Kamran W**, and **Jafri SM**. A Rare Presentation of Drug-Induced Pancreatitis After Cyclophosphamide Infusion. *Am J Gastroenterol* 2023; 118(10):S1538-S1538. Full Text

[Obri, Mark; Dawod, Sanad; Stephan, Johnathan; Kamran, Wasih] Henry Ford Hosp, Detroit, MI USA. [Qasawa, Austin] Wayne State Univ, Coll Med, Detroit, MI USA. [Fahoury, Alan] Univ Toledo, Coll Med, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. University System of Ohio; University of Toledo; Henry Ford Health System; Henry Ford Hospital

Gastroenterology
Obri M, **Harris K**, **Ali SA**, **Samad M**, **Rehman S**, **Chaudhary A**, and **Suresh S**. Delaying Endoscopy for Food Impaction Increases Hospital Admissions but Does Not Lead to More Patient Complications. *Am J Gastroenterol* 2023; 118(10):S417-S417. Full Text

[Obri, Mark; Harris, Kevin; Ali, Suhaib Alhaj; Rehman, Sheema; Chaudhary, Ammad; Suresh, Suraj] Henry Ford Hosp, Detroit, MI USA. [Samad, Momin] Henry Ford Hosp, Rochester Hills, MI USA.

Gastroenterology
Obri M, **Khan MZ**, **Chaudhary A**, **Piraka C**, and **Zuchelli T**. Isolated Gastric Metastasis of Renal Cell Carcinoma 11 Years After Initial Diagnosis Treated With Endoscopic Submucosal Dissection. *Am J Gastroenterol* 2023; 118(10):S2688-S2688. Full Text

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Gastroenterology
Obri M, **Nimri F**, **Dawod S**, **Youssef RM**, **Alluri S**, **Almajed MR**, **Stephan J**, **Ichkhanian Y**, **Watson A**, **Elatrache M**, **Pompa R**, **Dang DY**, **Singla S**, **Piraka C**, and **Zuchelli T**. Over Half of Liver Transplant Patients With Biliary Strictures Have. *Am J Gastroenterol* 2023; 118(10):S90-S90. Full Text

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Gastroenterology
Parikh ND, Jones PD, **Salgia RJ**, Bhan I, Grinspan LT, Jou J, Zhou K, Jalal P, Roccaro GA, Rangnekar AS, Benhammou JN, Diehl AM, Mehta N, Wedd JP, Yang JD, Kim AK, Duarte-Rojo A, Oloruntoba O, Tevar AD, Au JS, Blain Y, Rao S, Furtado F, Catalano O, Lewis S, Mendiratta-Lala M, King K, Sachdev L, Lee EW, Bruno J, Kamel I, Tolosa C, Kao KD, **Badawi I**, Przybyszewski E, Quirk L, Nathani P, Haydel B, Wong N, Albertian R, Chen A, Aloor FZ, Elkheshen A, Marvil C, Issac A, Clinton J, Woo SM, Yum J, Rieger E, Hutchison A, Turner A, Alsudaney M, Hernandez P, Xu ZY, Khalid A, Barrick B, Wang B, Tapper EB, Hao W, and Singal AG. DEVELOPMENT AND VALIDATION OF AN ALGORITHM FOR THE PREDICTION OF HIGH-RISK VARICES IN PATIENTS WITH UNRESECTABLE HEPATOCELLULAR CARCINOMA (HCC). *Hepatology* 2023; 78:S82-S83. Full Text

[Parikh, Neehar Dilip; Kao, Karissa D.] Univ Michigan, Ann Arbor, MI USA. [Jones, Patricia D.] Univ Miami, Miller Sch Med, Miami, FL USA. [Salgia, Reena J.] Henry Ford Hlth, Detroit, MI USA. [Bhan, Irun; Furtado, Felipe; Catalano, Onofrio; Przybyszewski, Eric] Massachusetts Gen Hosp, Boston, MA USA. [Bhan, Irun] Harvard Med Sch, Boston, MA USA. [Grinspan, Lauren T.; Lewis, Sara] Icahn Sch Med Mt Sinai, New York, NY USA. [Jou, Janice; Wong, Nicole] Oregon Hlth & Sci Univ, Portland, OR USA. [Zhou, Kali] Univ Southern Calif, Los Angeles, CA USA. [Jalal, Prasun; Aloor, Fuad Zain; Elkheshen, Ahmed] Baylor Coll Med, Houston, TX USA. [Roccaro, Giorgio A.; Marvil, Charles; Issac, Aaron] Emory Univ, Sch Med, Atlanta, GA USA. [Rangnekar, Amol S.; Clinton, Joseph; Woo, Stephanie M.] Medstar Georgetown Univ Hosp, Washington, DC USA. [Benhammou, Jihane N.; Lee, Edward Wolfgang; Yum, Jung] Univ Calif Los Angeles, Los Angeles, CA USA. [Diehl, Anna Mae; Hutchison, Alan; Turner, Alan] Univ Chicago, Chicago, IL USA. [Mehta, Neil] Univ Calif San Francisco, San Francisco, CA USA. [Wedd, Joel P.] Virginia Commonwealth Univ, Richmond, VA USA. [Yang, Ju Dong; Alsudaney, Manaf; Hernandez, Perla] Cedars Sinai Med Ctr, Los Angeles, CA USA. [Kim, Amy K.; Xu, Ziyi] Johns Hopkins Univ, Sch Med, Baltimore, MD USA. [Duarte-Rojo, Andres] Northwestern Univ, Feinberg Sch, Chicago, IL USA. [Oloruntoba, Omobonike] Duke Univ, Durham, NC USA. [Tevar, Amit D.] Univ Pittsburgh, Pittsburgh, PA USA. [Au, Jennifer S.] Scripps Clin, La Jolla, CA USA. [Blain, Yamile] Univ Miami, Miami, FL USA. [Rao, Sanjana] Univ Miami, Jackson Hlth Syst, Miami, FL USA. [Mendiratta-Lala, Mishal; Tapper, Elliot B.] Univ Michigan, Med Ctr, Ann Arbor, MI USA. [King, Kevin] UCLA, David Geffen Sch Med, Los Angeles, CA USA. [Sachdev, Lekha] Georgetown Univ, Washington, DC USA. [Bruno, Jill] Virginia Commonwealth Univ Hlth Syst, Richmond, VA USA. [Kamel, Ihab; Tolosa, Celestina] Johns Hopkins Univ, Baltimore, MD USA. [Badawi, Ihab] Henry Ford Hlth Syst, Detroit, MI USA. [Quirk, Lisa; Singal, Amit G.] Univ Texas Southwestern Med Ctr, Dallas, TX USA. [Nathani, Piyush] Univ Texas Southwestern, Dallas, TX USA. [Haydel, Brandy] Mt Sinai Recanati Miller Transplantat Inst, New York, NY USA. [Albertian, Robert] Univ Southern Calif, Los Angeles, CA USA. [Rieger, Erin] Columbia Univ, New York, NY USA. [Khalid, Abdullah; Barrick, Bethany] Scripps Hlth, San Diego, CA USA. [Wang, Bo; Hao, Wei] Univ Michigan, Sch Publ Hlth, Ann Arbor, MI USA. Miami; Henry Ford Health System; Harvard University; Massachusetts General Hospital; Harvard University; Harvard Medical School; Icahn School of Medicine at Mount Sinai; Oregon Health & Science University; University of Southern California; Baylor College of Medicine; Emory University; Georgetown University; University of California System; University of California Los Angeles; University of Chicago; University of California System; University of California San Francisco; Virginia Commonwealth University; Cedars Sinai Medical Center; Johns Hopkins University; Northwestern University; Feinberg School of Medicine; Duke University; Pennsylvania Commonwealth System of Higher Education (PCSHE); University of Pittsburgh; Scripps Research Institute; University of Miami; University of Miami; University of Michigan System; University of Michigan; University of California System; University of California Los Angeles; University of California Los Angeles Medical Center; David Geffen School of Medicine at UCLA; Georgetown University; Virginia Commonwealth University; Johns

Hopkins University; Henry Ford Health System; Henry Ford Hospital; University of Texas System; University of Texas Southwestern Medical Center Dallas; University of Texas System; University of Texas Southwestern Medical Center Dallas; Icahn School of Medicine at Mount Sinai; University of Southern California; Columbia University; University of Michigan System; University of Michigan

Gastroenterology
Patel PM, **Zreik H**, **Yasin Z**, **Ramanan S**, **Hari P**, **Singh B**, **Malik D**, and **Bern M**. Rare Case of Bowel Perforation After a Dose of Paclitaxel. *Am J Gastroenterol* 2023; 118(10):S1608-S1608. Full Text

[Patel, Parth M.] Henry Ford Hlth Syst, Boston, MA USA. [Zreik, Hassan; Yasin, Zarqa; Ramanan, Sruthi; Hari, Parneet; Singh, Bipneet; Malik, Devin; Bern, Merritt] Henry Ford Hlth Syst, Jackson, MI USA.

Gastroenterology
Rehman S, **Chaudhary A**, **Samad M**, and **Jafri SM**. Cryoglobulinemia-Induced Kidney Injury Secondary to Refractory Hepatitis C. *Am J Gastroenterol* 2023; 118(10):S2326-S2326. Full Text

[Rehman, Sheema; Chaudhary, Ammad] Henry Ford Hosp, Detroit, MI 48202 USA. [Samad, Momin] Henry Ford Hosp, Rochester Hills, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Health System; Henry Ford Hospital

Gastroenterology
Rehman S, **Chaudhary A**, **Veracruz N**, **Denha E**, Gumma J, and **Jafri SM**. An Unusual Case of Clostridioides Peritonitis From Small Intestinal Source. *Am J Gastroenterol* 2023; 118(10):S2326-S2326. Full Text

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Gastroenterology
Samad M, **Chaudhary A**, **Rehman S**, **Ali SA**, and **Jafri SM**. An Assessment of IPMN Screening in Liver Transplant Recipients. *Am J Gastroenterol* 2023; 118(10):S1035-S1035. Full Text

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Gastroenterology
Samad M, and **Jafri SM**. An Evaluation of Infections and Outcomes Following Intestinal Transplantation. *Am J Gastroenterol* 2023; 118(10):S1332-S1332. Full Text

[Samad, Momin] Henry Ford Hosp, Rochester Hills, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA.

Gastroenterology
Shaikh FP, and **Jafri SM**. Noncirrhotic Causes of Portal Hypertension. *Am J Gastroenterol* 2023; 118(10):S2454-S2454. Full Text

[Shaikh, Faryal P.; Jafri, Syed-Mohammed] Henry Ford Hosp, Clinton Township, MI USA.

Gastroenterology
Singh AD, Grewal U, Moond V, **Khan MZ**, McCarty TR, Chahal P, Bazarbashi AN, and Bhatt A. High Mortality Rates Despite Younger Age Among Patients With Intrahepatic Cholangiocarcinoma & Primary Sclerosing Cholangitis. *Am J Gastroenterol* 2023; 118(10):S36-S37. Full Text

[Singh, Achintya D.] Case Western Reserve Univ, MetroHlth Med Ctr, Cleveland, OH USA. [Grewal, Udhayvyir] Univ Iowa Hosp & Clin, Iowa City, OH USA. [Moond, Vishali] St Peters Univ Hosp, New Brunswick, NJ USA. [Moond, Vishali] Univ Med & Dent New Jersey, New Brunswick, NJ USA. [Khan, Muhammad Zarrar] Henry Ford Med Ctr, Detroit, MI USA. [McCarty, Thomas R.] Houston Methodist Hosp, Houston, TX USA. [Chahal, Prabhleen] Cleveland Clin Fdn, Cleveland, OH USA. [Bazarbashi, Ahmad Najdat] Washington Univ, Sch Med St Louis, St Louis, MO USA. [Bhatt, Amit] Cleveland Clin, Cleveland, OH USA. System; Saint Peter's University Hospital; Rutgers University System; Rutgers University New Brunswick; Rutgers University Biomedical & Health Sciences; Henry Ford Health System; Houston Methodist Hospital; The Methodist Hospital - Houston; Cleveland Clinic Foundation; Saint Louis University; Washington University (WUSTL); Cleveland Clinic Foundation

Gastroenterology
Sunkara PR, and **Jafri SM**. Cryptococcus Peritonitis as a Complication of Orthotopic Hepatitis C-Positive Liver Transplantation: A Case Report. *Am J Gastroenterol* 2023; 118(10):S2355-S2355. Full Text

[Sunkara, Pranit R.] Wayne State Univ, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA.

Gastroenterology
Sunkara PR, **Suresh S**, and **Jafri SM**. Drug- Induced Liver Injury from Over-the-Counter Nutritional Supplement Complicated by Bone Marrow Failure. *Am J Gastroenterol* 2023; 118(10):S2355-S2355. Full Text

[Sunkara, Pranit R.] Wayne State Univ, Detroit, MI USA. [Suresh, Suraj; Jafri, Syed-Mohammed] Henry Ford Hosp, Detroit, MI USA.

Gastroenterology
Sunkara PR, **Weise K**, and **Jafri SM**. Acute Liver Failure Due to Discontinuation of Hepatitis B Virus (HBV) Therapy. *Am J Gastroenterol* 2023; 118(10):S2355-S2356. Full Text

[Sunkara, Pranit R.] Wayne State Univ, Detroit, MI USA. [Weise, Kelly; Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA.

Gastroenterology
Venkat D, **Zuchelli T**, **Singla S**, and **Jafri SM**. Uncommon Manifestations of Biliary Strictures. *Am J Gastroenterol* 2023; 118(10):S1565-S1565. Full Text

[Venkat, Divya] Wayne State Univ, Sch Med, West Bloomfield, MI USA. [Zuchelli, Tobias; Singla, Sumit; Jafri, Syed-Mohammed] Henry Ford Hosp, Detroit, MI 48202 USA.

Gastroenterology
Visser J, **Suresh S**, **Varma A**, and **Jafri SM**. Management of Gastrointestinal Spirochetosis. *Am J Gastroenterol* 2023; 118(10):S2609-S2609. Full Text

[Visser, Jack] Henry Ford Hosp, Detroit, MI USA. [Suresh, Suraj] Henry Ford Hlth, Northville, MI USA. [Varma, Adarsh; Jafri, Syed-Mohammed] Henry Ford Hlth, Detroit, MI USA. Henry Ford Health System

Gastroenterology
White C, **Varma A**, and **Jafri SM**. Intestinal Metaplasia Advancing to Gastric Adenocarcinoma Following Cardiac Transplantation. *Am J Gastroenterol* 2023; 118(10):S2640-S2640. Full Text

[White, Ciara; Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. [Varma, Adarsh] Henry Ford Hlth, Detroit, MI USA.

Gastroenterology
Yasin Z, **Patel PM**, **Zreik H**, **Hari P**, **Singh B**, and **Alsheik E**. A Rare Case of Colonic Squamous Cell Carcinoma Metastasis Originating From Adenosquamous Cell Carcinoma of the Lung. *Am J Gastroenterol* 2023; 118(10):S1624-S1624. Full Text

[Yasin, Zarqa; Singh, Bipneet] Henry Ford Hlth, Jackson, MI USA. [Patel, Parth M.] Henry Ford Hlth Syst, Boston, MA USA. [Zreik, Hassan; Hari, Parneet] Henry Ford Hlth Syst, Jackson, MI USA. [Alsheik, Eva] Henry Ford Hlth Syst, Detroit, MI USA. System; Henry Ford Health System; Henry Ford Hospital

Gastroenterology
Younossi ZM, Yilmaz Y, Fan JG, Zheng MH, Alswat KA, Alqahtani SA, El-Kassas M, Castera L, Funuyet-Salas J, Romero-Gómez M, Wong VWS, Zelber-Sagi S, Treeprasertsuk S, Allen AM, Takahashi H, Kawaguchi T, Francque S, Fernandez MIC, Duseja AK, Schattenberg JM, Burra P, Carrieri MP, Arrese M, Rinella M, Singal AK, **Gordon SC**, Fuchs M, Eskridge W, Alkhouri N, Cusi K, Loomba R, Ranagan J, Kautz A, Ong J, Kugelmas M, Eguchi Y, Diago M, Newsome PN, Yu ML, Gerber L, Lam BP, Fornaresio L, Nader F, Henry L, Racila A, Golabi P, Stepanova M, and Lazarus JV. STIGMA IS A PREDICTOR OF IMPAIRMENT OF HEALTH RELATED QUALITY OF LIFE AMONG PATIENTS WITH NAFLD. *Hepatology* 2023; 78:S1768-S1774. Full Text

Z.M. Younossi, Inova Medicine, Inova Health System, Falls Church, VA, United States

Background: Stigma can be associated with impairment of patients' quality-of-life. Aim: Evaluate the association between stigma and HRQL among NAFLD patients. Methods: NAFLD patients were invited to complete the Chronic Liver Disease Questionnaire- NAFLD (CLDQ-NASH; 36 items, 6 domains, range 1-7, higher scores =better HRQL) and a stigma survey about history of stigmatization or discrimination due to chronic conditions, various aspects of disease burden [Liver Disease Burden (LDB) instrument; 35 items, 7 domains including Stigma, range 1-4, higher scores = greater disease burden], and perception of various diagnostic terms. Results: The CLDQ-NASH and the stigma surveys were completed by 377 NAFLD patients (9% <35 years, 52% male, 47% with ≥ 2 chronic comorbidities, 45% type 2 diabetes, 20% severe fibrosis or cirrhosis) from 12 countries (47% USA). Of included patients, 15% reported having experienced stigma or discrimination (at least sometimes) due to their liver disease (NAFLD) and 42% due to being overweight/ obese. In addition, 26%, 35%, 23%, 25% reported feeling uncomfortable with the diagnostic terms NAFLD , fatty liver , NASH and MAFLD , respectively. All aspects of NAFLD stigma (self-reported history of stigmatization due to the liver disease of NAFLD and having LDB Stigma score in top quartile) were associated with lower HRQL scores in all domains ($p \leq 0.01$) (Figure). In multivariate analysis adjusted for country of enrollment, history of stigmatization or discrimination due to the liver disease of NAFLD was the strongest independent predictor of lower HRQL scores in all domains (beta -0.63 to -0.92, $p < 0.001$) while history of stigmatization due to being overweight/ obese was associated with lower Activity domain (beta =-0.36, $p = 0.01$). Negative perception of the diagnostic terms NAFLD or NASH was not associated with HRQL scores (all $p > 0.05$) while that of fatty liver or MAFLD was associated with impairment in Emotional, Fatigue, and Worry domains of CLDQNASH ($p < 0.01$). Other predictors of lower HRQL scores included female sex, lack of college education, having ≥ 2 chronic comorbidities, history of weight loss due to medical reasons, and having severe fibrosis or cirrhosis ($p < 0.05$). Conclusion: In this survey, 15% of NAFLD patients reported having experienced stigma or discrimination due to their liver disease and this was an independent predictor of impaired HRQL. Efforts should be made to better understand and reduce the sources of stigmatization or discrimination in patients with NAFLD.

Gastroenterology
Youssef RM, **Obri M**, **Todter E**, **Salgia RJ**, and **Jesse M**. PSYCHOSOCIAL AND MEDICAL FACTORS ASSOCIATED WITH RECEIPT OF LIVER TRANSPLANT IN LISTED PATIENT WITH HEPATOCELLULAR CARCINOMA. *Hepatology* 2023; 78:S285. Full Text

R.M. Youssef, Henry Ford Health, United States

Background: Patients with hepatocellular carcinoma (HCC) are less likely to receive liver transplantation (LT) than patients without HCC. The aim of this study was to explore sociodemographic, psychosocial, and medical factors associated with progression to LT, versus delisting, in patients with HCC listed for LT. Methods: Prospectively maintained database from a single center tracking all patients diagnosed with HCC from 2005-2022. Amongst those listed for LT, the main outcome was receipt of transplant (versus delisting for any reason). Predictors included sociodemographic, psychosocial, and medical characteristics. Given the exploratory nature, predictors were included in the final multivariable logistic model if univariable logistic regression results approached significant ($p < 0.1$). Results: Among 341 patients listed with HCC; mean age 59.6 years (SD 6.8); 265 male (77.7%); racial composition was 246 White (72.1%), 50 Black (14.7%), and 45 “other” (13.2%). 261 (76.5%) underwent LT, 80 (23.5%) were delisted (any reason, majority due to disease progression/ medical deterioration). Variables included in the model were age at transplant listing, marital status, whether the patient underwent treatment for HCC, and histories of tobacco use, alcohol abuse, hepatic encephalopathy, diabetes, hypertension, and dyslipidemia. Final model presented in Table 1. Significant predictors of receipt of LT in the final model included younger age at transplant listing, no history of tobacco use, and no history of alcohol abuse. Conclusion: HCC patients are often delisted due to HCC disease progression and/or death while on the LT waitlist. Our data suggests that patients who are listed at a younger age, do not have a history of tobacco use, or of alcohol abuse are more likely to successfully receive LT. Also, contrary to hypotheses, race/ethnicity was not significant suggesting improved equity across these groups. (Table Presented).

Gastroenterology

Zreik H, **Hari P**, **Yasin Z**, **Patel PM**, **Singh B**, and **Bern M**. Rare Case of Intussusception in Adults: COVID-19 Induced Mesenteric Adenitis. *Am J Gastroenterol* 2023; 118(10):S1658-S1658. Full Text

[Zreik, Hassan; Hari, Parneet; Yasin, Zarqa; Patel, Parth M.; Singh, Bipneet; Bern, Merritt] Henry Ford Hlth Syst, Jackson, MI USA.

Hematology-Oncology

Abushukair H, Logothetis C, **Abu Rous F**, Saeed A, Aranha O, and Khushman M. THE ASSOCIATION BETWEEN MESOTHELIAL MEMBRANES METASTASIS AND RESPONSE TO IMMUNE CHECKPOINT INHIBITORS IN SOLID TUMORS. *J Immunother Cancer* 2023; 11:A590. Full Text

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Background Specific anatomic sites of metastasis (mets) such as liver and brain have been associated with poor response to immune checkpoint inhibitors (ICIs). The association between mesothelial membranes (MMs) mets and response to ICIs in solid tumors has not been established. Herein, we explored the association between MMs mets and response to ICIs. Methods A cohort of 1661 patients from the MSK's Tumor Mutational Burden (TMB) immunotherapy study was reviewed through cBioCancer Genomics Portal. Patients with identified sites of mets (N=901) were categorized according to the site of mets into Lung, Liver, Central Nervous System (CNS), Bone and MMs. Patients with mets to lymph nodes and other less common (N<50) sites were excluded from our analysis. The log rank test was used to compare Kaplan-Meier survival curves. Results Among the 901 patients with known site of mets, liver, lung, CNS, bone and MMs mets were reported in 139 (15.4%), 138 (15.3%), 64 (7.1%), 64 (7.1%) and 50 (5.5%) patients respectively. Other patterns of mets were reported in 446 (49.5%) patient. MMs mets to the pleura, peritoneum and pericardium were reported in 31, 18 and 1 patient respectively. The median overall survival (mOS) in patients with liver, lung, CNS, bone and MMs mets is 10, 29 , 24, 14 and 9 months (m) respectively. The mOS in patients with liver mets was worse than patients without liver mets (10 vs 24 m, $p < 0.001$). There was a trend for worse mOS in patients with MMs mets compared to patients with liver mets (9 vs 10 m, p=0.671). There was a trend for worse mOS in patients with MMs mets compared to patients without MMs mets (9 vs 16 m, p=0.148). The mOS in patients with MMs mets was worse compared to patients without MMs or liver mets (9 vs 25 m, p=0.018). This difference remained significant after adjusting for age and the ICI regimen type (anti- PD-(L)1, anti-CTLA-4, combination). The mOS in patients with pleural and peritoneal mets was 9 and 10 m respectively (p=0.76). Conclusions The association between liver mets and worse OS was reproduced in our analysis. A trend for worse OS was noticeable in patients MMs mets compared to patients with liver mets and to

patients with no MMs mets. Compared to patients without liver metastasis and no MMs metastases, patients with MMs metastases had worse OS. There was no statistical difference between peritoneal or pleural mets.

Hematology-Oncology
Al-Saheli Z, and **Donthireddy V**. Implementing Quality Improvement to Morbidity and Mortality Conferences: Focusing on Action Plans By Closing the Loops with Timely Follow Ups. *Blood* 2023; 142:4. Full Text

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Hematology-Oncology
Albusoul L, **Shahid M**, Vuyyala S, Otrock ZK, and **Kuriakose P**. Trend in Von Willebrand Factor Profile in Women With Von Willebrand Disease During Pregnancy and Postpartum. *Blood* 2023; 142:5499. Full Text

Introduction: Pregnancy is considered a hypercoagulable state, with levels of multiple coagulation factors including Factor VIII (FVIII) and von Willebrand Factor (VWF), progressively increasing throughout, reaching their peak levels during the third trimester. However, in women with von Willebrand disease (VWD), these changes are variable and could be blunted or absent due to the wide heterogeneity of phenotypes and pathophysiological mechanisms linked to this disorder, posing a significant clinical challenge. This study aims to describe the trend in the VWF profile in women with VWD during each trimester of pregnancy and in the postpartum period. Methods: This is a retrospective single-center study that included adult pregnant women diagnosed with VWD, who were followed at Henry Ford Health between 03/2012 and 11/2022. Patients with other bleeding disorders were excluded from the study. Data on baseline characteristics, including age, race, age at childbirth, and parity were collected. Additional data collected included VWF antigen (VWF:Ag) level, FVIII activity level, and VWF ristocetin cofactor (VWF:Rco) activity during the first, second, and third trimesters, as well as in the postpartum period. Results: A total of 33 cases were included in our study. At baseline, the mean VWF:Ag level in our patients was 50.5% (reference range 50%-150%). Compared to baseline, the VWF:Ag level increased by 48.71% in the first trimester, 80.59% in the second trimester, and 168.71% in the third trimester. Postpartum, the VWF:Ag level decreased by 51.29% compared to the third trimester; however, it remained 30.89% higher than baseline levels. While the FVIII level (reference range 50%-150%) was an average of 64.8% at baseline, it increased by 21.91% in the first trimester, 74.23% in the second trimester, and 143.67% in the third trimester, compared to baseline. Postpartum, the FVIII level decreased by 48.45% from the third trimester but remained 25.62% higher than baseline. Additionally, the VWF:Rco level was an average of 44.3% (reference range 51%-215%) at baseline. Compared to baseline, the VWF:Rco level increased by 61.85% in the first trimester, 90.52% in the second trimester, and 142.66% in the third trimester. It decreased by 49.12% postpartum compared to the third trimester but remained 23.48% higher than baseline. Conclusion: In women with VWD, VWF:Ag level, FVIII level, and VWF:Rco levels steadily increase during pregnancy, reaching their maximum levels during the third trimester. All three levels decreased in the postpartum period; however, they remain higher compared to baseline at a median follow up of 105 days after delivery.

Hematology-Oncology
Alshurafa A, Alhushki S, Alfaqheri D, Abushukair H, Alzghoul BN, and **Abu Rous F**. The Polymerase Epsilon Gene Expression and Mutation Predictive Significance in Patients Receiving Immune Checkpoint Inhibitors (icis) for Non-small Cell Lung Cancer (NSCLS). *Am J Respir Crit Care Med* 2024; 209. Full Text

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Rationale The DNA polymerase epsilon enzyme encoded by the POLE (polymerase epsilon) gene has drawn much interest as a potential biomarker for immunotherapy response. In this study, we used multi-omics analysis to assess the predictive and prognostic utility of POLE mutation in (NSCLC) patients treated with (ICIs). Methods Our study utilized The Cancer Genomic Atlas (TCGA) pan-cancer lung

adenocarcinoma (LUAD, n=566), squamous cell carcinoma (LUSC, n=487), and (MSK) Immunotherapy NSCLC (n=350) in our analysis. Clinical and genomic data were obtained through cBioportal. Using bulk tissue RNAseq, immune cell infiltration was assessed using the web-based TIMER2.0 tool. To further understand the synergy between POLE gene expression and immune cell infiltration, we conducted a subgroup analysis by different levels of POLE gene expression and different levels of immune cell infiltration using Cox proportional hazard model with correction for age, stage, gender, and race. Results POLE mutation frequencies in the combined LUAD and LUSC group were 5.1% and 5.4%, respectively. In the LUAD cohort, POLE mutations were significantly associated with poor overall survival outcomes (median: 30.54 vs. 49.84 months; Log-rank p=0.0269) as compared to POLE wild-type. Notably, POLE mutations were associated with better overall survival than POLE wild-type in patients receiving ICI for NSCLC (median: NA vs. 11.00; p=0.0365). Furthermore, in the NSCLC cohort, the tumor mutation burden was significantly higher in the POLE mutant group as compared to the wild-type (median: 19.89 vs 6.85; p<0.001). In addition, POLE mutations in LUAD were significantly (p<0.05) associated with increased infiltration of CD8+ T-cells and lower levels of macrophage M2 and cancer-associated fibroblasts infiltration. After adjusting for age, stage gender, and race, patients with high POLE gene expression experienced significant better overall survival benefit with high CD8+ T-cell infiltration compared to those with low CD8+ T-cell infiltration. Furthermore, in patients with high CD8+ T-cell infiltration, there was a trend for enhanced overall survival benefit in patients with high POLE gene expression compared to those with low gene expression. Conclusion Our analysis revealed a positive predictive value of POLE mutations in NSCLC patients receiving Immune checkpoint Inhibitors, and a negative prognostic effect in LUAD non-ICI-treated patients. Furthermore, our exploratory work highlights a potential synergistic effect between POLE expression and CD8+ Tcell infiltration. Further investigations are required to offer mechanistic insights into the impact of POLE mutations and expression.

Hematology-Oncology

Azmi AS, Uddin MH, Bannoura SF, Khan HM, **Diab M**, Kim S, Beal E, Tobon M, Chen H, **Beydoun R**, Dyson G, Mohammad RM, **Philip PA**, Al-Hallak MN, El-Rayes BF, and Pasche B. Nuclear exporter protein exportin 1 (XPO1) as a novel therapeutic target in pancreatic neuroendocrine tumors. 2024; 35((Azmi A.S.; Uddin M.H.; Bannoura S.F.; Khan H.M.; Kim S.; Beal E.; Tobon M.; Beydoun R.; Dyson G.; Mohammad R.M.; Al-Hallak M.N.; Pasche B.) Oncology, Wayne State University School of Medicine; Barbara Ann Karmanos Cancer Institute, Detroit, MI, United States):S97. Full Text

Background: Advanced pancreatic neuroendocrine tumors (pNETs) show minimal response to FDA approved therapies suggesting an urgent need for the identification of novel and effective therapeutic targets. Aberrant nuclear protein transport to the cytoplasm, often observed in cancer, causes mislocalization dependent inactivation of critical cellular proteins. The major nuclear exporter exportin-1 (XPO1) has been linked to cancer therapy resistance. Nevertheless, the role of XPO1 in pNET has not been explored. Major pNET growth regulators such as MEN1, DAXX and mTOR are recognized cargo proteins of XPO1 and thus their nucleo-cytoplasmic transport is regulated by XPO1. Here we explored the role of XPO1 in pNET subsistence and therapy resistance. Methods: We performed immunohistochemistry (IHC) analysis for XPO1 on 145 low grade pNET tumors, 35 normal and established cell lines. The impact of XPO1 inhibitor selinexor and analogs was evaluated in pNET 2D and 3D cultures, xenograft and primary explant cultures. Results: IHC on TMAs confirmed XPO1 over-expression in pNET tumor tissue. FDA approved and investigational XPO1 inhibitors selinexor and eltanexor suppressed BON-1 and QGP-1 pNET cell line growth at pharmacologically relevant concentrations. Selinexor synergized with everolimus and sunitinib leading to superior pNET cell death (CI<1). Immunofluorescence analysis showed nuclear retention of mTOR and MEN1 as well as perinuclear accumulation of DAXX in BON-1 pNET cell line. Selinexor suppressed phosphorylation of mTOR and its downstream targets P70S6K and RICTOR. We observed significant inhibition of MEN1 targets including suppression of FANCD2 and SMAD3 and activation of p53. Selinexor given at sub-optimal dose of 15 mg/kg twice a week for three weeks suppressed the growth of BON-1 and QGP-1 tumors. An examination of residual tumors showed reduction in mTOR downstream target pS6 and reduced nuclear expression of pAKT. Six day treatment with 300 nM selinexor demonstrated marked reduction in proliferation marker ki67 and nuclear retention of well recognized XPO1 cargo FOXO3a in the explant culture tissue. Conclusions: Our results indicate that XPO1 could be a novel therapeutic target

that warrants further clinical investigations in pNETs. Legal entity responsible for the study: The authors. Funding: National Cancer Institute. Disclosure: All authors have declared no conflicts of interest.

Hematology-Oncology
Bugazia S, **Gandhi N**, **Weerakoon N**, and **Kukreja G**. First Report of Asymptomatic Solitary High-Grade B-Cell Lymphoma NOS: An Enigmatic Entity. *Blood* 2023; 142:6253. Full Text

Background High-grade B cell lymphoma (HGBL) is a new disease entity introduced by WHO in 2016, including two types: HGBL with a double hit (DH) or triple hit (TH) and HGBL, not otherwise specified (NOS). HGBL DH/TH are defined by genetic rearrangements of specific oncogenes MYC, BCL2 and/or BCL6, while HGBL NOS is defined purely base on morphology in the absence of these genes. HGBL DH/TH is known for its poor prognostication given its propensity to rapidly progress and disseminate, however HGBL NOS remains ill-defined and poorly understood with no tangible literature describing its clinical nature and therapeutic susceptibility. Case presentation A 76-year-old post-menopausal woman with no significant PMH presented for evaluation of painless hematuria during a routine office visit. Evaluation with imaging showed a suspicious incidental liver mass concerning for possible metastatic or primary liver cancer. Obtained labs were unremarkable, including serum LDH, serological testing for hepatitis B/C and HIV1/2, and typical tumor markers. PET scan showed focal uptake of tracer in liver with no nodal involvement. Liver biopsy revealed diffuse infiltration by atypical lymphocytes. Immunohistochemical analysis showed CD20 and CD10 positivity, negative CD30, and high Ki-67 proliferation rate of 100%, however the absence of MYC, BCL6, BCL2, and t(8;14) rearrangements on FISH ruled out Burkitt and DH/TH lymphoma, consistent with HGBL-NOS. Following discussions with Henry Ford Lymphoma Tumor Board, patient was treated with six cycles of R-CHOP, where follow-up imaging indicated remission of her lymphoma. Conclusion This represents an extraordinary first report of HGBL NOS manifesting as an isolated primary hepatic lymphoma in the complete absence of clinical symptoms. The significance of this case lies in its atypical extra-nodal site of involvement and total absence of clinical symptoms and serological markers, underscoring the unfulfilled need to further describe this enigmatic entity.

Hematology-Oncology
Dziadziuszko R, Barlesi F, Kim JE, **Gadgeel SM**, Krzakowski M, Jeong JH, Daniele G, Chen D, Hu Y, Wilson TR, Simmons BP, and Thomas DM. Atezolizumab in patients (pts) with tumor mutational burden (TMB)–high tumors from the TAPISTRY trial. *J Clin Oncol* 2024; 42:LBA2509-LBA2509. Full Text

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Hematology-Oncology
Hermans C, Escobar M, Abajas Y, Acharya S, Alvarez-Román M, Batsuli G, Dargaud Y, Janbain M, **Kuriakose P**, Mahlangu J, Mancuso M, Miesbach W, Yuan S, Mitchell I, and Carcao M. Efficacy and Safety of Eptacog Beta (Recombinant Activated FVII) in Patients with Hemophilia A or B with Inhibitors According to Time to Initial Infusion: A Post-Hoc Analysis from PERSEPT-1. *Res Pract Thromb Haemost* 2023; 7. Full Text

Background: Early resolution of bleeding episodes (BEs) may reduce BE-related complications for patients with hemophilia A/B with inhibitors (PwHABI), including pain, musculoskeletal complications, absenteeism from work/school and hospitalization. The impact of time to initial dose of rFVIIa on bleed resolution is poorly understood/documented. Aims:We evaluated the impact of time to initial infusion and dosing regimen on bleed resolution and safety of eptacog beta. Methods: PERSEPT-1 was a Phase 3 trial of eptacog beta for the treatment of BEs in PwHABI (NCT02020369). Patients received an initial eptacog beta dose regimen (IDR) of either 75 or 225 μg/kg, followed by 75 μg/kg at predefined intervals over 24 hours until hemostasis was achieved. Primary endpoint was the proportion of successfully treated BEs (i.e. 'good'/ 'excellent' response) 12 hours after initial infusion. Safety assessments included physical examination, laboratory and immunogenicity testing, and assessment of adverse events (AEs). This post-hoc analysis evaluated the efficacy and safety of eptacog beta according to time between start of bleed and first infusion (<30 (N = 228), 30–60 (N = 105) and ≥60 (N = 73) min). Results: Across 468 BEs treated, the overall success proportion for the primary endpoint was 85.3% (95% CI 77.0–93.5) with 81.0% (70.9–91.0) and 90.3% (82.9–97.7) in the 75 and 225 μg/kg IDRs, respectively. Initial infusion at < 30 min was associated with numerically higher success proportion for both IDRs, compared with an initial infusion at 30–60 and ≥60 min; but the differences did not reach statistical significance. No significant differences were found when comparing both IDRs (Figure 1). Seven treatment-related AEs occurred in 2 patients, independently of the time between bleed start and first infusion. There were no thromboembolic events, hypersensitivity reactions, or deaths (Table 1). No neutralizing antibodies to eptacog beta were detected. Conclusion(s): Eptacog beta resulted in successful resolution of BEs with both IDRs with no difference in safety, regardless of the time to initial infusion. [Figure presented] [Table presented]

Hematology-Oncology

Hinojosa O, **Ammari O**, **Albusoul L**, **Kuriakose P**, and Otrock ZK. Post-Transfusion Purpura: A Literature Review. *Blood* 2023; 142:1294. Full Text

Introduction: Post-transfusion purpura (PTP) is a rare and occasionally life-threatening transfusion reaction characterized by severe thrombocytopenia usually within two weeks of blood transfusion. It is associated with the development of alloantibodies to human platelet antigens (HPAs). Due to its rarity, our knowledge of PTP is mostly based on reported cases or small cohorts. Methods: This is a systematic literature review of English language articles published in 2 large medical databases (Embase and Pubmed) using the search terms "post-transfusion purpura", "posttransfusion purpura", and "post transfusion purpura" between the years 1985 and 2023. Only articles reporting on patients older than 18 years were included. 684 articles were identified, 590 of them were excluded since they represented a combination of case reports of other conditions, laboratory, and epidemiological reports. The 94 articles left, represented case reports and case series of PTP encompassing 149 patients. 21 patients were removed since they represented duplicate cases. 17 patients were excluded due to missing information. 11 patients were excluded due to the presence of confounding clinical conditions. Results: A total of 100 cases were included in the study. The mean age was 56.7 years. 85% were female, 14% were male, and 1 was missing gender data. 62% of cases reported a baseline platelet count, ranging between 78,000 - 600,000 cells/μL. 65% of cases presented after a procedure- or surgery-related transfusion, of these 22 were related to cardiovascular procedures, while 16, 10, and 9 cases were related to gynecological, abdominal, and orthopedic surgeries respectively. A history of prior transfusions was only documented in 24% of cases. A prior pregnancy was reported in 63% of the cases. Red blood cell, fresh frozen plasma, and platelet transfusions were associated to 64%, 11%, and 9% of cases, respectively. The most common HPA antibody detected was HPA-1a (81%). HPA-1b, HPA-5b, and HPA-3a were the next most common antibodies, identified in 7%, 5%, and 5% cases, respectively. The median time from the first transfusion to the development of thrombocytopenia was 8 days, reaching a platelet nadir in 9 days. The platelet nadir ranged between 0 - 50,000 cells/ μL. Clinical presentation included post-transfusion fever (15%), petechial rash, epistaxis, and oral bleeding (65%, 17%, and 12, respectively), and bleeding from the genitourinary system, gastrointestinal tract, surgical incisions, lower respiratory tract, and central nervous system (38%, 28%, 6%, 6%, and 2% of cases, respectively). Death was reported in 9% of cases. The median time from PTP diagnosis to initiation of first treatment was 1 day. 83% of cases achieved an adequate response, defined as a platelet count > 100,000 cells/μL, after a mean/median time of 14.2/11.5 days (available in 68% of cases). Corticosteroids, intravenous immunoglobulin, and plasmapheresis were

administered in 68%, 63%, and 27%, of cases, respectively. 6 patients received HPA 1a negative platelet transfusions. Conclusions: The majority of reported PTP cases were females with a history of pregnancy or blood transfusions consistent with existing literature. Over 60% of cases were linked to a surgical procedure, with cardiovascular cases constituting the largest portion. Anti-HPA-1a represented the most commonly detected antibody, followed by HPA-1b, HPA-5b, and HPA-3a. The most common sites of bleeding were the gastrointestinal and genitourinary tracts. 9% died from PTP. The majority of patients (83%) achieved an adequate response, with the most common treatment modalities being corticosteroids, IV immunoglobulins, and plasmapheresis.

Hematology-Oncology

Jacob B, **Jamil M**, **Raslan S**, **Nasser Z**, **Springer K**, **Michael German A**, and **Kuriakose P**. Infusion Reactions with Alternative Therapies during the National Shortage of Iron Dextran. *Blood* 2023; 142:7338. Full Text

Introduction The national shortage of intravenous iron dextran has required patients to receive more alternative iron infusions, such as iron sucrose and sodium ferric gluconate/sucrose, since January 2023. While prior studies have evaluated rates of infusion reactions among some commonly used intravenous iron formulations, data is lacking among differing doses of iron formulations and especially in the setting of this iron dextran shortage. Clinicians at our institution generally observed more adverse reactions with alternative iron infusions during the national shortage of iron dextran compared to prior. Our study examines the infusion reactions of various iron therapies at differing doses and actions providers and patients took thereafter to assess the impact of the iron dextran national shortage on patients. Methods Patients were included who received iron infusions in three Henry Ford Hospital clinics in metropolitan Detroit, Michigan, from July 2022-June 2023 with the national iron dextran shortage impacting the health system since January 2023. Age, race, sex, reason for iron infusion, iron infusion formulation received, time of infusion, and dosing schedule of infusion were recorded for all participants. We assessed the symptoms experienced and actions taken for patients who had an infusion reaction. The number and type of infusion reactions between different iron infusion formulations and doses were then compared. Results Of the 880 unique patients assessed, 496 (56.4%) received iron dextran, iron sucrose, or sodium ferric gluconate/sucrose between July 2022 and December 2022 prior to the national iron dextran shortage and 384 (43.6%) patients had iron infusions between January 2023 and June 2023 during the shortage. Iron dextran accounted for most of the infusions (n= 356, 71.8%) prior to the shortage whereas iron sucrose was the majority (n=312, 81.3%) during the shortage. Prior to the national shortage, 30 iron infusions reactions occurred, with 18 (60%) associated with iron dextran, 9 (30%) with iron sucrose, and 3 (16.7%) with sodium ferric gluconate/sucrose. During the shortage, 44 reactions occurred, with 1 (2.27%) associated with iron dextran, 41 (93.1%) with iron sucrose, and 2 (4.54%) with sodium ferric gluconate/sucrose. The most reactions (n=41, 55.4%) occurred with iron sucrose at a dose of 500mg across the whole study period. Less reactions (n=9, 12.2%) were reported for iron sucrose at progressively lower doses, comparable to reactions with iron dextran at doses greater than 1000mg (n=8, 10.8%) and at lower doses of iron dextran (n=10, 13.5%). The most common reaction across all infusion types was nausea, vomiting, and/or diarrhea. After an iron infusion reaction, the infusion plan was then most commonly discontinued, with patients either switching to alternative iron infusion formulations, continuing the same infusion type with medications for symptoms, or continuing the same infusion type with lower dose and increased frequency. Conclusion More iron infusion reactions occurred after the national shortage of iron dextran since January 2023 in the setting of more frequent use of alternative iron therapies. The most common infusion formulation associated with a reaction was iron sucrose at its higher recommended dose of 500mg, compared with iron dextran and sodium ferric gluconate/sucrose. Providers should be aware of these associated adverse reactions with the different doses of alternative formulations when recommending infusions for patients, and the need for preemptive intervention.

Hematology-Oncology

Jamali T, **Pimentel J**, **Perry K**, Tocco J, **Tejwani S**, **Mayerhoff R**, and **Pompa R**. First Reported Case of Endoscopic En Bloc Resection of Esophageal Liposarcoma. *Am J Gastroenterol* 2023; 118(10):S2186-S2187. Full Text

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Hematology-Oncology
Jamil M, **Nasser Z**, **Jacob B**, **Mangal R**, and **Donthireddy V**. Efficacy of Direct Oral Anticoagulants Vs Warfarin Vs Low Molecular Weight Heparin in the Treatment of Acute Splanchnic Vein Thrombosis in Patients with Underlying Myeloproliferative Disorder. *Blood* 2023; 142:5533. Full Text

Introduction: Myeloproliferative neoplasms (MPNs) are hematopoietic stem cell disorders characterized by clonal proliferation of myeloid-lineage cells. Venous thrombosis poses a significant morbidity risk for MPN patients. The current recommended treatments for acute splanchnic vein thrombosis (SVT) are warfarin and low molecular weight heparin (LMWH). Direct oral anticoagulants (DOACs) are potential alternatives due to their predictable dose response and oral administration, but limited data exists for their use in acute SVTs. This retrospective study aims to assess the efficacy and outcomes of DOACs, LMWH, and warfarin in treating acute SVTs in patients with underlying MPN. Methods: We included patients of all ages with underlying myeloproliferative neoplasms and splanchnic vein thrombosis, with no underlying liver diseases, from Henry Ford Hospital Clinics in metropolitan Detroit, Michigan between 2013 and 2023. Patient data, which included age, gender, race, and BMI were recorded. The primary outcome was complete radiographic resolution (CRR) of the SVT, and secondary outcomes included recanalization, thrombosis progression, recurrent thrombosis, major bleeding, thrombocytopenia, and skin necrosis. The outcomes were compared between the three anticoagulant groups and patients using aspirin. Results: Among the 34 MPN patients with SVT, warfarin was prescribed most frequently (n=19), followed by enoxaparin (n=5) and DOACs (n=5). Although no significant differences were observed, warfarin showed the highest CRR rates (41.2%), while enoxaparin and DOACs had equal CRR rates (25%). DOACs showed recanalization rates similar to warfarin and higher than enoxaparin (44.4% and 47.1% vs. 20.0%, respectively). LMWH was associated with increased recurrent thrombosis rates (50.0%), while DOACs had a higher risk of major bleeding. All three anticoagulants had similar effects on thrombocytopenia and SVT progression. Aspirin use was linked to a higher risk of major bleeding (42.9%), but not using aspirin correlated with complete SVT resolution (30.8%), SVT progression (20.8%), recurrent thrombosis (29.2%), and thrombocytopenia (28.6%). Conclusions: Although limited by a small sample size, our study found no significant differences among the three anticoagulant groups. This contributes to establishing the role of DOACs in treating SVTs in patients with underlying MPN. Further studies with larger sample sizes are needed to explore the efficacy of DOACs compared to warfarin. Additionally, investigating the potential benefits of early thrombolysis in conjunction with anticoagulation for SVT patients with underlying MPN should be pursued, as the rates of complete resolution in these patients were low.

Hematology-Oncology
Karki U, Budhathoki P, Shah A, **Ghimire B**, Poudel SK, and Chisti MMM. Epidemiology and Survival Outcomes in Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN): A US Population-Based Study. *Blood* 2023; 142:3. Full Text

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Hematology-Oncology
Kulkarni R, **Hinojosa O**, and **Donthireddy V**. Real World Analysis of G6PD Testing Prior to the Use of Rasburicase in Hematologic Malignancies; A Single Center Experience. *Blood* 2023; 142:3. Full Text

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Hematology-Oncology
Patel PM, **Zreik H**, **Yasin Z**, **Ramanan S**, **Hari P**, **Singh B**, **Malik D**, and **Bern M**. Rare Case of Bowel Perforation After a Dose of Paclitaxel. *Am J Gastroenterol* 2023; 118(10):S1608-S1608. Full Text

[Patel, Parth M.] Henry Ford Hlth Syst, Boston, MA USA. [Zreik, Hassan; Yasin, Zarqa; Ramanan, Sruthi; Hari, Parneet; Singh, Bipneet; Malik, Devin; Bern, Merritt] Henry Ford Hlth Syst, Jackson, MI USA.

Hematology-Oncology
Pichardo R, **Ramo A**, Abu Omar Y, and **Dabak VS**. Factors Associated with in-Hospital Mortality in Patients with Burkitt Lymphoma - Analysis of the National Inpatient Sample (NIS). *Blood* 2023; 142:6291. Full Text

Introduction Burkitt Lymphoma (BL) is a highly aggressive B-cell non-Hodgkin Lymphoma, characterized by translocation and dysregulation of the MYC gene. BL comes in three distinct forms: endemic, sporadic, and immunodeficiency-related. BL has become a highly curable disease after the development of intense chemo-immunotherapy regimens, but given the low incidence of the disease, nationally representative studies on outcomes are scarce. We aim to highlight the most recent population-based factors associated with inpatient mortality and morbidity in patients with Burkitt's lymphoma. Methods The National Inpatient Sample database was queried from October 2015 to December 2020. Adults aged >= 18 with a primary diagnosis of BL were identified and stratified into those with and without the outcome of mortality. Complications included were queried using ICD codes most commonly found in the secondary diagnosis variables. Baseline characteristics, inpatient complications, and outcomes were compared using chi-squared and Wilcoxon rank-sum tests. Logistic regression analysis was performed to assess the risk of death before and after adjusting for multiple risk factors. Results We found 3,650 admissions with a primary diagnosis of BL, of which 320 (8.8%) patients died during the hospitalization. Patients who died had higher Charlson Comorbidity Index (CCI) >=3 (69%), tumor lysis syndrome (TLS) (41%), Sepsis (39%), and acute hypoxic respiratory failure (AHRF) (33%). No significant differences were found according to income, hospital bed-size or geographical region. In univariable analysis patients who died tended to be older with age >= 65 years (OR 2.55 (1.23 to 5.26) p=0.039), however, once adjusting for other variables there was no significant difference in mortality by age group, race, or gender. Multivariable analysis identified 3 factors with high association with mortality: acute renal failure (OR 3.07 (1.63 to 5.76), p<0.001), sepsis (OR 7.96 (3.85 to 16.4), p<0.001), and acute hypoxic respiratory failure (OR 2.70 (1.23 to 5.92), p=0.013). Conclusion BL remains a highly aggressive but potentially curable disease in patients able to tolerate intensive chemo-immunotherapy regimens. Our study highlights multiple factors that are independently associated with death include acute renal failure, sepsis, and acute hypoxic respiratory failure. Close monitoring should be placed on patients with the above complications to improve survival.

Hematology-Oncology
Pichardo R, **Ramo A**, Abu Omar Y, and **Dabak VS**. Prognostic Factors in Hospitalized Patients with HIV-Associated Burkitt's Lymphoma - Real World Data Analysis. *Blood* 2023; 142:7355. Full Text

Introduction Burkitt Lymphoma (BL) is a highly aggressive and rare B-cell non-Hodgkin Lymphoma, characterized by translocation and dysregulation of the MYC gene. BL comes in three distinct forms: endemic, sporadic, and immunodeficiency related, which is most commonly secondary to HIV. Despite improvements in antiretroviral therapy (ART), the reported incidence of BL has remained stable over time. BL is a highly curable disease in patients able to tolerate aggressive therapies. However, little is known about real-world outcomes in United States patients with HIV- related BL. Our study highlights multiple factors associated with inpatient mortality and morbidity. Methods The National Inpatient Sample database was queried from October 2015 to December 2020. Adults aged >= 18 with a primary diagnosis of BL were identified and stratified into those with and without HIV. Complications included were queried using ICD codes most found in the secondary diagnosis variables. Baseline characteristics, inpatient complications, and outcomes were compared using chi-squared and Wilcoxon rank-sum tests. Logistic regression analysis was performed to assess the risk of death before and after adjusting for multiple risk factors. Results We found 3,650 admissions with a primary diagnosis of BL, 400 (11%) of whom had HIV. Patients with HIV were younger, 49% were younger than 40 years old as compared to 29% in patients

with no HIV. There was a higher percentage of black patients 115 (29%), and most had Medicaid 170 (44%), there was no difference between income, hospital bed size or geographical region. Interestingly, in multivariable analysis, there were no significant differences in length of stay, race, or mortality between patients with and without HIV. The factors associated with mortality in HIV patients included acute renal failure OR 11.4 (1.22 to 107) and Sepsis OR 38.6 (1.62 to 921) Conclusion BL is an increasingly important disease in HIV-infected patients given that the incidence remains high despite advances in ART. This nationwide data analysis demonstrates the demographic characteristics of patients with HIV-associated BL in the US and the encouraging findings that outcomes are not significantly different between patients with and without HIV. Yet our study demonstrates the disproportionate distribution of HIV-BL in females and black patients. Further studies are needed to examine gender and racial disparities.

Hematology-Oncology

Prenen H, Lesimple T, Robert M, Machiels JP, Delafontaine BR, Tomasini P, Meniawy T, Kotecki N, Van Cutsem E, Piha-Paul SA, Schweizer MT, **Gadgeel S**, Kondo S, Ouali K, Kuboki Y, Daniel J, Ebiana V, Howe J, Spitz S, and Italiano A. A phase I study exploring the safety and tolerability of the small-molecule PD-L1 inhibitor INCB099280 in select advanced solid tumors. *Immunooncol Technol* 2023; 20. Full Text

Background: INCB099280, an oral, programmed death ligand 1 (PD-L1) inhibitor, has shown preliminary efficacy and acceptable safety in an ongoing Phase 1, open-label, multicenter study in patients (pts) with advanced solid tumors (Prenen, et al. SITC 2022). Here we present updated results. Methods: Eligible pts were ≥18 years with ECOG PS ≤1, and disease progression after available treatment (tx) or were ineligible for/without access to standard tx. In part 1, INCB099280 dose was escalated from 100 mg QD with a Bayesian optimal interval design. In part 2, 3 expansion cohorts with select tumor types were studied: 1) IO-naive pts, 2) IO-naive pts with MSI-H/dMMR tumors, 3) pts who progressed on anti-PD-1 mAb. Primary endpoints are INCB099280 safety, tolerability, and pharmacologically active/MTD determination. INCB099280 pharmacokinetics, objective response rate per RECIST v1.1, and biomarkers of pharmacologic activity were also analyzed. Results: As of June 22, 2023, 172 pts had received INCB099280 at doses from 100 mg QD to 800 mg BID (median age, 63 years [range, 21–86]; ≥2 prior lines of tx, 64.0%; prior IO, 14.5%; most common tumor types: anal [14.5%], cervical [8.7%], and colorectal [7.6%]). Dose was escalated to 800 mg BID; MTD was not reached. 5 dose levels were expanded in part 2 up to 800 mg BID. Overall, 137 pts (79.7%) discontinued treatment, 119 (69.2%) due to disease progression; 95.3% of pts had ≥1 tx-emergent adverse event (TEAE) (Table). Several responses have been observed, and updated results will be presented. In pts with complete response (n=2), baseline tumor mutational burden scores were high (34–49 mut/Mb) and ctDNA levels at cycle 4 day 1/end of tx had decreased by 92.3% from baseline. [Formula presented] Conclusions: INCB099280 was generally well tolerated at all doses tested. Updated results indicate promising antitumor activity and support future development of INCB099280 as monotherapy and in combination regimens for advanced solid tumors. Clinical trial identification: NCT04242199.

Hematology-Oncology

Ragni M, Hu B, Callis J, Manuel M, Santos J, Friedman K, Kouides P, **Kuriakose P**, Leavitt A, Lim M, Machin N, and Recht M. ATHN 11: Observational Study of Long-Term Outcomes of Liver Transplantation. *Res Pract Thromb Haemost* 2023; 7. Full Text

Background: As gene therapy (GT) is becoming a reality for hemophilia A and B (HA, HB), little is known about long-term phenotypic cures. Few data assess real-life impact of long-term GT factor correction. The analogy to liver transplantation (OLTX) is clear. As the United Network for Organ Sharing (UNOS) database lacked coding for hemophilia, we identified OLTX+ and OLTX- in ATHN-affiliated HTCs to compare post-OLTX FVIII, FIX on patient-reported outcomes (PRO) and quality of life (QoL). Aims: In the ATHN 11 multicenter observational study, Haem-A-QoL and PROMIS-29 were compared, OLTX+ vs OLTX-. Methods: Deidentified data from medical records were entered into ATHN electronic forms. OLTX- were matched to OLTX+ by age, race, HA, HB type and severity. Participants completed QoL tools. Demographic data were analyzed by descriptive statistics, and PRO and QoL were compared by OLTX status, using student's t-test and univariate regression models. Significance was set at 0.05. Results: Of 71 HA or HB patients cared for at 11 HTCs, 20 OLTX+ and 51 OLTX- were identified. There

was no difference between OLTX+ vs OLTX-, respectively, in median age, 59 vs 57 yr; race, 18(90.0%) vs 47(92.1%) Caucasian; type hemophilia 15(75.0%) vs 43(84.3%) HA; or severity, 39 (76.0%) vs 45(88.0%) with severe disease; or with target joint disease, 11 (55.0%) vs 25(49.0%). OLTX status was strongly associated with presence of a genetic mutation, $p < 0.001$, but not with three Haem-A-Qol scores (physical health, feelings, future health) or with the PROMIS score (physical function). QoL scores were most strongly correlated with history of target joint disease, followed by hemophilia severity and type, $p < 0.05$. Conclusion(s): Hemophilic target joint disease is more strongly correlated with QoL and PRO than disease severity, suggesting the irreversible impact of arthropathy on QoL and PRO. Further analysis will assess sustained factor levels and minimally important differences (MID).

Hematology-Oncology

Shastri A, Feldman EJ, Starodub AN, Feldman T, Rodriguez CP, Epstein-Peterson ZD, Stevens DA, Olszewski AJ, Huen AO, Porcu P, Reneau JC, Barta SK, Marchi E, **Mattour AH**, Pinter-Brown LC, Perea R, Donohue S, Dey J, Agarwal S, Karnik R, Gollerkeri A, Gollob J, and Smith SD. Preliminary Safety, Pharmacokinetics, Pharmacodynamics and Clinical Activity of KT-333, a Targeted Protein Degrader of STAT3, in Patients with Relapsed or Refractory Lymphomas, Large Granular Lymphocytic Leukemia, and Solid Tumors. *Blood* 2023; 142:3081. Full Text

Background: KT-333is a first-in-class, potent, highly selective, heterobifunctional small molecule degrader of the signal transducer and activator of transcription 3 (STAT3) protein. Aberrant activation of STAT3 resulting from activating mutations or deregulated cytokine signaling underlies various malignancies including peripheral T-cell lymphomas (PTCL), cutaneous T-cell lymphoma (CTCL), and large granular lymphocytic leukemia (LGL-L). Approximately 70% of human cancers including hematological malignancies and solid tumors exhibit increased levels of phosphorylated STAT3 (pSTAT3), a biomarker of pathway activation. In non-clinical studies, treatment with KT-333 resulted in durable tumor regressions with weekly (QW) or once every two weeks IV administration in STAT3-dependent T cell lymphomas. STAT3 degradation also sensitized immunocompetent mouse models of solid and liquid cancers to anti-PD1(ASH 2021, SITC 2021). Methods: The ongoing open-label, Phase 1a/1b study is evaluating the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and preliminary clinical activity of KT-333 administered as a QW IV infusion on Day 1, 8, 15 and 22 (28-day cycle) in patients (pts) with B- and T-cell lymphomas, Hodgkin's lymphoma and advanced solid tumors (ST) relapsed/refractory (R/R) to at least two prior systemic therapies and LGL-L and T-cell prolymphocytic leukemia R/R to at least one prior therapy. Cycle 1 and 2 blood samples are collected for KT-333 plasma concentrations and to measure changes in STAT3 protein expression in peripheral blood mononuclear cells (PBMCs) using targeted mass spectrometry. Whole blood RNA sequencing measures mRNA levels of STAT3 regulated targets. Plasma levels of inflammatory biomarkers are measured with Luminex. STAT3 degradation and other related biomarker changes in tumor are assessed in patients with accessible tumors. (NCT05225584). Results: As of July 10, 2023, 21 pts were treated at five dose levels (DL) in Phase 1a with a mean number of 5.8 doses. Pts included B-cell non-Hodgkin's lymphoma (n=1: DL5), Hodgkin's lymphoma (HL) (n=1: DL4), CTCL (n=3: DL1, 2 and 4), PTCL (n=1: DL2), LGL-L (n=2: DL5) and ST (n=13: DL1-4) with median age of 61 years (range 30,77) and ECOG performance status of 0 (n=7) or 1 (n=14). No DLTs and no KT-333 related serious adverse events (SAE) were reported. The most common AEs were Grade 1 and 2 and included constipation, fatigue, nausea and anemia. Best response among pts evaluable for response at data cut-off (not including CTCL or HL pts at DL4 or any DL5 pts) included one partial response after two cycles in a CTCL pt at DL2 and SD after two cycles in three ST pts treated at DL3 and DL4. PD data in blood available for DL1-4 demonstrated robust, dose-dependent, and sustained STAT3 degradation in PBMC. The mean maximum degradation of STAT3 by targeted mass spectrometry over the first two weeks in Cycle 1 by DL was (% (range; n)): DL1: 69.9% (52.6% to 84.1%; n=4), DL2: 73.5% (65.5% to 80.7%; n=3), DL3: 79.9% (72.3% to 90.4 %; n=3) and DL4: 86.6% (78.9% to 95.9 %; n=4) with absolute quantification of STAT3 peptides falling below lower limit of quantification of the assay for one pt in DL3 and two in DL4. STAT3 pathway inhibition in blood was demonstrated via transcriptional downregulation of a canonical JAK/STAT3 target, SOCS3, which correlated with changes in STAT3 protein levels. KT-333 also resulted in dose-dependent downregulation of STAT3-regulated inflammatory biomarkers C-reactive protein and serum amyloid A protein in plasma. KT-333 demonstrated linear PK with plasma exposure increasing with dose and reaching levels close to those predicted to be efficacious. Conclusion: The emerging clinical data demonstrate that KT-333 is a potent degrader of STAT3 as

demonstrated in PBMCs at doses that are well tolerated. These data provide the first evidence of STAT3 targeted protein degradation in humans with associated STAT3 pathway inhibition, along with potential early signs of antitumor activity, highlighting the potential of heterobifunctional degra ers for targeting previously undruggable transcription factors implicated in diseases. Based on non-clinical data and PK/PD modeling, the high levels of degradation achieved so far are expected to be clinically efficacious in STAT3-dependent malignancies. Accrual is ongoing, and analyses from additional patients will be presented at the meeting.

Hematology-Oncology
Singleton T, Acharya S, Ahuja S, Amos L, Bonzo D, Eason A, Escobar M, Knoll C, **Kuriakose P**, Lagrue E, Recht M, Sullivan S, Quon D, and Reding M. Preliminary Analysis of ATHN 16: Real-World Safety of Eptacog Beta. *Res Pract Thromb Haemost* 2023; 7. Full Text

Background: Eptacog beta (rFVIIa-jncw) received regulatory approval in the U.S. in 2020 for the treatment of bleeding events (BEs) in persons with hemophilia A/B with inhibitors (PwHABI), 12 years of age and older. The ATHN 16 study was designed by the American Thrombosis and Hemostasis Network (ATHN) and the investigators to collect real-world evidence on the safety of eptacog beta. Aims: To evaluate the safety of eptacog beta when used to treat BEs in participants with HAB with inhibitors with or without prophylactic treatment. Methods: ATHN 16 (NCT04647227) is a phase IV, multi-center, open-label safety study enrolling PwHABI, who are either on long-term prophylaxis (e. g., emicizumab) or episodic treatment. ATHN 16 received central IRB approval. After informed consent is obtained, each participant is provided nine (9) 75 µg/kg doses of eptacog beta to be administered as needed for bleed treatment. BEs are treated by the participant or by study staff at the time of an event. Actual dose administered (75 mcg/kg or 225 mcg/kg) is determined at the discretion of the treating physician. The safety of eptacog beta is evaluated based on events included in the European Haemophilia Safety Surveillance (EUHASS) protocol. There are no pre-specified efficacy endpoints. Results: Between August 2021 and October 2022, eleven subjects have been enrolled, ten of whom are on prophylactic emicizumab. Twenty-eight bleeding events have been treated (57% spontaneous, 36% traumatic, 8% other (surgery, activity/exercise) in four of the eleven enrolled participants. One adverse event (AE), unrelated to study product, was reported and resolved. One serious adverse event (SAE), unrelated to study product was reported and resolved. Conclusion(s): To date, the safety profile of eptacog beta, in the ATHN 16 participants treated with eptacog beta, is favorable and consistent with previous reports. [Table presented] [Table presented]

Hematology-Oncology
Wani K, and **Dabak VS**. Does Implementing Calendars Outlining Inpatient Chemotherapy Schedules in Patient Rooms Improve Patient's Experience? *Blood* 2023; 142:7275. Full Text

Background: Patients who receive inpatient chemotherapy for malignancy are dealing with both a physically and mentally challenging admission. Their chemotherapy regimen is predetermined and usually only discussed during rounds. Often times, patients feel overwhelmed and may miss the outline of their schedule. Furthermore, patients families may not be able to attend morning rounds and may miss the proposed schedule. This can lead to a feeling of loss of control in both the patient and their family, and thus, frustration. First year medicine residents are also overwhelmed with a large patient load and having to keep track of multiple chemotherapy regimens. We are hoping that by providing a calendar that outlines patient's anticipated chemotherapy schedule, we may be able to give patients a small sense of control back and help residents provide the best care to their patients. Ultimately, we hope that this leads to a better inpatient experience. Methods: Patients admitted to the hematology/oncology floor at Henry Ford Health Hospital in Detroit, Michigan over three months were screened, and those receiving inpatient chemotherapy were selected. Within this group, any patient that was getting inpatient chemotherapy for longer than three days was asked if they would like to participate in the study. If the patient agreed, they were provided a calendar that outlined their chemotherapy schedule. Calendars were updated if any adjustments were made to the schedule. At the end of their inpatient stay, patients filled out a questionnaire asking if the calendar helped them understand their schedule better. The primary resident caring for the patient was also asked if the calendar helped them keep track of their patient's schedule. Results: Overall, patients responded positively to the calendars. We have preliminary data on ten patients

and four providers from three months. On average, on a scale of 1-10 (with 1 indicating not helpful at all, and 10 indicating extremely helpful) patients rated the calendars helping them at a level of 7.5. Patients found that the calendars particularly helped their families who were not able to come visit in the hospital. Providers found the calendars extremely helpful, rating the calendars at a level of 10. We will continue to collect data and update our results. Conclusions: Implementing patient calendars in inpatient rooms helps patients keep track of their chemotherapy schedules and leads to a positive inpatient experience. We are hoping to implement this as a standard of care in all inpatient rooms on the hematology/oncology floor.

Hematology-Oncology

Wani K, **Gutta R**, **Mittal A**, **Jamil M**, **Springer K**, and **Kuriakose P**. Comparison of Maintenance Therapy Regimens of Patients Treated for Multiple Myeloma. *Blood* 2023; 142:6698. Full Text

Background: Despite significant progress in treatment modalities and improved survival and response rates in patients diagnosed with multiple myeloma (MM), it remains an incurable disease with a poor outcome, especially in high-risk groups. Though not all patients are eligible, autologous stem-cell transplantation (ASCT) remains an integral part of the treatment of patients with both newly diagnosed and relapsed MM. Regardless of whether patients receive a transplant, they do receive maintenance therapy, and recent evidence has demonstrated that maintenance therapies offer an advantage in progression free and overall survival. While Revlimid is the standard of care, data regarding the specifics of maintenance therapy in high-risk patients is limited and the overall impact of various regimens on survival needs to be further investigated. In our retrospective chart review we reviewed all adult patients with advanced MM within Henry Ford Cancer Institute in the last 10 years to determine the impact of maintenance therapy on progression free survival (PFS) and overall survival (OS). Methods: We conducted a retrospective chart review of adult patients with MM who underwent ASCT between January 1, 2012 to December 31, 2022. Those who received maintenance chemotherapy after transplant were included in the study. Patients who were lost to follow-up or who had largely incomplete records were excluded. Data points including age, ethnicity, cytogenetic analysis, risk category, maintenance regimen after transplant, last chemotherapy regimen, last follow-up, and date of death (if applicable) were recorded. Maintenance chemotherapy regimens were recorded as Revlimid versus other. Patients were split into 2 categories based on risk - high risk and standard risk. Kaplan-Meier plots were used to illustrate overall survival and time to relapse between groups for various variables. Statistical significance was set at $p<0.05$ Results: 158 patients were included in the study of which 44 were considered high-risk based on cytogenetics, 106 were standard-risk and 8 were missing. Most of the patients (n=137, 87.3%) received Revlimid, while 20 (12.7%) received maintenance therapy other than Revlimid, and for 1 patient, the type of maintenance therapy was unknown. Within the high-risk group, no statistical significance in OS or PFS was found between patients that received Revlimid versus those that did not. Furthermore, there was no statistical significance in OS and PFS within high risk versus standard cytogenetic risk groups. Conclusions: We did not see a difference in outcome based on risk and believe all patients would derive equal benefit from maintenance therapy We also did not see a difference in outcome between high and standard risk patients, and for the high-risk subgroup, there was a separation in curves suggesting that maintenance therapy has benefit compared to no maintenance.

Hematology-Oncology

Wani K, **Gutta R**, **Mittal A**, **Jamil M**, **Springer K**, and **Kuriakose P**. Impact of Race on Progression-Free Survival and Overall Survival in Patients with Multiple Myeloma. *Blood* 2023; 142:6661. Full Text

Background: Multiple myeloma (MM) is a disorder of plasma cells. Management typically includes induction therapy, autologous stem-cell transplantation (ASCT) and maintenance therapy. Despite significant progress in treatment modalities and improved survival and response rates in patients diagnosed with MM, it remains an incurable disease with a poor outcome, especially in high-risk groups. Black patients have been shown to have a higher incidence of MM than white patients. Multiple studies have been done to examine racial disparities among white and black patients, specifically in overall survival (OS) and progression free survival (PFS). However, data has been overall inconclusive with some studies suggesting there is a difference in survival based on race, while other studies suggesting the opposite. Thus, racial disparities among white and black patients' needs to be further investigated. In our retrospective chart review we reviewed all adult patients with advanced MM within Henry Ford Cancer

Institute in the last 10 years to determine the impact of maintenance therapy on PFS and overall survival OS. Methods: We conducted a retrospective chart review of adult patients with MM who underwent autologous stem cell transplantation (ASCT) between January 1, 2012 to December 31, 2022. Those who received maintenance chemotherapy after transplant were included in the study. Patients who were lost to follow-up or who had largely incomplete records were excluded. Data points including age, gender, race, date of transplant, maintenance chemotherapy regimen, last follow-up, and date of death (if applicable) were recorded. Kaplan-Meier plots were used to illustrate overall survival and time to relapse between various races. Statistical significance was set at $p<0.05$. Results: There were 158 patients included in the study. Of the 158 patients, 82 (51.9%) were male, and 76 (48.1%) were female. The average age of patients included was 61.66 + 9.30 years, spanning from 32 to 78 years old. There were 71 (44.9%) White patients, 76 (48.1%) Black patients, and 11 (7.0%) patients that were of another race. There was no statistical significance in PFS and OS between Black, White and Other race categories. Conclusions: We did not see a difference in outcome based on race and believe all patients would derive equal benefit from maintenance therapy. Further prospective studies are warranted to examine racial disparities in patients with multiple myeloma.

Hospital Medicine

Chaudhary A, **Denha E**, **Khan MZ**, **Rehman S**, Zaidi SMH, El Alayli A, Gharaibeh EZ, and Farooq U. Unraveling the Unusual: Autoimmune Hepatitis After a 5-day Course of Nitrofurantoin for Uncomplicated UTI. *Am J Gastroenterol* 2023; 118(10):S2311-S2311. Full Text

[Chaudhary, Ammad; Denha, Eric; Khan, Muhammad Zarrar; Rehman, Sheema] Henry Ford Hosp, Detroit, MI USA. [Zaidi, Syed Murtaza Haider] King Edward Med Univ, Lahore, Punjab, Pakistan. [El Alayli, Abdallah; Gharaibeh, Eyad Z.] St Louis Univ, St Louis, MO USA. [Farooq, Umer] Rochester Gen Hosp, Rochester, NY USA. Rochester General Hospital

Hospital Medicine

Hechtman RK, Paje D, Horowitz J, McLaughlin E, Tatarcuk C, Heath M, **Kaatz S**, Flanders S, Bernstein S, McSparron JI, Prescott HC, and Chopra V. Association Between Number of Lumens and Peripherally Inserted Central Catheter Complications in Patients Admitted to the Intensive Care Unit. *Am J Respir Crit Care Med* 2024; 209. Full Text

R.K. Hechtman, Division of Pulmonary and Critical Care, University of Michigan, Ann Arbor, MI, United States

Rationale: Among patients with peripherally inserted central catheters (PICCs), greater number of catheter lumens increases the risk of catheter-associated complications. However, multi-lumen central access is commonly used among patients admitted to the intensive care unit (ICU), and less is known about complications of PICCs in this population. We assessed the association between number of lumens and risk of PICC-related complications among patients admitted to the ICU. Methods: Between 11/2013 and 3/2023, professional abstractors at 69 hospitals in the Michigan Hospital Medicine Safety Consortium retrospectively collected medical record data of adults with PICCs placed in the ICU. Number of lumens, placement indications, and complications including catheter-associated blood stream infection (CLABSI), upper extremity venous thromboembolism (UE-VTE), and catheter occlusion were recorded. Chi-squared tests and Poisson regression were used to evaluate differences in event rates. Results: Of 18,494 PICCs placed among ICU patients, 7.9% were single lumen, 61.6% double lumen, and 30.5% triple lumen. Patients receiving single, double, and triple lumen PICCs were similar in age (median 64.1, 65.6, 64.2 years), sex (50.1%, 49.5%, 53.2% male), and comorbidity burden (median Charlson Comorbidity Score 3 for each). Single lumen PICCs were most commonly placed for antibiotics (48.3% vs 24.3% and 18.9% for double and triple lumens, respectively, $p<0.01$), while double and triple lumen PICCs were commonly placed for difficult access (42.4% and 37.9%, respectively, vs 28.1% for single lumen, $p<0.01$), for central access (29.3% and 44.0%, vs 19.3% for single lumen, $p<0.01$), or for multiple incompatible fluids (9.2% and 9.3%, vs 2.5% for single lumen, $p<0.01$). PICCs were removed within £14 days of placement for 48.4% of single, 62.6% of double, and 66.8% of triple lumen catheters ($p<0.01$). Upper extremity VTE occurred in 2.1% of single, 3.2% of double, and 3.1% of triple lumen PICCs ($p=0.029$). CLABSI occurred in 1.2% of single, 2.2% of double, and 2.2% of triple lumen PICCs ($p=0.013$). Catheter occlusion occurred

in 5.5% of single, 13.4% of double, and 15.5% of triple lumen PICCs (p<0.01). Composite of all three PICC-related complications per 1000 catheterdays was 4.1, 11.4, and 13.4 for single, double, and triple lumen catheters, respectively, (p<0.001 for difference across all 3 catheter types). Conclusion: Multi-lumen PICCs are associated with increased PICC-related complications among patients admitted to the ICU, although clinical indications varied and may explain some of the difference in complication rates. Nonetheless, selecting PICCs with the fewest lumens needed will likely reduce PICC-related complications.

Hospital Medicine
Ichkhanian Y, **Veracruz N**, **Al-Haddad M**, Albunni H, Schlachterman A, Gouda Z, Canakis A, Kim R, D'Souza L, Khashab M, **Nimri F**, **Ashraf T**, **Faisal MS**, **Jomaa D**, **Dababneh Y**, **Rehman S**, **Rizwan A**, **Singla S**, **Alsheik E**, **Ginnebaugh B**, **McFarlin K**, **Piraka C**, and **Zuchelli T**. Management of Patients After Failed Gastric Peroral Endoscopic Myotomy: A Multi-Center Study. *Am J Gastroenterol* 2023; 118(10):S1410-S1411. Full Text

[Ichkhanian, Yervant; Veracruz, Nicolette; Al-Haddad, Mohammad; Nimri, Faisal; Ashraf, Taha; Faisal, Muhammad Salman.; Jomaa, Diana; Dababneh, Yara; Rehman, Sheema; Rizwan, Aliza; Singla, Sumit; Alsheik, Eva; Ginnebaugh, Brian; McFarlin, Kellie; Piraka, Cyrus; Zuchelli, Tobias] Henry Ford Hosp, Detroit, MI USA. [Albunni, Hashem] Indiana Univ, Detroit, MI USA. [Schlachterman, Alexander; Gouda, Zane] Univ Maryland, Baltimore, MD USA. [Canakis, Andrew; Kim, Raymond] Stony Brook Univ Hosp, Stony Brook, NY USA. [D'Souza, Lionel; Khashab, Mouen] Johns Hopkins Med, Baltimore, MD USA. System; University System of Maryland; University of Maryland Baltimore; State University of New York (SUNY) System; State University of New York (SUNY) Stony Brook; Stony Brook University Hospital; Johns Hopkins University; Johns Hopkins Medicine

Hospital Medicine
Jomaa D, **Jamali T**, **Manivannan A**, **Zahedi S**, **Peleman A**, **Pillai S**, **Zalawadia A**, and **Fain C**. A Syndrome of Diarrhea, Anasarca, and Nail Dystrophy: A Curious Case of Cronkhite-Canada Syndrome. *Am J Gastroenterol* 2023; 118(10):S1990-S1991. Full Text

[Jomaa, Diana; Jamali, Taher; Zahedi, Sulmaz; Peleman, Andrew; Pillai, Shreejith; Zalawadia, Ashish; Fain, Christopher] Henry Ford Hosp, Detroit, MI USA. [Manivannan, Ahila] Henry Ford Hlth, Detroit, MI USA.

Hospital Medicine
Kaatz S, **Ellsworth S**, **Ryan N**, Kong X, Haymart B, and Barnes G. Potential of Racial Bias in Atrial Fibrillation Patients that are Switched from Warfarin to a Direct Oral Anticoagulant. *Res Pract Thromb Haemost* 2023; 7. Full Text

Background: Prior studies suggest racial discrepancy in the use of direct oral anticoagulants in patients with atrial fibrillation. Aims: Determine if there are residual differences in the proportion of African American and White patients that are switched from warfarin to a direct oral anticoagulant (DOAC) after controlling for demographic, comorbidities, insurance, and social determinants. Methods: Patients in the Michigan Anticoagulation Quality Improvement Initiative (MAQI2) ongoing registry from November 2009 to August 2022 with atrial fibrillation that were switched from warfarin to a DOAC were matched 1:1 with propensity score (greedy method). Median geographic household income based on zip code from census data could not be matched because of large differences and logistic regression was utilized on the matched populations. Results: 670 of 674 African American were well matched to 670 of 4952 White patients (Table 1) except for median household income (Table 2). Prior to matching, 936 of 4952 (18.9%) white and 100 of 674 (14.8%) African American patients were switched (P = 0.011). After matching, 120 (17.9%) and 99 (14.8%) of 670 white or African American patients were switched (P = 0.21). The odds ratio (OR) for switching was not different between races when controlling for median income (OR = 0.83, 95% CI 0.59–1.16). Conclusion(s): At first glance, African American patients with atrial fibrillation seem to be switched from warfarin to a DOAC less frequently. However, after controlling for differences in the populations, there is no longer any difference by race, arguing against implicit racial bias as a plausible explanation. Median household income is approximately a third lower in African American patients

attending our 6 anticoagulation clinics and likely represents the largest barrier to DOAC use. We are actively working on processes with patient assistance programs to decrease co-pays to allow all our patients to receive the best anticoagulant. [Table presented] [Table presented]

Hospital Medicine
Patell R, Angelini DE, **Ellsworth SR**, Lewis P, Lee JC, Nutescu EA, Amin A, Witt DM, Betensky M, Goldenberg N, Kouides P, Attia MD, Mourany L, Lake L, Rosovsky RP, Khorana AA, and **Kaatz S**. Estimating the Burden of Venous and Arterial Thrombotic Events in Hospitalized Adults with COVID-19; A National Multicenter Cohort Study. *Blood* 2023; 142:1262. Full Text

Background: Patients infected with Coronavirus Disease 2019 (COVID-19) have clinical and laboratory features consistent with a hypercoaguable state, particularly in more severely ill patients that require hospitalization. However, estimates of thrombotic complications in this high risk population vary widely. A geographic representative cohort to explore the rates of thrombotic events in patients hospitalized with COVID-19 in the United States would be useful to better understand the burden of thrombosis in this population. We aimed to assess the rates of venous and arterial thrombosis events during hospitalization in patients with COVID-19 in a national multicenter cohort study. Methods: We conducted a retrospective cohort study of hospitalized patients diagnosed with COVID-19 from January 1 2020 to January 2023. IRB approval was obtained at each site. Inclusion criteria included adults (> 21 years), hospitalized for >1 day and laboratory confirmation of polymerase chain reaction testing of severe acute respiratory syndrome coronavirus 2. Data were extracted by participating centers in a pre-specified instrument from the electronic medical record at each institution and pooled prior to analysis. Data sources included manual extraction by study investigators in 7 sites and electronic extraction based on billing codes at one site (Cleveland Clinic). Primary outcome was venous thrombotic events, including deep vein thrombosis (DVT), pulmonary embolism (PE). Unusual sites including splanchnic vein thrombosis and cerebral venous thrombosis were included if objectively demonstrated on imaging. Arterial thrombotic events including ischemic stroke, acute coronary syndrome were included as secondary outcomes. Data are presented as proportions, with binomial 95% confidence intervals (CI). Results: We included 33,769 patients from eight medical centers across the United States. Participating hospitals included all four census regions from the North East (Beth Israel Deaconess Medical Center, MA (n=1021) Rochester Regional Hospital, NY (n=99)), South (John Hopkins Medical Institute, ML (n=334); Baycare Health System, FL (n=3734), MidWest (Cleveland Clinic Foundation, OH (n=25467); Henry Ford Health System, MI (973); University of Illinois, IL (1192)) and West (University of California, CA (n=613)). (Figure) Of the total 33,433 hospitalized patients with COVID-19 included, 1684 patients developed a venous thrombotic event during the index hospitalization (5.0%, 95% CI 4.8-5.2) and 261 developed an arterial thrombotic event (0.8%, 95% CI, 95% CI 0.7-0.9). Rates of venous events by individual sites ranged from 2.6-8% and arterial events from 0.3-6.6%. Conclusion: In this national multicenter cohort study that included academic and community hospitals from all four US census regions, we estimated the rates of VTE were over five times more frequent than arterial events in hospitalized patients with COVID-19. Accurate estimates of thrombotic rates and trends can help plan targeted interventions related to strategies around thromboprophylaxis interventions and resource allocation for future surges of COVID-19 cases.

Hospital Medicine
Schaefer JK, Errickson J, Kong X, Ali MA, Chipalkatti N, Dorby P, Giuliano C, Haymart B, **Kaatz S**, Kurlander JE, **Krol GD**, Shankar S, Sood SL, Froehlich J, and Barnes GD. Outcomes of Oral Anticoagulation with Concomitant NSAID Use: A Registry Based Cohort Study. *Blood* 2023; 142:5129. Full Text

Introduction Nonsteroidal anti-inflammatory drugs (NSAIDs), available without a prescription, are some of the most commonly used drugs in the United States. For patients on oral anticoagulation (OAC), concomitant NSAID use can increase the risk of bleeding. Patients are often advised to avoid this drug combination, or else consider adding a proton pump inhibitor (PPI) or H2 receptor antagonists (H2RA) for gastroprotection when both NSAIDs and OAC are used. However, there are limited data on how NSAID use impacts thrombotic and hemorrhagic outcomes. Available data may be biased due to selection bias, confounding, misclassification, and variable NSAID exposure. We sought to determine the frequency of NSAID use among patients on OAC, the impact on clinical outcomes, and if gastroprotection may mitigate

bleeding risk. We hypothesized that NSAIDs would increase bleeding risk without impacting thrombotic risk. We did not anticipate gastroprotection would mitigate this risk. Methods We conducted a retrospective registry-based cohort study of adults starting a direct oral anticoagulant (DOAC) or warfarin therapy for the indications of venous thromboembolism and/or non-valvular atrial fibrillation between June 2011 and June 2023. As part of the Michigan Anticoagulation Quality Improvement Initiative (MAQI 2), warfarin-treated patients were followed by six anticoagulation clinics, and four of the six clinics contributed data for patients on DOACs. Patients were excluded if they had a history of valvular AF, less than 3 months of follow-up, or on more than one antiplatelet drug. Two propensity matched cohorts (OAC alone vs. OAC+NSAID) of patients were analyzed based on NSAID use at the time of study enrollment, using a 4:1 matching ratio. Both prescribed and over the counter NSAIDs were included, potentially with the former being more frequently captured in the study registry. The primary outcome was any new bleeding event. Secondary outcomes included new episodes of arterial or venous thrombosis, bleeding event type (major, fatal, life threatening, central nervous system, and non-major bleeding), emergency room visits, hospitalizations, transfusions, and death. Random chart audits were done to confirm the accuracy of the abstracted data. Event rates were compared using Poisson regression. Results Of 12,083 patients on OAC, 449 (3.7%) were on concomitant NSAIDs. After propensity matching, we compared 1,796 patients on OAC to 449 patients on OAC+NSAIDs. Patient demographics, co-morbidities, indication for anticoagulation, history of bleeding or clotting, medications, and duration of follow-up were well-balanced after matching. Patients were followed for an average of 30 months (standard deviation 34.2 months). For patients on OAC alone vs. OAC+NSAIDs, bleeding event rates were similar: 25.1 (95% confidence interval [CI] 23.7-26.6) versus 24.3 (95% CI 21.4-27.3) bleeds per 100 patient years (P=0.56). Rates of non-major, major, life-threatening, central nervous system, and fatal bleeding were also similar. Furthermore, rates of thrombosis, emergency room visits, hospitalizations, transfusion, and death were similar. A pre-defined subgroup analysis comparing patients on OAC+NSAIDs with gastrointestinal prophylaxis (PPIs or H2RAs, N=179) to patients on OAC+NSAIDs without gastrointestinal prophylaxis (N=270) also showed similar rates of bleeding and healthcare utilization. Conclusions Nearly 4% of patients were taking NSAIDs with OAC and outcomes were similar to patients on OAC alone. Study limitations include NSAIDs and gastroprotection were only reliably known at time of enrollment. In addition, the potential for unmeasured or unadjusted confounding inherent to observational studies. Further research is needed to determine if there is a “safe” level of NSAID use for patients on OAC and to better define the role of gastrointestinal prophylaxis.

Hospital Medicine

Schaefer JK, Errickson J, Kong X, Ali MA, Chipalkatti N, Haymart B, **Kaatz S**, **Krol GD**, Sood SL, Froehlich J, and Barnes GD. A Comparison of Bleeding Events Among Patients on Apixaban, Rivaroxaban, and Warfarin for Atrial Fibrillation and/or Venous Thromboembolism. *Blood* 2023; 142:135. Full Text

Introduction Apixaban and rivaroxaban are the most commonly used direct oral anticoagulants (DOACs) for atrial fibrillation (AF) and venous thromboembolism (VTE). Both have been compared to warfarin in landmark clinical trials. However, there are limited comparative efficacy data between these drugs in a real-world setting. We sought to assess patient characteristics and outcomes of apixaban, rivaroxaban, and warfarin in a non-trial based study cohort. Methods Retrospective registry-based cohort of adults starting apixaban, rivaroxaban, or warfarin therapy or switching between these anticoagulants for the indications of VTE and/or non-valvular AF. Through the Michigan Anticoagulation Quality Improvement Initiative (MAQI 2) collaborative of six anticoagulation clinics, warfarin treated patients were followed from January 2009 to June 2023. Four of these clinics contributed DOAC patient data from June 2011 to June 2023. Patients treated with other anticoagulants, with valvular AF, or with less than 3 months of follow-up were excluded. Propensity matched cohorts (apixaban versus warfarin [1:1], rivaroxaban versus warfarin [1:3], and apixaban versus rivaroxaban [1:1]) of patients were analyzed based on DOAC use at study enrollment, using 1:1-3:1 matching ratios. Patients were matched based on demographics, social history, comorbidities, medications, bleeding/thrombotic history, indication for anticoagulation, and follow-up. The primary outcome was any new bleeding event. Secondary outcomes included new episodes of thrombosis, bleeding event type (major, fatal, life threatening, central nervous system, and non-major bleeding), emergency room (ER) visits, hospitalizations, and death. Random chart audits were done to confirm the accuracy of the abstracted data. Event rates were compared using Poisson regression.

Results Of 13,435 patients on OAC who met the study inclusion criteria (3,536 on apixaban, 1,395 on rivaroxaban, and 8,504 on warfarin), the average age was 66.7 years (standard deviation [SD] 14.9 years), 51.1% identified as male, most (58.0%) were on anticoagulation for AF, and the average follow-up was 28.2 months (SD 30.7 months). After propensity matching, 3,527 patients on apixaban were compared to 3,527 patients on warfarin. Any bleeding was similar between groups, but major bleeding was higher with warfarin (3.4 versus 4.7 events/100 patient years, p<0.001). Thrombotic event rates were higher with apixaban (2.6 versus 2.1 events/100 patient years, p=0.026), including the thrombotic subtype of other thrombosis (1.0 versus 0.5 events/100 patient years, p<0.001). Rates of ER visits and hospitalizations for bleeding were higher with warfarin. Mortality was higher with warfarin (3.7 versus 4.4 deaths/100 patient years, p=0.027). After propensity matching, 1,395 patients on rivaroxaban were compared to 4,185 patients on warfarin. Any bleeding and major bleeding were higher with rivaroxaban (37.9 versus 24.9 events/100 patient years, p<0.001; 4.7 versus 3.6 events/100 patient years, p=0.041 respectively). Thrombotic event rates were similar, aside from a higher rate of the thrombotic subtype of other thrombosis with rivaroxaban (1.0 versus 0.3 events/100 patient years, p=0.002). ER visits, hospitalizations, and mortality were similar between rivaroxaban and warfarin. After propensity matching, 1,395 patients on apixaban were compared to 1,395 patients on rivaroxaban. Any bleeding and major bleeding were higher with rivaroxaban (37.9 versus 25.7 events/100 patient years, p<0.001; 4.7 versus 2.6 events/100 patient years, p<0.001). Thrombotic event rates were similar. ER visits occurred more frequently on rivaroxaban (12.8 versus 10.1 events/100 patient years, p=0.003) as did patient mortality (3.5 versus 2.6 deaths/100 patient years, p=0.047). Conclusions For patients on oral anticoagulation for AF and/or VTE we observed that bleeding was highest with rivaroxaban, followed by warfarin, and then apixaban. Rates of thrombosis were higher with apixaban compared to warfarin, seemingly largely driven by “other” thro botic events. Thrombotic event rates were otherwise similar between apixaban, rivaroxaban, and warfarin. We observed apixaban to be associated with lower mortality than rivaroxaban and warfarin. While these findings should be confirmed with randomized studies, they may have implications for anticoagulant selection.

Hospital Medicine

Siegal D, Arnaoutoglou E, Blostein M, Castellucci L, Eikelboom J, Gandhi R, Gross P, **Kaatz S**, Le Gal G, Schulman S, **Shah V**, Stamoulis K, Tafur A, Vogt K, Nixon J, St John M, Karunakaran M, Levoy-Jones B, and Douketis J. Management and Outcomes of Anticoagulated Patients in Urgent Surgery: The PAUSE-ER Study. *Res Pract Thromb Haemost* 2023; 7. Full Text

Background: Few data describe the perioperative management and outcomes of patients receiving oral anticoagulant (OAC) therapy who require urgent (unplanned) surgery. While limited available evidence suggests high rates of thromboembolism, bleeding and death in this setting, substantial knowledge gaps remain. Aims: We aimed to (i) determine the incidence of adverse events (thrombosis, bleeding, death) among OAC-treated patients requiring urgent surgery, (ii) examine management and resource utilization, and (iii) explore factors associated with adverse outcomes. Methods: PAUSE-ER was a prospective observational study conducted at 10 sites (Canada, US, Greece, Argentina). OAC-treated adults requiring OAC interruption for urgent (unplanned) surgery/invasive procedure (within 72 hours)were eligible. Patients undergoing elective (planned), or minimal bleed risk surgeries/procedures not requiring OAC interruption were excluded. Data were collected from medical records and telephone follow-up at 30 days. Results: 242 participants were enrolled (2019–2022). The mean age was 75 years and 50% were female. OAC use comprised apixaban (40%), warfarin (38%), rivaroxaban (16%), edoxaban (1%) and dabigatran (0.4%). The commonest indication for OAC was atrial fibrillation (74%). The most common surgeries were orthopedic (n = 84), general surgery (n = 42), vascular surgery (n = 16), neurosurgery (n = 16), interventional radiology procedures (n = 10), urologic surgery (n = 9), and cardiothoracic surgery (n = 8). Most patients (76%) received general anesthesia and 5% had neuraxial anesthesia. Perioperatively, patients received idarucizumab (n = 1), andexanet-alfa (n = 1), prothrombin complex concentrate (n = 45), plasma (n = 8), vitamin K (n = 61) and tranexamic acid (n = 31). At 30-days follow-up, 12 patients (5%) died, 18 (7%) had bleeding complications and 4 (2%) experienced thromboembolic events (ischemic stroke [n = 3] and pulmonary embolism [n = 1]). Conclusion(s): In the first prospective evaluation of unselected OAC-treated patients requiring urgent surgery, we showed that management was variable and adverse outcome rates appeared higher than those observed after elective (planned) surgery.

Further research aims to inform best practices for OAC management to reduce morbidity and mortality. [Figure presented]

Hospital Medicine
Taylor SP, Paje D, Heath M, Horowitz J, McLaughlin E, **Kaatz S**, Creutz E, Flanders S, Posa P, Younas M, and Prescott HC. Prevalence, Characteristics, and Outcomes of Sepsis Patients Admitted to Observation Versus Inpatient Status. *Am J Respir Crit Care Med* 2024; 209. Full Text

S.P. Taylor, University of Michigan, Ann Arbor, MI, United States

Rationale: Patients presenting early in their clinical course are often placed in observation status for further evaluation while discerning the need for inpatient admission. Given the frequent initial diagnostic uncertainty in sepsis, patients with sepsis may be initially hospitalized under observation status rather than inpatient status. Little is known about the prevalence, characteristics and clinical outcomes of patients with sepsis who are initially admitted under observation care. Methods: We conducted a retrospective cohort study of sepsis admissions (2020 to 2023) at 53 hospitals participating in the Michigan Hospital Medicine Safety Consortium. We ascertained sepsis cases consistent with CDC surveillance criteria. We excluded patients initially admitted to the intensive care (ICU) or moderate care units. Patient data were collected by trained abstractors at each hospital. The primary outcome was hospital mortality. Secondary outcomes were hospital length of stay (LOS), transfer to ICU , and intravenous (IV) antibiotic days. Mixed effects logistic regression models, with hospital included as a random effect, were used to adjust for age, Charlson comorbidity index, and organ dysfunctions at presentation.Results: Among 5,715 sepsis patients, 701 (12%) were initially admitted under observation status. The proportion of sepsis patients admitted under observation status varied from 1% to 83% across hospitals. Patients admitted under observation status were similar in age, comorbidity status, and predicted mortality risk compared to those admitted to inpatient status. Compared to patients admitted to inpatient status, fewer patients admitted under observation status received timely antibiotics (56% vs 74%) or full SEP-1 bundle compliant care (22% vs 34%). Adjusting for confounding variables, patients admitted under observation status had similar in-hospital mortality (OR, 0.96 [95%CI,0.62-1.48]), LOS (OR, 1.07 [95%CI,0.96-1.19]), and IV antibiotic days (OR, 1.03 [95%CI,0.97-1.09]) compared to those admitted as inpatients. Patients admitted under observation status had greater ICU transfer rates (OR, 1.54 [95%CI,1.09-2.18]) after adjustment for patient and hospital-level variation. This finding was not significant when removing the hospital-level effect. Conclusion: The use of observation status for sepsis varies widely across hospitals. Patients with sepsis admitted under observation status had similar frequency of hospital mortality, length of hospital stay and days of IV antibiotic treatment as those admitted under inpatient status. After adjusting for patient and hospital-level effects, admission under observation status was associated with higher rates of ICU transfer. This association is not significant when hospital-level effects are removed from the model, suggesting hospital-specific opportunities to improve the quality of sepsis care under observation status.

Hospital Medicine
Zreik H, **Singh B**, **Patel PM**, **Yasin Z**, **Hari P**, and **Alamelumangapuram CB**. Emerging Diagnostic Markers in Acute Ischemic Colitis. *Am J Gastroenterol* 2023; 118(10):S1658-S1658. Full Text

[Zreik, Hassan; Singh, Bipneet; Patel, Parth M.; Yasin, Zarqa; Hari, Parneet; Alamelumangapuram, Chidamber Bharath] Henry Ford Hlth Syst, Jackson, MI USA.

Infectious Diseases
Alvi RBR, **Mann Y**, **Brar S**, **Brar I**, and **Suleyman G**. Characterization of Mpox in Southeast Michigan. *Open Forum Infect Dis* 2023; 10:S1165-S1166. Full Text.

R.B.R. Alvi, Henry Ford Hospital, Detroit, MI, United States

Background. More than 30,000 cases of mpox have been identified in the United States. Data suggest that about 40% of affected persons are co-infected with HIV. Although most cases are self-limiting, patients with low CD4 counts are at increased risk of developing severe clinical manifestations and dying.

Methods. Retrospective case-control study comparing mpox cases among people with HIV (PWH) and HIV-uninfected persons from July to Dec 2022, at Henry Ford Health in Southeast Michigan. Demographic data, clinical characteristics, treatment, and outcomes were evaluated. Results. 54 patients were diagnosed with mpox. Overall, 42 (78%) were MSM or bisexual men, 36 (67%) Black, and 34 (63%) PWH; median age was 34.5 years (Table 1). The majority (63%) had prior sexually transmitted infections (STIs), which were more common in PWH (82% vs 30%, p< 0.001). About one-third had multiple sexual partners; more than half engaged in insertive or receptive anal intercourse. 32 (94%) of PWH were on ART, 26 (76%) had CD4 counts >200 and 19 (60%) had undetectable viral load; mean CD4 count was 602 and viral load 7942. Of the HIV-uninfected persons, 5 (25%) were on PrEP. Receipt of mpox vaccine was uncommon in either group. All patients presented with rash that was disseminated in 35%. Fever/chills, lymphadenopathy, headache, proctitis and pharyngitis were the most common manifestations and did not differ among the two groups. Concomitant STIs were present in 22 (48%) of 46 persons tested; syphilis co-infection was more prevalent among PWH (35% vs 25%, p< 0.006). Hospitalization and receipt of tecovirimat were similar between the two groups; no patients died. Demographics, Risk Factors, Clinical Manifestations and Outcomes of Mpox Patients Conclusion. Overall, there were no significant differences in clinical manifestations or outcomes between PWH and HIV-uninfected persons with mpox except for syphilis co-infection. Most of our PWH cohort was on ART and virally suppressed with high CD4 count. Hence, efforts should focus on rapid treatment of PWH with effective ART to achieve virological suppression and immunological recovery to minimize clinical complications and severe outcomes associated with opportunistic pathogens. Vaccinating all high-risk individuals, early mpox recognition and testing, and screening for additional STIs should be prioritized.

Infectious Diseases

Arena C, **Kenney RM**, **Eriksson E**, **Brar I**, and **Veve M**. Impact of Social Determinants of Health on Preferred Treatment of Trichomonas vaginalis and Chlamydia trachomatis. *Open Forum Infect Dis* 2023; 10:S850-S851. Full Text

C. Arena, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Henry Ford Hospital, Royal Oak, MI, United States

Background. The 2021 CDC Sexually Transmitted Infections (STI) Treatment Guideline modified preferred therapy for Trichomonas vaginalis (TV) and Chlamydia trachomatis (CT) from single dose to a 7-day course. Social Determinants of Health (SDOH) are non-medical factors that influence a person's life; little is known regarding the association between SDOH and TV and CT treatment. The study objective was to evaluate treatment of TV and CT infections after the guideline update and determine if health inequities exist with use of preferred therapy. Methods. IRB approved, retrospective cohort of patients ≥ 15 years with confirmed diagnosis of uncomplicated TV or CT in outpatient settings. Excluded: pregnant/ nursing, allergy to preferred therapy, unable to take oral. Primary outcome: proportion who received guideline preferred vs non-preferred (alternative, discordant, or null) antibiotic therapy. Logistic regression was used to identify variables associated with preferred treatment; SDOH were exposures of interest. Secondary outcomes: test of cure (≤ 3 months), any repeat positive test (recurrence/reinfection), any retreatment, expedited partner therapy (EPT) offered. A sample of 712 patients was needed to detect a 10% difference between two exposures (α=0.05, β=0.2). Results. 473 (66%) patients received preferred therapy; patient characteristics are in Table 1. Patients < 25 years had more asymptomatic disease compared to older patients (198 [54%] vs 150 [44%], P=0.01). Patients who received Emergency Department (ED) care were more likely to receive preferred therapy compared to outpatient clinics (201/264 [76%] vs 272/448 [61%], P=< 0.001). Black race, lower median income, and public insurance covaried with ED care. After adjusting for female sex, receipt of ED care was independently associated with preferred therapy (Table 2). 181 (25%) patients had 3-month test of cure performed; repeat positive test/retreatment was more frequent in patients who received non-preferred therapy (25 [11%] vs 24 [5%], P=0.01). EPT was offered in 35 (7%) and 8 (3%) patients in the preferred and non-preferred groups (P=0.03). Conclusion. Preferred therapy was more frequent in patients who received ED care. EDs represent an important safety net and provide high-level care for patients with SDOH barriers. (Table Presented).

Infectious Diseases

Birk NK, **Soman S**, **Kapur N**, **Pochhareddy V**, **Dillon WP**, **Veve M**, **Samuel L**, **Ramesh M**, and **Alangaden GJ**. Candidemia: Role of T2Candida® compared to Bact/Alert Virtuo blood culture system in a real-world setting. *Open Forum Infect Dis* 2023; 10:S356. Full Text

N.K. Birk, Henry Ford Hospital, Detroit, MI, United States

Background. Candidemia is the most common cause of invasive fungal infections with mortality rates up to 60%. The current standard for diagnosis of candidemia is traditional blood cultures (BC) but it has low sensitivity. The need for rapid identification of candidemia has led to the development of non-culture-based diagnostic platforms. T2Candida® (T2) is an FDA approved direct from blood PCR test. T2 detects 5 candida species (C. albicans/C. tropicalis, C. parapsilosis, & C. krusei/C. glabrata) with a turnaround time of three to five hours. T2 is used at our institution for the diagnosis of candidemia in the intensive care units (ICU) if prior blood cultures are negative. Patients with positive T2 results are managed the same as patients with positive BC. In February 2019, our health system switched from the VersaTREK™ to a more sensitive Bact/Alert Virtuo BC system. Our objective was to assess the impact of the new Virtuo system on the diagnosis of candidemia compared to T2 in a realworld setting. Methods. All T2 and concurrent BC results were retrospectively collected from January 2018 to January 2019 (VersaTREK™cohort) and March 2019 to March 2020 (Virtuo cohort) in our quaternary care facility in metro Detroit. Only patients with presumed candidemia were included (ICU patients with sepsis, recent exposure to anti-bacterial agents, and negative BC for candida in the past 7 days). Demographic data and the results of T2 and concurrent BC (obtained within 48 hours of T2) were analyzed for the presence or absence of candida. Indeterminate T2 results were excluded. Descriptive statistics were utilized to report the results. Results. A total of 522 and 348 T2 tests performed with concurrent BC through VersaTREK™and Virtuo systems respectively were included for analysis. In this ICU cohort with presumed candidemia, T2 remained superior: T2 positivity 45 (8.6%) vs. VersaTREK™ BC positivity 14 (2.7%) ($p < 0.001$) and T2 positivity 34 (9.8%) vs. Virtuo BC positivity 8 (2.3%) ($p < 0.001$) (Figure 1). The Virtuo cohort had overall fewer T2 tests performed. This may be because the more sensitive Virtuo system could have detected more cases of candidemia than VersaTREK™obviating the need for T2 test. Conclusion. T2 may still have a role in the early diagnosis of candidemia despite the use of newer sensitive blood culture systems.

Infectious Diseases

Caniff KE, Holger D, Lucas K, O'Donnell MA, Shields RK, Loo A, Khem R, Dahl N, Dubrovskaya Y, Marsh K, Cubillos AL, Chandler E, Knack O, Davis SL, **Alangaden GJ**, and Rybak MJ. Predictors of 30-Day Mortality Among Critically Ill Patients with Candidemia Identified by T2Candida Panel. *Open Forum Infect Dis* 2023; 10:S445. Full Text

K.E. Caniff, Anti-Infective Research Lab, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Royal Oak, MI, United States

Background. Candidemia is associated with mortality rates exceeding 40%. However, prior studies indicate mortality may be reduced when antifungal therapy is initiated within 12 hours. The T2Candida Panel is a diagnostic assay that detects Candida species directly from a whole blood specimen within 3-5 hours (T2 Biosystems, Lexington, MA). The objective of this study is to identify predictors of 30-day mortality in patients with candidemia identified by T2Candida Panel. Methods. This is a retrospective,multicenter study of critically ill patients with candidemia identified by T2Candida Panel from January 2016 - December 2022. Critically ill patients were defined as those who developed candidemia during an intensive care unit (ICU) stay or within 72 hours of ICU admission or discharge. T2Candida sites were chosen across the United States based on T2Candida utilization. Exclusion criteria were patients < 18 years of age, those with prophylactic indications for antifungal therapy, prisoners and pregnant patients. Multivariate logistic regression was conducted to identify factors associated with 30-day mortality measured from the T2Candida draw time. Results. There were 171 ICU patients from seven institutions with candidemia identified by T2Candida panel. The mean (standard deviation [SD]) age was 59.7 (14.8) years and 52.1% were male. Mean (SD) APACHE II and Charlson Comorbidity Index scores were 20.6 (7.1) and 4.9 (2.8), respectively. Empiric antifungal therapy was administered to 36.8% of

patients and the majority received infectious diseases (ID) consult (92.4%). Echinocandins were the most common agents used for empiric (72.7%) and definitive therapy (62.6%). Overall, 30-day mortality occurred in 36.0% and was not associated with antifungal de-escalation. Administration of empiric therapy (aOR 0.457, 95% CI 0.199-1.054) and ID consult (aOR 0.225, 95% CI 0.056-0.913) were associated with reduced odds of 30-day mortality. Conclusion. Empiric antifungal administration and ID consult were independently associated with reduced odds of 30-day mortality in patients with candidemia identified by T2Candida Panel. Future studies are needed to evaluate the impact of the T2Candida panel on antifungal stewardship.

Infectious Diseases
Cherian J, **Herc E**, **Yared NF**, **Brar I**, **Gudipati S**, and **Shallal A**. Factors that Increase Engagement on Social Media for an Infectious Diseases Fellowship Program. *Open Forum Infect Dis* 2023; 10:S427. Full Text

J. Cherian, Henry Ford Health, Detroit, MI, United States

Background. Social media is increasingly being used among Infectious Disease (ID) programs. It can be a valuable recruitment tool in addition to providing education, self-promotion, and increasing collaborations across the ID community. We sought to analyze factors associated with increased engagement for our ID fellowship program's Twitter account. Methods. We analyzed various metrics from consecutive Twitter posts and utilized the Twitter Analytics Dashboard to extract data from time of account inception. Impressions were defined as the number of times a tweet was seen by users, and engagements as a composite of interactions with a tweet. Tweet content was organized into educational, social, promotional, and other categories. Educational content was subcategorized into tweetorial, microbiology, question & answer (Q&A), and journal articles. A subset of tweets were analyzed for engagement from April 2022 to March 2023 for trends according to content and date the tweet was posted. Standard univariate descriptive statistical analyses, moods median test, and one-way analysis of variance was performed. Data analysis was performed using R version 3.4.0. Results. 460 tweets were posted from October 2020 to March 2023 (Figure 1). Educational subcategories showed a large amount of engagement related to microbiology, with specifically more retweets, likes, and profile clicks (Table 1). There was no difference in engagement based on time of day of tweet (Table 2), although profile clicks were significantly more likely if tweets occurred on a weekend (p=0.04). A subset of 284 tweets from April 2022 to March 2023 revealed that months where multiple content categories were tweeted resulted in the most engagement (Figure 2). Generally, more twitter posts correlated with more engagement with a Pearson correlation coefficient of 0.7. Figure 1. Tweet content by (a) overall categories and (b) educational categories. Conclusion. To increase engagement with social media, there should be frequent tweets with varied content categories. Subcategories of content such as microbiology tweets draw further interest and showcase a program's educational and clinical innovation.

Infectious Diseases
Dillon WP, **Muthanna Shadid A**, **Parsons A**, **Hardy M**, **Williams JD**, **McCorquodale J**, **Ramesh M**, and **Alangaden GJ**. Outcomes of Outpatient Parenteral Antimicrobial Therapy in the Solid Organ Transplant Population. *Open Forum Infect Dis* 2023; 10:S208-S209. Full Text

W.P. Dillon, Henry Ford Hospital, Detroit, MI, United States

Background. Outpatient parenteral antimicrobial therapy (OPAT) provides an effective and convenient means to complete extended courses of antimicrobial therapy for the treatment of serious infections. There is scant data addressing OPAT related outcomes such as readmission in solid organ transplant (SOT) recipients. Methods. In this observational cohort study, we analyzed all adult SOT recipients discharged from Henry Ford Hospital - an 877 bed quaternary care center in Detroit, Michigan - on OPAT between January 2015 and December 2020. The primary endpoint was 30-day all-cause readmission. The secondary endpoints included evaluation of risk factors associated with readmission (transplant type, reason for OPAT, OPAT related complications, length of treatment, length of stay, discharge disposition, and adequacy of infectious disease follow up and laboratory monitoring) and all-cause mortality at one year. Results. There were 201 patients discharged on OPAT. Demographics between study populations

were comparable (Table 1). A total of 83 out of 201 (41.3%) patients were readmitted. There were 38 (18.9%) patients readmitted for OPAT related complications and 45 (22.4%) for non-OPAT related reasons. Intestinal and multi-visceral transplants were associated with readmission (p=0.04 and p=0.02 respectively) while renal transplants were protective against readmission (p=0.02) (Table 1). Other factors associated with readmission include development of an OPAT related complication including treatment failure (p< 0.001) (Table 2). Patients discharged without Infectious Disease follow up were less likely to be readmitted (p=0.04) (Table 3) as these patients generally had less serious infections not meriting a follow up appointment. There was no difference in mortality at one year between study populations (Table 3). Conclusion. While the overall readmission rate of SOT discharged on OPAT is high, most readmissions were unrelated to OPAT. Patients with readmissions had higher rates of OPAT related complications and treatment failures. Further studies are warranted to optimize OPAT outcomes in the SOT population. (Table Presented).

Infectious Diseases

Failla AJ, and **Suleyman G**. Risk Factors and Outcomes Associated with Daptomycin-nonsusceptible Enterococcus Bloodstream Infections. *Open Forum Infect Dis* 2023; 10:S417. Full Text

A.J. Failla, Henry Ford Hospital, Detroit, MI, United States

Background. Enterococcus spp. are a common cause of nosocomial bloodstream infections (BSIs) with increasing resistance to currently available antibiotics and high mortality. Although the emergence of daptomycinnonsusceptible Enterococcus (DNSE) has been reported, risk factors and outcomes associated with acquisition of daptomycin (DAP) resistance are not well characterized. Methods. Retrospective cohort study of patients with enterococcal BSIs at Henry Ford Health in Southeast Michigan from 2014 to 2022. Cases included patients with DNSE; patients with persistent daptomycin (DAP)-susceptible Enterococcus (DSE) bacteremia (> 2 days of positive blood cultures) were used as controls. Outcomes included 30-day readmission and mortality. Results. 24 cases and 24 controls were included; median age was 67 years (IQR 59-72), 28 (58.3%) were male and 26 (54%) white. All patients were exposed to antibiotics within 90 days with no difference in DAP use between the two groups (8% vs 21%, p=0.220). The majority (90%) had prior hospitalization within the year, 44% were immune suppressed and 42% had end-stage renal disease. Hepatitis C virus (HCV) (17% vs 0, 0.037) and prior VRE (42% vs 21%, p < 0.001) were more prevalent among cases. Indwelling urinary catheter (IUC) use was more common in cases (83% vs 54%, p=0.029), but there was no difference in central venous catheter use (75% vs 58%, p=0.221). Most common source of infection was intra-abdominal in both groups (54% vs 75%, p=0.188). Although not statistically significant, need for intensive care unit admission was higher (75% vs 50%, p=0.074) and length of stay was longer (54 vs 32 days, p=0.063) in cases compared to controls; treatment duration was significantly longer in controls (23 vs 16 days, p=0.04). There was no significant difference in readmission (12.5% vs 25%, p=0.267) or mortality (58% vs 46%, p=0.386) between the two groups. (Table Presented) DNSE patient demographics, risk factors and outcomes Conclusion. DNSE is an emerging pathogen associated with HCV, prior VRE and IUC use in our cohort; however, prior daptomycin exposure was not a significant risk factor for DNSE. Despite the high mortality, there was no difference in outcome between the two groups. Mechanism of DNSE in patients without prior DAP exposure should be explored to prevent potential spread of resistance.

Infectious Diseases

Hanna ZW, **Alangaden GJ**, **Zervos M**, and **Suleyman G**. Evaluation of Risk Factors and Outcomes Associated with Daptomycin-nonsusceptible Staphylococcus aureus Bacteremia. *Open Forum Infect Dis* 2023; 10:S144. Full Text

Z.W. Hanna, Henry Ford Health, Detroit, MI, United States

Background. Staphylococcus aureus (SA) is a major cause of hospital-associated infections in the US with high morbidity and mortality. With SA developing resistance to many first-line antibiotics, daptomycin (DAP) has become a critical agent for SA therapy. However, increasing use of DAP has resulted in emergence of DAP-nonsusceptible (DNS) SA strains. We aim to elucidate risk factors associated with DNS SA and compare outcomes between patients with DAP-susceptible (DS) and DNS SA bacteremia

(SAB). Methods. Retrospective cohort analysis was performed on patients with DNS (cases) and DS (controls) SAB admitted to Henry Ford Health between 9/2005 and 3/2023. Patients with persistent (>7 days of positive blood cultures) DS SAB were used as controls. Demographic, risk factors, clinical characteristics, and outcomes were evaluated. Primary outcomes were 30-day relapse or progression, readmission and mortality; secondary endpoint was 90-day mortality. Results. A total of 122 patients included 59 (48%) cases and 63 (52%) controls. The majority were male (56.6%) with median age of 59. The study population had a high burden of comorbidities as outlined in the Table; central venous catheter use was significantly more common among cases (p=0.049). History of MRSA infection (p< 0.001) and prior hospitalization (p< 0.001) within 1-year, and antibiotic (p=0.017) use, particularly vancomycin (p=0.011), within 90 days were associated with DNS SA. Primary source of infection and infectious complications were not significantly different among cases and controls. There was no significant difference in outcomes between the two groups. Although not statistically significant, 90-mortality was higher in the DNS group (p=0.075). Conclusion. Our study highlights risk factors for DNS SA, including recent vancomycin use, and prior hospitalization and MRSA infection within 1 year. While there was no significant difference in outcomes between DNS and DS SAB, overall mortality was high. These findings highlight the need for continued surveillance of DNS SA and careful consideration of risk factors when selecting antimicrobial agents for complicated SA infections. Further studies are needed to identify potential mechanisms of vancomycin cross-resistance in DNS SA. (Table Presented).

Infectious Diseases

Hardy ME, **Kenney RM**, **Tibbetts R**, **Shallal A**, and **Veve M**. Leveraging Stewardship to Promote Narrower-spectrum Antibiotic Use for Low-risk AmpC Enterobacterales. *Open Forum Infect Dis* 2023; 10:S6. Full Text

M.E. Hardy, WVU Medicine, Morgantown, WV, United States

Background. AmpC β-lactamases are associated with development of ceftriaxone (CRO) resistance despite in vitro susceptibility, but the risk of AmpC derepression is not equal among Enterobacterales. The purpose of this study was to evaluate the impact of an AmpC stewardship intervention on definitive treatment of low-risk Enterobacterales. Methods. IRB approved, single pre-test, post-test quasi-experiment with a nonequivalent dependent variable at a 5-hospital system. An AmpC stewardship intervention was implemented 7/22 and included education, removal of microbiology comments indicating potential for CRO resistance on therapy, and modification of a blood PCR comment for Serratia marcescens to recommend CRO. Inclusion: adults ≥ 18 years pre- (7/21-12/21) and post-intervention (7/22-12/22) who received ≥ 72 hours of inpatient definitive therapy and had non-urine cultures growing S. marcescens, Providencia spp., Citrobacter koseri, C. amalonaticus, C. farmeri, or Morganella morganii. Exclusion: infection with CRO resistant organisms. Primary outcome: proportion of patients who received definitive CRO therapy. Secondary outcomes at 30 days: retreatment for the same organism, development of CRO-resistant organisms, or Clostridioides difficile infection (CDI). Results. 224 patients were included: 115 (51%) pre- and 109 (49%) postintervention. Table 1 describes patient, infection, and treatment characteristics. There were 79 (35%) patients with concurrent bacteremia. Definitive CRO therapy was prescribed more frequently after intervention 6 (5%) vs 72 (66%), P< 0.001. Median (IQR) total duration for pre- and post-groups (9 [7-17] vs 10 [7-18], P=0.46). After adjustment for intensive care, patients in the post-group were more likely to receive definitive CRO (adjOR, 35.4; 95%CI, 14.2-88.0) (Table 2). The proportion of patients who required retreatment was 18 (15%) and 11 (10%) for preand post-group patients (P=0.22). CRO resistance within 30 days occurred in 5 (4%) and 2 (2%) patients in the pre- and post-group (P=0.45). Table 1. Patient, infection, and treatment characteristics Conclusion. An antimicrobial stewardship intervention was associated with increased CRO prescribing and similar patient outcomes for low-risk AmpC Enterobacterales. (Table Presented).

Infectious Diseases

Joshi S, **Alvi RBR**, **Shanahan C**, **Ruby A**, **Chami E**, and **Suleyman G**. Clinical Characteristics and Outcomes in Patients with Healthcare Facility-Onset Clostridiodes difficile Infections. *Open Forum Infect Dis* 2023; 10:S386-S387. Full Text

S. Joshi, Henry Ford Hospital, Detroit, MI, United States

Background. Healthcare facility-onset (HCFO) Clostridiodes difficile infection (CDI) is the most common hospital-acquired infection. Although risk factors associated with CDI have been described, characterization and outcome of HFCO-CDI are limited. Methods. This was a retrospective observational study comparing disease severity among adult patients with HCFO-CDI from January 1, 2020, to December 31, 2022, at an 877-bed tertiary care hospital in Detroit. Patients were identified using National Healthcare Safety Network (NHSN) definition. CDI was classified as nonsevere, severe, or fulminant. Severe disease was defined as having white blood cell (WBC) count ≥ 15,000 cells/mm3 or acute kidney injury (AKI) defined as increase in creatinine of ≥ 0.3mg/dL within 48 hours of diagnosis. Fulminant disease included patients with ileus or toxic megacolon, or need for colectomy, intensive care unit or vasopressors. Risk factors, treatment and outcomes were evaluated. Results. 98 patients were diagnosed with HFCO CDI during the study period (Table 1); 37 (38%) were non-severe, 47 (38%) severe and 14 (24%) fulminant. Median age was 66 years, 50% were female and 45% white. Almost half were immune suppressed; 5% had prior CDI. Most patients (88%) were exposed to antibiotics (abx) prior to CDI with no difference between the groups (p=0.427); 61% received cephalosporins. Cirrhosis was more common among patients with fulminant disease (p=0.048) and receipt of chemotherapy was associated with severe and/or fulminant disease cases (p=0.049). AKI (p< 0.001), fever (p=0.030), and WBC >25,000 or < 2,000 cells/mm3 (p< 0.001) were more prevalent among patients with fulminant CDI; combination or alternative therapy was more common among fulminant cases (p< 0.001). Most were eligible, but only 6% received bezlotoxumab (BZX). Although outcomes were not significantly different between the groups, length of stay was longer and refractory disease and recurrence were more common in severe/fulminant CDI. Conclusion. In our HCFO-CDI cohort, most patients were exposed to abx, and cirrhosis and chemotherapy were associated with more severe CDI. Efforts should focus on appropriate abx utilization and increasing use of BZX to reduce burden of CDI and risk of recurrence and readmission.

Infectious Diseases

Kaur J, Gurdziel K, Wasinski B, Vakeesan N, Raza SH, Liu W, **Zervos M**, and **Suleyman G**. Genomic Epidemiology of SARS-CoV-2 in Metropolitan Detroit. *Open Forum Infect Dis* 2023; 10:S979. Full Text

J. Kaur, Henry Ford Health, Detroit, MI, United States

Background. The COVID-19 pandemic, resulting from the rapidly evolving SARS-CoV-2 virus, has drastically impacted health systems and economies worldwide. Genomic sequencing is critical for the surveillance of SARS-CoV-2 to monitor the rapidly evolving virus and identify new strains. Methods. 583 isolates from Henry Ford Health were retrospectively profiled across 3 years (117 isolates in 2020; 39 in 2021; 427 in 2022). DNA was extracted using Kingfisher viral isolation kit; RT-PCR screening was used to identify isolates with cycle threshold < 32 for whole genome sequencing (WGS). Libraries were generated using QIAseq DIRECT SARS-CoV-2 Kit, followed by Illumina sequencing (MiSeq or NovaSeq 6000; 300 cycles). Lineage analysis of the SARS-CoV-2 consensus genome sequences generated from samtools variant analysis pipeline was determined using Nextclade and Pangolin software. Results. Sequences were classified into 11 unique clades across 108 lineages by Nextclade and Pangolin, respectively. Almost three-fourths of the sequenced isolates were from 2022. 117 (20%) genomes were from the early pandemic (2020) and were clustered into 8 clades: 19A, 19B, 20A, 20B, 20C, 21 J (Delta) and 21L (Omicron). Most of the 2022 genomes (72%) were in clade 20C from lineage B.1, identified during the outbreak in Europe. 15 (13%) genomes had clade 19A (lineage B) and 1 had 19B (lineage A.3), identified early in the pandemic in Wuhan, China. Of the 39 (7%) genomes from 2021, the majority (82%) clustered into clade Delta 21J that originated in India. Only 2 (5%) of the genomes from 2021 had Alpha variant of concern (21I) from the lineage B1.1.7, which were suspected to be more transmissible. Of the 427 (73%) genomes from 2022, 393 (92%) had variants within Omicron variant of concern (21L), with 79 different lineages; 1 was Omicron variant 21K from the lineage BA1.1. Other clades observed in the 2022 batch were 19A (6%), 20A (0.2%), 20B (0.2%), 20C (0.2%) and 21M (1%). Conclusion. Our genomic surveillance data suggest that SARS-CoV-2 infections at the local level mirrored global outbreaks. This underscores the importance of robust genomic surveillance efforts to inform public health planning and practice.

Infectious Diseases

Parke DM, **Kenney RM**, **Bogojevich J**, **El-Khoury C**, **Joshi S**, **Brar S**, **MacDonald L**, **Salib C**, **MacDonald N**, **Veve M**, and **Suleyman G**. Barriers to Improving Outcomes among People Experiencing Homelessness and People Who Inject Drugs Hospitalized for Complicated Infections. *Open Forum Infect Dis* 2023; 10:S864-S865. Full Text

D.M. Parke, Henry Ford Health, Detroit, MI, United States

Background. People experiencing homelessness (PEH) and people who inject drugs (PWID) experience health disparities and worse outcomes. Challenges include suboptimal medication use, loss to follow-up, and non-compliance due to social determinant of health (SDOH) barriers, including lack of stable housing and transportation, limited financial resources, substance use, and addiction. Methods. This quality improvement project aimed to address SDOH barriers among hospitalized PEH and/or PWID requiring ≥ 2 weeks of antibiotics to improve antibiotic compliance and outcomes in Detroit from 6/2022-4/2023. Interventions included antibiotic education, addiction medicine and pharmacy discharge medication cost inquiry consults when indicated, ensuring oral antibiotics were in hand at discharge, strengthening discharge planning between inpatient and ambulatory case managers (ACM), and referrals to community-based organizations to address SDOHneeds. Results. 34 patients were included (8 PEH, 11 PWID, 15 both); 3 who died in the hospital were excluded. Multiple individual and structural barriers and challenges to improving adherence and outcomes were identified (Table 1). Loss to follow-up was a significant challenge among this cohort, primarily due to patients self-discharging (29%) and being unreachable (52%). 10 (37%) patients were offered SDOH services (Table 2). Patients also had significant behavioral health/substance use disorder needs and utilized healthcare at a very high rate, with 29% having an ED revisit and 44% being readmitted within 30 days after discharge. Several structural and SDOH barriers existed, including limited staff capacity and limited placement options after discharge, resulting in suboptimal treatment delivery. Conclusion. AddressingSDOHbarriers for PEHand PWIDis challenging but vital to improving outcomes. Qualitative research should be conducted to understand these barriers. Having an interdisciplinary team comprising of infectious diseases, pharmacy, addictionmedicine, casemanagement and population health is critical to address patient needs holistically. Strengthening internal processes and building additional communitybased partnerships will be essential to better meet patient needs after discharge. (Table Presented).

Infectious Diseases

Wells A, **Edmondson A**, **Mahal R**, and **Prascius S**. What Could Go Wrong? Utilizing a Failure Mode and Effects Analysis to Identify Endoscope Reprocessing Process Improvement Opportunities. *Am J Infect Control* 2024; 52(6):S3. Full Text

Background: When implemented correctly, endoscope reprocessing using high level disinfection (HLD) renders a reusable endoscope safe for the next patient. However, the amount and complexity of the steps of the HLD process make this challenging. An endoscopy department within a 191-bed acute care hospital with an average of 30 procedures per day had history of highly compliant HLD audits performed by the infection prevention team. However, due to staffing changes and increasing staff expectations, errors in the HLD process led to two patient exposures. Though mitigated swiftly, an improvement process was sought to prevent future patient exposures. Methods: The quality department chose to facilitate a Failure Mode and Effects Analysis (FMEA) to determine what other steps could fail next. Quality department leadership composed a multidisciplinary team to review the 70+ steps in channeled endoscope reprocessing to identify failure modes. First, the infection prevention/quality manager categorized the steps. Next, endoscopy nursing leadership, an endoscope reprocessing technician, surgical services leadership, and quality/risk management delineated the possible failure modes, causes, and effects for each step. The team scored the likelihood of each failure occurring and its severity, each on a scale of 1 to 4, to find areas in need of action plans. The likelihood and severity scores were multiplied to identify highest areas of risk. Results: Four steps of the HLD process had a risk score of eight or higher, and the group chose to focus on these for process improvement plans. These steps included portions of the manual endoscope cleaning process, new employee training and competency, and automated endoscope reprocessor parameter verification. Specific action plans will be created for these highest risk elements. Conclusions: There are often several opportunities for improvement of

complex processes such as HLD. Quality improvement tools such as the FMEA can assist infection prevention programs with prioritizing competing opportunities.

Infectious Diseases

Yared NF, **Gudipati S**, **Payne S**, **Alvi RBR**, **Cherian J**, **Di Lodivico J**, **Markowitz N**, and **Brar I**. Efficacy of Long-Acting Cabotegravir and Rilpivirine in a Diverse Group of Patients in a Real-World Setting. *Open Forum Infect Dis* 2023; 10:S749-S750. Full Text

N.F. Yared, Henry Ford Health System, Detroit, MI, United States

Background. Cabotegravir (CAB) + rilpivirine (RPV) is the first recommended complete long-acting (LA) regimen for maintenance of HIV-1 virologic suppression. The efficacy and safety of switching to CAB + RPV LA (CAR) has been shown in clinical trials. CAR injections offer less frequent dosing and address issues of adherence and disclosure related to daily oral cART. We describe the clinical characteristics and outcomes of switching a diverse group of people with HIV (PWH) to CAR in a real-world setting. Methods. A retrospective cohort study was performed to assess virologic efficacy of intramuscular CAR given every 4 or 8 weeks among adult PWH receiving care at Henry Ford Health ID Clinic by an interdisciplinary team of physicians, nurses, social workers, and a pharmacist. Efficacy was defined as HIV-1 RNA < 20 copies/mL at 3 months. Demographics, clinical characteristics, and outcomes were extracted from the electronic medical record. Results. We included the first 51 patients to receive CAR. Median age was 46 years (IQR 34 -59). Black individuals were 75%, cisgender males 84%, and transgender females 3.9% of participants. PWH were diagnosed a median of 12 years ago (IQR 11-17). At time of switch, 90% had HIV viral load (VL) < 20 copies/ml, and 9.8% of patients were viremic with < 75 copies/ml. Mean Cd4+ cell count was 871 cells/ µL (IQR 632-1603). Prior to switch, 80% had received ≥ 2 cART regimens, 75% had INSTI exposure, and 45% had NNRTI exposure. Among 38 patients with HIV-1 genotypes available prior to switch, 4 had either baseline NNRTI or INSTI mutations (Table 2). For patients with VL data at 3 months, 37 of 38 (98%) had an undetectable VL. Virologic failure occurred in 1 PWH with BMI 35 who had a Y188L RT mutation in a 2009 genotype which did not include RPV (2011 approval), with subsequent emergence of pan-NNRTI and INSTI resistance. Conclusion. A high degree of virologic suppression at 3 months was achieved among an older, diverse cohort of PWH cared for by an interdisciplinary team. Unrecognized baseline HIV resistance to NNRTI contributed to one virologic failure. It is important to assure that genotypic susceptibility interpretations are current and to carefully assess for eligibility before switching to CAR.

Internal Medicine

Albusoul L, **Shahid M**, Vuyyala S, Otrock ZK, and **Kuriakose P**. Trend in Von Willebrand Factor Profile in Women With Von Willebrand Disease During Pregnancy and Postpartum. *Blood* 2023; 142:5499. Full Text

Introduction: Pregnancy is considered a hypercoagulable state, with levels of multiple coagulation factors including Factor VIII (FVIII) and von Willebrand Factor (VWF), progressively increasing throughout, reaching their peak levels during the third trimester. However, in women with von Willebrand disease (VWD), these changes are variable and could be blunted or absent due to the wide heterogeneity of phenotypes and pathophysiological mechanisms linked to this disorder, posing a significant clinical challenge. This study aims to describe the trend in the VWF profile in women with VWD during each trimester of pregnancy and in the postpartum period. Methods: This is a retrospective single-center study that included adult pregnant women diagnosed with VWD, who were followed at Henry Ford Health between 03/2012 and 11/2022. Patients with other bleeding disorders were excluded from the study. Data on baseline characteristics, including age, race, age at childbirth, and parity were collected. Additional data collected included VWF antigen (VWF:Ag) level, FVIII activity level, and VWF ristocetin cofactor (VWF:Rco) activity during the first, second, and third trimesters, as well as in the postpartum period. Results: A total of 33 cases were included in our study. At baseline, the mean VWF:Ag level in our patients was 50.5% (reference range 50%-150%). Compared to baseline, the VWF:Ag level increased by 48.71% in the first trimester, 80.59% in the second trimester, and 168.71% in the third trimester. Postpartum, the VWF:Ag level decreased by 51.29% compared to the third trimester; however, it remained 30.89% higher than baseline levels. While the FVIII level (reference range 50%-150%) was an

average of 64.8% at baseline, it increased by 21.91% in the first trimester, 74.23% in the second trimester, and 143.67% in the third trimester, compared to baseline. Postpartum, the FVIII level decreased by 48.45% from the third trimester but remained 25.62% higher than baseline. Additionally, the VWF:Rco level was an average of 44.3% (reference range 51%-215%) at baseline. Compared to baseline, the VWF:Rco level increased by 61.85% in the first trimester, 90.52% in the second trimester, and 142.66% in the third trimester. It decreased by 49.12% postpartum compared to the third trimester but remained 23.48% higher than baseline. Conclusion: In women with VWD, VWF:Ag level, FVIII level, and VWF:Rco levels steadily increase during pregnancy, reaching their maximum levels during the third trimester. All three levels decreased in the postpartum period; however, they remain higher compared to baseline at a median follow up of 105 days after delivery.

Internal Medicine
Awan MR, Siddique M, Rahman SU, and **Chaudhary A**. Unmasking the Enigma: A Case of Idiopathic Non-Cirrhotic Portal Hypertension. *Am J Gastroenterol* 2023; 118(10):S2304-S2304. Full Text

[Awan, Muhammad Raheel; Rahman, Saad Ur] Carle Fdn Hosp, Urbana, IL USA. [Siddique, Mahreen] Childrens Hosp, Champaign, IL USA. [Siddique, Mahreen] Inst Child Hlth, Champaign, IL USA. [Chaudhary, Ammad] Henry Ford Hosp, Detroit, MI 48202 USA.

Internal Medicine
Bugazia S, **Gandhi N**, **Weerakoon N**, and **Kukreja G**. First Report of Asymptomatic Solitary High-Grade B-Cell Lymphoma NOS: An Enigmatic Entity. *Blood* 2023; 142:6253. Full Text

Background High-grade B cell lymphoma (HGBL) is a new disease entity introduced by WHO in 2016, including two types: HGBL with a double hit (DH) or triple hit (TH) and HGBL, not otherwise specified (NOS). HGBL DH/TH are defined by genetic rearrangements of specific oncogenes MYC, BCL2 and/or BCL6, while HGBL NOS is defined purely base on morphology in the absence of these genes. HGBL DH/TH is known for its poor prognostication given its propensity to rapidly progress and disseminate, however HGBL NOS remains ill-defined and poorly understood with no tangible literature describing its clinical nature and therapeutic susceptibility. Case presentation A 76-year-old post-menopausal woman with no significant PMH presented for evaluation of painless hematuria during a routine office visit. Evaluation with imaging showed a suspicious incidental liver mass concerning for possible metastatic or primary liver cancer. Obtained labs were unremarkable, including serum LDH, serological testing for hepatitis B/C and HIV1/2, and typical tumor markers. PET scan showed focal uptake of tracer in liver with no nodal involvement. Liver biopsy revealed diffuse infiltration by atypical lymphocytes. Immunohistochemical analysis showed CD20 and CD10 positivity, negative CD30, and high Ki-67 proliferation rate of 100%, however the absence of MYC, BCL6, BCL2, and t(8;14) rearrangements on FISH ruled out Burkitt and DH/TH lymphoma, consistent with HGBL-NOS. Following discussions with Henry Ford Lymphoma Tumor Board, patient was treated with six cycles of R-CHOP, where follow-up imaging indicated remission of her lymphoma. Conclusion This represents an extraordinary first report of HGBL NOS manifesting as an isolated primary hepatic lymphoma in the complete absence of clinical symptoms. The significance of this case lies in its atypical extra-nodal site of involvement and total absence of clinical symptoms and serological markers, underscoring the unfulfilled need to further describe this enigmatic entity.

Internal Medicine
Chaudhary A, **Denha E**, **Khan MZ**, **Rehman S**, Zaidi SMH, El Alayli A, Gharaibeh EZ, and Farooq U. Unraveling the Unusual: Autoimmune Hepatitis After a 5-day Course of Nitrofurantoin for Uncomplicated UTI. *Am J Gastroenterol* 2023; 118(10):S2311-S2311. Full Text

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Internal Medicine
Chaudhary A, **Fahad H**, Farooq U, El Alayli A, Awan MR, Gharaibeh EZ, and **Prostak J**. Burping, Fainting, and Laughing: The Hilarious Tale of a Hungry Heart. *Am J Gastroenterol* 2023; 118(10):S2633-S2633. Full Text

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Internal Medicine
Chaudhary A, **Fahad H**, **Francis A**, **Samad M**, **Rehman S**, **Baldwin H**, **Rana F**, Farooq U, El Alayli A, and **Jafri SM**. Unveiling the Influence of Age and Race on COVID-19 Incidence in Liver and Kidney Transplant Population. *Am J Gastroenterol* 2023; 118(10):S1074-S1074. Full Text

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Internal Medicine
Chaudhary A, **Fahad H**, **Samad M**, **Rehman S**, Francis A, Baldwin H, Rana F, Farooq U, **Ichkhanian Y**, and **Jafri SM**. Revolutionary Defense: Evusheld Triumphs in Combating Post Covid-ILD Among Liver and Kidney Transplant Recipients. *Am J Gastroenterol* 2023; 118(10):S1075-S1075. Full Text

[Chaudhary, Ammad; Fahad, Hamna; Rehman, Sheema; Ichkhanian, Yervant] Henry Ford Hosp, Detroit, MI 48202 USA. [Samad, Momin] Henry Ford Hosp, Rochester Hills, MI USA. [Francis, Ashley; Baldwin, Hope; Rana, Fariba] Wayne State Univ, Detroit, MI USA. [Farooq, Umer] Univ Rochester, Rochester, NY USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. Wayne State University; University of Rochester; Henry Ford Health System; Henry Ford Hospital

Internal Medicine
Chaudhary A, **Khan MZ**, **Fahad H**, **Muszkat Y**, and **Jafri SM**. TPN and Pregnancy: A Series of Successful Conceptions. *Am J Gastroenterol* 2023; 118(10):S2517-S2517. Full Text

[Chaudhary, Ammad; Khan, Muhammad Zarrar; Fahad, Hamna; Muszkat, Yakir] Henry Ford Hosp, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Hospital

Internal Medicine
Chaudhary AJ, **Fahad H**, **Samad M**, **Rehman S**, **Baldwin H**, **Francis A**, **Rana F**, **Ichkhanian Y**, **Jomaa D**, **Gupta K**, and **Jafri SM**. EVUSHELD IN LIVER AND KIDNEY TRANSPLANT PATIENTS , WAS IT WORTH IT? *Hepatology* 2023; 78:S310-S311. Full Text

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Background: Immunosuppression in patients with solid organ transplant has raised significant concerns regarding outcomes of COVID-19 infection. Pre-exposure use of monoclonal antibodies, specific to certain viral strains as an adjunct to vaccination has been proposed to enhance the immune response following the vaccine. In this study, we aimed to assess the efficacy of the emergency use of Evusheld in this sub-population. Methods: This was a retrospective chart review study conducted at a tertiary care center during the time period of 2022 , 2023 during which adult patients (age >18 y old) with liver, kidney or simultaneous Liver- Kidney transplant who received Evusheld were included. Patients' demographics, disease characteristics, and outcomes were recorded in de-identified datasheets. The primary outcome was incidence of COVID-19 positive PCR test. Secondary outcomes included: progression to Interstitial

lung disease (ILD), rate of hospitalization. The Wilcoxon rank sum test, Pearson's Chi-squared test, Fisher's exact test and Wilcoxon rank sum exact test were used for univariate analyses. Results: Among 1149 who received solid organ transplant, 273 (23.7%) patients were diagnosed with COVID-19 from the advent of the pandemic, to February 2023. Patients infected with COVID-19 were more likely to be younger (mean age 61.6 ± 10.9 y versus 63.4 ± 11.5 y, p =0.007), of white race (25.6% versus black 15.2 % and others 14.7 %, p= 0.014). In the total population 26% (296) received Evusheld. Among those who received Evusheld the incidence of covid was 13% (37/296) compared to 28% (236/853) in the patients who did not receive the Evusheld, p< 0.01. Data for post covid ILD was available in only 43.7% (118) patients. Among those with data available, prevalence of post covid ILD was 0%(0/22) and 8.1% (8/96) among those who did and did not receive evusheld respectively, p-value 0.045. Among those with data available, 16.1% (5/31) patients were hospitalized after getting Evusheld as compared to 20.7% (46/176) in patients who did not receive evusheld, p =0.689. Conclusion: Our data shows that Evusheild may have reduced incidence of COVID-19 and provided significant protection against post infectious ILD. It also showed that incidence of COVID-19 in post-transplant patients may be much higher than previously reported. Currently, the FDA has halted all use of Evusheild due to the combined frequency of non-susceptible SARSCoV- 2 variants nationally being more than 90%. However, they do recommend keeping the unexpired batches safe for future, in case new variants show susceptibility.

Internal Medicine

Dillon WP, **Muthanna Shadid A**, **Parsons A**, **Hardy M**, **Williams JD**, **McCorquodale J**, **Ramesh M**, and **Alangaden GJ**. Outcomes of Outpatient Parenteral Antimicrobial Therapy in the Solid Organ Transplant Population. *Open Forum Infect Dis* 2023; 10:S208-S209. Full Text

W.P. Dillon, Henry Ford Hospital, Detroit, MI, United States

Background. Outpatient parenteral antimicrobial therapy (OPAT) provides an effective and convenient means to complete extended courses of antimicrobial therapy for the treatment of serious infections. There is scant data addressing OPAT related outcomes such as readmission in solid organ transplant (SOT) recipients. Methods. In this observational cohort study, we analyzed all adult SOT recipients discharged from Henry Ford Hospital - an 877 bed quaternary care center in Detroit, Michigan - on OPAT between January 2015 and December 2020. The primary endpoint was 30-day all-cause readmission. The secondary endpoints included evaluation of risk factors associated with readmission (transplant type, reason for OPAT, OPAT related complications, length of treatment, length of stay, discharge disposition, and adequacy of infectious disease follow up and laboratory monitoring) and all-cause mortality at one year. Results. There were 201 patients discharged on OPAT. Demographics between study populations were comparable (Table 1). A total of 83 out of 201 (41.3%) patients were readmitted. There were 38 (18.9%) patients readmitted for OPAT related complications and 45 (22.4%) for non-OPAT related reasons. Intestinal and multi-visceral transplants were associated with readmission (p=0.04 and p=0.02 respectively) while renal transplants were protective against readmission (p=0.02) (Table 1). Other factors associated with readmission include development of an OPAT related complication including treatment failure (p< 0.001) (Table 2). Patients discharged without Infectious Disease follow up were less likely to be readmitted (p=0.04) (Table 3) as these patients generally had less serious infections not meriting a follow up appointment. There was no difference in mortality at one year between study populations (Table 3). Conclusion. While the overall readmission rate of SOT discharged on OPAT is high, most readmissions were unrelated to OPAT. Patients with readmissions had higher rates of OPAT related complications and treatment failures. Further studies are warranted to optimize OPAT outcomes in the SOT population. (Table Presented).

Internal Medicine

Faisal MS, **Ashraf T**, **Harris K**, **Khan MZ**, **Chaudhary A**, **Watson A**, **Dang DY**, **Pompa R**, **Elatrache M**, **Piraka C**, **Singla S**, and **Zuchelli T**. Cystic Duct Stenting vs Other Treatment Modalities for Management of Acute Cholecystitis in Patients With Decompensated Cirrhosis. *Am J Gastroenterol* 2023; 118(10):S957-S957. Full Text

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Internal Medicine
Faisal MS, **Shamaa O**, **Dang DY**, **Watson A**, **Elatrache M**, **Pompa R**, **Zuchelli T**, **Piraka C**, and **Singla S**. Safety and Efficacy of Biliary Radiofrequency Ablation in Management of Ampullary Lesions. *Am J Gastroenterol* 2023; 118(10):S2218-S2219. Full Text

[Faisal, Muhammad Salman; Shamaa, Omar] Henry Ford Hlth Syst, Detroit, MI USA. [Dang, Duyen; Watson, Andrew; Elatrache, Mazen; Pompa, Robert; Zuchelli, Tobias; Piraka, Cyrus; Singla, Sumit] Henry Ford Hosp, Detroit, MI 48202 USA. Henry Ford Hospital

Internal Medicine
Farooq U, Tarar Z, El Alayli A, Niu CG, **Chaudhary AJ**, and Qureshi K. EPIDEMIOLOGIC TRENDS IN COMORBIDITY BURDEN AND HEALTHCARE RESOURCE UTILIZATION IN NONALCOHOLIC STEATOHEPATITIS (NASH): A LONGITUDINAL STUDY. *Hepatology* 2023; 78:S953-S954. Full Text

[Farooq, Umer; El Alayli, Abdallah; Qureshi, Kamran] St Louis Univ, St Louis, MO USA. [Tarar, Zahid] Univ Missouri, Columbia, MO USA. [Niu, Chengu] Rochester Gen Hosp, Rochester, NY USA. [Chaudhary, Ammad Javaid] Henry Ford Hosp, Detroit, MI USA. Missouri Columbia; Rochester General Hospital; Henry Ford Health System; Henry Ford Hospital

Internal Medicine
Farooq U, Tarar Z, Niu C, El Alayli A, Abbasi AF, Hayat U, **Chaudhary A**, and Qureshi K. Epidemiologic Trends in Patient and Hospital Characteristics of Nonalcoholic Steatohepatitis: A Longitudinal Study. *Am J Gastroenterol* 2023; 118(10):S1142-S1143. Full Text

[Farooq, Umer; El Alayli, Abdallah; Qureshi, Kamran] St Louis Univ, St Louis, MO USA. [Tarar, Zahid] Univ Missouri, Columbia, MO USA. [Niu, Chengu] Rochester Gen Hosp, Rochester, NY USA. [Abbasi, Abu Fahad] Loyola Univ, Med Ctr, Maywood, IL USA. [Hayat, Umar] Geisinger Wyoming Valley Med Ctr, Wilkes Barre, PA USA. [Chaudhary, Ammad] Henry Ford Hosp, Detroit, MI USA. Missouri Columbia; Rochester General Hospital; Loyola University Chicago; Henry Ford Health System; Henry Ford Hospital

Internal Medicine
Gharaibeh EZ, El Alayli A, Onwuzo S, Boustany A, Farooq U, **Chaudhary A**, Thomas A, and Palagiri J. Glanzmann Thrombasthenia - Challenging Gastrointestinal Bleeding Without Definitive Management Guidelines. *Am J Gastroenterol* 2023; 118(10):S2037-S2038. Full Text

[Gharaibeh, Eyad Z.; El Alayli, Abdallah; Thomas, Alexander; Palagiri, Jennifer] St Louis Univ, St Louis, MO USA. [Onwuzo, Somtochukwu; Boustany, Antoine] Cleveland Clin Fdn, Fairview Pk, OH USA. [Farooq, Umer] St Louis Univ, Rochester, NY USA. [Chaudhary, Ammad] Henry Ford Hosp, Detroit, MI USA. System; Henry Ford Hospital

Internal Medicine
Hadi M, **Youssef RM**, Dourra M, **Obri M**, **Beidoun M**, and **Jafri SM**. A Late Diagnosis of Caroli Syndrome. *Am J Gastroenterol* 2023; 118(10):S1520-S1520. Full Text

[Hadi, Moustafa] Michigan State Univ, Coll Human Med, Detroit, MI USA. [Youssef, Rami M.; Obri, Mark; Jafri, Syed-Mohammed] Henry Ford Hosp, Detroit, MI 48202 USA. [Dourra, Mohsen] Corewell Hlth, Woodhaven, MI USA. [Beidoun, Mohamad] Henry Ford Hosp, Livonia, MI USA. Medicine; Henry Ford Health System; Henry Ford Hospital; Henry Ford Health System

Internal Medicine
Hinojosa O, **Ammari O**, **Albusoul L**, **Kuriakose P**, and Otrock ZK. Post-Transfusion Purpura: A Literature Review. *Blood* 2023; 142:1294. Full Text

Introduction: Post-transfusion purpura (PTP) is a rare and occasionally life-threatening transfusion reaction characterized by severe thrombocytopenia usually within two weeks of blood transfusion. It is associated with the development of alloantibodies to human platelet antigens (HPAs). Due to its rarity, our knowledge of PTP is mostly based on reported cases or small cohorts. Methods: This is a systematic literature review of English language articles published in 2 large medical databases (Embase and Pubmed) using the search terms “post-transfusion purpura”, “posttransfusion purpura”, and “post transfusion purpura” between the years 1985 and 2023. Only articles reporting on patients older than 18 years were included. 684 articles were identified, 590 of them were excluded since they represented a combination of case reports of other conditions, laboratory, and epidemiological reports. The 94 articles left, represented case reports and case series of PTP encompassing 149 patients. 21 patients were removed since they represented duplicate cases. 17 patients were excluded due to missing information. 11 patients were excluded due to the presence of confounding clinical conditions. Results: A total of 100 cases were included in the study. The mean age was 56.7 years. 85% were female, 14% were male, and 1 was missing gender data. 62% of cases reported a baseline platelet count, ranging between 78,000 - 600,000 cells/µL. 65% of cases presented after a procedure- or surgery-related transfusion, of these 22 were related to cardiovascular procedures, while 16, 10, and 9 cases were related to gynecological, abdominal, and orthopedic surgeries respectively. A history of prior transfusions was only documented in 24% of cases. A prior pregnancy was reported in 63% of the cases. Red blood cell, fresh frozen plasma, and platelet transfusions were associated to 64%, 11%, and 9% of cases, respectively. The most common HPA antibody detected was HPA-1a (81%). HPA-1b, HPA-5b, and HPA-3a were the next most common antibodies, identified in 7%, 5%, and 5% cases, respectively. The median time from the first transfusion to the development of thrombocytopenia was 8 days, reaching a platelet nadir in 9 days. The platelet nadir ranged between 0 - 50,000 cells/ µL. Clinical presentation included post-transfusion fever (15%), petechial rash, epistaxis, and oral bleeding (65%, 17%, and 12, respectively), and bleeding from the genitourinary system, gastrointestinal tract, surgical incisions, lower respiratory tract, and central nervous system (38%, 28%, 6%, 6%, and 2% of cases, respectively). Death was reported in 9% of cases. The median time from PTP diagnosis to initiation of first treatment was 1 day. 83% of cases achieved an adequate response, defined as a platelet count > 100,000 cells/µL, after a mean/median time of 14.2/11.5 days (available in 68% of cases). Corticosteroids, intravenous immunoglobulin, and plasmapheresis were administered in 68%, 63%, and 27%, of cases, respectively. 6 patients received HPA 1a negative platelet transfusions. Conclusions: The majority of reported PTP cases were females with a history of pregnancy or blood transfusions consistent with existing literature. Over 60% of cases were linked to a surgical procedure, with cardiovascular cases constituting the largest portion. Anti-HPA-1a represented the most commonly detected antibody, followed by HPA-1b, HPA-5b, and HPA-3a. The most common sites of bleeding were the gastrointestinal and genitourinary tracts. 9% died from PTP. The majority of patients (83%) achieved an adequate response, with the most common treatment modalities being corticosteroids, IV immunoglobulins, and plasmapheresis.

Internal Medicine

Ibrahim A, **Chaudhary A**, Sarowar A, Baldwin H, Khan MZ, and **Jafri SM**. Unveiling the Risk: Factors Affecting Clostridioides difficile Infection Incidence Within 1 Year of Liver Transplantation. *Am J Gastroenterol* 2023; 118(10):S1115-S1115. Full Text

[Ibrahim, Ahmed; Chaudhary, Ammad; Khan, Muhammad Zarrar] Henry Ford Hosp, Detroit, MI USA. [Sarowar, Arif; Baldwin, Hope] Wayne State Univ, Sch Med, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Health System; Henry Ford Hospital

Internal Medicine

Ibrahim AM, **Chaudhary AJ**, **Baldwin H**, **Sarowar A**, **Khan MZ**, and **Jafri SM**. EVALUATION OF THE EFFECT OF THE COVID-19 PANDEMIC ON THE RATE OF CLOSTRIDIUM DIFFICILE INFECTION FOLLOWING LIVER TRANSPLANTATION. *Hepatology* 2023; 78:S309-S310. Full Text

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Internal Medicine
Ichkhanian Y, **Veracruz N**, **Al-Haddad M**, Albunni H, Schlachterman A, Gouda Z, Canakis A, Kim R, D'Souza L, Khashab M, **Nimri F**, **Ashraf T**, **Faisal MS**, **Jomaa D**, **Dababneh Y**, **Rehman S**, **Rizwan A**, **Singla S**, **Alsheik E**, **Ginnebaugh B**, **McFarlin K**, **Piraka C**, and **Zuchelli T**. Management of Patients After Failed Gastric Peroral Endoscopic Myotomy: A Multi-Center Study. *Am J Gastroenterol* 2023; 118(10):S1410-S1411. Full Text

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Internal Medicine
Jaan A, Farooq U, Malik S, **Chaudhary A**, Inayat F, Chatha U, Khan A, Cryer B, and Mahmood S. Impact of Ethnicity on the Outcomes of Acute Pancreatitis: Insights From US National Inpatient Sample Database. *Am J Gastroenterol* 2023; 118(10):S12-S12. Full Text

[Jaan, Ali; Farooq, Umer; Malik, Sheza] Rochester Gen Hosp, Rochester, NY USA. [Chaudhary, Ammad] Henry Ford Hosp, Detroit, MI USA. [Inayat, Faisal] Allama Iqbal Med Coll, Lahore, Punjab, Pakistan. [Chatha, Uzair] Lahore Med & Dent Coll, Overland Pk, KS USA. [Khan, Ahmad] Case Western Reserve UHCMC, Cleveland, OH USA. [Cryer, Byron] Baylor Univ, Med Ctr, Dallas, TX USA. [Mahmood, Sultan] Beth Israel Deaconess Med Ctr, Boston, MA USA. Hospital; Baylor University; Baylor University Medical Center; Harvard University; Beth Israel Deaconess Medical Center

Internal Medicine
Jacob B, **Jamil M**, **Raslan S**, **Nasser Z**, **Springer K**, **Michael German A**, and **Kuriakose P**. Infusion Reactions with Alternative Therapies during the National Shortage of Iron Dextran. *Blood* 2023; 142:7338. Full Text

Introduction The national shortage of intravenous iron dextran has required patients to receive more alternative iron infusions, such as iron sucrose and sodium ferric gluconate/sucrose, since January 2023. While prior studies have evaluated rates of infusion reactions among some commonly used intravenous iron formulations, data is lacking among differing doses of iron formulations and especially in the setting of this iron dextran shortage. Clinicians at our institution generally observed more adverse reactions with alternative iron infusions during the national shortage of iron dextran compared to prior. Our study examines the infusion reactions of various iron therapies at differing doses and actions providers and patients took thereafter to assess the impact of the iron dextran national shortage on patients. Methods Patients were included who received iron infusions in three Henry Ford Hospital clinics in metropolitan Detroit, Michigan, from July 2022-June 2023 with the national iron dextran shortage impacting the health system since January 2023. Age, race, sex, reason for iron infusion, iron infusion formulation received, time of infusion, and dosing schedule of infusion were recorded for all participants. We assessed the symptoms experienced and actions taken for patients who had an infusion reaction. The number and type of infusion reactions between different iron infusion formulations and doses were then compared. Results Of the 880 unique patients assessed, 496 (56.4%) received iron dextran, iron sucrose, or sodium ferric gluconate/sucrose between July 2022 and December 2022 prior to the national iron dextran shortage and 384 (43.6%) patients had iron infusions between January 2023 and June 2023 during the shortage. Iron dextran accounted for most of the infusions (n= 356, 71.8%) prior to the shortage whereas iron sucrose was the majority (n=312, 81.3%) during the shortage. Prior to the national shortage, 30 iron infusions

reactions occurred, with 18 (60%) associated with iron dextran, 9 (30%) with iron sucrose, and 3 (16.7%) with sodium ferric gluconate/sucrose. During the shortage, 44 reactions occurred, with 1 (2.27%) associated with iron dextran, 41 (93.1%) with iron sucrose, and 2 (4.54%) with sodium ferric gluconate/sucrose. The most reactions (n=41, 55.4%) occurred with iron sucrose at a dose of 500mg across the whole study period. Less reactions (n=9, 12.2%) were reported for iron sucrose at progressively lower doses, comparable to reactions with iron dextran at doses greater than 1000mg (n=8, 10.8%) and at lower doses of iron dextran (n=10, 13.5%). The most common reaction across all infusion types was nausea, vomiting, and/or diarrhea. After an iron infusion reaction, the infusion plan was then most commonly discontinued, with patients either switching to alternative iron infusion formulations, continuing the same infusion type with medications for symptoms, or continuing the same infusion type with lower dose and increased frequency. Conclusion More iron infusion reactions occurred after the national shortage of iron dextran since January 2023 in the setting of more frequent use of alternative iron therapies. The most common infusion formulation associated with a reaction was iron sucrose at its higher recommended dose of 500mg, compared with iron dextran and sodium ferric gluconate/sucrose. Providers should be aware of these associated adverse reactions with the different doses of alternative formulations when recommending infusions for patients, and the need for preemptive intervention.

Internal Medicine

Jamil M, **Nasser Z**, **Jacob B**, **Mangal R**, and **Donthireddy V**. Efficacy of Direct Oral Anticoagulants Vs Warfarin Vs Low Molecular Weight Heparin in the Treatment of Acute Splanchnic Vein Thrombosis in Patients with Underlying Myeloproliferative Disorder. *Blood* 2023; 142:5533. Full Text

Introduction: Myeloproliferative neoplasms (MPNs) are hematopoietic stem cell disorders characterized by clonal proliferation of myeloid-lineage cells. Venous thrombosis poses a significant morbidity risk for MPN patients. The current recommended treatments for acute splanchnic vein thrombosis (SVT) are warfarin and low molecular weight heparin (LMWH). Direct oral anticoagulants (DOACs) are potential alternatives due to their predictable dose response and oral administration, but limited data exists for their use in acute SVTs. This retrospective study aims to assess the efficacy and outcomes of DOACs, LMWH, and warfarin in treating acute SVTs in patients with underlying MPN. Methods: We included patients of all ages with underlying myeloproliferative neoplasms and splanchnic vein thrombosis, with no underlying liver diseases, from Henry Ford Hospital Clinics in metropolitan Detroit, Michigan between 2013 and 2023. Patient data, which included age, gender, race, and BMI were recorded. The primary outcome was complete radiographic resolution (CRR) of the SVT, and secondary outcomes included recanalization, thrombosis progression, recurrent thrombosis, major bleeding, thrombocytopenia, and skin necrosis. The outcomes were compared between the three anticoagulant groups and patients using aspirin. Results: Among the 34 MPN patients with SVT, warfarin was prescribed most frequently (n=19), followed by enoxaparin (n=5) and DOACs (n=5). Although no significant differences were observed, warfarin showed the highest CRR rates (41.2%), while enoxaparin and DOACs had equal CRR rates (25%). DOACs showed recanalization rates similar to warfarin and higher than enoxaparin (44.4% and 47.1% vs. 20.0%, respectively). LMWH was associated with increased recurrent thrombosis rates (50.0%), while DOACs had a higher risk of major bleeding. All three anticoagulants had similar effects on thrombocytopenia and SVT progression. Aspirin use was linked to a higher risk of major bleeding (42.9%), but not using aspirin correlated with complete SVT resolution (30.8%), SVT progression (20.8%), recurrent thrombosis (29.2%), and thrombocytopenia (28.6%). Conclusions: Although limited by a small sample size, our study found no significant differences among the three anticoagulant groups. This contributes to establishing the role of DOACs in treating SVTs in patients with underlying MPN. Further studies with larger sample sizes are needed to explore the efficacy of DOACs compared to warfarin. Additionally, investigating the potential benefits of early thrombolysis in conjunction with anticoagulation for SVT patients with underlying MPN should be pursued, as the rates of complete resolution in these patients were low.

Internal Medicine

Jomaa D, **Dababneh Y**, **Nagirimadugu A**, **Oruganti P**, **Lu M**, **Melkonian C**, and **Kaur N**. Bridging Healthcare Disparities in Patients With Inflammatory Bowel Disease (IBD) in Underserved Communities: Results From a Telemedicine Intervention at a Large Tertiary Care Center. *Am J Gastroenterol* 2023; 118(12):S18. Full Text

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Background: The prevalence of IBD in the United States is greater than 3 million and rising, while the access to IBD specialists in rural areas remains limited. Urban areas associated with large healthcare systems have 263 specialists per 100,000 residents, whereas rural areas have only 30 specialists per residents. The specific aims of this study are to identify the impact access to specialty care has on frequency of IBD flares, emergency department (ED) visits, and hospitalizations. Methods: We conducted a retrospective chart review of adult patients (>18 years) with the diagnosis of IBD who reside in Michigan. Patients were divided into either pre or post periods, where preperiod was defined as before the initiation of telehealth services between 1/1/2018-12/31/2019, and post-period was defined as after the advent of telehealth, between 10/1/2021-10/31/2022, including both video visits as well as the Henry Ford Specialty Center, which offers IBD specialty care virtually. Patient's demographic information, IBD encounters, ED visits, hospitalizations were collected at the end of each study period. The outcomes of interest were the number of IBD-related outpatient encounters, ED visits, and hospitalizations in each period. Results: A total of 5520 IBD encounters were observed in both time periods from 4941 individual patients. Among the total 4941patients, 2992 patients were in the pre-period cohort, and 1949 patients were in the post-period cohort including 721 patients who were seen in both period cohorts. Patients' IBD encounters were significantly reduced in the post-period compared to those in the preperiod (RR=0.73, 95% CI 0.69-0.76 and p-value< 0.001). There was also a significant decrease in ED visits (RR=0.53, 95% CI 0.50-0.56) and hospitalizations in the post-period (RR=0.35, 95% CI 0.33- 0.37). In addition, we looked at the geospatial distribution in patients and found that there was a wider distribution of patients seeking care for their IBD in neighboring and rural counties in the postperiod compared to the pre-period. Conclusions: The IBD Center at Henry Ford Health serves more than 3,000 patients annually and an estimated 15% travel more than 60 miles for their care. Given the need to provide specialty care throughout Michigan, Henry Ford Health is offering telehealth services within a standard clinic to overcome the barriers of telehealth in IBD care. Our study shows that this effort has bridged access to medical care and increased distribution of patients in Michigan receiving specialty care for IBD. It also significantly reduced IBD flares, hospitalization, and ED visits for these patients.

Internal Medicine

Jomaa D, **Ichkhanian Y**, **Dababneh Y**, **Brown P**, **Dang D**, **Gonzalez H**, **Venkat D**, and **Zuchelli T**. A NATIONAL SURVEY ON THE RISING ROLE OF ENDOSCOPIC BARIATRIC PROCEDURES FOR THE MANAGEMENT OF NONALCOHOLIC STEATOHEPATITIS. *Hepatology* 2023; 78:S1230-S1231. Full Text

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Background: Weigh loss is the cornerstone of halting disease progression in patients with nonalcoholic fatty liver disease (NAFLD) and preventing nonalcoholic steatohepatitis (NASH). Patients who fail to lose weight through conservative modalities are often offered the option of bariatric surgeries, but most patients are either high-risk surgical candidates or prefer non-surgical modalities. Endoscopic Sleeve Gastrectomy (ESG) was introduced as a minimally invasive bariatric procedure that provides patients with acceptable weight loss and improvement in their metabolic disease that contributes to NAFLD and NASH. In the study, we aimed to conduct a national survey to evaluate practicing gastroenterologist's perception on the role of ESG for managing NASH. Methods: We conducted a descriptive study through a national survey of 15 questions. The survey was built through an online cloud-based software, and a link was emailed to a total of 493 U.S. GI fellowship programs. The email recipients were asked to forward the survey link to additional faculty members. There was no monetary compensation for filling out the survey. The survey was anonymous, and no physician or patient identifier was shared. Total estimated time for completing the survey was 4 minutes. Results: A total of 54 responses were obtained during the time period 01-09-2021 and 2-12-2021, with estimated completion rate of 50%. Survey questions were summarized in Table 1. The majority of participants, 72%, were from tertiary care academic center, mostly commonly located in the Midwest, (39%). About half (48%) of the institutions had an established multidisciplinary team to manage patients with NASH who failed to lose weight following conservative modalities, with 65% having an advanced endoscopist trained in bariatric endoscopy in the team. Providers were most commonly, advanced endoscopists (40%), hepatologists (26%), general

gastroenterologists, (18%), and gastroenterology fellows (11%). More than half of the participants (62%) encountered NASH patients sometimes with BMI > 40 kg/m2 who failed the current standard of care noninvasive weight loss measures, and refused surgical bariatric procedures, or deemed not to be a surgical candidate. Providers reported that endoscopic bariatric options, most commonly ESG (80%), are sometimes discussed with the patients in 46% of the times. Barriers for referral for endoscopic bariatric procedures in NASH patients were overwhelmingly due to lack of insurance coverage in 86% of the times while 32% of the participants thought that there was still not enough literature. Advanced endoscopists reported that they are unable to obtain insurance coverage for managing NASH patients in 78% of the time. Conclusion: NASH is projected to be the leading cause of cirrhosis, and the utilization of novel management modalities such as ESG are overwhelmingly impacted by the health insurance reimbursement policies.

Internal Medicine
Jomaa D, **Ichkhanian Y**, **Gupta K**, **Chaudhary AJ**, and **Jafri SM**. PREDICTIVE ROLE OF TRICUSPID REGURGITATION SEVERITY AMONG PERI-LIVER TRANSPLANT PATIENTS: RESULTS FROM A LARGE TERTIARY CARE CENTER. *Hepatology* 2023; 78:S338-S339. Full Text

[Jomaa, Diana; Ichkhanian, Yervant; Gupta, Kartik; Chaudhary, Ammad Javaid] Henry Ford Hosp, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Hospital

Internal Medicine
Jomaa D, **Jamali T**, **Manivannan A**, **Zahedi S**, **Peleman A**, **Pillai S**, **Zalawadia A**, and **Fain C**. A Syndrome of Diarrhea, Anasarca, and Nail Dystrophy: A Curious Case of Cronkhite-Canada Syndrome. *Am J Gastroenterol* 2023; 118(10):S1990-S1991. Full Text

[Jomaa, Diana; Jamali, Taher; Zahedi, Sulmaz; Peleman, Andrew; Pillai, Shreejith; Zalawadia, Ashish; Fain, Christopher] Henry Ford Hosp, Detroit, MI USA. [Manivannan, Ahila] Henry Ford Hlth, Detroit, MI USA.

Internal Medicine
Kaatz S, **Ellsworth S**, **Ryan N**, Kong X, Haymart B, and Barnes G. Potential of Racial Bias in Atrial Fibrillation Patients that are Switched from Warfarin to a Direct Oral Anticoagulant. *Res Pract Thromb Haemost* 2023; 7. Full Text

Background: Prior studies suggest racial discrepancy in the use of direct oral anticoagulants in patients with atrial fibrillation. Aims: Determine if there are residual differences in the proportion of African American and White patients that are switched from warfarin to a direct oral anticoagulant (DOAC) after controlling for demographic, comorbidities, insurance, and social determinants. Methods: Patients in the Michigan Anticoagulation Quality Improvement Initiative (MAQI2) ongoing registry from November 2009 to August 2022 with atrial fibrillation that were switched from warfarin to a DOAC were matched 1:1 with propensity score (greedy method). Median geographic household income based on zip code from census data could not be matched because of large differences and logistic regression was utilized on the matched populations. Results: 670 of 674 African American were well matched to 670 of 4952 White patients (Table 1) except for median household income (Table 2). Prior to matching, 936 of 4952 (18.9%) white and 100 of 674 (14.8%) African American patients were switched (P = 0.011). After matching, 120 (17.9%) and 99 (14.8%) of 670 white or African American patients were switched (P = 0.21). The odds ratio (OR) for switching was not different between races when controlling for median income (OR = 0.83, 95% CI 0.59–1.16). Conclusion(s): At first glance, African American patients with atrial fibrillation seem to be switched from warfarin to a DOAC less frequently. However, after controlling for differences in the populations, there is no longer any difference by race, arguing against implicit racial bias as a plausible explanation. Median household income is approximately a third lower in African American patients attending our 6 anticoagulation clinics and likely represents the largest barrier to DOAC use. We are actively working on processes with patient assistance programs to decrease co-pays to allow all our patients to receive the best anticoagulant. [Table presented] [Table presented]

Internal Medicine
Khan A, Naseem K, Sohail A, **Chaudhary AJ**, Mansoor E, and Sclair SN. HOSPITAL-RELATED OUTCOMES OF LIVER TRANSPLANTATION IN PATIENTS WITH AUTO-IMMUNE HEPATITIS: A NATIONWIDE ANALYSIS. *Hepatology* 2023; 78:S317-S317. Full Text

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Internal Medicine
Khan MZ, **Obri M**, **Chaudhary A**, **Elatrache M**, **Singla S**, **Watson A**, and **Zuchelli T**. Transcolonic Drainage of Walled-Off Pancreatic Necrosis: A Case Report. *Am J Gastroenterol* 2023; 118(10):S2245-S2245. Full Text

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Internal Medicine
Kulkarni R, **Hinojosa O**, and **Donthireddy V**. Real World Analysis of G6PD Testing Prior to the Use of Rasburicase in Hematologic Malignancies; A Single Center Experience. *Blood* 2023; 142:3. Full Text

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Internal Medicine
Manivannan A, **Davis W**, **Betcher S**, and **Pompa R**. Management of a Necrotic Pancreatic Pseudocyst - Avoiding the Dreaded Pseudoaneurysm Bleed. *Am J Gastroenterol* 2023; 118(10):S2182-S2183. Full Text

[Manivannan, Ahila; Betcher, Stephanie] Henry Ford Hlth, Detroit, MI USA. [Davis, William; Pompa, Robert] Henry Ford Hosp, Detroit, MI USA.

Internal Medicine
Manivannan A, Liapakis AM, Diehl AM, Verna E, Kumar V, **Salgia RJ**, **Wu T**, Lu M, Parikh ND, and **Jesse M**. INTERACTIONS BETWEEN RACE/ETHNICITY AND GENDER IN LIVER TRANSPLANTS: DO ACUITY CIRCLES MATTER? *Hepatology* 2023; 78:S277. Full Text

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Background: Despite continued efforts, there are welldocumented disparities in liver transplantation (LT) from listing through post-transplant. National policies on allocation of deceased donor liver transplants (DDLT) aim to provide consistent and equitable access. However, the impacts of Acuity Circles (AC) and interactions between race and gender on delisting due to deterioration/death or receipt of DDLT have been minimally explored. Methods: Using data from the United Network for Organ Sharing (UNOS), we studied listed adults for DDLT from April 3, 2017, to October 4, 2022, a 60-month period (30 mo pre- and post-AC). Fine-Gray subdistribution hazard model was used to study AC impact on LT while delisting due to deterioration/ death was used as a competing risk. The model focused on AC indicator by race by gender interactions, as well as AC by hepatocellular carcinoma (HCC) diagnosis interactions. Results: 59,592 patients (30,202 pre-AC, 29,390 post-AC) were studied. No 3- way (AC X race X gender) interaction was detected, indicating effect of race and gender on LT was consistent pre- and post-AC periods. However, there were significant gender by race or AC by HCC interactions (Table 1): patients with HCC had greater chance for LT than non-HCC, though post-AC this effect was reduced. AC increased LT 25% in patients without HCC. Across gender, White, Black, and Hispanic men were more likely to receive transplant compared to their female counterparts. Within gender, Black and Hispanic

women were less likely to receive transplant than White women, with no significant differences between White and Asian women. For men, there were no statistical difference in likelihood for transplant between White versus Black or Hispanic men, but Asian men had a lower likelihood for LT than White men. Additional significant predictors outlined in Table 1. Conclusion: Accounting for listing characteristics, AC did not significantly impact interactions between gender and race on receipt of LT. However, AC may have improved access to LT amongst those without HCC but may have diminished access amongst those with HCC post-AC. Regardless of AC, there were important gender-race interactions requiring closer examination, particularly where Black and Hispanic women appear disproportionately negatively impacted. The same patterns were not noted across male racial categories, suggesting future research and interventions should target those at greatest risk. (Table Presented).

Internal Medicine
Manivannan A, **Nagirimadugu A**, and **Kaur N**. Ulcerative Colitis in a Neovagina - An Unexpected Complication From M<spacing diaeresis>ullerian Agenesis. *Am J Gastroenterol* 2023; 118(10):S2116-S2116. Full Text

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Internal Medicine
Nimri FM, **Dawod S**, **Nimri R**, **Albusoul L**, **Shadid A**, **Maki M**, **Dababneh Y**, **Russell S**, and **Kutait A**. The Calm Before the Scope: A Look at Sedation Methods for Patients with History of Atrial Fibrillation Undergoing Screening Colonoscopy. *Am J Gastroenterol* 2023; 118(10):S560-S561. Full Text

[Nimri, Faisal M.; Dawod, Sanad; Albusoul, Linda; Shadid, Al Muthanna; Maki, Mohamed; Dababneh, Yara; Russell, Sarah; Kutait, Anas] Henry Ford Hosp, Detroit, MI USA. [Nimri, Rund] Jordan Univ Sci & Technol, Irbid, Jordan. Science & Technology

Internal Medicine
Obri M, **Ali SA**, **Alluri S**, **Samad M**, **Almajed MR**, **Ichkhanian Y**, and **Jafri SM**. SIMILAR REJECTION AND RETRANSPLANT RATES BUT DECREASED SURVIVAL AMONG AFRICAN AMERICAN PATIENTS FOLLOWING LIVER TRANSPLANTATION. *Hepatology* 2023; 78:S1320-S1321. Full Text

M. Obri, Henry Ford Health, United States

Background: There are known disparities in medicine in regards to sex and race. Investigation is important to evaluate these disparities and to aim to correct them, offering the best outcome for a diverse range of patients. The study aims to compare liver transplant outcomes based off of the race of the patient. Methods: A retrospective study was conducted at a single tertiary liver transplant center and was comprised of patients who underwent liver transplant from 2009 to 2019. The primary outcome was the rate of survival among different races. Secondary outcomes measured included the rate of rejection and re-transplant among different races in addition to the rate of survival among different sexes and donor types. Results: This study included 450 patients with race distribution of 83.6% white patients (n =376), 10.4% black patients (n=47), and 6.0% patients classified as 'Other' races (n=27). The primary outcome was the rate of survival compared amongst the three groups at 1 year, 3 years, and last known follow-up. Differences in survival rate among the three groups at 1 year was not statistically significant. At 3 years, the survival rate for white patients was 88.6%, black patients was 74.5%, and other patients was 92.6%; the chi-square statistics was 8.2 (p=0.016) which is statistically significant at p <0.05. At the last known follow-up, survival rate for white patients was 82.2%, black patients was 66.0%, and other patients was 88.9%; the chi-square statistic was 8.3 (p =0.016) which is significant. Re-transplant rates did not significantly differ between races with re-transplant rates among white, black, and other patients at 4.3%, 1.2%, and 3.7% respectively. Rejection rates did not significantly differ between races with white, black, and other patients at 24.5%, 31.9%, and 18.5% respectively. Comparisons of survival among patients with difference sexes did not demonstrate a statistically significant difference. Conclusion: Correlation exists between different patients races and survival among liver transplant patients. Patients who are black have a statistically lower survival rate (66.0%) compared to those who are white (82.2%) or other (88.9%). Further investigation with larger population sizes including epidemiological studies and subgroup

analyses is necessary to delineate the disparities which influence these outcomes. Published literature suggests that access to care, socioeconomic status, and racial biases are factors that influence healthcare access and affect outcomes.

Internal Medicine
Obri M, **Davis W**, **Faisal MS**, and **Watson A**. An Unusual Late Presentation of Caroli Syndrome. *Am J Gastroenterol* 2023; 118(10):S1538-S1539. Full Text

[Obri, Mark; Davis, William; Faisal, Muhammad Salman; Watson, Andrew] Henry Ford Hosp, Detroit, MI USA.

Internal Medicine
Obri M, **Davis W**, **Khan MZ**, **Fahad H**, **Curran J**, and **Pompa R**. A Case of Metastatic Seminoma Mimicking a Primary Pancreatic Tumor. *Am J Gastroenterol* 2023; 118(10):S1539-S1540. Full Text

[Obri, Mark; Davis, William; Khan, Muhammad Zarrar; Fahad, Hamna; Curran, John; Pompa, Robert] Henry Ford Hosp, Detroit, MI USA.

Internal Medicine
Obri M, **Dawod S**, Qasawa A, Fahoury A, **Stephan J**, **Kamran W**, and **Jafri SM**. A Rare Presentation of Drug-Induced Pancreatitis After Cyclophosphamide Infusion. *Am J Gastroenterol* 2023; 118(10):S1538-S1538. Full Text

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Internal Medicine
Obri M, **Harris K**, **Ali SA**, **Samad M**, **Rehman S**, **Chaudhary A**, and **Suresh S**. Delaying Endoscopy for Food Impaction Increases Hospital Admissions but Does Not Lead to More Patient Complications. *Am J Gastroenterol* 2023; 118(10):S417-S417. Full Text

[Obri, Mark; Harris, Kevin; Ali, Suhaib Alhaj; Rehman, Sheema; Chaudhary, Ammad; Suresh, Suraj] Henry Ford Hosp, Detroit, MI USA. [Samad, Momin] Henry Ford Hosp, Rochester Hills, MI USA.

Internal Medicine
Obri M, **Khan MZ**, **Chaudhary A**, **Piraka C**, and **Zuchelli T**. Isolated Gastric Metastasis of Renal Cell Carcinoma 11 Years After Initial Diagnosis Treated With Endoscopic Submucosal Dissection. *Am J Gastroenterol* 2023; 118(10):S2688-S2688. Full Text

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Internal Medicine
Obri M, **Nimri F**, **Dawod S**, **Youssef RM**, **Alluri S**, **Almajed MR**, **Stephan J**, **Ichkhanian Y**, **Watson A**, **Elatrache M**, **Pompa R**, **Dang DY**, **Singla S**, **Piraka C**, and **Zuchelli T**. Over Half of Liver Transplant Patients With Biliary Strictures Have. *Am J Gastroenterol* 2023; 118(10):S90-S90. Full Text

[Obri, Mark; Nimri, Faisal; Dawod, Sanad; Youssef, Rami M.; Alluri, Spandana; Almajed, Mohamed Ramzi; Stephan, Johnathan; Ichkhanian, Yervant; Watson, Andrew; Elatrache, Mazen; Pompa, Robert; Dang, Duyen; Singla, Sumit; Piraka, Cyrus; Zuchelli, Tobias] Henry Ford Hosp, Detroit, MI USA.

Internal Medicine
Omeish H, Thunaibat A, Omeish R, and Rashid M. Unveiling the Uncommon: Exploring Acute Appendicitis as a Complication of Colonoscopy and Colonoscopic EMR. *Am J Gastroenterol* 2023; 118(10):S1997-S1998. Full Text

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Internal Medicine
Patel PM, **Yasin Z**, **Zreik H**, **Singh H**, **Singh B**, **Hari P**, and Karagozian R. Retrospective Analyses of the Outcomes Among Hospitalized Liver Cirrhosis Patients, Including Those With COVID-19 Infection. *Am J Gastroenterol* 2023; 118(10):S1027-S1028. Full Text

[Patel, Parth M.; Karagozian, Raffi] Tufts Med Ctr, Boston, MA USA. [Yasin, Zarqa; Zreik, Hassan; Singh, Harjinder; Singh, Bipneet; Hari, Parneet] Henry Ford Hlth, Jackson, MI USA.

Internal Medicine
Patel PM, **Zreik H**, **Yasin Z**, **Ramanan S**, **Hari P**, **Singh B**, **Malik D**, and **Bern M**. Rare Case of Bowel Perforation After a Dose of Paclitaxel. *Am J Gastroenterol* 2023; 118(10):S1608-S1608. Full Text

[Patel, Parth M.] Henry Ford Hlth Syst, Boston, MA USA. [Zreik, Hassan; Yasin, Zarqa; Ramanan, Sruthi; Hari, Parneet; Singh, Bipneet; Malik, Devin; Bern, Merritt] Henry Ford Hlth Syst, Jackson, MI USA.

Internal Medicine
Patell R, Angelini DE, **Ellsworth SR**, Lewis P, Lee JC, Nutescu EA, Amin A, Witt DM, Betensky M, Goldenberg N, Kouides P, Attia MD, Mourany L, Lake L, Rosovsky RP, Khorana AA, and **Kaatz S**. Estimating the Burden of Venous and Arterial Thrombotic Events in Hospitalized Adults with COVID-19; A National Multicenter Cohort Study. *Blood* 2023; 142:1262. Full Text

Background: Patients infected with Coronavirus Disease 2019 (COVID-19) have clinical and laboratory features consistent with a hypercoaguable state, particularly in more severely ill patients that require hospitalization. However, estimates of thrombotic complications in this high risk population vary widely. A geographic representative cohort to explore the rates of thrombotic events in patients hospitalized with COVID-19 in the United States would be useful to better understand the burden of thrombosis in this population. We aimed to assess the rates of venous and arterial thrombosis events during hospitalization in patients with COVID-19 in a national multicenter cohort study. Methods: We conducted a retrospective cohort study of hospitalized patients diagnosed with COVID-19 from January 1 2020 to January 2023. IRB approval was obtained at each site. Inclusion criteria included adults (> 21 years), hospitalized for >1 day and laboratory confirmation of polymerase chain reaction testing of severe acute respiratory syndrome coronavirus 2. Data were extracted by participating centers in a pre-specified instrument from the electronic medical record at each institution and pooled prior to analysis. Data sources included manual extraction by study investigators in 7 sites and electronic extraction based on billing codes at one site (Cleveland Clinic). Primary outcome was venous thrombotic events, including deep vein thrombosis (DVT), pulmonary embolism (PE). Unusual sites including splanchnic vein thrombosis and cerebral venous thrombosis were included if objectively demonstrated on imaging. Arterial thrombotic events including ischemic stroke, acute coronary syndrome were included as secondary outcomes. Data are presented as proportions, with binomial 95% confidence intervals (CI). Results: We included 33,769 patients from eight medical centers across the United States. Participating hospitals included all four census regions from the North East (Beth Israel Deaconess Medical Center, MA (n=1021) Rochester Regional Hospital, NY (n=99)), South (John Hopkins Medical Institute, ML (n=334); Baycare Health System, FL (n=3734), MidWest (Cleveland Clinic Foundation, OH (n=25467); Henry Ford Health System, MI (973); University of Illinois, IL (1192)) and West (University of California, CA (n=613)). (Figure) Of the total 33,433 hospitalized patients with COVID-19 included, 1684 patients developed a venous thrombotic event during the index hospitalization (5.0%, 95% CI 4.8-5.2) and 261 developed an arterial thrombotic event (0.8%, 95% CI, 95% CI 0.7-0.9). Rates of venous events by individual sites ranged from 2.6-8%

and arterial events from 0.3-6.6%. Conclusion: In this national multicenter cohort study that included academic and community hospitals from all four US census regions, we estimated the rates of VTE were over five times more frequent than arterial events in hospitalized patients with COVID-19. Accurate estimates of thrombotic rates and trends can help plan targeted interventions related to strategies around thromboprophylaxis interventions and resource allocation for future surges of COVID-19 cases.

Internal Medicine
Rehman S, **Chaudhary A**, **Samad M**, and **Jafri SM**. Cryoglobulinemia-Induced Kidney Injury Secondary to Refractory Hepatitis C. *Am J Gastroenterol* 2023; 118(10):S2326-S2326. Full Text

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Internal Medicine
Rehman S, **Chaudhary A**, **Veracruz N**, **Denha E**, Gumma J, and **Jafri SM**. An Unusual Case of Clostridioides Peritonitis From Small Intestinal Source. *Am J Gastroenterol* 2023; 118(10):S2326-S2326. Full Text

[Rehman, Sheema; Chaudhary, Ammad; Veracruz, Nicolette; Denha, Eric] Henry Ford Hosp, Detroit, MI 48202 USA. [Gumma, Julius] Michigan State Univ, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. University; Henry Ford Health System; Henry Ford Hospital

Internal Medicine
Salam R, Affas S, **Affas R**, and Hassan M. Racial Disparities in Graft and Patient Survival After Orthotopic Liver Transplantation. *Am J Gastroenterol* 2023; 118(10):S1166-S1167. Full Text

[Salam, Reshad] Michigan State Univ, Ascension Providence Hosp, Southfield, MI USA. [Affas, Saif] Ascension Providence Hosp, Troy, MI USA. [Affas, Raffe] Henry Ford Hosp, Detroit, MI USA. [Hassan, Mona] Univ Toledo, Toledo, OH USA. Hospital; University System of Ohio; University of Toledo

Internal Medicine
Samad M, **Chaudhary A**, **Rehman S**, **Ali SA**, and **Jafri SM**. An Assessment of IPMN Screening in Liver Transplant Recipients. *Am J Gastroenterol* 2023; 118(10):S1035-S1035. Full Text

[Samad, Momin] Henry Ford Hosp, Rochester Hills, MI USA. [Chaudhary, Ammad; Rehman, Sheema; Ali, Suhaib Alhaj] Henry Ford Hosp, Detroit, MI USA. [Jafri, Syed-Mohammed] Henry Ford Hlth Syst, Detroit, MI USA. Henry Ford Health System; Henry Ford Hospital

Internal Medicine
Samad M, and **Jafri SM**. An Evaluation of Infections and Outcomes Following Intestinal Transplantation. *Am J Gastroenterol* 2023; 118(10):S1332-S1332. Full Text

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Internal Medicine
Schaefer JK, Errickson J, Kong X, Ali MA, Chipalkatti N, Dorby P, Giuliano C, Haymart B, **Kaatz S**, Kurlander JE, **Krol GD**, Shankar S, Sood SL, Froehlich J, and Barnes GD. Outcomes of Oral Anticoagulation with Concomitant NSAID Use: A Registry Based Cohort Study. *Blood* 2023; 142:5129. Full Text

Introduction Nonsteroidal anti-inflammatory drugs (NSAIDs), available without a prescription, are some of the most commonly used drugs in the United States. For patients on oral anticoagulation (OAC), concomitant NSAID use can increase the risk of bleeding. Patients are often advised to avoid this drug combination, or else consider adding a proton pump inhibitor (PPI) or H2 receptor antagonists (H2RA) for

gastroprotection when both NSAIDs and OAC are used. However, there are limited data on how NSAID use impacts thrombotic and hemorrhagic outcomes. Available data may be biased due to selection bias, confounding, misclassification, and variable NSAID exposure. We sought to determine the frequency of NSAID use among patients on OAC, the impact on clinical outcomes, and if gastroprotection may mitigate bleeding risk. We hypothesized that NSAIDs would increase bleeding risk without impacting thrombotic risk. We did not anticipate gastroprotection would mitigate this risk. Methods We conducted a retrospective registry-based cohort study of adults starting a direct oral anticoagulant (DOAC) or warfarin therapy for the indications of venous thromboembolism and/or non-valvular atrial fibrillation between June 2011 and June 2023. As part of the Michigan Anticoagulation Quality Improvement Initiative (MAQI 2), warfarin-treated patients were followed by six anticoagulation clinics, and four of the six clinics contributed data for patients on DOACs. Patients were excluded if they had a history of valvular AF, less than 3 months of follow-up, or on more than one antiplatelet drug. Two propensity matched cohorts (OAC alone vs. OAC+NSAID) of patients were analyzed based on NSAID use at the time of study enrollment, using a 4:1 matching ratio. Both prescribed and over the counter NSAIDs were included, potentially with the former being more frequently captured in the study registry. The primary outcome was any new bleeding event. Secondary outcomes included new episodes of arterial or venous thrombosis, bleeding event type (major, fatal, life threatening, central nervous system, and non-major bleeding), emergency room visits, hospitalizations, transfusions, and death. Random chart audits were done to confirm the accuracy of the abstracted data. Event rates were compared using Poisson regression. Results Of 12,083 patients on OAC, 449 (3.7%) were on concomitant NSAIDs. After propensity matching, we compared 1,796 patients on OAC to 449 patients on OAC+NSAIDs. Patient demographics, co-morbidities, indication for anticoagulation, history of bleeding or clotting, medications, and duration of follow-up were well-balanced after matching. Patients were followed for an average of 30 months (standard deviation 34.2 months). For patients on OAC alone vs. OAC+NSAIDs, bleeding event rates were similar: 25.1 (95% confidence interval [CI] 23.7-26.6) versus 24.3 (95% CI 21.4-27.3) bleeds per 100 patient years (P=0.56). Rates of non-major, major, life-threatening, central nervous system, and fatal bleeding were also similar. Furthermore, rates of thrombosis, emergency room visits, hospitalizations, transfusion, and death were similar. A pre-defined subgroup analysis comparing patients on OAC+NSAIDs with gastrointestinal prophylaxis (PPIs or H2RAs, N=179) to patients on OAC+NSAIDs without gastrointestinal prophylaxis (N=270) also showed similar rates of bleeding and healthcare utilization. Conclusions Nearly 4% of patients were taking NSAIDs with OAC and outcomes were similar to patients on OAC alone. Study limitations include NSAIDs and gastroprotection were only reliably known at time of enrollment. In addition, the potential for unmeasured or unadjusted confounding inherent to observational studies. Further research is needed to determine if there is a “safe” level of NSAID use for patients on OAC and to better define the role of gastrointestinal prophylaxis.

Internal Medicine

Schaefer JK, Errickson J, Kong X, Ali MA, Chipalkatti N, Haymart B, **Kaatz S**, **Krol GD**, Sood SL, Froehlich J, and Barnes GD. A Comparison of Bleeding Events Among Patients on Apixaban, Rivaroxaban, and Warfarin for Atrial Fibrillation and/or Venous Thromboembolism. *Blood* 2023; 142:135. Full Text

Introduction Apixaban and rivaroxaban are the most commonly used direct oral anticoagulants (DOACs) for atrial fibrillation (AF) and venous thromboembolism (VTE). Both have been compared to warfarin in landmark clinical trials. However, there are limited comparative efficacy data between these drugs in a real-world setting. We sought to assess patient characteristics and outcomes of apixaban, rivaroxaban, and warfarin in a non-trial based study cohort. Methods Retrospective registry-based cohort of adults starting apixaban, rivaroxaban, or warfarin therapy or switching between these anticoagulants for the indications of VTE and/or non-valvular AF. Through the Michigan Anticoagulation Quality Improvement Initiative (MAQI 2) collaborative of six anticoagulation clinics, warfarin treated patients were followed from January 2009 to June 2023. Four of these clinics contributed DOAC patient data from June 2011 to June 2023. Patients treated with other anticoagulants, with valvular AF, or with less than 3 months of follow-up were excluded. Propensity matched cohorts (apixaban versus warfarin [1:1], rivaroxaban versus warfarin [1:3], and apixaban versus rivaroxaban [1:1]) of patients were analyzed based on DOAC use at study enrollment, using 1:1-3:1 matching ratios. Patients were matched based on demographics, social history, comorbidities, medications, bleeding/thrombotic history, indication for anticoagulation, and follow-up. The

primary outcome was any new bleeding event. Secondary outcomes included new episodes of thrombosis, bleeding event type (major, fatal, life threatening, central nervous system, and non-major bleeding), emergency room (ER) visits, hospitalizations, and death. Random chart audits were done to confirm the accuracy of the abstracted data. Event rates were compared using Poisson regression. Results Of 13,435 patients on OAC who met the study inclusion criteria (3,536 on apixaban, 1,395 on rivaroxaban, and 8,504 on warfarin), the average age was 66.7 years (standard deviation [SD] 14.9 years), 51.1% identified as male, most (58.0%) were on anticoagulation for AF, and the average follow-up was 28.2 months (SD 30.7 months). After propensity matching, 3,527 patients on apixaban were compared to 3,527 patients on warfarin. Any bleeding was similar between groups, but major bleeding was higher with warfarin (3.4 versus 4.7 events/100 patient years, p<0.001). Thrombotic event rates were higher with apixaban (2.6 versus 2.1 events/100 patient years, p=0.026), including the thrombotic subtype of other thrombosis (1.0 versus 0.5 events/100 patient years, p<0.001). Rates of ER visits and hospitalizations for bleeding were higher with warfarin. Mortality was higher with warfarin (3.7 versus 4.4 deaths/100 patient years, p=0.027). After propensity matching, 1,395 patients on rivaroxaban were compared to 4,185 patients on warfarin. Any bleeding and major bleeding were higher with rivaroxaban (37.9 versus 24.9 events/100 patient years, p<0.001; 4.7 versus 3.6 events/100 patient years, p=0.041 respectively). Thrombotic event rates were similar, aside from a higher rate of the thrombotic subtype of other thrombosis with rivaroxaban (1.0 versus 0.3 events/100 patient years, p=0.002). ER visits, hospitalizations, and mortality were similar between rivaroxaban and warfarin. After propensity matching, 1,395 patients on apixaban were compared to 1,395 patients on rivaroxaban. Any bleeding and major bleeding were higher with rivaroxaban (37.9 versus 25.7 events/100 patient years, p<0.001; 4.7 versus 2.6 events/100 patient years, p<0.001). Thrombotic event rates were similar. ER visits occurred more frequently on rivaroxaban (12.8 versus 10.1 events/100 patient years, p=0.003) as did patient mortality (3.5 versus 2.6 deaths/100 patient years, p=0.047). Conclusions For patients on oral anticoagulation for AF and/or VTE we observed that bleeding was highest with rivaroxaban, followed by warfarin, and then apixaban. Rates of thrombosis were higher with apixaban compared to warfarin, seemingly largely driven by “other” thro botic events. Thrombotic event rates were otherwise similar between apixaban, rivaroxaban, and warfarin. We observed apixaban to be associated with lower mortality than rivaroxaban and warfarin. While these findings should be confirmed with randomized studies, they may have implications for anticoagulant selection.

Internal Medicine

Siegal D, Arnaoutoglou E, Blostein M, Castellucci L, Eikelboom J, Gandhi R, Gross P, **Kaatz S**, Le Gal G, Schulman S, **Shah V**, Stamoulis K, Tafur A, Vogt K, Nixon J, St John M, Karunakaran M, Levoy-Jones B, and Douketis J. Management and Outcomes of Anticoagulated Patients in Urgent Surgery: The PAUSE-ER Study. *Res Pract Thromb Haemost* 2023; 7. Full Text

Background: Few data describe the perioperative management and outcomes of patients receiving oral anticoagulant (OAC) therapy who require urgent (unplanned) surgery. While limited available evidence suggests high rates of thromboembolism, bleeding and death in this setting, substantial knowledge gaps remain. Aims: We aimed to (i) determine the incidence of adverse events (thrombosis, bleeding, death) among OAC-treated patients requiring urgent surgery, (ii) examine management and resource utilization, and (iii) explore factors associated with adverse outcomes. Methods: PAUSE-ER was a prospective observational study conducted at 10 sites (Canada, US, Greece, Argentina). OAC-treated adults requiring OAC interruption for urgent (unplanned) surgery/invasive procedure (within 72 hours)were eligible. Patients undergoing elective (planned), or minimal bleed risk surgeries/procedures not requiring OAC interruption were excluded. Data were collected from medical records and telephone follow-up at 30 days. Results: 242 participants were enrolled (2019–2022). The mean age was 75 years and 50% were female. OAC use comprised apixaban (40%), warfarin (38%), rivaroxaban (16%), edoxaban (1%) and dabigatran (0.4%). The commonest indication for OAC was atrial fibrillation (74%). The most common surgeries were orthopedic (n = 84), general surgery (n = 42), vascular surgery (n = 16), neurosurgery (n = 16), interventional radiology procedures (n = 10), urologic surgery (n = 9), and cardiothoracic surgery (n = 8). Most patients (76%) received general anesthesia and 5% had neuraxial anesthesia. Perioperatively, patients received idarucizumab (n = 1), andexanet-alfa (n = 1), prothrombin complex concentrate (n = 45), plasma (n = 8), vitamin K (n = 61) and tranexamic acid (n = 31). At 30-days follow-up, 12 patients (5%) died, 18 (7%) had bleeding complications and 4 (2%) experienced thromboembolic events (ischemic

stroke [n = 3] and pulmonary embolism [n = 1]). Conclusion(s): In the first prospective evaluation of unselected OAC-treated patients requiring urgent surgery, we showed that management was variable and adverse outcome rates appeared higher than those observed after elective (planned) surgery. Further research aims to inform best practices for OAC management to reduce morbidity and mortality. [Figure presented]

Internal Medicine
Thunaibat A, **Omeish H**, and Rashid M. Necrotizing Pancreatitis Complicated by ARDS and GI Bleeding: A Case Report. *Am J Gastroenterol* 2023; 118(10):S1555-S1556. Full Text

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Internal Medicine
Wani K, and **Dabak VS**. Does Implementing Calendars Outlining Inpatient Chemotherapy Schedules in Patient Rooms Improve Patient's Experience? *Blood* 2023; 142:7275. Full Text

Background: Patients who receive inpatient chemotherapy for malignancy are dealing with both a physically and mentally challenging admission. Their chemotherapy regimen is predetermined and usually only discussed during rounds. Often times, patients feel overwhelmed and may miss the outline of their schedule. Furthermore, patients families may not be able to attend morning rounds and may miss the proposed schedule. This can lead to a feeling of loss of control in both the patient and their family, and thus, frustration. First year medicine residents are also overwhelmed with a large patient load and having to keep track of multiple chemotherapy regimens. We are hoping that by providing a calendar that outlines patient's anticipated chemotherapy schedule, we may be able to give patients a small sense of control back and help residents provide the best care to their patients. Ultimately, we hope that this leads to a better inpatient experience. Methods: Patients admitted to the hematology/oncology floor at Henry Ford Health Hospital in Detroit, Michigan over three months were screened, and those receiving inpatient chemotherapy were selected. Within this group, any patient that was getting inpatient chemotherapy for longer than three days was asked if they would like to participate in the study. If the patient agreed, they were provided a calendar that outlined their chemotherapy schedule. Calendars were updated if any adjustments were made to the schedule. At the end of their inpatient stay, patients filled out a questionnaire asking if the calendar helped them understand their schedule better. The primary resident caring for the patient was also asked if the calendar helped them keep track of their patient's schedule. Results: Overall, patients responded positively to the calendars. We have preliminary data on ten patients and four providers from three months. On average, on a scale of 1-10 (with 1 indicating not helpful at all, and 10 indicating extremely helpful) patients rated the calendars helping them at a level of 7.5. Patients found that the calendars particularly helped their families who were not able to come visit in the hospital. Providers found the calendars extremely helpful, rating the calendars at a level of 10. We will continue to collect data and update our results. Conclusions: Implementing patient calendars in inpatient rooms helps patients keep track of their chemotherapy schedules and leads to a positive inpatient experience. We are hoping to implement this as a standard of care in all inpatient rooms on the hematology/oncology floor.

Internal Medicine
Wani K, **Gutta R**, **Mittal A**, **Jamil M**, **Springer K**, and **Kuriakose P**. Comparison of Maintenance Therapy Regimens of Patients Treated for Multiple Myeloma. *Blood* 2023; 142:6698. Full Text

Background: Despite significant progress in treatment modalities and improved survival and response rates in patients diagnosed with multiple myeloma (MM), it remains an incurable disease with a poor outcome, especially in high-risk groups. Though not all patients are eligible, autologous stem-cell transplantation (ASCT) remains an integral part of the treatment of patients with both newly diagnosed and relapsed MM. Regardless of whether patients receive a transplant, they do receive maintenance therapy, and recent evidence has demonstrated that maintenance therapies offer an advantage in progression free and overall survival. While Revlimid is the standard of care, data regarding the specifics of maintenance therapy in high-risk patients is limited and the overall impact of various regimens on survival needs to be further investigated. In our retrospective chart review we reviewed all adult patients

with advanced MM within Henry Ford Cancer Institute in the last 10 years to determine the impact of maintenance therapy on progression free survival (PFS) and overall survival (OS). Methods: We conducted a retrospective chart review of adult patients with MM who underwent ASCT between January 1, 2012 to December 31, 2022. Those who received maintenance chemotherapy after transplant were included in the study. Patients who were lost to follow-up or who had largely incomplete records were excluded. Data points including age, ethnicity, cytogenetic analysis, risk category, maintenance regimen after transplant, last chemotherapy regimen, last follow-up, and date of death (if applicable) were recorded. Maintenance chemotherapy regimens were recorded as Revlimid versus other. Patients were split into 2 categories based on risk - high risk and standard risk. Kaplan-Meier plots were used to illustrate overall survival and time to relapse between groups for various variables. Statistical significance was set at $p<0.05$ Results: 158 patients were included in the study of which 44 were considered high-risk based on cytogenetics, 106 were standard-risk and 8 were missing. Most of the patients (n=137, 87.3%) received Revlimid, while 20 (12.7%) received maintenance therapy other than Revlimid, and for 1 patient, the type of maintenance therapy was unknown. Within the high-risk group, no statistical significance in OS or PFS was found between patients that received Revlimid versus those that did not. Furthermore, there was no statistical significance in OS and PFS within high risk versus standard cytogenetic risk groups. Conclusions: We did not see a difference in outcome based on risk and believe all patients would derive equal benefit from maintenance therapy We also did not see a difference in outcome between high and standard risk patients, and for the high-risk subgroup, there was a separation in curves suggesting that maintenance therapy has benefit compared to no maintenance.

Internal Medicine

Wani K, **Gutta R**, **Mittal A**, **Jamil M**, **Springer K**, and **Kuriakose P**. Impact of Race on Progression-Free Survival and Overall Survival in Patients with Multiple Myeloma. *Blood* 2023; 142:6661. Full Text

Background: Multiple myeloma (MM) is a disorder of plasma cells. Management typically includes induction therapy, autologous stem-cell transplantation (ASCT) and maintenance therapy. Despite significant progress in treatment modalities and improved survival and response rates in patients diagnosed with MM, it remains an incurable disease with a poor outcome, especially in high-risk groups. Black patients have been shown to have a higher incidence of MM than white patients. Multiple studies have been done to examine racial disparities among white and black patients, specifically in overall survival (OS) and progression free survival (PFS). However, data has been overall inconclusive with some studies suggesting there is a difference in survival based on race, while other studies suggesting the opposite. Thus, racial disparities among white and black patients' needs to be further investigated. In our retrospective chart review we reviewed all adult patients with advanced MM within Henry Ford Cancer Institute in the last 10 years to determine the impact of maintenance therapy on PFS and overall survival OS. Methods: We conducted a retrospective chart review of adult patients with MM who underwent autologous stem cell transplantation (ASCT) between January 1, 2012 to December 31, 2022. Those who received maintenance chemotherapy after transplant were included in the study. Patients who were lost to follow-up or who had largely incomplete records were excluded. Data points including age, gender, race, date of transplant, maintenance chemotherapy regimen, last follow-up, and date of death (if applicable) were recorded. Kaplan-Meier plots were used to illustrate overall survival and time to relapse between various races. Statistical significance was set at $p<0.05$. Results: There were 158 patients included in the study. Of the 158 patients, 82 (51.9%) were male, and 76 (48.1%) were female. The average age of patients included was 61.66 + 9.30 years, spanning from 32 to 78 years old. There were 71 (44.9%) White patients, 76 (48.1%) Black patients, and 11 (7.0%) patients that were of another race. There was no statistical significance in PFS and OS between Black, White and Other race categories. Conclusions: We did not see a difference in outcome based on race and believe all patients would derive equal benefit from maintenance therapy. Further prospective studies are warranted to examine racial disparities in patients with multiple myeloma.

Internal Medicine

Yasin Z, **Hari P**, **Zreik H**, Patel PM, **Singh B**, and **Ullah N**. A Rare Case of Non-Celiac Adult-Onset Autoimmune Enteropathy With Villous Atrophy. *Am J Gastroenterol* 2023; 118(10):S2502-S2502. Full Text

[Yasin, Zarqa; Hari, Parneet; Zreik, Hassan; Singh, Bipneet] Henry Ford Hlth, Jackson, MI USA. [Patel, Parth M.] Henry Ford Hlth Syst, Boston, MA USA. [Ullah, Nadeem] Henry Ford Jackson Hosp, Jackson, MI USA.

Internal Medicine
Yasin Z, **Patel PM**, **Zreik H**, **Hari P**, **Singh B**, and **Alsheik E**. A Rare Case of Colonic Squamous Cell Carcinoma Metastasis Originating From Adenosquamous Cell Carcinoma of the Lung. *Am J Gastroenterol* 2023; 118(10):S1624-S1624. Full Text

[Yasin, Zarqa; Singh, Bipneet] Henry Ford Hlth, Jackson, MI USA. [Patel, Parth M.] Henry Ford Hlth Syst, Boston, MA USA. [Zreik, Hassan; Hari, Parneet] Henry Ford Hlth Syst, Jackson, MI USA. [Alsheik, Eva] Henry Ford Hlth Syst, Detroit, MI USA. System; Henry Ford Health System; Henry Ford Hospital

Internal Medicine
Youssef RM, **Obri M**, **Todter E**, **Salgia RJ**, and **Jesse M**. PSYCHOSOCIAL AND MEDICAL FACTORS ASSOCIATED WITH RECEIPT OF LIVER TRANSPLANT IN LISTED PATIENT WITH HEPATOCELLULAR CARCINOMA. *Hepatology* 2023; 78:S285. Full Text

R.M. Youssef, Henry Ford Health, United States

Background: Patients with hepatocellular carcinoma (HCC) are less likely to receive liver transplantation (LT) than patients without HCC. The aim of this study was to explore sociodemographic, psychosocial, and medical factors associated with progression to LT, versus delisting, in patients with HCC listed for LT. Methods: Prospectively maintained database from a single center tracking all patients diagnosed with HCC from 2005-2022. Amongst those listed for LT, the main outcome was receipt of transplant (versus delisting for any reason). Predictors included sociodemographic, psychosocial, and medical characteristics. Given the exploratory nature, predictors were included in the final multivariable logistic model if univariable logistic regression results approached significant ($p < 0.1$). Results: Among 341 patients listed with HCC; mean age 59.6 years (SD 6.8); 265 male (77.7%); racial composition was 246 White (72.1%), 50 Black (14.7%), and 45 “other” (13.2%). 261 (76.5%) underwent LT, 80 (23.5%) were delisted (any reason, majority due to disease progression/ medical deterioration). Variables included in the model were age at transplant listing, marital status, whether the patient underwent treatment for HCC, and histories of tobacco use, alcohol abuse, hepatic encephalopathy, diabetes, hypertension, and dyslipidemia. Final model presented in Table 1. Significant predictors of receipt of LT in the final model included younger age at transplant listing, no history of tobacco use, and no history of alcohol abuse. Conclusion: HCC patients are often delisted due to HCC disease progression and/or death while on the LT waitlist. Our data suggests that patients who are listed at a younger age, do not have a history of tobacco use, or of alcohol abuse are more likely to successfully receive LT. Also, contrary to hypotheses, race/ethnicity was not significant suggesting improved equity across these groups. (Table Presented).

Internal Medicine
Zahedi S, **Almajed M**, **Antishin S**, and **Bradley P**. A Breath-Taking Triad, Rare Case of Pseudo-Meigs Syndrome in a Patient With Benign Leiomyoma. *Am J Respir Crit Care Med* 2024; 209. Full Text

S. Zahedi, Internal Medicine, Henry Ford Health Care System, Detroit, MI, United States

Meigs syndrome is a clinical diagnosis based on the triad of ovarian tumors, ascites and pleural effusions. Meigs syndrome is an incredibly rare phenomenon and accounts for only 1% of ovarian tumors; most commonly ovarian fibromas. Pseudo-Meigs is a mimicker of Meigs syndrome occurring when other benign ovarian or pelvic tumors result in the same triad. The pathophysiology of Meigs syndrome is unclear. The most accepted theory is that the tumor results in pressure on the lymphatic system in the abdomen, resulting the accumulation of a transudative ascitic fluid which is subsequently transmitted to the pleural cavity. Since there are known cases of atypical Meigs syndrome, in which pleural effusions are present in the absence of ascites, another theory is that fluid enters the pleural cavity through stromal edema from lymphatic channels. The final postulated theory is that growth hormones such as vascular endothelial factor result in increased capillary permeability and accumulation of transudative fluid. We

present a case of a 50-year-old woman who was sent to the hospital after anemia was noted on outpatient labs. Her medical history was notable for uterine fibroids. She reported menorrhagia but had no symptoms otherwise. An ultrasound revealed multiple uterine masses consistent with fibroids. She was hospitalized and managed symptomatically for anemia during which time she developed acute hypoxia. She underwent Chest CTA which revealed pulmonary edema, moderate bilateral pleural effusions, and small-volume ascites. Thoracentesis revealed a transudative effusion; gram stain, wet mount and cytology were all negative. Serum tumor markers including CEA, alpha fetoprotein, carbohydrate 19-9, and CA 125 were all negative. Liver function tests were within normal limits. She subsequently underwent a laparoscopic hysterectomy; biopsy of pelvic masses revealed benign leiomyomas. In the two years after the hysterectomy, she did not have re-accumulation of the ascites or pleural fluid. Newly-identified pleural effusions warrant an extensive workup and astute clinical acumen, especially in the absence of a clear etiology. Uterine tumors are a rare cause of pleural effusions and often understandably overlooked by clinicians. This case highlights the importance of considering uterine tumors when evaluating causes of transudative pleural effusions. Identifying Meigs Syndrome and Pseudo-Meigs Syndrome as potential causative factors allows a pathway towards recurrence prevention. Tumor resection results in resolution of ascites and pleural effusions and saves patients from unnecessary thoracentesis and paracentesis. Eliminating the iatrogenic risks of these procedures, such as pneumothorax, bleeding, infection, and bowel perforation.

Internal Medicine

Zahedi S, **Parsons A**, Vahabzadeh A, and **Franco-Palacios DJ**. Success of Mechanical Circulatory Support as a Bridge to Treatment in Acute Right Ventricular Failure. *Am J Respir Crit Care Med* 2024; 209. Full Text

S. Zahedi, Internal Medicine, Henry Ford Health Care System, Detroit, MI, United States

Right ventricular (RV) failure is associated with significant morbidity and mortality and carries inhospital mortality rates estimated to be 70-75%. RV failure may occur secondary to acute inferior myocardial infarction, decompensated heart failure, pulmonary embolism, or pulmonary hypertension. While medical therapy aimed at optimizing the contractility of the heart, paired with preload and afterload management are useful therapeutic modalities, in cases of significant right heart failure they are ineffective and mechanical support may be needed. A 40-year-old man with a past medical history of hypertension, polysubstance abuse and previous pulmonary embolism (PE) presented to the emergency department after being found wandering in the street confused. Patient was hypoxic, agitated, and hypotensive. A CT PE showed a large extrinsic thrombus in the distal left main PA and causing complete occlusion of the left lower lobe arteries as well as lobar and segmental thrombus in the right lower lobe. The main PA was dilated, and the RV wall was hypertrophic. Troponins were elevated (1800 ng/L). Echocardiogram showed moderate enlarged RV with diminished RV systolic function. RV systolic pressure was unable to be estimated. Patient was intubated in the ED and on high intensity heparin. His hypotension initially responded to IV fluids but later became hemodynamically unstable requiring rapid increase in norepinephrine. Due to worsening RV failure, he was placed on VA ECMO (fem-fem configuration) with rapid hemodynamic improvement and as a bridge to percutaneous thrombectomy. After pulmonary angiography revealed chronic thrombus attempts for thrombectomy were aborted. Inotropic support with milrinone and addition of afterload reduction with inhaled nitric oxide allowed for weaning off VA ECMO. Sildenafil and IV furosemide were started, and the patient was successfully decannulated. The initial concern was for acute on chronic PE. Although initially VA ECMO in this case was used for hemodynamic compensation to attempt percutaneous thrombectomy, it ultimately served as a bridge to PAH therapy in a patient presenting with new diagnosis CTEPH and RV failure. His urine was positive for cocaine. It is possible that patient RV failure was precipitated by acute cocaine toxicity inducing vasoconstriction in the setting of unknown chronic thromboembolic pulmonary hypertension. The patient will follow-up in the PH clinic to decide on appropriate vasodilator therapy and referral to a CTEPH center. VA ECMO's ability to provide rapid and complete off-loading of the right heart as a bridge to treatment should be considered in medically refractory cases and rapid cardiovascular decompensation.

Internal Medicine
Zreik H, **Hari P**, **Yasin Z**, **Patel PM**, **Singh B**, and **Bern M**. Rare Case of Intussusception in Adults: COVID-19 Induced Mesenteric Adenitis. *Am J Gastroenterol* 2023; 118(10):S1658-S1658. Full Text

[Zreik, Hassan; Hari, Parneet; Yasin, Zarqa; Patel, Parth M.; Singh, Bipneet; Bern, Merritt] Henry Ford Hlth Syst, Jackson, MI USA.

Internal Medicine
Zreik H, **Singh B**, **Patel PM**, **Yasin Z**, **Hari P**, and **Alamelumangapuram CB**. Emerging Diagnostic Markers in Acute Ischemic Colitis. *Am J Gastroenterol* 2023; 118(10):S1658-S1658. Full Text

[Zreik, Hassan; Singh, Bipneet; Patel, Parth M.; Yasin, Zarqa; Hari, Parneet; Alamelumangapuram, Chidamber Bharath] Henry Ford Hlth Syst, Jackson, MI USA.

Neurology
Ali M, **deCarvalho A**, **Ewing J**, **Snyder J**, and **Mikkelsen T**. TUMOR PARAMETERS AFFECTED BY NANOCOMBRESTATIN THERAPY IN AN EXPERIMENTAL RAT MODEL OF GLIOMA. *Neuro Oncol* 2023; 25:1. Full Text

[Ali, Meser; Snyder, James; Mikkelsen, Tom] Henry Ford Hosp, Detroit, MI 48202 USA. [deCarvalho, Ana; Ewing, James] Henry Ford Hlth, Detroit, MI USA.

Neurology
Chen L, **Xiong Y**, **Chopp M**, **Pnag HY**, **Zhang ZG**, **Mahmood A**, and **Zhang YL**. THERAPEUTIC EFFECTS OF VEPOLOXAMER ON FUNCTIONAL OUTCOMES AFTER TRAUMATIC BRAIN INJURY IN MALE AND FEMALE RATS. *J Neurotrauma* 2023; 40(15-16):A116-A116. Full Text

[Chen, Liang; Xiong, Ye; Pnag, Haiyan; Mahmood, Asim; Zhang, Yanlu] Henry Ford Hlth Syst, Dept Neurosurg, Detroit, MI USA. [Chopp, Michael; Zhang, Zheng Gang] Henry Ford Hlth Syst, Dept Neurol, Detroit, MI USA. [Chopp, Michael] Oakland Univ, Dept Phys, Rochester, MI 48063 USA. Henry Ford Hospital; Oakland University

Neurology
LeWitt PA, Todi SV, Qadri Z, Bangash Z, Chbihi Z, Ranxhi B, and Tsou WL. Linking Biomarkers and Pathways: Investigating Polyamines' Influence on a-Synuclein in Parkinson's Disease. *Mov Disord* 2023; 38:S11-S12. Full Text

[LeWitt, Peter A.] Henry Ford Hosp, Detroit, MI USA. [LeWitt, Peter A.; Todi, Sokol V.; Qadri, Zaina; Bangash, Zoya; Chbihi, Zach; Ranxhi, Bedri; Tsou, Wei-Ling] Wayne State Univ, Sch Med, Detroit, MI USA.

Neurology
McCann R, Zhou YZ, Mojica C, Zeldich E, **Xin HQ**, Rosene D, Medalla M, and Moore T. EXTRACELLULAR VESICLE TREATMENT REDUCES INFLAMMATION AND INCREASES NEURONAL MARKERS IN A MONKEY MODEL OF CORTICAL INJURY. *J Neurotrauma* 2023; 40(15-16):A108-A109. Full Text

[McCann, Ryan; Zhou, Yuzin; Mojica, Chromewell; Zeldich, Ella; Rosene, Douglas; Medalla, Maria; Moore, Tara] Boston Univ, Chobanian & Avedisian Sch Med, Boston, MA 02215 USA. [Xin, Hongqi] Henry Ford Hlth Syst, Detroit, MI USA.

Neurology
Nagaraja T, **Datta I**, **Morosini N**, **Bartlett S**, Ayloo B, **Cabral G**, Avritt F, **Hasselbach L**, **Parasar P**, **De Carvalho A**, **Singh J**, **Knight R**, **Brown S**, **Ewing J**, **Noushmehr H**, and **Lee I**. IMAGING, HISTOLOGICAL AND MOLECULAR CHARACTERIZATION AND COMPARISON OF POST-ABLATION

RECURRENT TUMOR WITH THE PRIMARY TUMOR IN A PRECLINICAL GLIOBLASTOMA MODEL. *Neuro Oncol* 2023; 25:v301. Full Text

T. Nagaraja, Henry Ford Health, Detroit, MI, United States

Recurrent glioblastoma (rGBM) is highly aggressive and invasive. A reliable preclinical model that recapitulates these features is not presently available. The objective was to generate a preclinical rGBM model, characterize and compare its imaging, histological and molecular signatures in comparison to the primary tumor. Immune-suppressed, RNU/RNU female rats were implanted with U251N tumor cells in one brain hemisphere (n=33). Tumor progression in all rats was followed by longitudinal dynamic contrast enhanced-magnetic resonance imaging (DCE-MRI). In 24 rats the tumor was ablated under diffusion-weighted imaging (DWI)-guided laser interstitial thermal therapy (LITT) at post-implantation 2-weeks. Cohorts from twenty ablated rats were euthanized at post-LITT 24 h, 2- and 4-weeks and, along with 5 unablated controls, used for hematoxylin and eosin (H&E) and Ki67 staining. Tissues from 4 other unablated and 4 recurrent tumors at post-LITT 2-weeks were used for RNAseq. All the rats survived the LITT procedure. Unablated controls showed increased tumor burden by postimplantation 2 weeks and were euthanized. In the LITT group, MRI showed little tumor tissue at 24 h, evidence of recurrence at 2 weeks and significant tumor tissue at 4 weeks and matched with histological evidence for tumor recurrence. Compared to the primary tumor, H&E staining showed increased vascular hyperplasia, mitotic bodies and hypoxic regions with pseudopalisading necrosis in the recurrent tumor. Increased KI67 staining in recurrent tumors suggested higher rates of proliferation and evidence of infiltration into host tissue. Pathway analyses demonstrated differentially expressed genes in the canonical pathways of hypoxia-inducible factor-alpha (HIF-1α), nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) and OX40 signaling. The genes for the following functions were significantly affected: cell cycle, cellular movement and cell morphology. Reliable preclinical rGBM models are few. These data suggest that this model replicates the features of human rGBM and can be useful in testing putative anti-glioma therapies.

Neurology

Wen P, Alexander B, Berry D, Buxton M, Cavenee W, Colman H, De Groot J, Ellingson B, Gordon G, Hyddmark E, Khasraw M, Lim M, Mellinghoff I, **Mikkelsen T**, Perry J, Powell A, Sulman E, Tanner K, Weller M, Yung WKA, Blondin N, Brenner A, Butt O, De La Fuente M, Drappatz J, Iwamoto F, Kim L, Lee E, Mantica M, Nabors B, Newton H, Schiff D, **Walbert T**, Weathers SP, Cloughesy T, and Lassman A. GBM AGILE PLATFORM TRIAL FOR NEWLY DIAGNOSED AND RECURRENT GBM: RESULTS OF FIRST EXPERIMENTAL ARM, REGORAFENIB. *Neuro Oncol* 2023; 25:v97-v98. Full Text

P. Wen, Dana-Farber/Brigham and Women's Cancer Center, Boston, MA, United States

GBM AGILE (NCT03970447;https://www.gcaresearch.org/research/ gbm-agile) is a phase 3 Bayesian adaptive platform trial that efficiently tests multiple arms against common control, with 6 arms included to date. Primary endpoint is overall survival (OS). Stage 1 experimental arms are adaptively randomized against other arms. Demonstrated efficacy in stage 1 leads to fixed randomization stage 2. Stages 1 and 2 are combined for registration. Control randomization is fixed. Regorafenib, a multikinase-inhibitor, entered into GBM AGILE as the first arm and therefore was equally ran-domized against control. Regorafenib showed OS benefit in recurrent disease (RD) in randomized phase 2 REGOMA trial. METHODS: Patient subtypes in GBM AGILE are newly diagnosed unmethylated (NDU), RD, and-not considered for regorafenib-ND methylated (NDM). Arm indications (signatures) are combinations of subtypes. Control is temozolomide (ND) and lomustine (RD). Efficacy is assessed by OS hazard ratio(HR), arm/control. Efficacy is demonstrated when Bayesian probability of benefit (HR< 1.00) ≥ 98% (roughly analogous P-value: 0.02). Futility occurs at any monthly analysis when Bayesian predictive power (PP) is < 25% for all signatures. Follow-up continues for 12 months after arm's accrual stops. RESULTS for regorafenib: When PP for all 3 pre-defined signatures was < 25%, regorafenib's accrual was stopped for futility. Regorafenib/control sample sizes were 49/51, 126/128, 175/179 for signatures NDU, RD, and both. Respective PPs: 0.138, 0.030, 0.025-none close to 0.25. Respective mean HRs: 1.26, 1.25, 1.23. Probabilities of benefit (HR< 1.00): 0.35, 0.18, 0.17. At final analysis, mean HRs were 1.07, 1.12, 1.10 with final probabilities of benefit (HR< 1.00) equal to 0.43, 0.24, 0.24-none close to 0.98.

CONCLUSION: GBM AGILE efficiently and compellingly addressed regorafenib's role in GBM, in RD and NDU. These findings are germane as they fail to confirm the REGOMA results in RD. GBM AGILE continues to efficiently assess other therapies, including utilizing concurrent and previously accrued controls.

Neurology
Zhang YL, **Chen L**, **Ding GL**, **Li L**, **Pang HY**, **Jiang Q**, **Chopp M**, **Zhang ZG**, **Mahmood A**, and **Xiong Y**. DYSREGULATED AQUAPORIN 4 EXPRESSION AND POLARITY, INCREASED NEUROINFLAMMATION AND AXONAL INJURY ARE ASSOCIATED WITH LONG-TERM FUNCTIONAL DEFICITS AFTER MILD CLOSED HEAD INJURY. *J Neurotrauma* 2023; 40(15-16):A96-A96. Full Text

[Zhang, Yanlu; Chen, Liang; Pang, Haiyan; Mahmood, Asim; Xiong, Ye] Henry Ford Hlth, Dept Neurosurg, Detroit, MI USA. [Ding, Guangliang; Li, Lian; Jiang, Quan; Chopp, Michael; Zhang, Zheng Gang] Henry Ford Hlth, Dept Neurol, Detroit, MI USA. [Chopp, Michael] Oakland Univ, Dept Phys, Rochester, MI 48063 USA.

Neurosurgery
Akbari H, Bakas S, Garcia J, Kazerooni AF, Sako C, Villanueva-Meyer J, Baid U, Mamourian E, Brem S, Lustig RA, Nasrallah MP, O'Rourke DM, Calabrese E, Rudie J, Chang S, Rauschecker A, LaMontagne P, Marcus DS, Balana C, Capellades J, Puig J, Barnholtz-Sloan J, Badve C, Sloan A, Waite K, Colen R, Choi YS, Ahn SS, Dicker AP, Flanders AE, Shi W, **Griffith B**, **Poisson LM**, **Rogers LR**, Booth TC, Jain R, Chakravarti A, Palmer J, Cepeda S, Wiestler B, Di Stefano AL, Alexander K, Melhem ER, Woodworth GF, Kamel PI, Tiwari P, Aboian M, Mohan S, and Davatzikos C. ROBUSTNESS OF PROGNOSTIC STRATIFICATION IN DE NOVO GLIOBLASTOMA PATIENTS ACROSS 22 GEOGRAPHICALLY DISTINCT INSTITUTIONS: INSIGHTS FROM THE RESPOND CONSORTIUM. *Neuro Oncol* 2023; 25:v187. Full Text

H. Akbari, University of Pennsylvania, Philadelphia, United States

PURPOSE: Glioblastoma is the most prevalent primary malignant brain tumor in adults, with a median overall survival (OS) of approximately 15 months and only limited advancements in prognostication and survival prediction. This study aims to evaluate an AI-based prognostic stratification model for OS prediction trained on the ReSPOND consortium data and to validate its performance on an independent dataset. METHODS: The AI model was trained on a cohort of 2,293 glioblastoma patients from 22 institutions across three continents. For validation, an independent cohort of 78 treatment-naïve patients was used from three institutions. Preoperative structural MRI scans were utilized for feature extraction. Automated segmentation defined three tumor sub-compartments: enhancing, necrotic, and peritumoral T2-FLAIR abnormality. The AI predictor incorporated variables such as patient age, normalized tumor sub-compartment volume, spatial distribution characteristics, and morphologic descriptors. The overall survival predictor index provided a continuous value between 0 and 1 for patient stratification that higher values indicating longer predicted OS. Generalizability was assessed using Leave-One-Cohort-Out-Cross-Validation (LOCOCV) for training data, and the model was subsequently applied to the validation cohort. RESULTS: Survival analysis demonstrated a concordance index of 0.64 for LOCOCV training data and 0.59 for the independent validation data, indicating effective prognostic stratification of patients. CONCLUSION: Multi-parametric AI assisted image analysis extracts prognostic biomarkers, which correlate with OS in glioblastoma patients. The generalizability of this method was validated using the extensive centralized glioblastoma imaging dataset registry from the ReSPOND consortium and an independent dataset, demonstrating its generalizability across diverse patient populations and acquisition settings. This model holds promise for robust prognostic stratification and prediction in de novo glioblastoma patients.

Neurosurgery
Ali M, **deCarvalho A**, **Ewing J**, **Snyder J**, and **Mikkelsen T**. TUMOR PARAMETERS AFFECTED BY NANOCOMBRESTATIN THERAPY IN AN EXPERIMENTAL RAT MODEL OF GLIOMA. *Neuro Oncol* 2023; 25:1. Full Text

[Ali, Meser; Snyder, James; Mikkelsen, Tom] Henry Ford Hosp, Detroit, MI 48202 USA. [deCarvalho, Ana; Ewing, James] Henry Ford Hlth, Detroit, MI USA.

Neurosurgery
Chen L, **Xiong Y**, **Chopp M**, **Pnag HY**, **Zhang ZG**, **Mahmood A**, and **Zhang YL**. THERAPEUTIC EFFECTS OF VEPOLOXAMER ON FUNCTIONAL OUTCOMES AFTER TRAUMATIC BRAIN INJURY IN MALE AND FEMALE RATS. *J Neurotrauma* 2023; 40(15-16):A116-A116. Full Text

[Chen, Liang; Xiong, Ye; Pnag, Haiyan; Mahmood, Asim; Zhang, Yanlu] Henry Ford Hlth Syst, Dept Neurosurg, Detroit, MI USA. [Chopp, Michael; Zhang, Zheng Gang] Henry Ford Hlth Syst, Dept Neurol, Detroit, MI USA. [Chopp, Michael] Oakland Univ, Dept Phys, Rochester, MI 48063 USA. Henry Ford Hospital; Oakland University

Neurosurgery
Fortunato J, Walsh L, Polacek L, Panageas K, Reiner A, **Walbert T**, Thomas A, Buthorn J, Sigler A, Prigerson H, Applebaum A, and Diamond E. ILLNESS UNDERSTANDING AND RELIGIOUSNESS IN PATIENTS WITH RECURRENT GLIOBLASTOMA. *Neuro Oncol* 2023; 25:v255-v256. Full Text

J. Fortunato, Memorial Sloan Kettering Cancer Center, New York, NY, United States

BACKGROUND: Glioblastoma (GBM) is an aggressive neurologic malignancy with invariably poor prognosis. However, there is evidence that patients with GBM often have unrealistic perceptions of their prognosis. Strong religious beliefs have been shown to be associated with limited illness understanding (IU) in patients with advanced cancer, but IU and religiousness have not been investigated in patients with GBM. METHODS: Patients enrolled in a prospective multi-center study of recurrent GBM (Coping with Glioblastoma; NCT02375841) completed surveys after a clinical encounter with their oncologist revealing GBM progression. Psychometrically validated measures assessed parameters of IU and religiousness. IU was compared between participants with at least a moderate or high degree of religiousness (vs. not) using Fishers-exact test. RESULTS: Twenty-four adult patients (median age 57) completed surveys. Fifteen (63%) identified their illness as terminal. Six patients (25%) correctly identified their life expectancy (months), eight patients predicted life expectancy of years (33%) and ten (42%) did not know or answer. Eleven (46%) reported being moderately or very religious, while nine (38%) were slightly or not at all religious. There was significantly less frequent awareness of terminal illness amongst patients identifying as religious, spiritual, or as feeling God's presence (all $p < 0.05$). There was significantly less frequent IU amongst patients identifying as spiritual or believing in miracles (both $p < 0.05$). CONCLUSION: IU is infrequent in recurrent GBM and is significantly less frequent in patients endorsing religiousness and spirituality. Strategies to improve IU, broadly and in alignment with religious and spiritual beliefs, are warranted.

Neurosurgery
Garcia M, Brachman D, Lee S, Peach MS, Wanebo J, Smith K, Chen C, Kotecha R, Ahluwalia M, Hanft S, Nowlan A, McCracken D, Floyd J, Shah M, Richardson A, Patel T, Pham H, Ryan R, Wasilewski A, Shen C, **Robin A**, Ranjan T, Bojanowski-Hoang K, DiNapoli V, Chamoun R, Choutka O, Mercado C, Haydon D, Leng L, Rodriguez A, Deb N, Patel A, Piccioni D, Campbell L, Patel S, and Hall A. IMPACT OF COLLAGEN TILE BRACHYTHERAPY AS TREATMENT FOR RECURRENT GLIOBLASTOMAS ON FUNCTIONAL STATUS AND QUALITY OF LIFE. *Neuro Oncol* 2023; 25:1. Full Text

[Garcia, Michael; Brachman, David; Wanebo, John; Smith, Kris; Campbell, Lisa; Patel, Sita; Hall, Angela] GT Med Technol, Tempe, AZ USA. [Lee, Stuart] ECU Hlth, Greenville, NC USA. [Peach, Matthew Sean] Vidant ECU, Washington, NC USA. [Wanebo, John; Smith, Kris] Barrow Neurol Inst, Phoenix, AZ 85013 USA. [Chen, Clark] Univ Minnesota, Minneapolis, MN USA. [Kotecha, Rupesh; Ahluwalia, Manmeet] Baptist Hlth South Florida, Miami Canc Inst, Miami, FL USA. [Hanft, Simon] Westchester Med Ctr, Valhalla, NY USA. [Nowlan, Adam; McCracken, David] Piedmont Atlanta Hosp, Atlanta, GA USA. [Floyd, John] UT Hlth Sci Ctr San Antonio, San Antonio, TX USA. [Shah, Mitesh; Richardson, Angela] Indiana Univ, Neurosci Ctr, Indianapolis, IN USA. [Patel, Toral] UT SouthWestern Med Ctr, Dallas, TX USA. [Huong Pham; Ryan, Robert] Virginia Mason Med Ctr, Seattle, WA 98101 USA. [Wasilewski, Andrea]

Abbott NW Hosp, Minneapolis, MN USA. [Shen, Colette] UNC Hlth, Chapel Hill, NC USA. [Robin, Adam] Henry Ford West Bloomfield Hosp, Detroit, MI USA. [Ranjan, Tulika] Tampa Gen Hosp, Tampa, FL USA. [Bojanowski-Hoang, Kimberly] Emory Univ Hosp, Atlanta, GA USA. [DiNapoli, Vincent] Mayfield Clin, Cincinnati, OH USA. [Chamoun, Roukoz] Univ Kansas Hlth Syst, Kansas City, KS USA. [Choutka, Ondrej] St Alphonsus Reg Med Ctr, Boise, ID USA. [Mercado, Catherine] Orlando Hlth Syst, Orlando, FL USA. [Haydon, Devon] BayCare Hosp, Clearwater, FL USA. [Leng, Lewis] Sutter Hlth, San Francisco, CA USA. [Rodriguez, Analiz] Univ Arkansas Med Sci, Little Rock, AR USA. [Deb, Nimisha] St Lukes Univ Hlth Network, Bethlehem, PA USA. [Patel, Akash] Baylor Coll Med, Houston, TX USA. [Piccioni, David] Univ Calif San Diego, San Diego, CA USA. University of Minnesota Twin Cities; Westchester Medical Center; University of Texas System; University of Texas Health Science Center at San Antonio; Indiana University System; Indiana University-Purdue University Indianapolis; University of Texas System; University of Texas Southwestern Medical Center Dallas; Virginia Mason Medical Center; Henry Ford Health System; Tampa General Hospital; Emory University; Saint Alphonsus Regional Medical Center; University of Arkansas System; University of Arkansas Medical Sciences; Baylor College of Medicine; University of California System; University of California San Diego

Neurosurgery
Gilbert M, **Zhu S**, **Shah M**, **Siddiqui S**, **Rogers LR**, and **Siddiqui F**. INSTITUTION SPECIFIC CLINICAL TRIAL MATCHING WEB APPLICATION FOR CENTRAL NERVOUS SYSTEM METASTASES. *Neuro Oncol* 2023; 25:v156. Full Text

M. Gilbert, Henry Ford Health System, Detroit, United States

BACKGROUND: Current clinical trials evaluating treatment options for patients with brain metastases are tailored to a number of clinical factors, including type of underlying cancer, number of brain metastases, size and volume of brain metastasis, prior treatment, and genomic characterization. A multidisciplinary brain metastasis tumor board was established at our institution in January 2023. Subsequently, an institution specific clinical trial matching web application was developed in-house to screen and match subjects for trials accruing at our institution. METHODS: We reviewed our institution's list of phase III surgical, radiation, and medical oncology clinical trials specific for brain metastasis to identify the most discriminating inclusion criteria that can be used as a basis for branching and differentiation. These disease specific trials were then individually assessed according to these criteria and these results were populated in a common separated value (CSV) file. RESULTS: A web application was created using Python for analysis of the CSV and incorporating branching logic. HTML, CSS, and JavaScript were used for building the webpage interface. The web application is hosted on our institutional server and can be utilized to search available clinical trials for each patient being presented during tumor board. CONCLUSION: We developed an institution specific web application that can be used to screen patients for various clinical trials. By developing this application and hosting it internally, we are able to edit the components at our discretion. The methodology for this web-build can be applied to other disease sites or institutions. This web application is useful for screening our institution's clinical trial portfolio to identify potential gaps, and can also be used to avoid competing trials. This web application significantly reduces the time to identify protocol eligibility and has increased clinical trial enrollment.

Neurosurgery
Gongala S, Garcia J, Korakavi N, Patil N, Akbari H, Tippareddy C, Sloan A, Barnholtz-Sloan J, Bakas S, Kazerooni AF, Sako C, Baid U, Brem S, Lustig RA, Capellades J, Nasrallah M, O'Rourke DM, La Montagne P, Marcus DS, Balana C, Puig J, Waite K, Colen R, Choi YS, Lee SK, Dicker AP, Flanders AE, Shi W, **Griffith B**, **Poisson LM**, **Rogers LR**, Booth TC, Jain R, Chakravarti A, Palmer J, Mohan S, Tiwari P, Aboian M, Ahn SS, Davatzikos C, and Badve C. SEX-SPECIFIC DIFFERENCES IN GLIOBLASTOMA IN THE RESPOND CONSORTIUM. *Neuro Oncol* 2023; 25:v118. Full Text

S. Gongala, Department of Radiology, University Hospitals Seidman Cancer Center, Cleveland, United States

AIM: The goal of this study was to understand sex-specific differences in the molecular, clinical and radiological tumor parameters and survival outcomes of Glioblastoma (GBM) patients within the

international GBM dataset, known as the ReSPOND (Radiomic Signatures for PrecisiON Diagnostics) consortium. METHODS: Sex-based differences were retrospectively studied in 1922 GBM patients from the ReSPOND consortium which includes information from over 14 institutions across 3 continents. The parameters include age, Methylguanine-DNA Methyltransferase (MGMT) promoter methylation status, isocitrate dehydrogenase 1 (IDH1) mutation status, Karnofsky performance status (KPS), extent of resection (EOR), tumor epicenter, volumes, laterality and spatial extent. Non-parametric tests, log-rank test and cox-proportional hazard analysis were performed to understand sex-based differences in tumor parameters, survival rates and hazard ratios. Spatial atlases were generated to understand radiological parameters such as tumor spatial extent. RESULTS: GBM in was diagnosed at a median age of 62.6 years in females compared to 61 years in males ($p = 0.001$). Additionally, 44% females compared to 37% males ($p = 0.04$) had methylated MGMT and 79% females compared to 73% males ($p = 0.004$) had IDH1 wildtype. The tumor volumes were smaller in females (necrotic core, edema, and enhancing tumor) compared to males. Females exhibited a higher prevalence of right hemisphere (39.6%) and right temporal lobe tumors (19.7%), while males showed a higher prevalence of left hemisphere (40.3%) left temporal lobe tumors (23.7%). No significant sex-based differences in OS and PFS was observed in overall sample, although longer PFS was observed in elderly (above 60 years) female patients. CONCLUSION: This is a first international large cohort study looking at sex-based differences in GBM patients using the ReSPOND consortium data. Several sex-specific differences in the distribution of various tumor phenotypes were noted, however sex was not a contributing factor in OS and PFS.

Neurosurgery
Hazy A, Grills I, Ogaily M, Stender M, and **Rogers LR**. RADIATION MYELOPATHY AFTER STANDARD DOSE RADIATION: POTENTIAL RADIATION SENSITIZING EFFECTS OF SYSTEMIC THERAPY. *Neuro Oncol* 2023; 25:v46-v47. Full Text

A. Hazy, Corewell Health, Royal Oak, MI, United States

Radiation myelopathy is an uncommon adverse effect of spinal irradiation. It is especially rare following conventional palliative fractionation regimens for vertebral metastasis. We present two cases of delayed thoracic radiation myelopathy in patients with breast cancer. In both cases, palliative radiation of 30 Gy in ten fractions was administered to thoracic spinal metastases. Neither patient received concurrent systemic therapy. One began trastuzumab emtansine nine days after finishing radiation and the other started palbociclib three months afterwards, which was switched to capecitabine at disease progression. Each patient developed progressive leg weakness and numbness, ten months following radiation and eleven months following radiation (four weeks following capecitabine), respectively. MRI showed edema and focal contrast enhancement within the radiation field in each. Both were treated with high-dose corticosteroid, vitamin E, and pentoxifylline. Neither patient returned to their neurologic baseline and remain with significant deficits, requiring assistance with ambulation. Serial MRIs revealed eventual reduction in cord enhancement and edema, followed by cord atrophy in one case. The cumulative radiation dose of 30 Gy is typically within the safety tolerance of the spinal cord, so it is speculative if post-radiation systemic therapy played a role in the development of myelopathy. The timing is particularly convincing in the patient who developed symptoms within four weeks of starting capecitabine. These cases are similar to recently reported instances of radiation myelopathy after standard dose spinal radiation followed by chemotherapy or immunotherapy. Recognition of the potential radiation sensitizing effects of systemic therapy should lead clinicians to consider radiation myelopathy early if spinal cord symptoms develop and to consider the timing of initiation of potential sensitizing drugs when spinal radiation has been given.

Neurosurgery
Horbinski C, Drumm M, McCord M, Kostelecky N, Smith H, Ahrendsen J, Jamshidi P, Castellani R, **Herrgott G**, **Noushmehr H**, Zhang D, Silverbush D, Dos Santos L, Walshon J, Steffens A, and McCortney K. Multidimensional characterization of supratentorial adult-type diffuse gliomas that migrate to the brainstem. *J Neuropathol Exp Neurol* 2024; 83(6):504-505. Full Text

C. Horbinski, Northwestern University, United States

Background: We previously showed that cerebral diffuse gliomas usually spread to the brainstem at the final stages of disease, and that this, not tonsillar herniation, most likely accounts for brainstem-type symptoms commonly observed at the end of life (PMID: 31711239). It remains unknown whether glioma cells that spread to the brainstem are different from glioma that remains near the original tumor site ("stationary"). Methods: We analyzed original premortem tumors, postmortem stationary tumors, and postmortem tumors that infiltrated the brainstem from 20 patients (5 IDHmut astrocytomas, 15 IDHwt GBM). Each site was analyzed for expression of key markers by immunohistochemistry, genomic DNA methylation profiling (including deconvolution analysis of immune populations), and whole exome sequencing. Results: Compared to stationary tumors, glioma subclones that migrated to the brainstem had higher Ki67 proliferation indices (P=0.003), expressed fewer mesenchymal markers (P<0.001), lost OLIG2 expression (P<0.001), and were normoxic as indicated by HIF1a (P=0.03). Brainstem tumors also had fewer admixed macrophages and lymphocytes (P<0.05), except for patients who received immunotherapy during their disease courses. In those cases, lymphocytes and macrophages were elevated in the brainstems (but not in stationary tumors) relative to the brainstems of patients without immunotherapy (P<0.01). Microvascular proliferation was not found in any glioma-infiltrated brainstems. Whereas IDHmut astrocytomas retained their methylation profiles, 40% of the RTK-II subset of IDHwt GBM shifted methylation subclass, most commonly to RTK-I. There was no consistent pattern of mutations in brainstem subclones vs. premortem or stationary tumors, and tumor mutation burden was similar in all three settings (P=0.17). Conclusions: Together, these data suggest that, while brainstem subclones mostly retain the molecular patterns of their supratentorial origins, protein expression shifts in consistent patterns, perhaps as a consequence of the glioma cells having moved to a new microenvironment. This study sheds new light on the characteristics of end-stage glioma spread.

Neurosurgery

Lee I, Judy K, Schulder M, Hanft S, Evans L, Wu J, Aulakh S, Wong E, Agarwal V, Ramakrishna R, Elder JB, Gill B, Quiñones-Hinojosa A, Brennan C, Perez-Olle R, Diwanji M, Pennock G, Scott C, Andrews D, and Boockvar J. A RANDOMIZED, MULTICENTER, DOUBLEBLIND, PHASE 2B STUDY OF IGV-001, AN AUTOLOGOUS CELL IMMUNOTHERAPY WITH ANTISENSE OLIGO IMV-001 TARGETING IGF-1R, VS PLACEBO, IN NEWLY DIAGNOSED GLIOBLASTOMA PATIENTS. *Neuro Oncol* 2023; 25:v260-v261. Full Text

I. Lee, Henry Ford Health, Detroit, MI, United States

Glioblastoma (GBM) is the most common primary brain malignancy in adults. Standard of care (SOC) for suspected GBM begins with maximal safe resection followed by adjuvant radiotherapy and temozolomide, and maintenance temozolomide. Imvax has developed the Goldspire™ platform to create IGV-001, an autologous biologic-device combination product for the treatment of newly diagnosed GBM (ndGBM). IGV-001 consists of autologous GBM tumor cells and an antisense oligonucleotide against IGF-1R mRNA (IMV-001), irradiated and administered via biodiffusion chambers implanted in the abdomen. Together, these com- ponents stimulate immunogenic cell death and antigen release. IGV-001 was well tolerated and multiple efficacy signals were observed in a Phase 1b study in patients with ndGBM, including significant improvements in progression-free survival (PFS), radiographic evidence of tumor response, and changes in immune response biomarkers. A Phase 2b randomized, multicenter, double-blind, placebo-controlled study has been initiated to assess the safety and efficacy of IGV-001 in patients with ndGBM (NCT04485949). After surgical resection, patients will be treated with IGV-001 or placebo followed by SOC. 25 US sites have been selected with a target enrollment of 93 patients (2:1 randomization) and the study is open to enrollment. Key inclusion criteria are 18 to 70 years of age, Karnofsky performance status score ≥ 70, diagnosis of GBM based on the treating neurosurgeon's best clinical judgement, confirmed measurable disease pre-operatively, tumor located in the supratentorial compartment, and adequate bone marrow and organ function. Key exclusion criteria include bihemispheric disease, multicentric disease, or treatment with Tumor Treating Fields prior to documented progression. The primary outcome is PFS, defined as the time from randomization to first progression, as determined by blinded central radiology review, or death. Secondary outcomes include overall survival, defined as the time from randomization to death due to any cause, and safety.

Neurosurgery

Lita A, Sjöberg J, PĂcioianu D, Siminea N, Celiku O, PĂun A, Gilbert M, **Noushmehr H**, Petre I, and Larion M. RAMAN-BASED AI PLATFORM TO ACCELERATE THE DIAGNOSIS AND MANAGEMENT OF GLIOMAS VIA RAPID METHYLATION PROFILING. *Neuro Oncol* 2023; 25:v182. Full Text

A. Lita, Neuro-Oncology Branch, National Cancer Institute, Bethesda, MD, United States

BACKGROUND: DNA methylation profiling and subtyping of gliomas has become an integral part of the diagnosis and treatment of glioma patients but remains a challenge due to the sample preparation and time requirements of the existing methylation profiling technology. We hypothesized that machine learning and Raman spectroscopy, which creates fast molecular fingerprints of samples in situ based on chemical signatures rather than the use of exogenous dyes, can provide a fast alternative to the existing approaches for methylation profiling and classification of gliomas. METHODS: Raman spectroscopy at the spatial resolution of less than 300nm was used for molecular fingerprinting of the regions of interest using 1mm2 Formalin-Fixed Paraffin-Embedded (FFPE) tissue spots from 45 patient samples with known LGm1 to LGm6 methylation subtypes. Spectral information (over 1738 frequencies) was used to construct tumor/non-tumor, IDH1WT/IDH1mut, and methylation-subtype classifiers. Oversampling was used to obtain subtype-balanced data distributions. Supervised wrapper methods and random forests were used to identify the top 20 most discriminatory Raman frequencies. Stimulated Raman spectroscopy was used to validate the findings. RESULTS: We developed APOLLO - a novel platform based on spontaneous Raman spectroscopy and machine learning - for predicting the DNA methylation subtypes of FFPE glioma tissue specimens. APOLLO discriminates tumors from non-tumor areas with 98% accuracy and discriminates IDH1mut versus IDH1WT tumors with 82% accuracy. APOLLO also achieved high discriminatory power between G-CIMP-high and G-CIMP-low molecular phenotypes (ROC of 0.75), subtypes of lower-grade IDH1mut gliomas with significantly different clinical outcomes. We determined that the Raman shifts important for discriminating IDH1mut versus IDH1wt tumors are associated with novel lipid-metabolism signatures of IDH1mut glioma. CONCLUSIONS: The development of APOLLO allows fast, reliable, and accurate prediction of methylation subtypes of glioma which can speed diagnosis and, once validated on fresh tissue, can be implemented in the operating room.

Neurosurgery

Meng Y, Mughal N, **Datta I**, Nuga O, **Irtenkauf S**, **Hasselbach L**, **Quenneville K**, **Brown S**, and **DeCarvalho A**. GLIOBLASTOMA PATIENT SPECIFIC TRANSCRIPTOME REMODELING IN RESPONSE TO MDM2 ANTAGONIST TREATMENT OF WILD-TYPE P53 CANCER STEM CELLS IS ASSOCIATED WITH SENSITIVITY AND STRATEGIES FOR COMBINATION THERAPY. *Neuro Oncol* 2023; 25:v224-v225. Full Text

Y. Meng, Henry Ford Health, Detroit, United States

Over 70% of glioblastomas are p53 wild-type and these patients could benefit from p53 reactivation treatment. Here we determined the sensitivity of a glioblastoma patient-derived cancer stem cells (CSCs) panel to three MDM2 antagonists (MDM2a) to test to what extent transcriptional reprogramming is affected by genomic background and correlates to response to acute treatment with MDM2 antagonists. IC50 concentrations and area above the curve (AAC) were measured from dose response curves obtained from 4 and 7-day treatment. The inhibitors were specific to wt-p53 CSCs, but these presented a wide range of sensitivity. Seven wt-p53 CSCs were treated RG7112 IC50 concentrations or DMSO control for 24h (n=4). RNA was isolated for Illumina Truseq stranded mRNA libraries sequenced at 30M depth. Quantified raw counts were processed using NOISeq R package to determine differentially expressed genes (DEG) between control and treated samples. In addition to the expected high representation of upregulated p53 targets in all cell lines, we observed significan cell specific transcriptome alterations, including enrichment of survival pathways, such as mTOR, ERK and NFkB in the less sensitive CSC lines, which did not readily correlate with the individual genomic landscapes. E2F targets, G2-M cell cycle check point and DNA-repair pathways were highly enriched in the downregulated genes. Combination of MDM2a with radiation treatment (RT) was synergistic to a subset of CSCs. As validation we found that MDM2a treatment was effective in sensitizing a resistant orthotopic mouse glioblastoma PDX to fractionated RT, with maximum efficacy when treatment started 24h prior to RT vs

simultaneously (Log-rank Mantel-Cox test: p=0.0006 vs 0.0277). The integration of the treatment-mediated transcriptional patterns with differential sensibility to MDM2 antagonists and genomic landscape of the CSC panel provides a platform to identify targets for combination therapies, which is the most promising clinical application of the reactivation of wt-p53 in GBMs.

Neurosurgery
Nagaraja T, **Datta I**, **Morosini N**, **Bartlett S**, Ayloo B, **Cabral G**, Avritt F, **Hasselbach L**, **Parasar P**, **De Carvalho A**, **Singh J**, **Knight R**, **Brown S**, **Ewing J**, **Noushmehr H**, and **Lee I**. IMAGING, HISTOLOGICAL AND MOLECULAR CHARACTERIZATION AND COMPARISON OF POST-ABLATION RECURRENT TUMOR WITH THE PRIMARY TUMOR IN A PRECLINICAL GLIOBLASTOMA MODEL. *Neuro Oncol* 2023; 25:v301. Full Text

T. Nagaraja, Henry Ford Health, Detroit, MI, United States

Recurrent glioblastoma (rGBM) is highly aggressive and invasive. A reliable preclinical model that recapitulates these features is not presently available. The objective was to generate a preclinical rGBM model, characterize and compare its imaging, histological and molecular signatures in comparison to the primary tumor. Immune-suppressed, RNU/RNU female rats were implanted with U251N tumor cells in one brain hemisphere (n=33). Tumor progression in all rats was followed by longitudinal dynamic contrast enhanced-magnetic resonance imaging (DCE-MRI). In 24 rats the tumor was ablated under diffusion-weighted imaging (DWI)-guided laser interstitial thermal therapy (LITT) at post-implantation 2-weeks. Cohorts from twenty ablated rats were euthanized at post-LITT 24 h, 2- and 4-weeks and, along with 5 unablated controls, used for hematoxylin and eosin (H&E) and Ki67 staining. Tissues from 4 other unablated and 4 recurrent tumors at post-LITT 2-weeks were used for RNAseq. All the rats survived the LITT procedure. Unablated controls showed increased tumor burden by postimplantation 2 weeks and were euthanized. In the LITT group, MRI showed little tumor tissue at 24 h, evidence of recurrence at 2 weeks and significant tumor tissue at 4 weeks and matched with histological evidence for tumor recurrence. Compared to the primary tumor, H&E staining showed increased vascular hyperplasia, mitotic bodies and hypoxic regions with pseudopalisading necrosis in the recurrent tumor. Increased KI67 staining in recurrent tumors suggested higher rates of proliferation and evidence of infiltration into host tissue. Pathway analyses demonstrated differentially expressed genes in the canonical pathways of hypoxia-inducible factor-alpha (HIF-1α), nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) and OX40 signaling. The genes for the following functions were significantly affected: cell cycle, cellular movement and cell morphology. Reliable preclinical rGBM models are few. These data suggest that this model replicates the features of human rGBM and can be useful in testing putative anti-glioma therapies.

Neurosurgery
Ozair A, Drappatz J, Ye X, Berens M, Peng S, Rath S, Dhruv H, **Walbert T**, Holdhoff M, Lesser G, Cloughesy T, Sloan A, Couce M, Peereboom D, Nabors B, Wen P, **Rogers L**, Grossman S, and Ahluwalia M. EXCEPTIONAL RESPONDERS TO BASE EXCISION REPAIR (BER) INHIBITION FOR RECURRENT GLIOBLASTOMA DISPLAY ENRICHMENT FOR DNA DAMAGE RESPONSE PATHWAYS: RNA SEQUENCING ANALYSIS FROM A MULTICENTER TRIAL. *Neuro Oncol* 2023; 25:v99. Full Text

A. Ozair, Miami Cancer Institute Baptist Health South Florida, Miami, FL, United States

INTRODUCTION: Therapies for glioblastoma recurrence after surgery and chemoradiation are warranted. TRC102 (methoxyamine), a small molecule DNA base-excision repair (BER) inhibitor, reverses temozolomide (TMZ) resistance in preclinical glioma models. We had investigated efficacy of TRC102+TMZ for recurrent glioblastoma (rGBM) through a multicenter trial. This work sought to report translational findings from RNA sequencing performed on patients with available tumor tissue. METHOD: A two-arm, two-stage, non-randomized, Phase II trial of TRC102+TMZ for adults with rGBM named BERT was conducted. Arm 1 included bevacizumab-naive patients at first recurrence, with primary aim of estimating response rates using RANO criteria. If sufficient activity was identified, arm 2 was planned in bevacizumab-refractory patients. Secondary aims were to determine overall survival (OS), progression-

free survival (PFS), 6-month PFS, and toxicity. Exploratory aims were correlating clinical outcomes with MPG expression and MGMT methylation. Differential gene expression profiling was analyzed using DESeq2 GSVA (RRID:SCR-015687) and transformed into enrichment scores for 'hallmark of DNA repair' pathways from Molecular Signatures Database (MSigDB, RRID:SCR-016863) to assign mechanistic signatures of therapeutic vulnerability. RESULTS: Arm 1 enrolled 19 patients with median of two treatment cycles, but objective responses were not observed. Hence, arm 2 did not open. Median OS was 11.1 months (95%CI 8.2-17.9). Median PFS was 1.9 months (95%CI 1.8-3.7). MGMT promoter was unmethylated in 14/19 patients, and MPG expression was present in 8/14 cases with available tumor tissue. MGMT methylation and MPG non-expression were associated with better OS and PFS. However, two 'exceptional responders' had PFS ≥11 months, with MGMT methylated and MPG expressed. RNA sequencing of their tumor tissue demonstrated significant enrichment for DNA damage response (DDR) pathways (MSigDB), chromosomal instability gene signatures (CIN70, CIN25), and proliferative gene signatures (PCNA25). CONCLUSION: rGBM patients with elevated levels of MPG and DDR molecular signature may have impaired BER and respond better to TRC102+TMZ.

Neurosurgery

Peereboom D, Lindsay R, Badruddoja M, Nabors LB, Kumthekar P, Lieberman F, Schiff D, Sherman J, Butowski N, Dunbar E, Fink K, Iwamoto F, Moertel C, Schulder M, **Walbert T**, Chattopadhyay P, Habboubi N, Grzegorzewski K, Brooks C, and Reardon D. A PHASE 2 STUDY OF A NOVEL IMMUNOTHERAPY SL-701 IN ADULTS WITH RECURRENT GLIOBLASTOMA: EXPLORING THE PROGNOSTIC VALUE OF TREATMENTINDUCED CD8+CD57+ T-CELLS AS A MARKER FOR SURVIVAL. *Neuro Oncol* 2023; 25:v56. Full Text

D. Peereboom, Cleveland Clinic, Cleveland, OH, United States

Recurrent glioblastoma (GBM) remains a challenging disease with limited therapeutic options and poor prognosis. SL-701 is a novel immunotherapy composed of synthetic peptides designed to elicit an anti-tumor immune response against the overexpressed GBM antigens IL-13Rα2, ephrinA2, and survivin. In this study, we present updated findings from a phase 2 clinical trial (NCT02078648) evaluating SL-701+poly-ICLC+bevacizumab, where the 12-month overall survival (OS) was 50%. Using high-parameter flow cytometry, we compared the quality of the treatment induced T-cell response in patients with an OS < 12m (n = 15) versus OS >12m (n = 12). Among the patients assessed, 89% exhibited heterogeneous T-cell responses against SL-701, with no discernible correlation between the response to a specific peptide and survival. Consequently, we focused on identifying other characteristics of the pan-SL701-specific T-cell response with an association to survival. Assessing all time points collected, patients with an OS >12m generated a significantly higher frequency of SL-701-specific CD8 T-cells (79% increase, $P < 0.005$) and a lower frequency of CD4+ T-cells (36% decrease, $P < 0.05$) compared to patients with a lower OS. Moreover, the ratio of CD8:CD4 T-cells was 2-fold higher in patients with an OS >12m indicating a CD8-enriched response, whereas patients with an OS < 12m had a lower ratio of CD8:CD4 associated with CD4 enriched responses. Notably, patients with an OS >12m, expressed CD57 (identifying highly cytotoxic, differentiated memory T-cells) on 40% of their T-cells compared to 18% in patients with an OS < 12m ($P < 0.05$). Furthermore, the ratio of SL-701 specific CD57:CD107A expressing cells trended 20% lower in patients with an OS >12m, indicative of a replicating, cytotoxic T-cell response that is not terminally differentiated. These qualitative differences in the immune response, detectable as early as week 8 post treatment, may serve as biomarkers for monitoring and predicting survival. Deep sequencing of SL-701- specific T-cells is planned.

Neurosurgery

Schiff D, Bindra RS, Li J, Ye X, Ellingson B, **Walbert T**, Campian J, Nabors B, Lieberman F, Ozer B, Desai A, Omuro A, Wen P, Desideri S, Danda N, and Grossman S. PHASE II AND PHASE 0 RESULTS OF ABTC 1801: A MULTI-ARM CLINICAL TRIAL OF THE PARP INHIBITOR PAMIPARIB WITH VERY LOW DOSE METRONOMIC TEMOZOLOMIDE IN RECURRENT IDH MUTANT GLIOMAS. *Neuro Oncol* 2023; 25:v84. Full Text

D. Schiff, University of Virginia, School of Medicine, Charlottesville, United States

BACKGROUND: Preclinical studies have demonstrated that IDH1-mutant (IDHmt) gliomas harbor a BRCAness phenotype with a defect in homologous recombination that confers PARP inhibitor sensitivity. METHODS: The phase II component of ABTC 1801 examined the efficacy of the combination of pamiparib (BeiGene BGB-290) with low dose metronomic temozolomide in recurrent IDHmt grade 2 and 3 gliomas. In this two-stage design, Arm A enrolled patients who had failed two lines and Arm B a single line of alkylator therapy. Pamiparib and temozolomide doses based on phase I results was 60 mg BID and 20 mg daily. Primary endpoint was objective response rate (ORR). RESULTS: 39 patients (Arm A 15, Arm B 24) enrolled in the phase II. Median age was 45 (range: 25-69), 56% male, and median KPS 90. 72% of tumors were MGMT methylated. There were no confirmed responses in Arm A and one in Arm B; neither arm met the threshold for additional accrual. One-third of subjects discontinued treatment for reasons other than progressive disease. Estimated median PFS was 5.8 months in Arm A and 11.3 months in Arm B. Seven subjects (Arm A 3, Arm B 4) developed DLT during treatment. Grade 3+ toxicity was principally hematologic; 9 patients had grade 3 anemia, 7 grade 3 and 3 grade 4 neutropenia, and 3 grade 3 thrombocytopenia. In enhancing and non-enhancing tumors from 8 surgical arm patients, median unbound drug tumor/plasma ratios were 0.98 and 0.92, respectively; and median unbound pamiparib tumor concentrations were 209 and 188 nmol/L (or nmol/kg), respectively, which were >20-fold the in vitro IC50 for PARP inhibition. CONCLUSIONS: While pamiparib appeared to achieve sufficient pharmacologically active concentrations in both enhancing and non-enhancing tumors, combination with temozolomide did not produce a meaningful ORR in IDHmt recurrent gliomas. Cumulative hematologic toxicity was substantial.

Neurosurgery

Wen P, Alexander B, Berry D, Buxton M, Cavenee W, Colman H, De Groot J, Ellingson B, Gordon G, Hyddmark E, Khasraw M, Lim M, Mellinghoff I, **Mikkelsen T**, Perry J, Powell A, Sulman E, Tanner K, Weller M, Yung WKA, Blondin N, Brenner A, Butt O, De La Fuente M, Drappatz J, Iwamoto F, Kim L, Lee E, Mantica M, Nabors B, Newton H, Schiff D, **Walbert T**, Weathers SP, Cloughesy T, and Lassman A. GBM AGILE PLATFORM TRIAL FOR NEWLY DIAGNOSED AND RECURRENT GBM: RESULTS OF FIRST EXPERIMENTAL ARM, REGORAFENIB. *Neuro Oncol* 2023; 25:v97-v98. Full Text

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GBM AGILE (NCT03970447;https://www.gcaresearch.org/research/ gbm-agile) is a phase 3 Bayesian adaptive platform trial that efficiently tests multiple arms against common control, with 6 arms included to date. Primary endpoint is overall survival (OS). Stage 1 experimental arms are adaptively randomized against other arms. Demonstrated efficacy in stage 1 leads to fixed randomization stage 2. Stages 1 and 2 are combined for registration. Control randomization is fixed. Regorafenib, a multikinase-inhibitor, entered into GBM AGILE as the first arm and therefore was equally ran-domized against control. Regorafenib showed OS benefit in recurrent disease (RD) in randomized phase 2 REGOMA trial. METHODS: Patient subtypes in GBM AGILE are newly diagnosed unmethylated (NDU), RD, and-not considered for regorafenib-ND methylated (NDM). Arm indications (signatures) are combinations of subtypes. Control is temozolomide (ND) and lomustine (RD). Efficacy is assessed by OS hazard ratio(HR), arm/control. Efficacy is demonstrated when Bayesian probability of benefit (HR< 1.00) ≥ 98% (roughly analogous P-value: 0.02). Futility occurs at any monthly analysis when Bayesian predictive power (PP) is < 25% for all signatures. Follow-up continues for 12 months after arm's accrual stops. RESULTS for regorafenib: When PP for all 3 pre-defined signatures was < 25%, regorafenib's accrual was stopped for futility. Regorafenib/control sample sizes were 49/51, 126/128, 175/179 for signatures NDU, RD, and both. Respective PPs: 0.138, 0.030, 0.025-none close to 0.25. Respective mean HRs: 1.26, 1.25, 1.23. Probabilities of benefit (HR< 1.00): 0.35, 0.18, 0.17. At final analysis, mean HRs were 1.07, 1.12, 1.10 with final probabilities of benefit (HR< 1.00) equal to 0.43, 0.24, 0.24-none close to 0.98. CONCLUSION: GBM AGILE efficiently and compellingly addressed regorafenib's role in GBM, in RD and NDU. These findings are germane as they fail to confirm the REGOMA results in RD. GBM AGILE continues to efficiently assess other therapies, including utilizing concurrent and previously accrued controls.

Neurosurgery
Zhang YL, **Chen L**, **Ding GL**, **Li L**, **Pang HY**, **Jiang Q**, **Chopp M**, **Zhang ZG**, **Mahmood A**, and **Xiong Y**. DYSREGULATED AQUAPORIN 4 EXPRESSION AND POLARITY, INCREASED NEUROINFLAMMATION AND AXONAL INJURY ARE ASSOCIATED WITH LONG-TERM FUNCTIONAL DEFICITS AFTER MILD CLOSED HEAD INJURY. *J Neurotrauma* 2023; 40(15-16):A96-A96. Full Text

[Zhang, Yanlu; Chen, Liang; Pang, Haiyan; Mahmood, Asim; Xiong, Ye] Henry Ford Hlth, Dept Neurosurg, Detroit, MI USA. [Ding, Guangliang; Li, Lian; Jiang, Quan; Chopp, Michael; Zhang, Zheng Gang] Henry Ford Hlth, Dept Neurol, Detroit, MI USA. [Chopp, Michael] Oakland Univ, Dept Phys, Rochester, MI 48063 USA.

Nursing
Plemmons J, **Saleh M**, **Johnson P**, and **Kirk N**. QAPI 124 - Effect of Education and Performance Feedback to Eliminate Central Line Associated Blood Stream Infections on an Internal Medicine Unit...Association for Professionals in Infection Control and Epidemiology (APIC) 51st Annual Conference and Exposition, June 3-5, 2024, San Antonio, Texas. *Am J Infect Control* 2024; 52(6):S61-S61. Full Text

Henry Ford Hospital, Henry Ford Health
Henry Ford Health

Nursing
Wells A, **Edmondson A**, **Mahal R**, and **Prascius S**. What Could Go Wrong? Utilizing a Failure Mode and Effects Analysis to Identify Endoscope Reprocessing Process Improvement Opportunities. *Am J Infect Control* 2024; 52(6):S3. Full Text

Background: When implemented correctly, endoscope reprocessing using high level disinfection (HLD) renders a reusable endoscope safe for the next patient. However, the amount and complexity of the steps of the HLD process make this challenging. An endoscopy department within a 191-bed acute care hospital with an average of 30 procedures per day had history of highly compliant HLD audits performed by the infection prevention team. However, due to staffing changes and increasing staff expectations, errors in the HLD process led to two patient exposures. Though mitigated swiftly, an improvement process was sought to prevent future patient exposures. Methods: The quality department chose to facilitate a Failure Mode and Effects Analysis (FMEA) to determine what other steps could fail next. Quality department leadership composed a multidisciplinary team to review the 70+ steps in channeled endoscope reprocessing to identify failure modes. First, the infection prevention/quality manager categorized the steps. Next, endoscopy nursing leadership, an endoscope reprocessing technician, surgical services leadership, and quality/risk management delineated the possible failure modes, causes, and effects for each step. The team scored the likelihood of each failure occurring and its severity, each on a scale of 1 to 4, to find areas in need of action plans. The likelihood and severity scores were multiplied to identify highest areas of risk. Results: Four steps of the HLD process had a risk score of eight or higher, and the group chose to focus on these for process improvement plans. These steps included portions of the manual endoscope cleaning process, new employee training and competency, and automated endoscope reprocessor parameter verification. Specific action plans will be created for these highest risk elements. Conclusions: There are often several opportunities for improvement of complex processes such as HLD. Quality improvement tools such as the FMEA can assist infection prevention programs with prioritizing competing opportunities.

Nursing
Wells A, **Prascius S**, and **Assenova T**. Two Years of Zero Harm: A Multi-Faceted Approach for Achieving Two Years Without a Catheter-Associated Urinary Tract Infection (CAUTI). *Am J Infect Control* 2024; 52(6):S44. Full Text

Background: After experiencing five catheter-associated urinary tract infections (CAUTI) in 2019 (standardized infection ratio [SIR] 0.69) and six in 2020 (SIR 0.6), a 191-bed acute care hospital was determined to find a sustainable way to reduce the number of infections. Methods: Many interventions were introduced to reduce the number of CAUTIs, consisting of education, alternative device

implementation, and electronic medical record (EMR) tools. Registered nurses (RN) and nurse assistants (NA) were reeducated on the importance of aseptic urine specimen collection and indwelling urinary catheter (IUC) maintenance bundles at annual skills fairs. The infection prevention (IP) and nursing team explored alternative external male urine collection devices such as condom catheters and moisture-wicking urinary pouches. The IP team performed audits with nursing unit leaders on IUC maintenance bundle compliance and reported the data monthly to unit staff and leadership. Additionally, inappropriate urine cultures decreased through the implementation of a urine culture hard stop in the EMR to ensure urine specimens were ordered and sent only if truly indicated. Results: After implementation of these interventions, the hospital had one reportable CAUTI in 2021. In 2022 and 2023, zero were reported. The standardized infection ratio (SIR) declined from 0.69 in 2019 to 0 in 2022 and 2023. Conclusions: The IP and nursing department credits the sustenance of zero harm to the culture of high reliability created by the above interventions. Team members providing direct patient care are aware of the expectations related to CAUTI prevention. The facility plans to continue diligent daily review of IUCs, prevent placement of IUCs if another viable option exists, educate team members on IUC maintenance expectations, and ensure all urine cultures ordered when the IUC has been in place for three or more days are reviewed by an infectious disease physician for appropriateness.

Obstetrics, Gynecology and Women's Health Services
Arruga Novoa y Novoa V, **Chamseddine P**, **Shalabi F**, **Vilkins A**, and **Abood J**. Retroperitoneal Myolipoma Excision Via vNOTES. *J Minim Invasive Gynecol* 2023; 30(11):S62. Full Text

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Study Objective: To illustrate the excision of a retroperitoneal myolipoma via VNOTES (vaginal natural orifice transluminal endoscopic surgery). Design: Stepwise demonstration of surgical technique with narrated video footage. Setting: Myolipoma is a rare benign soft tissue tumor composed of smooth muscle cells and adipocytes. It can occur in different locations including the retroperitoneal space, abdominal cavity, pericardium and spinal cord. Retroperitoneal myolipoma can be misdiagnosed radiologically as ovarian teratoma due to the adipose tissue component and location in the pelvis. Techniques used until now by gynecologic surgeons for retroperitoneal mass resection were either classic laparoscopy or laparotomy. This video highlights the vaginal approach. Patients or Participants: 65-year-old female who presented with right flank pain. Pelvic ultrasound and MRI revealed a 7 × 6 × 4 cm pelvic mass concerning for right ovarian dermoid. Interventions: VNOTES approach for resection of retroperitoneal mass with concomitant bilateral salpingoophorectomy. Measurements and Main Results: The key surgical steps are as follows: • Review of pelvic anatomy from VNOTES perspective. • Identification of retroperitoneal mass. • Techniques to increase surgical exposure from vaginal approach. • Dissection of retroperitoneal space with care to avoid the ureter. • Resection of myolipoma. Conclusion: This video demonstrates that with appropriate identification of key anatomical landmarks and surgical technique, vNOTES is a feasible procedure for retroperitoneal mass excision.

Obstetrics, Gynecology and Women's Health Services
Arruga Novoa y Novoa V, **Sitarik A**, **Su WT**, **Bossick A**, **Wegienka G**, **Chamseddine P**, **Vilkins A**, and **Abood J**. 9430 The Impact of Anxiety and Depression on Regret after Hysterectomy. *J Minim Invasive Gynecol* 2023; 30(11):S70-S70. Full Text

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Obstetrics, Gynecology and Women's Health Services
Shalabi F, **Novoa V**, **Bossick A**, **Su WT**, **Sitarik A**, **Wegienka G**, **Vilkins A**, and **Abood J**. 10357 Does Sexual Function Prior to Hysterectomy Impact Post-Operative Regret? *J Minim Invasive Gynecol* 2023; 30(11):S116-S117. Full Text

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Study Objective: To investigate the pattern of regret after hysterectomy as it relates to sexual function. Design: Prospective cohort study of women undergoing hysterectomy. Setting: Academic tertiary medical center. Patients or Participants: 456 women who underwent hysterectomy for benign indications. Interventions: None. Measurements and Main Results: Participants undergoing hysterectomy for benign indications and without concurrent urogynecologic surgery were recruited and asked to complete a baseline survey 2-weeks prior to their scheduled procedure, as well as seven follow-up surveys up to 12-months post-operatively. Using latent class analysis, overall regret scores were derived from five validated survey questions and were used to determine patterns of regret following hysterectomy. Three classes were identified: high regret that remained high over time (Class 1); high regret that lowered over time (Class 2); and low regret that remained low (Class 3). Women who reported they were moderately dissatisfied with their sexual life prior to surgery were more likely to be in Class 1 relative to the Class 3 compared with women who were very satisfied with their sexual life (multinomial logistic regression, risk ratio=4.92, 95% CI: 1.48, 16.31). Conclusion: Self-reported sexual dissatisfaction prior to surgery is associated with postoperative regret. Gynecologists and their patients may take this into consideration during preoperative counseling.

Orthopedics/Bone and Joint Center
Castle J, **Jiang E**, **Wager S**, **Brown S**, **Kasto J**, **Gasparro M**, **Muh S**, **Makhni E**, **Moutzouros V**, and **Gaudiani M**. Worse Postoperative Outcomes and Higher Reoperation in Smokers Compared to Nonsmokers for Arthroscopic Rotator Cuff Repair...AOSSM 2023 – American Orthopaedic Society for Sports Medicine Annual Meeting, July 13-16, 2023, Washington, DC. *Orthop J Sports Med* 2023; 11:95-98. Full Text

Henry Ford Health System
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Objectives: Smoking significantly impairs healing potential and is a significant risk factor for complications after various orthopaedic surgeries. The purpose of this study was to determine if a cohort of former or current smokers at time of surgery met the minimally clinical important difference (MCID) for Patient-Reported Outcomes Measurement Information System Upper Extremity (PROMIS- UE), Depression (PROMIS-D), and Pain Interference (PROMIS-PI) scores in comparison to nonsmoking patients. Methods: A retrospective review of a prospectively collected database of patients undergoing arthroscopic rotator cuff was performed. Patients who completed preoperative and 6-month postoperative PROMIS scores were included. The MCID was calculated using a distribution technique with a threshold of 0.5 standard deviations above the mean. A cohort of nonsmokers was compared to a cohort of patients currently or former smokers at time of surgery in terms of their clinical outcomes and PROMIS scores. A sub-analysis was also performed where a cohort of nonsmokers were propensity matched 1:1 to a cohort of current/former smokers via age, body mass index (BMI), and tear size. Results: A total of 182 patients, 80 current or former smokers and 102 nonsmokers, who underwent rotator cuff repair were included in the study. Smokers had statistically different sized tears with more rated massive and more reoperations (16.3% vs 5.9%, P=0.02). No differences were found in preoperative PROMIS scores, change in PROMIS scores, proportion meeting MCID for PROMIS scores, and retear rate. In the sub-analysis, 74 current or former smokers were matched to 74 nonsmokers. Smokers had a lower change in PROMIS-UE (8.6 ± 9.8 vs 12.3 ± 10.0, P=0.007) and PROMIS-PI (-9.1 ± 8.5 vs -12.8 ± 10.1, P=0.03) postoperatively. Fewer met MCID for PROMIS UE postoperatively (60.3% vs 82.4%, P=0.003) and more had reoperations (16.2% vs 4.1%, P=0.02). Conclusions: Patients who smoke currently or had a history of smoking preoperatively demonstrated smaller improvements in function, pain scores, and were less likely to meet MCID for PROMIS-UE when compared to nonsmokers after arthroscopic rotator cuff repair. Smokers were more likely to undergo reoperations within 6 months.

Orthopedics/Bone and Joint Center
Castle J, **Kasto J**, **Jay J**, **Haan J**, **Serra S**, **Vyskocil J**, **Lutchka J**, **Wolterink T**, **Sanii R**, and **Muh S**. ROTATOR CUFF REPAIR WITH BIOINDUCTIVE ALLOGRAFT PATCH ACHIEVES EQUIVALENT PATIENT-REPORTED OUTCOMES AT 2 YEARS POSTOPERATIVELY. *JSES International* 2023; 7(5):1085. Full Text

Background: To compare patient reported outcomes, range of motion (ROM), and complications of patients undergoing arthroscopic rotator cuff repair (RCR) augmented with a bioinductive patch compared to standard repair. Methods: A retrospective review was conducted of patients undergoing primary RCR with and without bioinductive bovine collagen patch augmentation for MRI or Ultrasound confirmed supraspinatus/infraspinatus tears from 2016 to 2021. Exclusion criteria included the following: open RCR, ipsilateral shoulder surgery, active infection, or less than 6-week postoperative follow-up. Patch RCR was matched 2:1 to controls based on age, sex, BMI, tear size, and the number of tendons involved. Patient Reported Outcome Information System (PROMIS) for upper extremity function (-UE), pain interference (-PI), and depression (-D) scores were recorded up to 2 years. Results: Overall, 81 patients underwent RCR with patch augmentation and were matched to 162 controls. No significant differences were found between groups in terms of age (p=0.62), sex, smoking, diabetes, partial vs. full-thickness tears, and tear size. ROM in forward-flexion (FF) and abduction were significantly increased at 6-month follow-up for the augmented group compared to controls (FF 156.8±21.6 vs. 148.1±23.2 degrees, p<0.01; abduction 133.1±33.2 vs. 114.1±36.5 degrees, p=0.019) but not at 1-year follow-up. No differences were seen for PROMIS-UE, PROMIS-PI, or PROMIS-D scores. The augmented group had ten complications (12.3%) and the control had 20 (12.3%). The augmented group had four retears (4.9%) of which three required revision compared to 11 retears for the control (6.8%) of which eight required revision. The augmented group had six cases (7.4%) of adhesive capsulitis, five of which took place in mid-late 2020, compared to the four cases (2.5%) of adhesive capsulitis (three before mid 2019 and one in early 2021) seen in the control and all patients underwent manipulation under anesthesia. Conclusions: Bioinductive patch augmentation for RCR demonstrated increased ROM at six months and equivalent physical function, pain in daily life, and depression levels at 2 years when compared to standard RCR. There was a lower retear rate in the augmented group compared to the controls. The increased incidence of postoperative adhesive capsulitis in the augment group is a concern and needs to be further evaluated.

Orthopedics/Bone and Joint Center

Dimitrion P, **Toor J**, **Ge J**, **Wang Q**, Allen CE, **Zhou L**, and **Mi QS**. HDAC3 Is Required for Pathognomonic Features of Langerhans Cell Histiocytes. *Blood* 2023; 142:676. Full Text

Langerhans cell histiocytosis (LCH) is a pediatric inflammatory myeloid neoplasm that develops due to dysregulated myeloid cell development. BRAFV600E is the most common disease-causing mutation and constitutively activates the mitogen-activated protein kinase (MAPK) pathway in myeloid lineage precursors leading to the key pathognomonic features of LCH cells. Enhanced myelopoiesis and reduced CCR7 expression promote accumulation of LCH cells in tissues by simultaneously increasing the production of pathological DCs and preventing tissue egress. Furthermore, LCH cells acquire an oncogene induced senescence-associated secretory phenotype (SASP) that depends on mammalian target of rapamycin (mTOR), which is hallmarked by increased expression of anti-apoptotic proteins, inflammatory cytokines, and matrix metalloproteinases enhancing survival of LCH cells and promoting recruitment of inflammatory immune cells forming characteristic granulomatous lesions. These pathognomonic features result in the accumulation of LCH cells in any organ causing a wide range of clinical symptoms. Frontline therapy for LCH involves combination chemotherapy and steroidal anti-inflammatories, or MAPK inhibitors, which have significant toxicity and fail to eliminate disease causing precursors. New therapeutic approaches are urgently needed. Here, using multiple genetic mouse models, we show that normal epidermal Langerhans cells (LCs) depend on HDAC3 for their development, differentiation, and survival. Integrative RNA and chromatin-immunoprecipitation-sequencing show loss of HDAC3 abrogates the expression of master regulators of myeloid development and function including Csf1r, Spi1, Id2 and Runx3. LCH cells are also known to rely on Csf1r and Pu.1 for their development and homeostasis, thus we hypothesized that LCH cells similarly rely on HDAC3 for their development and survival. CD11c Cre LSL-BRAFV600E (BRAFV600E CD11c) mice develop severe multifocal LCH with pronounced lesion development in their livers and lungs, hepatosplenomegaly, and a reduced lifespan due to the accumulation of pathological dendritic cells (DCs). We generated BRAFV600E CD11c HDAC3 fl/fl (BRAFV600E HD3KO) mice, which produce pathological DCs that simultaneously express BRAFV600E and harbor a conditional deletion in the deacetylase domain of HDAC3. Compared to BRAFV600E CD11c mice, BRAFV600E HD3KO mice exhibited significantly less hepatosplenomegaly, reduced lesional burden (Panel A), attenuated disease progression, and improved

survival indicating reduced LCH disease burden. Compared to BRAFV600E CD11c flow cytometry showed BRAFV600E HD3KO had reduced numbers of LCH cells in lungs and livers linking improved disease outcomes to abrogation of pathological DCs. Flow cytometric analysis of circulating myeloid cells further found reduced frequency of circulating DCs and DC progenitors, indicating that a lack of HDAC3 activity prevents the development of pathological DCs (Panel B). LCH-like cells can be generated in vitro by culturing BRAFV600E CD11c bone marrow with granulocyte-monocyte colony-stimulating factor (GM-CSF), providing a valuable drug screening tool. Treating LCH-like cells with RGFP966, an HDAC3-specific inhibitor, increased apoptosis indicated by annexin-V and DAPI staining, reduced expression of Bcl-2, increased CCR7 expression, and decreased S6 phosphorylation (an indication of decreased mTOR activity), showing that pharmacological inhibition of HDAC3 may prove therapeutically efficacious by abrogating pathognomonic features of LCH cells. Together, our findings identify HDAC3 as a critical epigenetic regulator for both healthy and pathological LCs. We further show, HDAC3 is required for multiple pathognomonic features of LCH cells and could be a promising drug target. Furthermore, if HDAC3 is required for the development of pathological DC and DC progenitors, HDAC3 blockade would address a great need in treatment of patients with LCH.

Orthopedics/Bone and Joint Center

Evans H, **Kasto J**, **Tsitlakidou D**, **Castle J**, **Jay J**, **Akins J**, **Jiang E**, **Sanii R**, and **Muh S**. THE USE OF NON-OPIOID MULTIMODAL ANALGESIA FOR TOTAL SHOULDER ARTHROPLASTY: A RETROSPECTIVE STUDY. *JSES International* 2023; 7(5):2004. Full Text

Background: The purpose of this study was to compare the pain level and the amount of opioid consumed in postoperative total shoulder arthroplasty (TSA) patients who were treated with a standard opioid-including regimen versus a non-opioid multimodal analgesia regimen. Methods: We retrospectively reviewed two consecutive cohorts who underwent TSA—either anatomic or reverse—by a single surgeon. The opioid cohort included patients from early 2016 to late 2020 and were given 80 tablets of Percocet 5 mg/325 mg that followed a dose reduction plan to 60, 40, and 20 tablets for consecutive refills (max of 3 refills). The non-opioid cohort included patients from late 2020 to mid 2022 and consisted of preoperative oral analgesics (Celecoxib, Pregabalin, and Tramadol); intraoperative IV Dexamethasone and Acetaminophen, and local infiltration of Ropivacaine, Epinephrine and Ketorolac; and postoperative oral Dexamethasone and oral analgesics (Pregabalin, Tizanidine, Magnesium, Ibuprofen, and Acetaminophen). Visual Analog Scale (VAS) scores for pain (preoperative, and 10-days, 6-weeks, 3-months, and 6-months postoperative) and opioid consumption (preoperative, and 10-days, 6-weeks, and 3-months postoperative) using Morphine Milligram Equivalents (MME) were compared and analyzed using the nonparametric Wilcoxon rank-sum test for both cohorts. Total MME was calculated as max consumption. Results: There were 249 patients in the opioid cohort and 127 in the non-opioid cohort. No between-group differences were found in demographic factors—including age, sex, race, BMI, smoking status—or anatomic versus reverse TSA. Patients treated with the non-opioid protocol had lower mean VAS scores at preoperative (6.4 vs 7.4, $p<0.05$), 10-day (3.5 vs 4.2, $p<0.05$), and 6-week postoperative time points (2.1 vs 2.8, $p<0.05$). Opioid consumption was lower in the non-opioid multimodal cohort at all time periods ($p<0.005$). Complications such as 90-day hospital readmissions and revision surgery at one-year were not significantly different between the groups. Conclusions: A non-opioid multimodal postoperative regime is reliable and well tolerated by patients undergoing Total Shoulder Arthroplasty. They have lower early postoperative VAS scores (10-days and 6-weeks) and a significant reduction in opioid utilization. One-year postoperative complications between both groups were similar indicating that a non-opioid regimen is effective in safely controlling postoperative pain.

Orthopedics/Bone and Joint Center

James C, **Haan J**, **Wager S**, **Hegde Y**, **Wolterink T**, and **Muh S**. CLINICAL AND RADIOGRAPHIC OUTCOMES IN OPERATIVE VS NONOPERATIVE TREATMENT OF HUMERAL SHAFT FRACTURES. *JSES International* 2023; 7(5):1808. Full Text

Background: Humeral shaft fractures represent 1-5% of all fractures and are increasing in incidence. There is conflicting literature regarding the superiority of operative versus nonoperative treatment of these fractures. We hypothesized that patients treated operatively would have a faster time to radiographic union and improved functional outcomes relative to patients treated nonoperatively. Methods: This was a

retrospective cohort study performed at a single healthcare system. All humeral shaft fractures treated between 2010-2020 were identified using ICD-9, -10, and CPT codes. Information on demographics, fracture, treatment, and outcomes was collected through chart and radiograph review. These measures were compared between patients treated operatively and nonoperatively. Results: A total of 517 adult patients with unilateral humeral shaft fractures were identified, 233 were treated nonoperatively and 284 were treated operatively. Patients treated operatively had a mean age of 50.2 years relative to 59.9 years in patients treated nonoperatively ($p < 0.001$). A higher proportion of the nonoperative group were female and unemployed than the operative group ($p = 0.007$ and $p < 0.001$ respectively). Operatively treated patients had significantly faster time to radiographic union at a median of 113 days versus a median of 161 days in nonoperatively-treated patients ($p = 0.001$). The operative group was made weight-bearing as tolerated at a median of 84 days, significantly less time than the nonoperative group at a median of 98 days ($p = 0.002$). There was no difference in complication rates between groups. There were no differences in range of motion at time of radiographic union. However, at time of last follow-up, patients treated operatively were up to two times more likely to achieve full shoulder forward elevation than those treated nonoperatively ($p = 0.011$). Conclusions: Operative treatment of humeral shaft fractures leads to faster time to union and earlier weight bearing without increased rate of complications.

Orthopedics/Bone and Joint Center
Jay J, **Kasto J**, **Castle J**, **Burdick G**, **Dash M**, **Muh S**, and **Sanii R**. INFLUENCE OF DIABETES MELLITUS ON OUTCOMES AFTER SHOULDER ARTHROPLASTY. *JSES International* 2023; 7(5):1943. Full Text

Background: The prevalence of type 2 diabetes mellitus (DM) in the United States is approximately 11% and increasing. Following joint replacement, diabetic patients have close to a threefold increase in risk for postoperative complications. However, there is a relative paucity of studies examining this association for total shoulder arthroplasty (TSA). This present study aimed to address this gap in knowledge by determining the differences in outcomes after TSA in patients with and without DM. Additionally, this study also aimed to determine whether a dose-response relationship exists between Hemoglobin A1c (HbA1c) and adverse or suboptimal outcomes after TSA. Methods: A total of 812 patients who underwent primary TSA (anatomic or reverse) between 2014 and 2019 were identified by querying the electronic medical record system at our institution. Patients with less than 1-year postoperative follow-up or incomplete outcomes data were excluded. Medical charts were reviewed to identify patients with a preoperative diagnosis of DM and to record the most recent HbA1c measurement prior to the date of surgery for all patients. Primary outcome measures were shoulder range of motion (ROM) and visual analog scale (VAS) pain scores. Secondary outcomes were emergency department (ED) and hospital readmission rates and peri- and postoperative complications. Results: A total of 595 patients were included in this study with 151 (25%) having a preoperative diagnosis of DM. Both the DM and non-DM groups experienced significant improvements in ROM and VAS score following surgery ($p<0.05$) and were not significantly different between the two groups. Our analysis also indicated that diabetics have no significant differences in length of stay, postoperative complications, infection rates, hospital readmissions, and all-case ED visitations, when compared to non-diabetic patients. Lastly, HbA1c did not significantly correlate with peri- or postoperative complications, improvement in VAS score or ROM, or readmission rates. Conclusions: Patients with DM benefited significantly from shoulder arthroplasty and achieved satisfactory pain relief and improvement in shoulder mobility. Furthermore, HbA1c does not seem correlate with increased risk of post-operative complications. Longer term follow up is needed.

Orthopedics/Bone and Joint Center
Kazanjian A, **Akins J**, **Burdick G**, **Kasto J**, **Sanii R**, and **Muh S**. EARLY POSTOPERATIVE IMPROVEMENT IN PATIENT-REPORTED OUTCOMES FOLLOWING OPERATIVE VERSUS NONOPERATIVE TREATMENT FOR PROXIMAL HUMERUS FRACTURES. *JSES International* 2023; 7(5):1799. Full Text

Background: The significance of early improvements in patient-reported outcomes following treatment for proximal humerus fracture (PHF) has not been well established. This study compares early improvement in patient-reported outcomes following PHF between patients who were treated conservatively vs. surgically. The primary outcome was Patient Reported Outcome Measurement Information System

(PROMIS) Upper Extremity (-UE) and Pain Interference (-PI) scores at 6-weeks, 3-months, and 6-months from date of injury or date of operation for nonsurgical and surgical patients, respectively. Methods: This single surgeon, retrospective chart review was conducted on 76 patients treated for PHF between 2/2019 and 7/2021. Exclusion criteria were presentation >4 weeks and follow up <6 weeks from the date of injury, and pathologic fractures. The final cohort included 47 patients treated nonoperatively and 8 treated operatively (3 reverse total shoulder arthroplasty, 5 open reduction and internal fixation). Data points included age, sex, race, smoking status, diagnosis of insulin-dependent diabetes mellitus, Neer classification, glenohumeral dislocation, open fracture, and PROMIS-UE and PROMIS-PI scores. Results: There was no significant differences in age, gender, race, smoking status, dominant side injury, open fractures, or insulin-dependent diabetes mellitus between the groups. Patients with 1- or 2-part fractures versus 3- or 4-part fractures was not significantly different. Those with glenohumeral dislocation were more likely to be treated operatively, (operative (n=2, 25%), nonoperative (n=2, 4.26%), p=0.037). PROMIS-UE scores were not statistically different between the groups at any time point. PROMIS-PI scores were found to be significantly lower in the operative group at both 3- and 6-months postoperatively (3-months, nonoperative 57.46 ± 7.38, operative 49.25 ± 6.85, p=0.048; 6-months, nonoperative 61.80 ± 9.31, operative 46.33 ± 6.35, p=0.046) but not at 6-weeks postoperatively. Forward flexion and abduction were not found to be significantly different between the two groups. Conclusions: Patients treated with operative intervention had significantly reduced pain as evaluated on the PROMIS-PI at both 3- and 6-month time points, but no significant differences in either function or range of motion as evaluated on PROMIS-UE. However, Early pain reduction may be a factor to consider when discussing treatment options with patients who sustain a PHF.

Orthopedics/Bone and Joint Center
Schell L, **Muh S**, Jacobsen S, Roche C, Elwell J, Barfield W, Eichinger J, and Friedman R. CLINICAL OUTCOMES BASED ON FINAL BASEPLATE VERSION IN REVERSE TOTAL SHOULD ARTHROPLASTY. *JSES International* 2023; 7(5):944. Full Text

Background: While surgeons attempt to place the baseplate of a reverse total shoulder arthroplasty (rTSA) close to neutral version, outcomes based on the final version remain unknown. The purpose of this study is to determine the clinical and radiographic outcomes of rTSA based on the amount of retroversion the baseplate is placed in to determine if increasing retroversion affects the outcomes. Methods: All primary rTSA patients in a multicentered international database with a 2-year minimum follow-up implanted with computer navigation so the final baseplate version is known were included. A single medialized glenoid/lateralized humerus rTSA implant system was used. Patients were stratified by their final version: <0° (anteversion), 0 to 5° of retroversion, 6-10°, and >10°. Motion, outcome scores and radiographic outcomes were compared between groups using ANOVA with Tukey HSD post tests and chi square. Results: Four hundred and fourteen patients (189 females/225 males) were identified, with a mean follow-up of 30 months. Demographics were similar between the 4 groups. The mean native version was 10.3°, and the mean postoperative version was 3.1°. Preoperatively, 46% were >10°, 25% 6-10°, 18% 0-5° and 11% anteverted. Postoperatively, 3% were >10°, 23% 6-10°, 68% 0-5° and 6% anteverted. Postoperatively, there were no significant differences between the 4 groups with regards to outcome scores or motion, except for abduction greater in the >10° retroversion group that exceeded the MCID. At follow-up, pain scores, patient satisfaction, notching and complications were similar between the groups. Conclusions: This study demonstrated that computer navigation was highly efficacious, placing 97% of patient in 10° or less of retroversion or in anteversion. Except for abduction, there were no significant differences with regards to motion, pain relief, outcome scores, patient satisfaction or complications between the different groups based on the final implanted version. rTSA baseplates can be placed in anteversion or up to 10° of retroversion. The outcomes of patients left in 15° or greater retroversion could not be answered by this study since the use computer navigation left very few patients with postoperative retroversion >10°.

Orthopedics/Bone and Joint Center
Tramer J, Benkalfate T, Titelman R, Savoie F, Noel C, Roche C, Wright T, Roberts C, Simovitch R, and **Muh S**. COMPARISON OF HUMERAL HEAD RESURFACING VERSUS STEMLESS HUMERAL COMPONENTS IN ANATOMIC TOTAL SHOULDER ARTHROPLASTY: A MULTICENTER

INVESTIGATION WITH MINIMUM TWO YEAR FOLLOW UP. *JSES International* 2023; 7(5):2082. Full Text

Background: The purpose of this investigation was to compare minimum two-year outcomes of anatomic total shoulder arthroplasty (aTSA) performed with humeral head resurfacing (HHR) versus stemless implants. Methods: A retrospective review of a large multicenter database was conducted. All patients who underwent aTSA with either HHR or stemless implants with minimum two-year follow-up were evaluated. Range of motion (ROM) and patient reported outcomes (PROs) including Constant Score, Simple Shoulder test (SST), American Shoulder and Elbow score, University of California Los Angeles shoulder score, Shoulder Pain and Disability Index and Shoulder Arthroplasty Smart score were collected for all patients pre- and post-surgery. Radiographic data was collected to determine the presence of radiolucent lines as well as evaluation of implant sizing and anatomic shoulder restoration. Results: Overall, 127 patients were included with 49 receiving HHR and 78 stemless aTSA. The HHR group were significantly older (69.3±8.6 versus 64.3±8.7, P<0.01), had a lower BMI (27.7±4.3 versus 31.5±7.2, p<0.01) and a higher percentage were females (87.8% versus 35.9%, p<0.01) compared to the stemless group. Both groups demonstrated significant improvements in all PROs and ROM from pre- to post-surgery (p<0.05). At final follow-up the stemless group had significantly greater active abduction (148.5±27.7 versus 115.6±22.4, p<0.01), forward flexion (154.3±20.6 versus 140.6±15.3, p<0.01) and external rotation (52.14±14.9 versus 34.4±19.8, p=0.01). The stemless group exhibited better scores on the SST (10.4±2.0 versus 9.5±1.9, p=0.01), but no other PROs demonstrated significant difference. Radiographic evaluation of HHR patients demonstrated overstuffing, oversizing, and lucent lines around the glenoid component in 8.7%, 39.1%, and 13.0% of implants, respectively. Radiographic evaluation of stemless patients demonstrated radiolucent lines around humeral component and glenoid component in 4.2% and 18.8% of implants, respectively. One patient in the stemless aTSA group required a revision surgery for aseptic glenoid loosening, otherwise no other major complications were reported. Conclusions: Anatomic TSA performed both with stemless implants and HHR resulted in significant improvements in ROM and multiple PROs at minimum two year follow up with a low complication rate. The HHR group had significantly worse pre-operative ROM and PROs which lead to greater magnitudes of improvement at final follow up.

Orthopedics/Bone and Joint Center
Yining L, Marigi E, Alder K, Mickley J, Camp C, Levy B, Krych A, and **Okoroha K**. Identifying Racial Disparity in Utilization and Outcomes of Hip Arthroscopy using Machine Learning...AOSSM 2023 – American Orthopaedic Society for Sports Medicine Annual Meeting, July 13-16, 2023, Washington, DC. *Orthop J Sports Med* 2023; 11:504-507. Full Text

Mayo Clinic
Henry Ford Hospital

Objectives: Background: Arthroscopic diagnosis and treatment of femoroacetabular pathology has been increasingly used in the past thirty years with interventions resulting in improved hip function and ultimate delay of hip arthroplasty in a minimally invasive manner. Unfortunately, previous investigations have observed decreased rates of access, utilization of, and outcomes following orthopedic interventions such as hip arthroplasty in underrepresented patients. The purpose of this study is to examine racial differences in procedural rates, outcomes, and complications in patients undergoing hip arthroscopy. Methods: Methods: The State Ambulatory Surgery and Services Database (SASD) and State Emergency Department Database (SEDD) of New York were queried for patients undergoing hip arthroscopy from 2011 to 2017. The primary outcomes investigated were utilization over time, total charges billed per encounter, 90-day emergency department visits, and revision hip arthroscopy. Patients were stratified into White and non-White race, and intergroup differences were evaluated with descriptive statistics. Subgroup analysis was performed with linear mixed-effects models to identify significant interactions between race and individual variables that contributed to any differences in the outcomes of interest. Temporal trends in utilization of hip arthroscopy and concomitant procedures between the two groups were analyzed with Poisson regression modeling. Finally, targeted maximum likelihood estimation (TMLE) was performed to provide nonparametric estimates of the specific differences in the outcomes studied using machine learning ensembles while controlling for patient risk factors. Results: Results: A total of

9,745 patients underwent hip arthroscopy during the study period, with 1,081 patients of non-White race (11.9%). Results of Poisson regression demonstrated an annual increase of 1.11 in the incidence rate of hip arthroscopy among White patients, compared to 1.03 for non-White patients (p<0.001), with this disparity projected to increase by 2040. Based on TMLE utilizing an ensemble of machine learning models, non-White patients were significantly more likely to incur higher costs (OR: 1.30, 95% CI: 1.24-1.37, p<0.001) and visit the emergency department within 90-days (OR: 1.09, 95% CI: 1.01, 1.18, p=0.05), but had negligible differences in reoperation rates at 90 days to 2 years (OR: 1.13, 95% CI: 0.78-1.63, p=0.53). Subgroup analysis identified higher likelihood for 90-day emergency department admissions among non-White patients compared to White patients, which were significantly compounded by Medicare insurance (OR: 2.95, 95% CI 1.46-5.95, p=0.002), median income in the lowest quartile (OR: 1.84, 95% CI: 1.2-2.61, p=0.012), and residence in low-income neighborhoods (OR: 2.05, 95% CI: 1.313.2, p=0.006). Subgroup analysis for charges billed and reoperation did not identify significant findings. Conclusions: Conclusion: Hip arthroscopy remains an increasingly utilized surgical technique for the treatment of a myriad of hip disorders. Unfortunately, racial disparities exist and are worsening over time. Irrespective of insurance status, non-white patients undergo hip arthroscopy at a lower rate, incur higher costs, and more frequently experience unexpected returns to the emergency department. Improved initiatives to improve the disparity in access to and outcomes following hip arthroscopy must be addressed to further its utility for all patients.

Otolaryngology – Head and Neck Surgery

Jamali T, **Pimentel J**, **Perry K**, Tocco J, **Tejwani S**, **Mayerhoff R**, and **Pompa R**. First Reported Case of Endoscopic En Bloc Resection of Esophageal Liposarcoma. *Am J Gastroenterol* 2023; 118(10):S2186-S2187. Full Text

[Jamali, Taher] Henry Ford Hlth, Farmington Hills, MI USA. [Pimentel, Jason; Perry, Kyle; Tejwani, Sheela; Mayerhoff, Ross] Henry Ford Hlth, Detroit, MI USA. [Tocco, Jack] Pinnacle GI Partners, Troy, MI USA. [Pompa, Robert] Henry Ford Hosp, Detroit, MI USA. System; Henry Ford Hospital

Pathology and Laboratory Medicine

Baba O. Qualitopix: Artificial intelligence-based quantitative quality assurance of immunohistochemistry stain-ing-The Henry Ford Health experience. *Am J Clin Pathol* 2023; 160:S101-S102. Full Text

O. Baba, Pathology and Laboratory Medicine, Henry Ford Health, Detroit, MI, United States

Introduction/Objective: Immunohistochemistry (IHC) offers crucial patient data for diagnosis, prognosis, and treatment. Pathologists currently assess stain quality subjectively, comparing control sections to patient tissue. Qualitopix (Visiopharm, Denmark) is a cloud-based platform that enables objective, quantitative analysis of staining consistency through external cell line controls. Methods/Case Report: Over six months, we tested 1121 slides from five cell-line blocks with epitopes of different intensities for ER, PR, Ki-67, Her-2 Neu, and PD-L1. Slides were stained using Ventana Benchmark Ultra (Roche, Basel, Switzerland) for ER, PR, and Her-2 and Dako Omnis (Agilent, Santa Clara, California, United states) for Ki-67 and PD-L1. They were scanned with DP 200 scanner (Roche) and uploaded to Qualitopix for image analysis. Cells were detected using artificial intelligence and classified based on diaminobenzidine (DAB) staining intensity, reported as H-scores (0-100). Outliers were determined at 1 standard deviation. a selection of outliers was rescanned. Inter- scanner comparisons and repeatability studies were performed for ER and 50 within and between the DP 200 and HT scanners (Roche). Results (if a Case Study enter NA): Our analysis revealed a 26-34% rate of outliers at 1 SD for the five stains, 10 times higher than the currently reported number from our lab. Most outliers (70-100%) remained out of range at rescanning, suggesting pre-analytical technical issues. 5-33% of slides failed analysis due to technical errors. Poor discrimination between sequential cores of varying intensity for ER and Ki-67 was noted. Inter-scanner comparison and repeatability studies demonstrated precise and consistent H-scores within and across both scanning platforms for ER and PR. Conclusion: Qualitopix offers automated, objective, and quantitative quality assurance for IHC stain quality assessment, a hitherto manual, subjective and qualitative-driven process. Our findings emphasize the need for continuous IHC quality monitoring. The origin of outliers, technical failures, and their correlation with pathologist's subjective findings require further investigation.

Pathology and Laboratory Medicine
Bava EP, **Epelman M**, **Yeldo N**, **Uribe-Marquez S**, and **Lopez-Plaza I**. Use of Plasmapheresis in Heparin Induced Thrombocytopenia in Patients Undergoing Urgent Cardiac Surgery. *Am J Clin Pathol* 2023; 160:S115-S116. Full Text

[Bava, Ejas Palathingal; Epelman, Mathew; Yeldo, Nicholas; Uribe-Marquez, Santiago; Lopez-Plaza, Ileana] Henry Ford Hosp, Dept Pathol & Lab Med, Detroit, MI USA.

Pathology and Laboratory Medicine
Bava EP, and **Shaw B**. Mosaic Trisomy 1q Caused by a Novel Unbalanced Structural Rearrangement and Its Mechanism of Origin: A Rare Case of Cytogenetic Anomaly, Congenital Abnormalities, and Neonatal Death. *J Mol Diagn* 2023; 25(11):S26-S26. Full Text.

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Pathology and Laboratory Medicine
Birk NK, **Soman S**, **Kapur N**, **Pochhareddy V**, **Dillon WP**, **Veve M**, **Samuel L**, **Ramesh M**, and **Alangaden GJ**. Candidemia: Role of T2Candida® compared to Bact/Alert Virtuo blood culture system in a real-world setting. *Open Forum Infect Dis* 2023; 10:S356. Full Text

N.K. Birk, Henry Ford Hospital, Detroit, MI, United States

Background. Candidemia is the most common cause of invasive fungal infections with mortality rates up to 60%. The current standard for diagnosis of candidemia is traditional blood cultures (BC) but it has low sensitivity. The need for rapid identification of candidemia has led to the development of non-culture-based diagnostic platforms. T2Candida® (T2) is an FDA approved direct from blood PCR test. T2 detects 5 candida species (C. albicans/C. tropicalis, C. parapsilosis, & C. krusei/C. glabrata) with a turnaround time of three to five hours. T2 is used at our institution for the diagnosis of candidemia in the intensive care units (ICU) if prior blood cultures are negative. Patients with positive T2 results are managed the same as patients with positive BC. In February 2019, our health system switched from the VersaTREK™ to a more sensitive Bact/Alert Virtuo BC system. Our objective was to assess the impact of the new Virtuo system on the diagnosis of candidemia compared to T2 in a realworld setting. Methods. All T2 and concurrent BC results were retrospectively collected from January 2018 to January 2019 (VersaTREK™cohort) and March 2019 to March 2020 (Virtuo cohort) in our quaternary care facility in metro Detroit. Only patients with presumed candidemia were included (ICU patients with sepsis, recent exposure to anti-bacterial agents, and negative BC for candida in the past 7 days). Demographic data and the results of T2 and concurrent BC (obtained within 48 hours of T2) were analyzed for the presence or absence of candida. Indeterminate T2 results were excluded. Descriptive statistics were utilized to report the results. Results. A total of 522 and 348 T2 tests performed with concurrent BC through VersaTREK™and Virtuo systems respectively were included for analysis. In this ICU cohort with presumed candidemia, T2 remained superior: T2 positivity 45 (8.6%) vs. VersaTREK™ BC positivity 14 (2.7%) ($p < 0.001$) and T2 positivity 34 (9.8%) vs. Virtuo BC positivity 8 (2.3%) ($p < 0.001$) (Figure 1). The Virtuo cohort had overall fewer T2 tests performed. This may be because the more sensitive Virtuo system could have detected more cases of candidemia than VersaTREK™obviating the need for T2 test. Conclusion. T2 may still have a role in the early diagnosis of candidemia despite the use of newer sensitive blood culture systems.

Pathology and Laboratory Medicine
Gaddam S, **Kisha S**, **Tawil T**, **Theisen B**, and **Husain S**. Clinicopathologic Features of Autoimmune Metaplastic Atrophic Gastritis (AMAG) in an Underserved Community. *Am J Clin Pathol* 2023; 160:S32-S33. Full Text.

[Gaddam, S.; Kisha, S.; Tawil, T.; Theisen, B.; Husain, S.] Henry Ford Hosp, Pathol, Detroit, MI 48202 USA.

Pathology and Laboratory Medicine
Hardy ME, **Kenney RM**, **Tibbetts R**, **Shallal A**, and **Veve M**. Leveraging Stewardship to Promote Narrower-spectrum Antibiotic Use for Low-risk AmpC Enterobacterales. *Open Forum Infect Dis* 2023; 10:S6. Full Text

M.E. Hardy, WVU Medicine, Morgantown, WV, United States

Background. AmpC β-lactamases are associated with development of ceftriaxone (CRO) resistance despite in vitro susceptibility, but the risk of AmpC derepression is not equal among Enterobacterales. The purpose of this study was to evaluate the impact of an AmpC stewardship intervention on definitive treatment of low-risk Enterobacterales. Methods. IRB approved, single pre-test, post-test quasi-experiment with a nonequivalent dependent variable at a 5-hospital system. An AmpC stewardship intervention was implemented 7/22 and included education, removal of microbiology comments indicating potential for CRO resistance on therapy, and modification of a blood PCR comment for Serratia marcescens to recommend CRO. Inclusion: adults ≥ 18 years pre- (7/21-12/21) and post-intervention (7/22-12/22) who received ≥ 72 hours of inpatient definitive therapy and had non-urine cultures growing S. marcescens, Providencia spp., Citrobacter koseri, C. amalonaticus, C. farmeri, or Morganella morganii. Exclusion: infection with CRO resistant organisms. Primary outcome: proportion of patients who received definitive CRO therapy. Secondary outcomes at 30 days: retreatment for the same organism, development of CRO-resistant organisms, or Clostridioides difficile infection (CDI). Results. 224 patients were included: 115 (51%) pre- and 109 (49%) postintervention. Table 1 describes patient, infection, and treatment characteristics. There were 79 (35%) patients with concurrent bacteremia. Definitive CRO therapy was prescribed more frequently after intervention 6 (5%) vs 72 (66%), P< 0.001. Median (IQR) total duration for pre- and post-groups (9 [7-17] vs 10 [7-18], P=0.46). After adjustment for intensive care, patients in the post-group were more likely to receive definitive CRO (adjOR, 35.4; 95%CI, 14.2-88.0) (Table 2). The proportion of patients who required retreatment was 18 (15%) and 11 (10%) for preand post-group patients (P=0.22). CRO resistance within 30 days occurred in 5 (4%) and 2 (2%) patients in the pre- and post-group (P=0.45). Table 1. Patient, infection, and treatment characteristics Conclusion. An antimicrobial stewardship intervention was associated with increased CRO prescribing and similar patient outcomes for low-risk AmpC Enterobacterales. (Table Presented).

Pathology and Laboratory Medicine
Saikia K, **Ziying Z**, **Wang ZB**, **Azordegan N**, and Scialla A. Endometrial stromal tumor presenting as multiple endometrial polyps with limited infiltration; a novel presentation. *Am J Clin Pathol* 2023; 160:S57-S57. Full Text

[Saikia, K.; Ziying, Z.; Wang, Z. B.; Azordegan, N.] Henry Ford Hosp, Pathol, Detroit, MI 48202 USA. [Scialla, A.] Cleveland Clin, Pathol, Cleveland, OH 44106 USA. Foundation

Pediatrics
Jordan H, Glynn M, Seim LG, **Shah U**, Taddei TH, Thomas E, Wong RJ, and Verma M. A PUBLIC HEALTH INITIATIVE FROM THE AMERICAN LIVER FOUNDATION DEMONSTRATES THE FEASIBILITY OF A SCREENING PROGRAM FOR FATTY LIVER DISEASE. *Hepatology* 2023; 78:S753-S754. Full Text

[Jordan, Helene; Glynn, Megan; Seim, Lynn Gardiner] Amer Liver Fdn, San Diego, CA USA. [Shah, Uzma] Henry Ford Hlth, Detroit, MI USA. [Taddei, Tamar H.] Yale Univ, New Haven, CT USA. [Thomas, Emmanuel] Univ Miami, Miller Sch Med, Schiff Ctr Liver Dis, Coral Gables, FL 33124 USA. [Wong, Robert J.] Stanford Univ, Sch Med, Stanford, CA 94305 USA. [Verma, Manisha] Einstein Healthcare Network, Bronx, NY USA. University

Pharmacy
Arena C, **Kenney RM**, **Eriksson E**, **Brar I**, and **Veve M**. Impact of Social Determinants of Health on Preferred Treatment of Trichomonas vaginalis and Chlamydia trachomatis. *Open Forum Infect Dis* 2023; 10:S850-S851. Full Text

C. Arena, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Henry Ford Hospital, Royal Oak, MI, United States

Background. The 2021 CDC Sexually Transmitted Infections (STI) Treatment Guideline modified preferred therapy for Trichomonas vaginalis (TV) and Chlamydia trachomatis (CT) from single dose to a 7-day course. Social Determinants of Health (SDOH) are non-medical factors that influence a person's life; little is known regarding the association between SDOH and TV and CT treatment. The study objective was to evaluate treatment of TV and CT infections after the guideline update and determine if health inequities exist with use of preferred therapy. Methods. IRB approved, retrospective cohort of patients ≥ 15 years with confirmed diagnosis of uncomplicated TV or CT in outpatient settings. Excluded: pregnant/ nursing, allergy to preferred therapy, unable to take oral. Primary outcome: proportion who received guideline preferred vs non-preferred (alternative, discordant, or null) antibiotic therapy. Logistic regression was used to identify variables associated with preferred treatment; SDOH were exposures of interest. Secondary outcomes: test of cure (≤ 3 months), any repeat positive test (recurrence/reinfection), any retreatment, expedited partner therapy (EPT) offered. A sample of 712 patients was needed to detect a 10% difference between two exposures (α=0.05, β=0.2). Results. 473 (66%) patients received preferred therapy; patient characteristics are in Table 1. Patients < 25 years had more asymptomatic disease compared to older patients (198 [54%] vs 150 [44%], P=0.01). Patients who received Emergency Department (ED) care were more likely to receive preferred therapy compared to outpatient clinics (201/264 [76%] vs 272/448 [61%], P=< 0.001). Black race, lower median income, and public insurance covaried with ED care. After adjusting for female sex, receipt of ED care was independently associated with preferred therapy (Table 2). 181 (25%) patients had 3-month test of cure performed; repeat positive test/retreatment was more frequent in patients who received non-preferred therapy (25 [11%] vs 24 [5%], P=0.01). EPT was offered in 35 (7%) and 8 (3%) patients in the preferred and non-preferred groups (P=0.03). Conclusion. Preferred therapy was more frequent in patients who received ED care. EDs represent an important safety net and provide high-level care for patients with SDOH barriers. (Table Presented).

Pharmacy

Belza AC, **Efta J**, **MacDonald N**, **Kenney RM**, and **Patel N**. Putting a CAP on Discharge Antimicrobial Therapy: Evaluation of a Systematic Transitions of Care Process for Patients with Community Acquired Pneumonia (CAP) and Chronic Obstructive Pulmonary Disease (COPD). *Open Forum Infect Dis* 2023; 10:S540-S541. Full Text

A.C. Belza, Henry Ford Health - Detroit, Fraser, MI, United States

Background. Prescribing excess antibiotic duration at hospital discharge is common. A collaborative, pharmacist-led Antimicrobial Stewardship Transition of Care (ASP TOC) intervention implemented in our hospital was associated with improved discharge prescribing and reduced patient harm. However, the sustainability of this pharmacy service was challenging. To improve sustainability, the electronic scoring system (ESS) in the electronic medical record, used by inpatient pharmacists to prioritize patient care and identify interventions, had implemented an ASP TOC decision support in 2023. The purpose of this study was to evaluate the implementation of ASP TOC in the ESS. Methods. This IRB-approved retrospective quasi-experiment included patients discharged on oral antibiotics for community-acquired pneumonia or chronic obstructive pulmonary disease exacerbation (LRTI) from 11/2021 to 2/2022 (preintervention) or 11/2022 to 2/2023 (post-intervention). The primary endpoint was optimized discharge antimicrobial regimen, defined as guideline concordant selection, dose, and duration. 194 patients were required to achieve 80% power and detect 20% reduction of non-optimized therapy. Multivariable logistic regression was used to identify factors associated with optimized regimens. Results. 200 patients were included. Similar baseline demographics were found in both the pre-intervention group and post-intervention group (Table 1). Optimized discharge regimens improved from 69% in the pre-intervention group to 82% in the post-intervention group (p = 0.033). ASP TOC interventions by the pharmacist increased from 4% to 25% in the post-intervention group (p < 0.001). After adjustment for the type of LRTI, ASP TOC intervention was independently associated with optimized discharge regimens (aOR 6.57; 95% CI 1.51-28.63). Conclusion. After launch of the ASP TOC decision support, there was an increase in optimized discharge

regimens and ASP TOC interventions completed. Pharmacist use of ASP TOC decision support through an ESS can aid in improving discharge prescribing by the primary medical team, leading to improved outcomes. (Table Presented).

Pharmacy

Birk NK, **Soman S**, **Kapur N**, **Pochhareddy V**, **Dillon WP**, **Veve M**, **Samuel L**, **Ramesh M**, and **Alangaden GJ**. Candidemia: Role of T2Candida® compared to Bact/Alert Virtuo blood culture system in a real-world setting. *Open Forum Infect Dis* 2023; 10:S356. Full Text

N.K. Birk, Henry Ford Hospital, Detroit, MI, United States

Background. Candidemia is the most common cause of invasive fungal infections with mortality rates up to 60%. The current standard for diagnosis of candidemia is traditional blood cultures (BC) but it has low sensitivity. The need for rapid identification of candidemia has led to the development of non-culture-based diagnostic platforms. T2Candida® (T2) is an FDA approved direct from blood PCR test. T2 detects 5 candida species (C. albicans/C. tropicalis, C. parapsilosis, & C. krusei/C. glabrata) with a turnaround time of three to five hours. T2 is used at our institution for the diagnosis of candidemia in the intensive care units (ICU) if prior blood cultures are negative. Patients with positive T2 results are managed the same as patients with positive BC. In February 2019, our health system switched from the VersaTREK™ to a more sensitive Bact/Alert Virtuo BC system. Our objective was to assess the impact of the new Virtuo system on the diagnosis of candidemia compared to T2 in a realworld setting. Methods. All T2 and concurrent BC results were retrospectively collected from January 2018 to January 2019 (VersaTREK™cohort) and March 2019 to March 2020 (Virtuo cohort) in our quaternary care facility in metro Detroit. Only patients with presumed candidemia were included (ICU patients with sepsis, recent exposure to anti-bacterial agents, and negative BC for candida in the past 7 days). Demographic data and the results of T2 and concurrent BC (obtained within 48 hours of T2) were analyzed for the presence or absence of candida. Indeterminate T2 results were excluded. Descriptive statistics were utilized to report the results. Results. A total of 522 and 348 T2 tests performed with concurrent BC through VersaTREK™and Virtuo systems respectively were included for analysis. In this ICU cohort with presumed candidemia, T2 remained superior: T2 positivity 45 (8.6%) vs. VersaTREK™ BC positivity 14 (2.7%) ($p < 0.001$) and T2 positivity 34 (9.8%) vs. Virtuo BC positivity 8 (2.3%) ($p < 0.001$) (Figure 1). The Virtuo cohort had overall fewer T2 tests performed. This may be because the more sensitive Virtuo system could have detected more cases of candidemia than VersaTREK™obviating the need for T2 test. Conclusion. T2 may still have a role in the early diagnosis of candidemia despite the use of newer sensitive blood culture systems.

Pharmacy

Brochu JM, **Kenney RM**, **Herbin S**, **Gunaga S**, and **Veve M**. Risk Factors for Unplanned Healthcare Encounters in Patients Discharged from the Emergency Department with Extended-spectrum β-lactamase Urinary Tract Infections. *Open Forum Infect Dis* 2023; 10:S1259-S1260. Full Text

J.M. Brochu, Henry Ford Hospital, Detroit, MI, United States

Background. The management of extended spectrum β-lactamase (ESBL) urinary tract infections (UTIs) in the emergency department (ED) has not been well documented in literature. The purpose of this study was to describe treatment and outcomes of patients with ESBL UTIs in the ED, which can inform best practices for antimicrobial stewardship. Methods. This IRB approved, retrospective cohort analysis included patients who were discharged from the ED with an ESBL UTI between January 2020 and November 2022. The primary outcome of interest was any unplanned healthcare encounter related to the UTI within 30 days of the index ED visit, which included phone/ virtual visits, clinic visits, ED visits, and hospitalizations. Patients ≥18 years of age treated for symptomatic UTI with a monomicrobial urine culture were included, while those with altered mental status, history of renal transplant, abnormal urinary tract, or were on active antibiotic therapy prior to the ED visit were excluded. Patient characteristics, initial and definitive antibiotic therapy, culture results including pathogen and susceptibilities were described. Logistic regression analysis was used to identify any exposures that were independently associated with unplanned healthcare encounters related to the UTI. Results. 162 patients were included; 103 (64%) had

an unplanned healthcare encounter. Patient characteristics are depicted in Table 1. Complicated lower UTI was most frequent occuring in 71 patients (44%). Susceptibility data revealed that nitrofurantoin was effective in 121 (75%) patients, aminoglycosides in 117 (72%) patients, TMP/SMX in 66 (41%) patients, and quinolones in 62 (38%) patients. 76 (74%) patients with unplanned encounters received an inactive empiric prescription: β-lactams being prescribed to 52 (51%) patients with cephalexin used for 49/52 (94%). Of the 81 patients with lower UTI, 20 (25%) initially received a prescription for nitrofurantoin. Factors associated with an unplanned healthcare encounter are described in Table 2. Abbreviations: Un-Adj OR = unadjusted odds ratio; Adj OD = adjusted odds ratio Conclusion. Patients discharged from the ED with an ESBL UTI were at higher risk for unplanned healthcare encounters if they had CKD or were initially prescribed an oral β-lactam. Prescribing first line therapy with nitrofurantoin for lower UTI is a potential area for improvement.

Pharmacy

Caniff KE, Holger D, Lucas K, O'Donnell MA, Shields RK, Loo A, Khem R, Dahl N, Dubrovskaya Y, Marsh K, Cubillos AL, Chandler E, Knack O, Davis SL, **Alangaden GJ**, and Rybak MJ. Predictors of 30-Day Mortality Among Critically Ill Patients with Candidemia Identified by T2Candida Panel. *Open Forum Infect Dis* 2023; 10:S445. Full Text

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Background. Candidemia is associated with mortality rates exceeding 40%. However, prior studies indicate mortality may be reduced when antifungal therapy is initiated within 12 hours. The T2Candida Panel is a diagnostic assay that detects Candida species directly from a whole blood specimen within 3-5 hours (T2 Biosystems, Lexington, MA). The objective of this study is to identify predictors of 30-day mortality in patients with candidemia identified by T2Candida Panel. Methods. This is a retrospective,multicenter study of critically ill patients with candidemia identified by T2Candida Panel from January 2016 - December 2022. Critically ill patients were defined as those who developed candidemia during an intensive care unit (ICU) stay or within 72 hours of ICU admission or discharge. T2Candida sites were chosen across the United States based on T2Candida utilization. Exclusion criteria were patients < 18 years of age, those with prophylactic indications for antifungal therapy, prisoners and pregnant patients. Multivariate logistic regression was conducted to identify factors associated with 30-day mortality measured from the T2Candida draw time. Results. There were 171 ICU patients from seven institutions with candidemia identified by T2Candida panel. The mean (standard deviation [SD]) age was 59.7 (14.8) years and 52.1% were male. Mean (SD) APACHE II and Charlson Comorbidity Index scores were 20.6 (7.1) and 4.9 (2.8), respectively. Empiric antifungal therapy was administered to 36.8% of patients and the majority received infectious diseases (ID) consult (92.4%). Echinocandins were the most common agents used for empiric (72.7%) and definitive therapy (62.6%). Overall, 30-day mortality occurred in 36.0% and was not associated with antifungal de-escalation. Administration of empiric therapy (aOR 0.457, 95% CI 0.199-1.054) and ID consult (aOR 0.225, 95% CI 0.056-0.913) were associated with reduced odds of 30-day mortality. Conclusion. Empiric antifungal administration and ID consult were independently associated with reduced odds of 30-day mortality in patients with candidemia identified by T2Candida Panel. Future studies are needed to evaluate the impact of the T2Candida panel on antifungal stewardship.

Pharmacy

Fitzmaurice M, **Franco-Palacios DJ**, **Henderson R**, **Olexsey K**, **Pinto J**, **Poparad-Stezar A**, **Stagner LD**, and **Allenspach L**. A Case Series Describing Response to Rabbit Anti-thymocyte Globulin for the Treatment of Bronchiolitis Obliterans Syndrome in Patients With Chronic Lung Allograft Dysfunction. *Am J Respir Crit Care Med* 2024; 209. Full Text

M. Fitzmaurice, Henry Ford Health, Detroit, MI, United States

Background: Chronic allograft dysfunction (CLAD) is a frequent complication and main reason for morbidity and decreased survival after lung transplant. Besides augmented immunosuppression and azithromycin, few other salvage therapies exist. Anti-thymocyte globulin therapy (ATG) is commonly

offered to patients. The goal is to attenuate the rate of disease progression, stabilize or improve forced expiratory volume in 1 second (FEV1). Few centers have reported their treatment response with thymoglobulin and with varying doses. Methods: We reviewed all patients treated at our center with ATG for CLAD from 2015 to 2023. Their treatment response and side effects are described in 16 patients (BOS in 14, BOS + RAS in 2). Results: Median age 61, 81% were men, 15 patients underwent bilateral lung transplant. Most common indication was pulmonary fibrosis (6/16, 37%), followed by emphysema, cystic fibrosis and sarcoidosis. All patients received standard induction. Triple maintenance immunosuppression with calcineurin and cell cycle inhibitors and steroids were used in 68% of patients. Most patients (14/16, 87%) were taking azithromycin 250 mg three times weekly. The median cumulative ATG dose was 2.25 mg/kg with a median of 2 doses per course. Median time from transplant to BOS development was 24 months. Most patients (80%) had BOS stages 3 (9/16; 56%) and 4 (3/16, 18%). The median rate of FEV1 decline was - 142 mL/month. Eight patients had follow-up spirometry at 6 months post ATG. All eight (8/16, 50%) had attenuated decline or improvement in FEV1 in 4 and 4 patients, respectively. Four patients with shorter follow-up post ATG (2 to 4.5 months) have also responded to ATG (1 unchanged, 2 improved and 1 attenuated decline in FEV1). At the time of data censoring, responders had a median survival of 11 months. Baseline FEV1 was lower in non-responders. Five of them declined rapidly and died. Serum sickness was diagnosed in one patient post ATG. Three patients required dose reductions or slower infusion rate due to tolerability. Conclusions: Attenuated decline, stabilization, or improvement in FEV1 was seen in 68% (11/16) of patients at any time post ATG. Four patients with early BOS (stages 1 and 2) had improved FEV1 after ATG. Even in patients with late CLAD (BOS s-3 and 4, or on chronic oxygen therapy) ATG was of some benefit (partial response in 6/12, 50%). Our outcomes are consistent with previous reports and suggest that ATG at lower cumulative doses could benefit patients with CLAD.

Pharmacy

Hardy ME, **Kenney RM**, **Tibbetts R**, **Shallal A**, and **Veve M**. Leveraging Stewardship to Promote Narrower-spectrum Antibiotic Use for Low-risk AmpC Enterobacterales. *Open Forum Infect Dis* 2023; 10:S6. Full Text

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Background. AmpC β-lactamases are associated with development of ceftriaxone (CRO) resistance despite in vitro susceptibility, but the risk of AmpC derepression is not equal among Enterobacterales. The purpose of this study was to evaluate the impact of an AmpC stewardship intervention on definitive treatment of low-risk Enterobacterales. Methods. IRB approved, single pre-test, post-test quasi-experiment with a nonequivalent dependent variable at a 5-hospital system. An AmpC stewardship intervention was implemented 7/22 and included education, removal of microbiology comments indicating potential for CRO resistance on therapy, and modification of a blood PCR comment for Serratia marcescens to recommend CRO. Inclusion: adults ≥ 18 years pre- (7/21-12/21) and post-intervention (7/22-12/22) who received ≥ 72 hours of inpatient definitive therapy and had non-urine cultures growing S. marcescens, Providencia spp., Citrobacter koseri, C. amalonaticus, C. farmeri, or Morganella morganii. Exclusion: infection with CRO resistant organisms. Primary outcome: proportion of patients who received definitive CRO therapy. Secondary outcomes at 30 days: retreatment for the same organism, development of CRO-resistant organisms, or Clostridioides difficile infection (CDI). Results. 224 patients were included: 115 (51%) pre- and 109 (49%) postintervention. Table 1 describes patient, infection, and treatment characteristics. There were 79 (35%) patients with concurrent bacteremia. Definitive CRO therapy was prescribed more frequently after intervention 6 (5%) vs 72 (66%), P< 0.001. Median (IQR) total duration for pre- and post-groups (9 [7-17] vs 10 [7-18], P=0.46). After adjustment for intensive care, patients in the post-group were more likely to receive definitive CRO (adjOR, 35.4; 95%CI, 14.2-88.0) (Table 2). The proportion of patients who required retreatment was 18 (15%) and 11 (10%) for preand post-group patients (P=0.22). CRO resistance within 30 days occurred in 5 (4%) and 2 (2%) patients in the pre- and post-group (P=0.45). Table 1. Patient, infection, and treatment characteristics Conclusion. An antimicrobial stewardship intervention was associated with increased CRO prescribing and similar patient outcomes for low-risk AmpC Enterobacterales. (Table Presented).

Pharmacy

Ismail G, **Donald NM**, **Kenney RM**, **Mulugeta S**, **Gendjar S**, and **Daifi C**. 332. Factors Associated with Readmission in Patients with End-Stage Renal Disease on Hemodialysis Discharged on Outpatient Parenteral Antimicrobial Therapy. *Open Forum Infect Dis* 2023; 10:S211-S212. Full Text

G. Ismail, Henry Ford Health System, Dearborn, MI, United States

Background. Outpatient parenteral antimicrobial therapy (OPAT) is a popular option for patients who require extended treatment with antimicrobials. OPAT in patients with end stage renal disease (ESRD) on hemodialysis (HD) has unique considerations and regimens that facilitate vein preservation as a priority. This study aimed to characterize patients with ESRD on HD discharged on OPAT and identify factors associated with poor outcomes. Methods. This was an IRB-approved retrospective cohort of patients ≥ 18 years with ESRD on HD who were discharged between 1/1/20 and 8/30/22 with at least one week of OPAT. Enrolled patients were divided into two equal groups depending on their 60-day readmission status. Patients were excluded if they were admitted on OPAT prior to admission or expired within 30 days of the initial OPAT discharge, incarcerated, or if the discharge was self-directed. To identify risk factors for readmission, patients who had an unplanned all-cause 30-day readmission were compared with those not readmitted. Other safety measures collected include transitions of care process measures, pharmacist collaboration with patient education and follow-up monitoring. Results. 162 patients (67 females, 95 males; median age 59 years) were included. The most common reason for OPAT was bloodstream infection (51%). Vancomycin was the most prescribed (50%). Nine patients in the readmitted group reported adverse events compared to 31 in the readmitted group (p = < 0.001). Patients in the non-readmitted were statistically more likely to have a pharmacist infection treatment plan note prior to discharge (p = 0.036) and statistically more likely to attend infectious disease (ID) follow-up appointments (p = 0.001). A multivariable regression identified that being female, having diabetes mellitus, or congestive heart failure are associated with increased risk of unfavorable outcomes (Adjusted odd ratio = 3.352, 1.75, and 1.671 respectively). Conclusion. This study suggests that OPAT optimization and patient education by a pharmacist, and attending follow-up ID appointments reduced the risk of readmission for patients with ESRD on HD.

Pharmacy

Jacob B, **Jamil M**, **Raslan S**, **Nasser Z**, **Springer K**, **Michael German A**, and **Kuriakose P**. Infusion Reactions with Alternative Therapies during the National Shortage of Iron Dextran. *Blood* 2023; 142:7338. Full Text

Introduction The national shortage of intravenous iron dextran has required patients to receive more alternative iron infusions, such as iron sucrose and sodium ferric gluconate/sucrose, since January 2023. While prior studies have evaluated rates of infusion reactions among some commonly used intravenous iron formulations, data is lacking among differing doses of iron formulations and especially in the setting of this iron dextran shortage. Clinicians at our institution generally observed more adverse reactions with alternative iron infusions during the national shortage of iron dextran compared to prior. Our study examines the infusion reactions of various iron therapies at differing doses and actions providers and patients took thereafter to assess the impact of the iron dextran national shortage on patients. Methods Patients were included who received iron infusions in three Henry Ford Hospital clinics in metropolitan Detroit, Michigan, from July 2022-June 2023 with the national iron dextran shortage impacting the health system since January 2023. Age, race, sex, reason for iron infusion, iron infusion formulation received, time of infusion, and dosing schedule of infusion were recorded for all participants. We assessed the symptoms experienced and actions taken for patients who had an infusion reaction. The number and type of infusion reactions between different iron infusion formulations and doses were then compared. Results Of the 880 unique patients assessed, 496 (56.4%) received iron dextran, iron sucrose, or sodium ferric gluconate/sucrose between July 2022 and December 2022 prior to the national iron dextran shortage and 384 (43.6%) patients had iron infusions between January 2023 and June 2023 during the shortage. Iron dextran accounted for most of the infusions (n= 356, 71.8%) prior to the shortage whereas iron sucrose was the majority (n=312, 81.3%) during the shortage. Prior to the national shortage, 30 iron infusions reactions occurred, with 18 (60%) associated with iron dextran, 9 (30%) with iron sucrose, and 3 (16.7%) with sodium ferric gluconate/sucrose. During the shortage, 44 reactions occurred, with 1 (2.27%)

associated with iron dextran, 41 (93.1%) with iron sucrose, and 2 (4.54%) with sodium ferric gluconate/sucrose. The most reactions (n=41, 55.4%) occurred with iron sucrose at a dose of 500mg across the whole study period. Less reactions (n=9, 12.2%) were reported for iron sucrose at progressively lower doses, comparable to reactions with iron dextran at doses greater than 1000mg (n=8, 10.8%) and at lower doses of iron dextran (n=10, 13.5%). The most common reaction across all infusion types was nausea, vomiting, and/or diarrhea. After an iron infusion reaction, the infusion plan was then most commonly discontinued, with patients either switching to alternative iron infusion formulations, continuing the same infusion type with medications for symptoms, or continuing the same infusion type with lower dose and increased frequency. Conclusion More iron infusion reactions occurred after the national shortage of iron dextran since January 2023 in the setting of more frequent use of alternative iron therapies. The most common infusion formulation associated with a reaction was iron sucrose at its higher recommended dose of 500mg, compared with iron dextran and sodium ferric gluconate/sucrose. Providers should be aware of these associated adverse reactions with the different doses of alternative formulations when recommending infusions for patients, and the need for preemptive intervention.

Pharmacy

Mulbah JL, Morita K, Mentzer L, and Schultz SK. Microbiology and Predictors of Gram-Negative Infections in Persons Who Inject Drugs with Injection-Related Infections Requiring Hospitalization. *Open Forum Infect Dis* 2023; 10:S962-S963. Full Text

J.L. Mulbah, Henry Ford Health, Detroit, MI, United States

Background. Intravenous drug use predisposes users to life-threatening bacterial infections primarily caused by gram-positive organisms. Studies have seen an uptrend in gram-negative injection-related infections in persons who inject drugs (PWID). Therefore, this study aimed to assess the microbiology of injection-related infections in PWID and evaluate risk factors that may predispose these patients to infections caused by gram-negative organisms. Methods. This retrospective chart review of adult PWID hospitalized with an injection-related infection (skin & soft tissue infection, bacteremia, septic arthritis, endocarditis, epidural abscess, and osteomyelitis) included patients aged >18 years with bacterial growth on specimens collected within 72 hours of admission from September 1, 2021, to March 31, 2022. Data analysis utilized descriptive statistics, chi-square tests, and Mann-Whitney U tests where appropriate. Results. A total of 259 patients were included in the study. 243 (93.8%) patients grew gram-positive organisms, while only 16 (6.2%) grew gram-negative organisms. The majority of patients were male (60%), the median age was 38 (IQR [33-44]), and 10% had a prior infection with MRSA. The distribution of injection-related infections included SSTIs (79.9%), bacteremia (34.7%), septic arthritis (12%), infective endocarditis (10.4%), osteomyelitis (8.5%), and epidural abscess (3.5%). The most commonly observed organisms were MRSA (36%), S. pyogenes (43%), and MSSA (9%). The gram-negative organisms isolated are shown in Figure 1. Approximately 84% of patients received overtreatment with an anti-pseudomonal agent; however, only 2% required its use. SSTIs with lower extremity involvement were found to be associated with gram-negative infections within this cohort, as shown in Table 1. Conclusion. In this study, despite less than 10% of patients growing gramnegative organisms on culture, approximately 80% received gram-negative treatment. Knowledge of the microbiology of infections in PWID can aid prescribers in optimizing empiric therapy for injection-related infections and preserving the core principles of antimicrobial stewardship.

Pharmacy

Parke DM, **Kenney RM**, **Bogojevich J**, **El-Khoury C**, **Joshi S**, **Brar S**, **MacDonald L**, **Salib C**, **MacDonald N**, **Veve M**, and **Suleyman G**. Barriers to Improving Outcomes among People Experiencing Homelessness and People Who Inject Drugs Hospitalized for Complicated Infections. *Open Forum Infect Dis* 2023; 10:S864-S865. Full Text

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Background. People experiencing homelessness (PEH) and people who inject drugs (PWID) experience health disparities and worse outcomes. Challenges include suboptimal medication use, loss to follow-up, and non-compliance due to social determinant of health (SDOH) barriers, including lack of stable housing

and transportation, limited financial resources, substance use, and addiction. Methods. This quality improvement project aimed to address SDOH barriers among hospitalized PEH and/or PWID requiring ≥ 2 weeks of antibiotics to improve antibiotic compliance and outcomes in Detroit from 6/2022-4/2023. Interventions included antibiotic education, addiction medicine and pharmacy discharge medication cost inquiry consults when indicated, ensuring oral antibiotics were in hand at discharge, strengthening discharge planning between inpatient and ambulatory case managers (ACM), and referrals to community-based organizations to address SDOHneeds. Results. 34 patients were included (8 PEH, 11 PWID, 15 both); 3 who died in the hospital were excluded. Multiple individual and structural barriers and challenges to improving adherence and outcomes were identified (Table 1). Loss to follow-up was a significant challenge among this cohort, primarily due to patients self-discharging (29%) and being unreachable (52%). 10 (37%) patients were offered SDOH services (Table 2). Patients also had significant behavioral health/substance use disorder needs and utilized healthcare at a very high rate, with 29% having an ED revisit and 44% being readmitted within 30 days after discharge. Several structural and SDOH barriers existed, including limited staff capacity and limited placement options after discharge, resulting in suboptimal treatment delivery. Conclusion. AddressingSDOHbarriers for PEHand PWIDis challenging but vital to improving outcomes. Qualitative research should be conducted to understand these barriers. Having an interdisciplinary team comprising of infectious diseases, pharmacy, addictionmedicine, casemanagement and population health is critical to address patient needs holistically. Strengthening internal processes and building additional communitybased partnerships will be essential to better meet patient needs after discharge. (Table Presented).

Pharmacy

Shields RK, Abbo LM, Ackley R, Aitken SL, Albrecht B, Babiker A, Cifuentes R, Claeys KC, DeSear K, Gallagher JC, Gregory E, Heil EL, Hickey C, Klatt M, Kline EG, Kubat RC, Kufel WD, Lee JH, Lim A, Lingg T, MacDougall C, Mathers A, McCreary EK, Moore WJ, Olson S, Oxer J, Pearson JC, Pham C, Polk C, Satlin MJ, Satola SW, Shah S, Solanki YB, Tamma P, Vega A, Veena V, **Veve M**, Wangchinda W, Witt LS, Wu J, and Pogue JM. A multicenter, observational study to compare the effectiveness of Ceftazidime-Avibactam versus Ceftolozane-Tazobactam for multidrug-resistant Pseudomonas aeruginosa infections in the United States (CACTUS). *Open Forum Infect Dis* 2023; 10:S49-S50. Full Text

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Background. Ceftolozane-tazobactam (CT) and ceftazidime-avibactam (CZA) are front-line agents for treatment of multidrug-resistant (MDR) Pseudomonas aeruginosa; however, real-world comparative-effectiveness data are lacking. Methods. CACTUS is a retrospective, matched, multicenter study to compare the efficacy of CT and CZA among patients with bacteremia or pneumonia due to MDR P. aeruginosa. CT and CZA patients were matched 1:1 within each study site by the presence/absence of septic shock/severe sepsis, infection site, and time to treatment initiation. The primary outcome was clinical success at day 30 defined as survival, resolution of signs/symptoms with the intended treatment course, and absence of recurrent infections. Patients with cystic fibrosis or COVID-19 infection within 90 days were excluded. Results. 234 patients were included from 20 sites. Patient demographics, severity of illness, infection types, and treatment durations were similar for patients treated with CT or CZA (Table 1). The overall median age was 61 years, 61% were male, and the median Charlson score was 5. At study drug initiation, 77% of patients were in the ICU, 67% received mechanical ventilation and the median SOFA score was 7. 79% of patients were treated for pneumonia; 72% of which occurred in ventilated patients. The median time from index culture to treatment initiation was 72 hours in both groups; CT patients were more likely to receive a prolonged infusion of ≥3 hours (36% vs 19%; P=0.005). Clinical success occurred in 62% and 55% of patients receiving CT and CZA, respectively (P=0.35; Table 1). Corresponding rates of success for pneumonia were 63% and 52%, respectively (P=0.13; Figure 1). All-cause, 30-day mortality rate was 20% and 19%, respectively. Microbiologic failures, recurrent infections, and development of resistance within 90 days were similar between groups. Time to a composite endpoint of recurrent infection or death within 90 days was similar between groups in the overall analysis and the subgroup of patients with pneumonia (Figure 2). Conclusion. In this interim analysis of the CACTUS study, patients treated with CT and CZA had similar clinical outcomes. We plan to continue enrollment up to 420 patients to detect if any differences exist in the efficacy of CT and CZA for MDR P. aeruginosa infections. (Figure Presented).

Pharmacy

Yared NF, **Gudipati S**, **Payne S**, **Alvi RBR**, **Cherian J**, **Di Lodivico J**, **Markowitz N**, and **Brar I**. Efficacy of Long-Acting Cabotegravir and Rilpivirine in a Diverse Group of Patients in a Real-World Setting. *Open Forum Infect Dis* 2023; 10:S749-S750. Full Text

N.F. Yared, Henry Ford Health System, Detroit, MI, United States

Background. Cabotegravir (CAB) + rilpivirine (RPV) is the first recommended complete long-acting (LA) regimen for maintenance of HIV-1 virologic suppression. The efficacy and safety of switching to CAB + RPV LA (CAR) has been shown in clinical trials. CAR injections offer less frequent dosing and address issues of adherence and disclosure related to daily oral cART. We describe the clinical characteristics and outcomes of switching a diverse group of people with HIV (PWH) to CAR in a real-world setting. Methods. A retrospective cohort study was performed to assess virologic efficacy of intramuscular CAR given every 4 or 8 weeks among adult PWH receiving care at Henry Ford Health ID Clinic by an interdisciplinary team of physicians, nurses, social workers, and a pharmacist. Efficacy was defined as HIV-1 RNA < 20 copies/mL at 3 months. Demographics, clinical characteristics, and outcomes were extracted from the electronic medical record. Results. We included the first 51 patients to receive CAR. Median age was 46 years (IQR 34 -59). Black individuals were 75%, cisgender males 84%, and transgender females 3.9% of participants. PWH were diagnosed a median of 12 years ago (IQR 11-17). At time of switch, 90% had HIV viral load (VL) < 20 copies/ml, and 9.8% of patients were viremic with < 75 copies/ml. Mean Cd4+ cell count was 871 cells/ μL (IQR 632-1603). Prior to switch, 80% had received ≥ 2 cART regimens, 75% had INSTI exposure, and 45% had NNRTI exposure. Among 38 patients with HIV-1 genotypes available prior to switch, 4 had either baseline NNRTI or INSTI mutations (Table 2). For patients with VL data at 3 months, 37 of 38 (98%) had an undetectable VL. Virologic failure occurred in 1 PWH with BMI 35 who had a Y188L RT mutation in a 2009 genotype which did not include RPV (2011 approval), with subsequent emergence of pan-NNRTI and INSTI resistance. Conclusion. A high degree of virologic suppression at 3 months was achieved among an older, diverse cohort of PWH cared for by an interdisciplinary team. Unrecognized baseline HIV resistance to NNRTI contributed to one virologic failure. It is important to assure that genotypic susceptibility interpretations are current and to carefully assess for eligibility before switching to CAR.

Public Health Sciences

Akbari H, Bakas S, Garcia J, Kazerooni AF, Sako C, Villanueva-Meyer J, Baid U, Mamourian E, Brem S, Lustig RA, Nasrallah MP, O'Rourke DM, Calabrese E, Rudie J, Chang S, Rauschecker A, LaMontagne P, Marcus DS, Balana C, Capellades J, Puig J, Barnholtz-Sloan J, Badve C, Sloan A, Waite K, Colen R, Choi YS, Ahn SS, Dicker AP, Flanders AE, Shi W, **Griffith B**, **Poisson LM**, **Rogers LR**, Booth TC, Jain R, Chakravarti A, Palmer J, Cepeda S, Wiestler B, Di Stefano AL, Alexander K, Melhem ER, Woodworth GF, Kamel PI, Tiwari P, Aboian M, Mohan S, and Davatzikos C. ROBUSTNESS OF PROGNOSTIC STRATIFICATION IN DE NOVO GLIOBLASTOMA PATIENTS ACROSS 22 GEOGRAPHICALLY DISTINCT INSTITUTIONS: INSIGHTS FROM THE RESPOND CONSORTIUM. *Neuro Oncol* 2023; 25:v187. Full Text

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PURPOSE: Glioblastoma is the most prevalent primary malignant brain tumor in adults, with a median overall survival (OS) of approximately 15 months and only limited advancements in prognostication and survival prediction. This study aims to evaluate an AI-based prognostic stratification model for OS prediction trained on the ReSPOND consortium data and to validate its performance on an independent dataset. METHODS: The AI model was trained on a cohort of 2,293 glioblastoma patients from 22 institutions across three continents. For validation, an independent cohort of 78 treatment-naïve patients was used from three institutions. Preoperative structural MRI scans were utilized for feature extraction. Automated segmentation defined three tumor sub-compartments: enhancing, necrotic, and peritumoral T2-FLAIR abnormality. The AI predictor incorporated variables such as patient age, normalized tumor sub-compartment volume, spatial distribution characteristics, and morphologic descriptors. The overall survival predictor index provided a continuous value between 0 and 1 for patient stratification that higher

values indicating longer predicted OS. Generalizability was assessed using Leave-One-Cohort-Out-Cross-Validation (LOCOCV) for training data, and the model was subsequently applied to the validation cohort. RESULTS: Survival analysis demonstrated a concordance index of 0.64 for LOCOCV training data and 0.59 for the independent validation data, indicating effective prognostic stratification of patients. CONCLUSION: Multi-parametric AI assisted image analysis extracts prognostic biomarkers, which correlate with OS in glioblastoma patients. The generalizability of this method was validated using the extensive centralized glioblastoma imaging dataset registry from the ReSPOND consortium and an independent dataset, demonstrating its generalizability across diverse patient populations and acquisition settings. This model holds promise for robust prognostic stratification and prediction in de novo glioblastoma patients.

Public Health Sciences
Arruga Novoa y Novoa V, **Sitarik A**, **Su WT**, **Bossick A**, **Wegienka G**, **Chamseddine P**, **Vilkins A**, and **Abood J**. 9430 The Impact of Anxiety and Depression on Regret after Hysterectomy. *J Minim Invasive Gynecol* 2023; 30(11):S70-S70. Full Text

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Public Health Sciences
Connolly JG, Rodriguez-Watson CV, Lem J, Behr S, Dickerson J, Go AS, Reynolds K, Roblin D, **Cassidy-Bushrow AE**, Mendelsohn A, Clary A, McMahill-Walraven CN, Adgent M, Selvan M, Pawloski PA, and Kuntz J. Cohort study of serious angioedema in association with sacubitril/valsartan use in black patients with heart failure. *Pharmacoepidemiol Drug Saf* 2023; 32:475-476. Full Text

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Public Health Sciences
Czarnota P, Wilbrink R, Khatri B, Stolarczyk A, Frazee CP, Li C, Marlin C, Wright K, Tessneer K, Radfar L, James J, Scofield R, **Adrianto I**, Rasmussen A, Guthridge J, Farris AD, and Lessard C. New Histological Approach in Spatial Transcriptomics Implicates Glandular Cell Involvement in Pathophysiology of Sjogren's Disease. *Arthritis Rheumatol* 2023; 75:62-63. Full Text

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Public Health Sciences

DeCuir J, Zhu Y, Gaglani M, Ginde AA, Mohr N, Gibbs K, Hager D, Frosch A, Mohamed A, Johnson N, Steingrub JS, Peltan I, Martin ET, Bender W, Wilson J, Qadir N, Mallow C, Kwon JH, Exline M, Lauring AS, Columbus C, **Vaughn I**, Safdar B, Chappell J, Baughman A, Womack KN, Swan SA, McMorrow ML, Self W, and Surie D. 2083. Waning of Bivalent mRNA Vaccine Effectiveness Against COVID-19-associated Hospitalization Among Immunocompetent Adults Aged ≥65 Years - IVY Network, 20 U.S. States, September 8, 2022-April 1, 2023. *Open Forum Infect Dis* 2023; 10:S90-S91. Full Text

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Background. On September 1, 2022, the Advisory Committee on Immunization Practices recommended a bivalent mRNA COVID-19 booster dose for persons who had completed at least a primary COVID-19 vaccination series ≥2 months earlier. Early data showed high effectiveness of a bivalent booster in preventing COVID-19-associated hospitalization within 45 days of receipt; however, little is known about the durability of this protection. Methods. Data from the Investigating Respiratory Viruses in the Acutely Ill (IVY) Network were used to conduct a case-control analysis measuring bivalent vaccine effectiveness (VE) against COVID-19-associated hospitalization over time. During September 8, 2022-April 1, 2023, immunocompetent, hospitalized adults aged ≥65 years with COVID-19-like illness were enrolled at 25 hospitals in 20 U.S. states. COVID-19 case-patients tested positive for SARS-CoV-2 by a nucleic acid or antigen test within 10 days of illness onset, while control-patients tested negative for SARS-CoV-2 during the same interval. Multivariable logistic regression was used to measure absolute and relative bivalent VE adjusted for age, sex, race and ethnicity, admission date, and U.S. Health and Human Services region. Unvaccinated patients and patients who received 2-4 doses of monovalent-only mRNA vaccine were used as the reference group for absolute and relative VE, respectively. Bivalent VE was calculated for 7-89 days and 90-179 days from booster dose receipt to illness onset. Results. A total of 2,787 immunocompetent, hospitalized adults aged ≥65 years were enrolled in the IVY Network during the study period (1,236 COVID-19 casepatients and 1,551 control patients). Absolute VE of a bivalent booster dose against COVID-19-associated hospitalization was 58% (95% CI=42%-70%) after 7-89 days and 27% (95% CI= -7% to 50%) after 90-179 days. Relative VE of a bivalent booster dose was 54% (95% CI=41%-64%) after 7-89 days and 19% (95% CI= -8% to 39%) after 90-179 days (Figure). Conclusion. Bivalent mRNA vaccination provided moderate protection against COVID-19-associated hospitalization within 90 days of receipt among adults aged ≥65 years, with waning protection after 90 days. Additional booster doses could improve protection against COVID-19-associated hospitalization among older adults.

Public Health Sciences

Ghanem A, **Rose CM**, **Li P**, and **Elshaikh MA**. INFLUENCE of COMORBIDITY on the RISK of DEATH: A SINGLE INSTITUTION STUDY of 1915 WOMEN with EARLY-STAGE UTERINE CANCER. *Int J Gynecol Cancer* 2023; 33:A160. Full Text

M.A. Elshaikh, Henry Ford Cancer Institute, Detroit, United States

Introduction/Background The study goal is to utilize a validated comorbidity scoring to determine its impact on recurrence-free (RFS), disease-specific (DSS) and overall survival (OS) in women with early-stage uterine endometrioid carcinoma (EC). Methodology We identified 1915 patients with EC stages I-II who underwent hysterectomy. Charlson Comorbidity Index (CCI) at time of hysterectomy was calculated by trained physician. Survival endpoints was correlated with CCI. Univariate and multivariate modeling with Cox regression analysis was used to determine significant predictors of OS, DSS, and RFS. Results After a median follow-up of 104 months, 529 deaths were recorded, only 87 patients died from EC [16%], and 442 [84%] from other causes). Median CCI score for the study cohort was 0 (range, 0 to 12). On the basis of CCI, patients were grouped as follows: 0 score (group 1, n=1083), score 1-2 (group 2, n = 690), and score of 3 or more (group 3, n = 142). By CCI grouping, the 5-year RFS, DSS, and OS were 94%, 96%, and 97% for group 1, 92%, 94%, and 78% for group 2, and 86%, 95% and 60% for group 3 (P< 0.0001). The cause of death in the first 10 years after hysterectomy in our study was mainly non-uterine cancer-related (80% vs. 20% for uterine cancer-related) causes. On multivariate analyses, higher CCI, lymphovascular space invasion (LVSI), higher tumor grade, and older age were significant predictors of shorter OS. On multivariate analysis for DSS and RFS, only high tumor grade and LVSI were significant

predictors. Conclusion The cause of death for women with early-stage EC is mainly nonuterine cancer-related. Comorbidity score is a significant predictor of OS in our study cohort. Comorbidity scores may be useful as a stratification factor in any prospective clinical trial for women with early-stage EC.

Public Health Sciences
Gongala S, Garcia J, Korakavi N, Patil N, Akbari H, Tippareddy C, Sloan A, Barnholtz-Sloan J, Bakas S, Kazerooni AF, Sako C, Baid U, Brem S, Lustig RA, Capellades J, Nasrallah M, O'Rourke DM, La Montagne P, Marcus DS, Balana C, Puig J, Waite K, Colen R, Choi YS, Lee SK, Dicker AP, Flanders AE, Shi W, **Griffith B**, **Poisson LM**, **Rogers LR**, Booth TC, Jain R, Chakravarti A, Palmer J, Mohan S, Tiwari P, Aboian M, Ahn SS, Davatzikos C, and Badve C. SEX-SPECIFIC DIFFERENCES IN GLIOBLASTOMA IN THE RESPOND CONSORTIUM. *Neuro Oncol* 2023; 25:v118. Full Text

S. Gongala, Department of Radiology, University Hospitals Seidman Cancer Center, Cleveland, United States

AIM: The goal of this study was to understand sex-specific differences in the molecular, clinical and radiological tumor parameters and survival outcomes of Glioblastoma (GBM) patients within the international GBM dataset, known as the ReSPOND (Radiomic Signatures for PrecisiON Diagnostics) consortium. METHODS: Sex-based differences were retrospectively studied in 1922 GBM patients from the ReSPOND consortium which includes information from over 14 institutions across 3 continents. The parameters include age, Methylguanine-DNA Methyltransferase (MGMT) promoter methylation status, isocitrate dehydrogenase 1 (IDH1) mutation status, Karnofsky performance status (KPS), extent of resection (EOR), tumor epicenter, volumes, laterality and spatial extent. Non-parametric tests, log-rank test and cox-proportional hazard analysis were performed to understand sex-based differences in tumor parameters, survival rates and hazard ratios. Spatial atlases were generated to understand radiological parameters such as tumor spatial extent. RESULTS: GBM in was diagnosed at a median age of 62.6 years in females compared to 61 years in males ($p = 0.001$). Additionally, 44% females compared to 37% males ($p = 0.04$) had methylated MGMT and 79% females compared to 73% males ($p = 0.004$) had IDH1 wildtype. The tumor volumes were smaller in females (necrotic core, edema, and enhancing tumor) compared to males. Females exhibited a higher prevalence of right hemisphere (39.6%) and right temporal lobe tumors (19.7%), while males showed a higher prevalence of left hemisphere (40.3%) left temporal lobe tumors (23.7%). No significant sex-based differences in OS and PFS was observed in overall sample, although longer PFS was observed in elderly (above 60 years) female patients. CONCLUSION: This is a first international large cohort study looking at sex-based differences in GBM patients using the ReSPOND consortium data. Several sex-specific differences in the distribution of various tumor phenotypes were noted, however sex was not a contributing factor in OS and PFS.

Public Health Sciences
Gonzalez H, **Gordon SC**, Daida YG, Schmidt MA, **Zhou YR**, **Wu T**, **Rupp L**, **Trudeau S**, and Lu M. SUSTAINED VIROLOGICAL RESPONSE REDUCES RISK OF PORTAL VEIN THROMBOSIS IN HEPATITIS C PATIENTS WITH CIRRHOSIS. *Hepatology* 2023; 78:S710-S711. Full Text

[Gonzalez, Humberto; Gordon, Stuart C.; Zhou, Yueren; Wu, Trueman; Rupp, Lora; Trudeau, Sheri] Henry Ford Hlth, Detroit, MI USA. [Gordon, Stuart C.] Wayne State Univ, Sch Med, Detroit, MI USA. [Daida, Yihe G.] Kaiser Permanente Hawaii, Honolulu, HI USA. [Schmidt, Mark A.] Kaiser Permanente Northwest, Washington, DC USA. [Lu, Mei] 156 Pocatello Rd, Middletown, NY USA.

Public Health Sciences
Jacob B, **Jamil M**, **Raslan S**, **Nasser Z**, **Springer K**, **Michael German A**, and **Kuriakose P**. Infusion Reactions with Alternative Therapies during the National Shortage of Iron Dextran. *Blood* 2023; 142:7338. Full Text

Introduction The national shortage of intravenous iron dextran has required patients to receive more alternative iron infusions, such as iron sucrose and sodium ferric gluconate/sucrose, since January 2023. While prior studies have evaluated rates of infusion reactions among some commonly used intravenous iron formulations, data is lacking among differing doses of iron formulations and especially in the setting

of this iron dextran shortage. Clinicians at our institution generally observed more adverse reactions with alternative iron infusions during the national shortage of iron dextran compared to prior. Our study examines the infusion reactions of various iron therapies at differing doses and actions providers and patients took thereafter to assess the impact of the iron dextran national shortage on patients. Methods Patients were included who received iron infusions in three Henry Ford Hospital clinics in metropolitan Detroit, Michigan, from July 2022-June 2023 with the national iron dextran shortage impacting the health system since January 2023. Age, race, sex, reason for iron infusion, iron infusion formulation received, time of infusion, and dosing schedule of infusion were recorded for all participants. We assessed the symptoms experienced and actions taken for patients who had an infusion reaction. The number and type of infusion reactions between different iron infusion formulations and doses were then compared. Results Of the 880 unique patients assessed, 496 (56.4%) received iron dextran, iron sucrose, or sodium ferric gluconate/sucrose between July 2022 and December 2022 prior to the national iron dextran shortage and 384 (43.6%) patients had iron infusions between January 2023 and June 2023 during the shortage. Iron dextran accounted for most of the infusions (n= 356, 71.8%) prior to the shortage whereas iron sucrose was the majority (n=312, 81.3%) during the shortage. Prior to the national shortage, 30 iron infusions reactions occurred, with 18 (60%) associated with iron dextran, 9 (30%) with iron sucrose, and 3 (16.7%) with sodium ferric gluconate/sucrose. During the shortage, 44 reactions occurred, with 1 (2.27%) associated with iron dextran, 41 (93.1%) with iron sucrose, and 2 (4.54%) with sodium ferric gluconate/sucrose. The most reactions (n=41, 55.4%) occurred with iron sucrose at a dose of 500mg across the whole study period. Less reactions (n=9, 12.2%) were reported for iron sucrose at progressively lower doses, comparable to reactions with iron dextran at doses greater than 1000mg (n=8, 10.8%) and at lower doses of iron dextran (n=10, 13.5%). The most common reaction across all infusion types was nausea, vomiting, and/or diarrhea. After an iron infusion reaction, the infusion plan was then most commonly discontinued, with patients either switching to alternative iron infusion formulations, continuing the same infusion type with medications for symptoms, or continuing the same infusion type with lower dose and increased frequency. Conclusion More iron infusion reactions occurred after the national shortage of iron dextran since January 2023 in the setting of more frequent use of alternative iron therapies. The most common infusion formulation associated with a reaction was iron sucrose at its higher recommended dose of 500mg, compared with iron dextran and sodium ferric gluconate/sucrose. Providers should be aware of these associated adverse reactions with the different doses of alternative formulations when recommending infusions for patients, and the need for preemptive intervention.

Public Health Sciences

Jomaa D, **Dababneh Y**, **Nagirimadugu A**, **Oruganti P**, **Lu M**, **Melkonian C**, and **Kaur N**. Bridging Healthcare Disparities in Patients With Inflammatory Bowel Disease (IBD) in Underserved Communities: Results From a Telemedicine Intervention at a Large Tertiary Care Center. *Am J Gastroenterol* 2023; 118(12):S18. Full Text

D. Jomaa, Henry Ford Health, Detroit, MI, United States

Background: The prevalence of IBD in the United States is greater than 3 million and rising, while the access to IBD specialists in rural areas remains limited. Urban areas associated with large healthcare systems have 263 specialists per 100,000 residents, whereas rural areas have only 30 specialists per residents. The specific aims of this study are to identify the impact access to specialty care has on frequency of IBD flares, emergency department (ED) visits, and hospitalizations. Methods: We conducted a retrospective chart review of adult patients (>18 years) with the diagnosis of IBD who reside in Michigan. Patients were divided into either pre or post periods, where preperiod was defined as before the initiation of telehealth services between 1/1/2018-12/31/2019, and post-period was defined as after the advent of telehealth, between 10/1/2021-10/31/2022, including both video visits as well as the Henry Ford Specialty Center, which offers IBD specialty care virtually. Patient's demographic information, IBD encounters, ED visits, hospitalizations were collected at the end of each study period. The outcomes of interest were the number of IBD-related outpatient encounters, ED visits, and hospitalizations in each period. Results: A total of 5520 IBD encounters were observed in both time periods from 4941 individual patients. Among the total 4941patients, 2992 patients were in the pre-period cohort, and 1949 patients were in the post-period cohort including 721 patients who were seen in both period cohorts. Patients' IBD encounters were significantly reduced in the post-period compared to those in the preperiod (RR=0.73,

95% CI 0.69-0.76 and p-value< 0.001). There was also a significant decrease in ED visits (RR=0.53, 95% CI 0.50-0.56) and hospitalizations in the post-period (RR=0.35, 95% CI 0.33- 0.37). In addition, we looked at the geospatial distribution in patients and found that there was a wider distribution of patients seeking care for their IBD in neighboring and rural counties in the postperiod compared to the pre-period. Conclusions: The IBD Center at Henry Ford Health serves more than 3,000 patients annually and an estimated 15% travel more than 60 miles for their care. Given the need to provide specialty care throughout Michigan, Henry Ford Health is offering telehealth services within a standard clinic to overcome the barriers of telehealth in IBD care. Our study shows that this effort has bridged access to medical care and increased distribution of patients in Michigan receiving specialty care for IBD. It also significantly reduced IBD flares, hospitalization, and ED visits for these patients.

Public Health Sciences

Kim RY, Rendle KA, Mitra N, **Neslund-Dudas C**, Greenlee RT, Burnett-Hartman AN, Honda SA, **Simoff MJ**, Schapira MM, Croswell JM, Jeon J, Meza R, Ritzwoller DP, and Vachani A. Longitudinal Adherence to Recommended Lung Cancer Screening Follow-up: A Multicenter Cohort Study. *Am J Respir Crit Care Med* 2024; 209. Full Text

R.Y. Kim, Pulmonary,Allergy,and Critical Care, University of Pennsylvania, Philadelphia, PA, United States

RATIONALE: Disparities in lung cancer screening (LCS) adherence by type of screening program and patient race across one round of LCS have previously been identified. However, real-world data are limited regarding adherence to LCS recommendations across multiple rounds of screening. We sought to determine adherence to Lung Imaging Reporting and Data System (Lung- RADS) recommendations across two rounds of LCS, stratified by program centralization and patient race. METHODS: We performed a multicenter retrospective cohort study of 55-75 year-old patients who formerly or currently smoked and received baseline LCS (T0) between 1/1/2015 and 6/30/2019 at healthcare systems within the Population-based Research to Optimize the Screening Process (PROSPR)-Lung Consortium. We collected electronic health record and billing data to calculate adherence to Lung-RADS recommendations across two LCS rounds (T1, T2) via a previously validated approach. Among individuals adherent at T1, T2 adherence was determined based on T1 Lung-RADS score if available or any follow-up chest CT or relevant diagnostic procedure within 15 months of T1. We used descriptive statistics and stratified multivariable modified Poisson regression models to assess differences in T2 adherence by LCS program type and patient race. RESULTS: Of the 12,310 individuals receiving LCS (median age: 65 years [IQR: 60-69 years]; 73.2% White; 14.1% Black), 7,755 (63.0%) were screened at decentralized and 4,555 (37.0%) at centralized programs. Adherence to Lung-RADS recommendations was higher at centralized compared to decentralized programs at both T1 (72.3% vs 41.4%; P<0.001) and T2 (74.0% vs 63.0%; P<0.001). Among the 6,506 individuals adherent at T1, there was no significant difference in T2 adherence by race at either decentralized (Black: 60.9% vs White: 63.5%; P=0.254) or centralized programs (Black: 74.7% vs White: 72.3%; P=0.599). Overall adjusted T2 adherence rates for Black and White patients were 54.5% vs 56.6% (P=0.138) and 86.9% vs 84.1% (P=0.095) at decentralized and centralized programs, respectively (Figure). When stratifying by baseline Lung-RADS score and controlling for all measured confounders, there was no difference in T2 adherence by race, except for slightly higher adherence among Black compared to White patients screened at centralized programs with positive baseline screens (adjusted risk ratio: 1.17 [95% CI: 1.05-1.31]). CONCLUSIONS: LCS program centralization is associated with increased longitudinal LCS adherence to Lung-RADS recommendations across two rounds of LCS. We did not observe any significant racial disparities in longitudinal LCS adherence among individuals who were adherent during the first round of screening, regardless of baseline screening result or program centralization.

Public Health Sciences

Kim RY, Rendle KA, Mitra N, **Neslund-Dudas C**, Greenlee RT, Burnett-Hartman AN, Honda SA, **Simoff MJ**, Schapira MM, Croswell JM, Meza R, Ritzwoller DP, and Vachani A. Racial Disparities in Annual Lung Cancer Screening Follow-up: An Updated Analysis of a Multicenter Cohort Study. *Am J Respir Crit Care Med* 2024; 209. Full Text

R.Y. Kim, Pulmonary,Allergy,and Critical Care, University of Pennsylvania, Philadelphia, PA, United States

RATIONALE: We previously demonstrated that adherence to annual lung cancer screening (LCS) is higher at centralized compared to decentralized programs, with program decentralization associated with racial disparities in adherence. Here we report an updated analysis with a larger sample and additional years of follow-up data to examine racial disparities in LCS follow-up among individuals with negative baseline screens recommended for ongoing annual LCS. METHODS: We performed a multicenter retrospective cohort study of 55-75 year-old patients who formerly or currently smoked and received baseline LCS between 1/1/2015 and 6/30/2019 at healthcare systems within the Population-based Research to Optimize the Screening Process (PROSPR)- Lung Consortium. We restricted our analysis to individuals with negative baseline screens (Lung Imaging Reporting and Data System [Lung-RADS] 1 or 2) and excluded those with a prior lung cancer diagnosis and those who died within 30 months of baseline LCS. Using electronic health record and billing data, we identified all follow-up chest computed tomography (CT) imaging within 30 months of baseline LCS and evaluated the association between LCS program centralization and patient race with annual LCS adherence using descriptive statistics, multivariable modified Poisson regression, and kernel density plots. RESULTS: Of the 10,353 patients with a negative baseline screen (median age: 64 years [IQR: 60-69 years]; median pack-year smoking history: 40 [IQR: 32-52]; median Charlson Comorbidity Index: 1 [IQR: 0-2]), 7,507 (72.5%) identified as White, 1,499 (14.5%) as Black, and 6,063 (58.6%) as currently smoking. Of these individuals, 6,648 (64.2%) were screened at decentralized programs, and 3,705 (35.8%) at centralized programs. At decentralized programs, Black patients, compared to White patients, were less likely to have a follow-up chest CT within 10-15 months of baseline LCS (28.5% vs 40.3%; P<0.001) and more likely to have delayed imaging follow-up within 15-30 months (29.5% vs 23.7%; P<0.001) or no follow-up imaging within 30 months (36.3% vs 30.4%; P<0.001). In contrast, at centralized programs Black individuals had similar follow-up rates compared to White individuals at 10-15 months (67.5% vs 71.5%; P=0.360), 15-30 months (19.3% vs 15.0%; P=0.206), and no follow-up within 30 months (7.9% vs 7.6%; P=0.906; Figure). Multivariable adjusted adherence for Black and White patients were 30.8% vs 38.2% (P<0.001) and 71.1% vs 74.5% (P=0.172) at decentralized and centralized programs, respectively. CONCLUSIONS: This updated multicenter analysis confirms that program centralization is associated with reduced racial disparities in annual LCS adherence and represents a feasible systemic approach to promoting health equity in LCS.

Public Health Sciences

Manivannan A, Liapakis AM, Diehl AM, Verna E, Kumar V, **Salgia RJ**, **Wu T**, Lu M, Parikh ND, and **Jesse M**. INTERACTIONS BETWEEN RACE/ETHNICITY AND GENDER IN LIVER TRANSPLANTS: DO ACUITY CIRCLES MATTER? *Hepatology* 2023; 78:S277. Full Text

A. Manivannan, Henry Ford Health, New Haven, CT, United States

Background: Despite continued efforts, there are welldocumented disparities in liver transplantation (LT) from listing through post-transplant. National policies on allocation of deceased donor liver transplants (DDLT) aim to provide consistent and equitable access. However, the impacts of Acuity Circles (AC) and interactions between race and gender on delisting due to deterioration/death or receipt of DDLT have been minimally explored. Methods: Using data from the United Network for Organ Sharing (UNOS), we studied listed adults for DDLT from April 3, 2017, to October 4, 2022, a 60-month period (30 mo pre- and post-AC). Fine-Gray subdistribution hazard model was used to study AC impact on LT while delisting due to deterioration/ death was used as a competing risk. The model focused on AC indicator by race by gender interactions, as well as AC by hepatocellular carcinoma (HCC) diagnosis interactions. Results: 59,592 patients (30,202 pre-AC, 29,390 post-AC) were studied. No 3- way (AC X race X gender) interaction was detected, indicating effect of race and gender on LT was consistent pre- and post-AC periods. However, there were significant gender by race or AC by HCC interactions (Table 1): patients with HCC had greater chance for LT than non-HCC, though post-AC this effect was reduced. AC increased LT 25% in patients without HCC. Across gender, White, Black, and Hispanic men were more likely to receive transplant compared to their female counterparts. Within gender, Black and Hispanic women were less likely to receive transplant than White women, with no significant differences between

White and Asian women. For men, there were no statistical difference in likelihood for transplant between White versus Black or Hispanic men, but Asian men had a lower likelihood for LT than White men. Additional significant predictors outlined in Table 1. Conclusion: Accounting for listing characteristics, AC did not significantly impact interactions between gender and race on receipt of LT. However, AC may have improved access to LT amongst those without HCC but may have diminished access amongst those with HCC post-AC. Regardless of AC, there were important gender-race interactions requiring closer examination, particularly where Black and Hispanic women appear disproportionately negatively impacted. The same patterns were not noted across male racial categories, suggesting future research and interventions should target those at greatest risk. (Table Presented).

Public Health Sciences

Parke DM, **Kenney RM**, **Bogojevich J**, **El-Khoury C**, **Joshi S**, **Brar S**, **MacDonald L**, **Salib C**, **MacDonald N**, **Veve M**, and **Suleyman G**. Barriers to Improving Outcomes among People Experiencing Homelessness and People Who Inject Drugs Hospitalized for Complicated Infections. *Open Forum Infect Dis* 2023; 10:S864-S865. Full Text

D.M. Parke, Henry Ford Health, Detroit, MI, United States

Background. People experiencing homelessness (PEH) and people who inject drugs (PWID) experience health disparities and worse outcomes. Challenges include suboptimal medication use, loss to follow-up, and non-compliance due to social determinant of health (SDOH) barriers, including lack of stable housing and transportation, limited financial resources, substance use, and addiction. Methods. This quality improvement project aimed to address SDOH barriers among hospitalized PEH and/or PWID requiring ≥ 2 weeks of antibiotics to improve antibiotic compliance and outcomes in Detroit from 6/2022-4/2023. Interventions included antibiotic education, addiction medicine and pharmacy discharge medication cost inquiry consults when indicated, ensuring oral antibiotics were in hand at discharge, strengthening discharge planning between inpatient and ambulatory case managers (ACM), and referrals to community-based organizations to address SDOHneeds. Results. 34 patients were included (8 PEH, 11 PWID, 15 both); 3 who died in the hospital were excluded. Multiple individual and structural barriers and challenges to improving adherence and outcomes were identified (Table 1). Loss to follow-up was a significant challenge among this cohort, primarily due to patients self-discharging (29%) and being unreachable (52%). 10 (37%) patients were offered SDOH services (Table 2). Patients also had significant behavioral health/substance use disorder needs and utilized healthcare at a very high rate, with 29% having an ED revisit and 44% being readmitted within 30 days after discharge. Several structural and SDOH barriers existed, including limited staff capacity and limited placement options after discharge, resulting in suboptimal treatment delivery. Conclusion. AddressingSDOHbarriers for PEHand PWIDis challenging but vital to improving outcomes. Qualitative research should be conducted to understand these barriers. Having an interdisciplinary team comprising of infectious diseases, pharmacy, addictionmedicine, casemanagement and population health is critical to address patient needs holistically. Strengthening internal processes and building additional communitybased partnerships will be essential to better meet patient needs after discharge. (Table Presented).

Public Health Sciences

Shalabi F, **Novoa V**, **Bossick A**, **Su WT**, **Sitarik A**, **Wegienka G**, **Vilkins A**, and **Abood J**. 10357 Does Sexual Function Prior to Hysterectomy Impact Post-Operative Regret? *J Minim Invasive Gynecol* 2023; 30(11):S116-S117. Full Text

F. Shalabi, Obstetrics and Gynecology, Henry Ford Health, Detroit, MI, United States

Study Objective: To investigate the pattern of regret after hysterectomy as it relates to sexual function. Design: Prospective cohort study of women undergoing hysterectomy. Setting: Academic tertiary medical center. Patients or Participants: 456 women who underwent hysterectomy for benign indications. Interventions: None. Measurements and Main Results: Participants undergoing hysterectomy for benign indications and without concurrent urogynecologic surgery were recruited and asked to complete a baseline survey 2-weeks prior to their scheduled procedure, as well as seven follow-up surveys up to 12-months post-operatively. Using latent class analysis, overall regret scores were derived from five

validated survey questions and were used to determine patterns of regret following hysterectomy. Three classes were identified: high regret that remained high over time (Class 1); high regret that lowered over time (Class 2); and low regret that remained low (Class 3). Women who reported they were moderately dissatisfied with their sexual life prior to surgery were more likely to be in Class 1 relative to the Class 3 compared with women who were very satisfied with their sexual life (multinomial logistic regression, risk ratio=4.92, 95% CI: 1.48, 16.31). Conclusion: Self-reported sexual dissatisfaction prior to surgery is associated with postoperative regret. Gynecologists and their patients may take this into consideration during preoperative counseling.

Public Health Sciences
Wani K, **Gutta R**, **Mittal A**, **Jamil M**, **Springer K**, and **Kuriakose P**. Comparison of Maintenance Therapy Regimens of Patients Treated for Multiple Myeloma. *Blood* 2023; 142:6698. Full Text

Background: Despite significant progress in treatment modalities and improved survival and response rates in patients diagnosed with multiple myeloma (MM), it remains an incurable disease with a poor outcome, especially in high-risk groups. Though not all patients are eligible, autologous stem-cell transplantation (ASCT) remains an integral part of the treatment of patients with both newly diagnosed and relapsed MM. Regardless of whether patients receive a transplant, they do receive maintenance therapy, and recent evidence has demonstrated that maintenance therapies offer an advantage in progression free and overall survival. While Revlimid is the standard of care, data regarding the specifics of maintenance therapy in high-risk patients is limited and the overall impact of various regimens on survival needs to be further investigated. In our retrospective chart review we reviewed all adult patients with advanced MM within Henry Ford Cancer Institute in the last 10 years to determine the impact of maintenance therapy on progression free survival (PFS) and overall survival (OS). Methods: We conducted a retrospective chart review of adult patients with MM who underwent ASCT between January 1, 2012 to December 31, 2022. Those who received maintenance chemotherapy after transplant were included in the study. Patients who were lost to follow-up or who had largely incomplete records were excluded. Data points including age, ethnicity, cytogenetic analysis, risk category, maintenance regimen after transplant, last chemotherapy regimen, last follow-up, and date of death (if applicable) were recorded. Maintenance chemotherapy regimens were recorded as Revlimid versus other. Patients were split into 2 categories based on risk - high risk and standard risk. Kaplan-Meier plots were used to illustrate overall survival and time to relapse between groups for various variables. Statistical significance was set at $p<0.05$ Results: 158 patients were included in the study of which 44 were considered high-risk based on cytogenetics, 106 were standard-risk and 8 were missing. Most of the patients (n=137, 87.3%) received Revlimid, while 20 (12.7%) received maintenance therapy other than Revlimid, and for 1 patient, the type of maintenance therapy was unknown. Within the high-risk group, no statistical significance in OS or PFS was found between patients that received Revlimid versus those that did not. Furthermore, there was no statistical significance in OS and PFS within high risk versus standard cytogenetic risk groups. Conclusions: We did not see a difference in outcome based on risk and believe all patients would derive equal benefit from maintenance therapy We also did not see a difference in outcome between high and standard risk patients, and for the high-risk subgroup, there was a separation in curves suggesting that maintenance therapy has benefit compared to no maintenance.

Public Health Sciences
Wani K, **Gutta R**, **Mittal A**, **Jamil M**, **Springer K**, and **Kuriakose P**. Impact of Race on Progression-Free Survival and Overall Survival in Patients with Multiple Myeloma. *Blood* 2023; 142:6661. Full Text

Background: Multiple myeloma (MM) is a disorder of plasma cells. Management typically includes induction therapy, autologous stem-cell transplantation (ASCT) and maintenance therapy. Despite significant progress in treatment modalities and improved survival and response rates in patients diagnosed with MM, it remains an incurable disease with a poor outcome, especially in high-risk groups. Black patients have been shown to have a higher incidence of MM than white patients. Multiple studies have been done to examine racial disparities among white and black patients, specifically in overall survival (OS) and progression free survival (PFS). However, data has been overall inconclusive with some studies suggesting there is a difference in survival based on race, while other studies suggesting the opposite. Thus, racial disparities among white and black patients' needs to be further investigated. In

our retrospective chart review we reviewed all adult patients with advanced MM within Henry Ford Cancer Institute in the last 10 years to determine the impact of maintenance therapy on PFS and overall survival OS. Methods: We conducted a retrospective chart review of adult patients with MM who underwent autologous stem cell transplantation (ASCT) between January 1, 2012 to December 31, 2022. Those who received maintenance chemotherapy after transplant were included in the study. Patients who were lost to follow-up or who had largely incomplete records were excluded. Data points including age, gender, race, date of transplant, maintenance chemotherapy regimen, last follow-up, and date of death (if applicable) were recorded. Kaplan-Meier plots were used to illustrate overall survival and time to relapse between various races. Statistical significance was set at $p<0.05$. Results: There were 158 patients included in the study. Of the 158 patients, 82 (51.9%) were male, and 76 (48.1%) were female. The average age of patients included was 61.66 + 9.30 years, spanning from 32 to 78 years old. There were 71 (44.9%) White patients, 76 (48.1%) Black patients, and 11 (7.0%) patients that were of another race. There was no statistical significance in PFS and OS between Black, White and Other race categories. Conclusions: We did not see a difference in outcome based on race and believe all patients would derive equal benefit from maintenance therapy. Further prospective studies are warranted to examine racial disparities in patients with multiple myeloma.

Public Health Sciences

Yuengling K, Surie D, DeCuir J, Zhu Y, Gaglani M, Ginde AA, Gibbs K, Prekker M, Mohamed A, Johnson N, Peltan I, Bender W, Mallow C, Kwon JH, Lauring AS, Columbus C, **Vaughn I**, Safdar B, Chappell J, Baughman A, Swan SA, Johnson C, McMorrow ML, Self W, and Martin ET. Severity of Illness among Adults Hospitalized with Respiratory Syncytial Virus Compared with COVID-19 and Influenza-IVY Network, 25 Hospitals, 20 U.S. States, January 31, 2022 - April 11, 2023. *Open Forum Infect Dis* 2023; 10:S49. Full Text

K. Yuengling, GDIT/Centers for Disease Control and Prevention, Los Angeles, CA, United States

Background. Data on the severity of RSV-associated hospitalizations in adults compared with COVID-19- and influenza-associated hospitalizations are limited. We compared characteristics and clinical outcomes among adults hospitalized with RSV vs. COVID-19, and RSV vs. influenza. Methods. Adults aged ≥18 years hospitalized with acute respiratory illness (ARI) who tested positive for RSV, SARS-CoV-2, or influenza by nucleic acid amplification or antigen test were enrolled at 25 hospitals in 20 U.S. states participating in the Investigating Respiratory Viruses in the Acutely Ill (IVY) Network during January 31, 2022 to April 11, 2023. Patients with respiratory viral co-infections were excluded. Clinical data were abstracted from medical charts. Advanced respiratory support was defined as receipt of high flow nasal cannula, non-invasive ventilation, or invasive mechanical ventilation (IMV) during hospitalization. Characteristics were compared using Chi-square tests. Severe illness was compared for RSV vs. COVID-19 and RSV vs. influenza using multivariable logistic regression models adjusted for age, sex, race and ethnicity, number of chronic medical condition categories, admission date, and geographic region. Results. Of 8,334 hospitalized adults included, 6% tested positive for RSV (n=478), 80% for SARS-CoV-2 (n=6,664), and 14% for influenza (n=1,192). Median age of patients with RSV was 65 years (IQR = 53-75), similar to patients with COVID-19 and influenza (Table 1). Shortness of breath was more frequently reported by patients with RSV compared to patients with COVID-19 (78% vs. 62%, P< 0.0001) and influenza (78% vs 72%, P=0.005). Patients with RSV were more likely to be hypoxemic compared to those with COVID-19 (aOR 1.92, 95% CI = 1.52-2.42) (Table 2). Patients with RSV were also more likely to receive advanced respiratory support compared to those with COVID-19 (aOR 1.88, 95% CI = 1.51-2.33) or influenza (aOR 1.83, 95% CI = 1.4-2.4); however, use of IMV did not differ between these groups. Conclusion. In this prospective, multicenter network, prevalence of RSV among adults enrolled with ARI was lower than patients with COVID-19 and influenza; however, adults hospitalized with RSV experienced more severe respiratory illness compared to patients hospitalized with COVID-19 or influenza. (Table Presented).

Pulmonary and Critical Care Medicine

Fitzmaurice M, **Franco-Palacios DJ**, **Henderson R**, **Olexsey K**, **Pinto J**, **Poparad-Stezar A**, **Stagner LD**, and **Allenspach L**. A Case Series Describing Response to Rabbit Anti-thymocyte Globulin for the

Treatment of Bronchiolitis Obliterans Syndrome in Patients With Chronic Lung Allograft Dysfunction. *Am J Respir Crit Care Med* 2024; 209. Full Text

M. Fitzmaurice, Henry Ford Health, Detroit, MI, United States

Background: Chronic allograft dysfunction (CLAD) is a frequent complication and main reason for morbidity and decreased survival after lung transplant. Besides augmented immunosuppression and azithromycin, few other salvage therapies exist. Anti-thymocyte globulin therapy (ATG) is commonly offered to patients. The goal is to attenuate the rate of disease progression, stabilize or improve forced expiratory volume in 1 second (FEV1). Few centers have reported their treatment response with thymoglobulin and with varying doses. Methods: We reviewed all patients treated at our center with ATG for CLAD from 2015 to 2023. Their treatment response and side effects are described in 16 patients (BOS in 14, BOS + RAS in 2). Results: Median age 61, 81% were men, 15 patients underwent bilateral lung transplant. Most common indication was pulmonary fibrosis (6/16, 37%), followed by emphysema, cystic fibrosis and sarcoidosis. All patients received standard induction. Triple maintenance immunosuppression with calcineurin and cell cycle inhibitors and steroids were used in 68% of patients. Most patients (14/16, 87%) were taking azithromycin 250 mg three times weekly. The median cumulative ATG dose was 2.25 mg/kg with a median of 2 doses per course. Median time from transplant to BOS development was 24 months. Most patients (80%) had BOS stages 3 (9/16; 56%) and 4 (3/16, 18%). The median rate of FEV1 decline was - 142 mL/month. Eight patients had follow-up spirometry at 6 months post ATG. All eight (8/16, 50%) had attenuated decline or improvement in FEV1 in 4 and 4 patients, respectively. Four patients with shorter follow-up post ATG (2 to 4.5 months) have also responded to ATG (1 unchanged, 2 improved and 1 attenuated decline in FEV1). At the time of data censoring, responders had a median survival of 11 months. Baseline FEV1 was lower in non-responders. Five of them declined rapidly and died. Serum sickness was diagnosed in one patient post ATG. Three patients required dose reductions or slower infusion rate due to tolerability. Conclusions: Attenuated decline, stabilization, or improvement in FEV1 was seen in 68% (11/16) of patients at any time post ATG. Four patients with early BOS (stages 1 and 2) had improved FEV1 after ATG. Even in patients with late CLAD (BOS s-3 and 4, or on chronic oxygen therapy) ATG was of some benefit (partial response in 6/12, 50%). Our outcomes are consistent with previous reports and suggest that ATG at lower cumulative doses could benefit patients with CLAD.

Pulmonary and Critical Care Medicine

Hechtman RK, Munroe E, McLaughlin E, Horowitz J, Heath M, Creutz E, Posa P, **Jayaprakash N**, Blamoun J, Angus DC, Flanders S, and Prescott HC. Preventable Mortality Among Previously Healthy Patients With Sepsis. *Am J Respir Crit Care Med* 2024; 209. Full Text

R.K. Hechtman, Division of Pulmonary and Critical Care Medicine, University of Michigan, Ann Arbor, MI, United States

Rationale: Sepsis is the leading cause of in-hospital mortality. However, many patients with sepsis are elderly or have significant comorbidities, so it is unclear how many deaths may be preventable with optimal care. By contrast, deaths among patients who were healthy prior to hospitalization may reflect preventable deaths. We completed a multi-hospital study of previously healthy patients who died following sepsis to assess for evidence of preventability. Methods: Multicenter, retrospective cohort study of adults hospitalized with community-onset sepsis at 10 hospitals in the Michigan Hospital Medicine Safety Consortium (HMS-Sepsis), a Collaborative Quality Initiative within Blue Cross Blue Shield of Michigan. Data on sepsis hospitalizations were abstracted into the HMSSepsis registry by professional abstractors. We identified a cohort of previously healthy patients by serially excluding frail, multimorbid patients while retaining ≥10% of hospitalizations, then identified patients with 90-day mortality. We asked attending physicians at hospital systems with ≥5 previously healthy deaths to conduct chart reviews. They completed a 10-question survey evaluating patients' baseline health, quality of sepsis management, and potential preventability of death on a 6-point Likert scale from “definitely not preventable” and “slight evidence for preventability” to “definitely preventable”. Results: Of 10,380 patients in the HMS-Sepsis registry, 1,075 were classified as previously healthy. Of these, 109 (10.1%) died within 90 days, including 85 (7.9%) at hospitals with ≥5 previously healthy deaths. Physicians completed reviews for 36/85

(42.3%). Among these, mean age was 55.8, 58.7% were female, and 76.1% died during sepsis hospitalization. Patients were predominantly ASA Class I (N=11, 30.5%) or Class II (N=20, 55.5%) and 77.8% had an estimated life expectancy of >5 years if they had been cured of sepsis. 6 deaths (16.7%) were felt to be “possibly preventable”, 10 deaths (27.8%) had “slight evidence for preventability”, and 20 deaths (55.5%) were classified as “definitely not preventable”. Of deaths graded not preventable or having only slight evidence for preventability, the most common reason was severity of illness at presentation (N=22, 73.3%). Of the 6 deaths graded possibly preventable, the most common reasons were development of iatrogenic/nosocomial complications and surrogate decision maker elected to discontinue life sustaining measures. Conclusion: In this statewide cohort of sepsis hospitalizations, we identified previously healthy patients who died following sepsis. On physician review, nearly half of deaths were judged to have evidence of potential preventability. Most “not preventable” deaths were attributed to severity of illness at presentation, which suggests opportunity for community-level intervention.

Pulmonary and Critical Care Medicine

Kim RY, Rendle KA, Mitra N, **Neslund-Dudas C**, Greenlee RT, Burnett-Hartman AN, Honda SA, **Simoff MJ**, Schapira MM, Croswell JM, Jeon J, Meza R, Ritzwoller DP, and Vachani A. Longitudinal Adherence to Recommended Lung Cancer Screening Follow-up: A Multicenter Cohort Study. *Am J Respir Crit Care Med* 2024; 209. Full Text

R.Y. Kim, Pulmonary,Allergy,and Critical Care, University of Pennsylvania, Philadelphia, PA, United States

RATIONALE: Disparities in lung cancer screening (LCS) adherence by type of screening program and patient race across one round of LCS have previously been identified. However, real-world data are limited regarding adherence to LCS recommendations across multiple rounds of screening. We sought to determine adherence to Lung Imaging Reporting and Data System (Lung- RADS) recommendations across two rounds of LCS, stratified by program centralization and patient race. METHODS: We performed a multicenter retrospective cohort study of 55-75 year-old patients who formerly or currently smoked and received baseline LCS (T0) between 1/1/2015 and 6/30/2019 at healthcare systems within the Population-based Research to Optimize the Screening Process (PROSPR)-Lung Consortium. We collected electronic health record and billing data to calculate adherence to Lung-RADS recommendations across two LCS rounds (T1, T2) via a previously validated approach. Among individuals adherent at T1, T2 adherence was determined based on T1 Lung-RADS score if available or any follow-up chest CT or relevant diagnostic procedure within 15 months of T1. We used descriptive statistics and stratified multivariable modified Poisson regression models to assess differences in T2 adherence by LCS program type and patient race. RESULTS: Of the 12,310 individuals receiving LCS (median age: 65 years [IQR: 60-69 years]; 73.2% White; 14.1% Black), 7,755 (63.0%) were screened at decentralized and 4,555 (37.0%) at centralized programs. Adherence to Lung-RADS recommendations was higher at centralized compared to decentralized programs at both T1 (72.3% vs 41.4%; P<0.001) and T2 (74.0% vs 63.0%; P<0.001). Among the 6,506 individuals adherent at T1, there was no significant difference in T2 adherence by race at either decentralized (Black: 60.9% vs White: 63.5%; P=0.254) or centralized programs (Black: 74.7% vs White: 72.3%; P=0.599). Overall adjusted T2 adherence rates for Black and White patients were 54.5% vs 56.6% (P=0.138) and 86.9% vs 84.1% (P=0.095) at decentralized and centralized programs, respectively (Figure). When stratifying by baseline Lung-RADS score and controlling for all measured confounders, there was no difference in T2 adherence by race, except for slightly higher adherence among Black compared to White patients screened at centralized programs with positive baseline screens (adjusted risk ratio: 1.17 [95% CI: 1.05-1.31]). CONCLUSIONS: LCS program centralization is associated with increased longitudinal LCS adherence to Lung-RADS recommendations across two rounds of LCS. We did not observe any significant racial disparities in longitudinal LCS adherence among individuals who were adherent during the first round of screening, regardless of baseline screening result or program centralization.

Pulmonary and Critical Care Medicine

Kim RY, Rendle KA, Mitra N, **Neslund-Dudas C**, Greenlee RT, Burnett-Hartman AN, Honda SA, **Simoff MJ**, Schapira MM, Croswell JM, Meza R, Ritzwoller DP, and Vachani A. Racial Disparities in Annual Lung

Cancer Screening Follow-up: An Updated Analysis of a Multicenter Cohort Study. *Am J Respir Crit Care Med* 2024; 209. Full Text

R.Y. Kim, Pulmonary,Allergy,and Critical Care, University of Pennsylvania, Philadelphia, PA, United States

RATIONALE: We previously demonstrated that adherence to annual lung cancer screening (LCS) is higher at centralized compared to decentralized programs, with program decentralization associated with racial disparities in adherence. Here we report an updated analysis with a larger sample and additional years of follow-up data to examine racial disparities in LCS follow-up among individuals with negative baseline screens recommended for ongoing annual LCS. METHODS: We performed a multicenter retrospective cohort study of 55-75 year-old patients who formerly or currently smoked and received baseline LCS between 1/1/2015 and 6/30/2019 at healthcare systems within the Population-based Research to Optimize the Screening Process (PROSPR)- Lung Consortium. We restricted our analysis to individuals with negative baseline screens (Lung Imaging Reporting and Data System [Lung-RADS] 1 or 2) and excluded those with a prior lung cancer diagnosis and those who died within 30 months of baseline LCS. Using electronic health record and billing data, we identified all follow-up chest computed tomography (CT) imaging within 30 months of baseline LCS and evaluated the association between LCS program centralization and patient race with annual LCS adherence using descriptive statistics, multivariable modified Poisson regression, and kernel density plots. RESULTS: Of the 10,353 patients with a negative baseline screen (median age: 64 years [IQR: 60-69 years]; median pack-year smoking history: 40 [IQR: 32-52]; median Charlson Comorbidity Index: 1 [IQR: 0-2]), 7,507 (72.5%) identified as White, 1,499 (14.5%) as Black, and 6,063 (58.6%) as currently smoking. Of these individuals, 6,648 (64.2%) were screened at decentralized programs, and 3,705 (35.8%) at centralized programs. At decentralized programs, Black patients, compared to White patients, were less likely to have a follow-up chest CT within 10-15 months of baseline LCS (28.5% vs 40.3%; P<0.001) and more likely to have delayed imaging follow-up within 15-30 months (29.5% vs 23.7%; P<0.001) or no follow-up imaging within 30 months (36.3% vs 30.4%; P<0.001). In contrast, at centralized programs Black individuals had similar follow-up rates compared to White individuals at 10-15 months (67.5% vs 71.5%; P=0.360), 15-30 months (19.3% vs 15.0%; P=0.206), and no follow-up within 30 months (7.9% vs 7.6%; P=0.906; Figure). Multivariable adjusted adherence for Black and White patients were 30.8% vs 38.2% (P<0.001) and 71.1% vs 74.5% (P=0.172) at decentralized and centralized programs, respectively. CONCLUSIONS: This updated multicenter analysis confirms that program centralization is associated with reduced racial disparities in annual LCS adherence and represents a feasible systemic approach to promoting health equity in LCS.

Pulmonary and Critical Care Medicine

McIntosh J, **Moonka D**, and **Jayaprakash N**. When the Critical Illness Dominoes Fall, Unforeseen Events Post BRTO. *Am J Respir Crit Care Med* 2024; 209. Full Text

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Introduction: Gastric variceal bleeding is a complication of cirrhosis with portal hypertension (PHT) associated with significant morbidity and mortality. Management of suspected variceal bleeding includes resuscitation, medical therapy, endoscopic intervention and early consideration for advanced procedures such as TIPS, BRTO, surgery or liver transplant. Herein, we describe a rare adverse event following BRTO. Case: A 39 year old male with alcoholic cirrhosis and PHT, gastric varices (GV) and Gastroesophageal varices (GOV), presented to emergency department (ED) with hematemesis. He was intubated and transfused per massive transfusion protocol for large volume hematemesis. A Minnesota tube was placed emergently. Medical therapy was initiated including IV pantoprazole, octreotide, ceftriaxone. An endoscopy within 24 hours revealed a large GOV without stigmata of recent bleeding and GV with stigmata of recent bleeding. The GOV were banded and the GV identified as the source of hematemesis. To address the GV, he was taken to Interventional radiology (IR) for a Balloon-occluded Retrograde Transvenous Obliteration (BRTO) procedure. 12 hours later the patient developed abdominal distension, lactic acidosis and sudden rise in norepinephrine requirements refractory to fluid resuscitation. CT abdomen with contrast showed diffuse hypo enhancement and thickening of the bowel favored to be

related to mesenteric ischemia secondary to mesenteric venous hypertension (MVH). As a solution, a TIPS procedure was performed to reduce MVH. MICU course was complicated by ARDS, Renal failure required SLED, multiple transfusion of blood products for correction of coagulopathy. Discussion: A BRTO is an advanced procedure for intervention of GV as the source For GV as the source of the variceal bleeding in decompensated liver cirrhosis, advanced options such as BRTO are available as secondary prevention for further bleeding. This case highlights an adverse event associated with BRTO that has not been commonly reported. Intensivists, while not performing advanced procedures for these patients, must have heightened awareness of all complications and adverse events related to BRTO, because early recognition can result in expedited care to decrease severity of morbidity or mortality.

Pulmonary and Critical Care Medicine

Zahedi S, **Almajed M**, **Antishin S**, and **Bradley P**. A Breath-Taking Triad, Rare Case of Pseudo-Meigs Syndrome in a Patient With Benign Leiomyoma. *Am J Respir Crit Care Med* 2024; 209. Full Text

S. Zahedi, Internal Medicine, Henry Ford Health Care System, Detroit, MI, United States

Meigs syndrome is a clinical diagnosis based on the triad of ovarian tumors, ascites and pleural effusions. Meigs syndrome is an incredibly rare phenomenon and accounts for only 1% of ovarian tumors; most commonly ovarian fibromas. Pseudo-Meigs is a mimicker of Meigs syndrome occurring when other benign ovarian or pelvic tumors result in the same triad. The pathophysiology of Meigs syndrome is unclear. The most accepted theory is that the tumor results in pressure on the lymphatic system in the abdomen, resulting the accumulation of a transudative ascitic fluid which is subsequently transmitted to the pleural cavity. Since there are known cases of atypical Meigs syndrome, in which pleural effusions are present in the absence of ascites, another theory is that fluid enters the pleural cavity through stromal edema from lymphatic channels. The final postulated theory is that growth hormones such as vascular endothelial factor result in increased capillary permeability and accumulation of transudative fluid. We present a case of a 50-year-old woman who was sent to the hospital after anemia was noted on outpatient labs. Her medical history was notable for uterine fibroids. She reported menorrhagia but had no symptoms otherwise. An ultrasound revealed multiple uterine masses consistent with fibroids. She was hospitalized and managed symptomatically for anemia during which time she developed acute hypoxia. She underwent Chest CTA which revealed pulmonary edema, moderate bilateral pleural effusions, and small-volume ascites. Thoracentesis revealed a transudative effusion; gram stain, wet mount and cytology were all negative. Serum tumor markers including CEA, alpha fetoprotein, carbohydrate 19-9, and CA 125 were all negative. Liver function tests were within normal limits. She subsequently underwent a laparoscopic hysterectomy; biopsy of pelvic masses revealed benign leiomyomas. In the two years after the hysterectomy, she did not have re-accumulation of the ascites or pleural fluid. Newly-identified pleural effusions warrant an extensive workup and astute clinical acumen, especially in the absence of a clear etiology. Uterine tumors are a rare cause of pleural effusions and often understandably overlooked by clinicians. This case highlights the importance of considering uterine tumors when evaluating causes of transudative pleural effusions. Identifying Meigs Syndrome and Pseudo-Meigs Syndrome as potential causative factors allows a pathway towards recurrence prevention. Tumor resection results in resolution of ascites and pleural effusions and saves patients from unnecessary thoracentesis and paracentesis. Eliminating the iatrogenic risks of these procedures, such as pneumothorax, bleeding, infection, and bowel perforation.

Pulmonary and Critical Care Medicine

Zahedi S, **Parsons A**, Vahabzadeh A, and **Franco-Palacios DJ**. Success of Mechanical Circulatory Support as a Bridge to Treatment in Acute Right Ventricular Failure. *Am J Respir Crit Care Med* 2024; 209. Full Text

S. Zahedi, Internal Medicine, Henry Ford Health Care System, Detroit, MI, United States

Right ventricular (RV) failure is associated with significant morbidity and mortality and carries inhospital mortality rates estimated to be 70-75%. RV failure may occur secondary to acute inferior myocardial infarction, decompensated heart failure, pulmonary embolism, or pulmonary hypertension. While medical therapy aimed at optimizing the contractility of the heart, paired with preload and afterload management

are useful therapeutic modalities, in cases of significant right heart failure they are ineffective and mechanical support may be needed. A 40-year-old man with a past medical history of hypertension, polysubstance abuse and previous pulmonary embolism (PE) presented to the emergency department after being found wandering in the street confused. Patient was hypoxic, agitated, and hypotensive. A CT PE showed a large extrinsic thrombus in the distal left main PA and causing complete occlusion of the left lower lobe arteries as well as lobar and segmental thrombus in the right lower lobe. The main PA was dilated, and the RV wall was hypertrophic. Troponins were elevated (1800 ng/L). Echocardiogram showed moderate enlarged RV with diminished RV systolic function. RV systolic pressure was unable to be estimated. Patient was intubated in the ED and on high intensity heparin. His hypotension initially responded to IV fluids but later became hemodynamically unstable requiring rapid increase in norepinephrine. Due to worsening RV failure, he was placed on VA ECMO (fem-fem configuration) with rapid hemodynamic improvement and as a bridge to percutaneous thrombectomy. After pulmonary angiography revealed chronic thrombus attempts for thrombectomy were aborted. Inotropic support with milrinone and addition of afterload reduction with inhaled nitric oxide allowed for weaning off VA ECMO. Sildenafil and IV furosemide were started, and the patient was successfully decannulated. The initial concern was for acute on chronic PE. Although initially VA ECMO in this case was used for hemodynamic compensation to attempt percutaneous thrombectomy, it ultimately served as a bridge to PAH therapy in a patient presenting with new diagnosis CTEPH and RV failure. His urine was positive for cocaine. It is possible that patient RV failure was precipitated by acute cocaine toxicity inducing vasoconstriction in the setting of unknown chronic thromboembolic pulmonary hypertension. The patient will follow-up in the PH clinic to decide on appropriate vasodilator therapy and referral to a CTEPH center. VA ECMO's ability to provide rapid and complete off-loading of the right heart as a bridge to treatment should be considered in medically refractory cases and rapid cardiovascular decompensation.

Radiation Oncology

Ghanem A, **Rose CM**, **Li P**, and **Elshaikh MA**. INFLUENCE of COMORBIDITY on the RISK of DEATH: A SINGLE INSTITUTION STUDY of 1915 WOMEN with EARLY-STAGE UTERINE CANCER. *Int J Gynecol Cancer* 2023; 33:A160. Full Text

M.A. Elshaikh, Henry Ford Cancer Institute, Detroit, United States

Introduction/Background The study goal is to utilize a validated comorbidity scoring to determine its impact on recurrence-free (RFS), disease-specific (DSS) and overall survival (OS) in women with early-stage uterine endometrioid carcinoma (EC). Methodology We identified 1915 patients with EC stages I-II who underwent hysterectomy. Charlson Comorbidity Index (CCI) at time of hysterectomy was calculated by trained physician. Survival endpoints was correlated with CCI. Univariate and multivariate modeling with Cox regression analysis was used to determine significant predictors of OS, DSS, and RFS. Results After a median follow-up of 104 months, 529 deaths were recorded, only 87 patients died from EC [16%], and 442 [84%] from other causes). Median CCI score for the study cohort was 0 (range, 0 to 12). On the basis of CCI, patients were grouped as follows: 0 score (group 1, n=1083), score 1-2 (group 2, n = 690), and score of 3 or more (group 3, n = 142). By CCI grouping, the 5-year RFS, DSS, and OS were 94%, 96%, and 97% for group 1, 92%, 94%, and 78% for group 2, and 86%, 95% and 60% for group 3 (P< 0.0001). The cause of death in the first 10 years after hysterectomy in our study was mainly non-uterine cancer-related (80% vs. 20% for uterine cancer-related) causes. On multivariate analyses, higher CCI, lymphovascular space invasion (LVSI), higher tumor grade, and older age were significant predictors of shorter OS. On multivariate analysis for DSS and RFS, only high tumor grade and LVSI were significant predictors. Conclusion The cause of death for women with early-stage EC is mainly nonuterine cancer-related. Comorbidity score is a significant predictor of OS in our study cohort. Comorbidity scores may be useful as a stratification factor in any prospective clinical trial for women with early-stage EC.

Radiation Oncology

Gilbert M, **Zhu S**, **Shah M**, **Siddiqui S**, **Rogers LR**, and **Siddiqui F**. INSTITUTION SPECIFIC CLINICAL TRIAL MATCHING WEB APPLICATION FOR CENTRAL NERVOUS SYSTEM METASTASES. *Neuro Oncol* 2023; 25:v156. Full Text

M. Gilbert, Henry Ford Health System, Detroit, United States

BACKGROUND: Current clinical trials evaluating treatment options for patients with brain metastases are tailored to a number of clinical factors, including type of underlying cancer, number of brain metastases, size and volume of brain metastasis, prior treatment, and genomic characterization. A multidisciplinary brain metastasis tumor board was established at our institution in January 2023. Subsequently, an institution specific clinical trial matching web application was developed in-house to screen and match subjects for trials accruing at our institution. METHODS: We reviewed our institution's list of phase III surgical, radiation, and medical oncology clinical trials specific for brain metastasis to identify the most discriminating inclusion criteria that can be used as a basis for branching and differentiation. These disease specific trials were then individually assessed according to these criteria and these results were populated in a common separated value (CSV) file. RESULTS: A web application was created using Python for analysis of the CSV and incorporating branching logic. HTML, CSS, and JavaScript were used for building the webpage interface. The web application is hosted on our institutional server and can be utilized to search available clinical trials for each patient being presented during tumor board. CONCLUSION: We developed an institution specific web application that can be used to screen patients for various clinical trials. By developing this application and hosting it internally, we are able to edit the components at our discretion. The methodology for this web-build can be applied to other disease sites or institutions. This web application is useful for screening our institution's clinical trial portfolio to identify potential gaps, and can also be used to avoid competing trials. This web application significantly reduces the time to identify protocol eligibility and has increased clinical trial enrollment.

Radiation Oncology

Meng Y, Mughal N, **Datta I**, Nuga O, **Irtenkauf S**, **Hasselbach L**, **Quenneville K**, **Brown S**, and **DeCarvalho A**. GLIOBLASTOMA PATIENT SPECIFIC TRANSCRIPTOME REMODELING IN RESPONSE TO MDM2 ANTAGONIST TREATMENT OF WILD-TYPE P53 CANCER STEM CELLS IS ASSOCIATED WITH SENSITIVITY AND STRATEGIES FOR COMBINATION THERAPY. *Neuro Oncol* 2023; 25:v224-v225. Full Text

Y. Meng, Henry Ford Health, Detroit, United States

Over 70% of glioblastomas are p53 wild-type and these patients could benefit from p53 reactivation treatment. Here we determined the sensitivity of a glioblastoma patient-derived cancer stem cells (CSCs) panel to three MDM2 antagonists (MDM2a) to test to what extent transcriptional reprogramming is affected by genomic background and correlates to response to acute treatment with MDM2 antagonists. IC50 concentrations and area above the curve (AAC) were measured from dose response curves obtained from 4 and 7-day treatment. The inhibitors were specific to wt-p53 CSCs, but these presented a wide range of sensitivity. Seven wt-p53 CSCs were treated RG7112 IC50 concentrations or DMSO control for 24h (n=4). RNA was isolated for Illumina Truseq stranded mRNA libraries sequenced at 30M depth. Quantified raw counts were processed using NOISeq R package to determine differentially expressed genes (DEG) between control and treated samples. In addition to the expected high representation of upregulated p53 targets in all cell lines, we observed significan cell specific transcriptome alterations, including enrichment of survival pathways, such as mTOR, ERK and NFkB in the less sensitive CSC lines, which did not readily correlate with the individual genomic landscapes. E2F targets, G2-M cell cycle check point and DNA-repair pathways were highly enriched in the downregulated genes. Combination of MDM2a with radiation treatment (RT) was synergistic to a subset of CSCs. As validation we found that MDM2a treatment was effective in sensitizing a resistant orthotopic mouse glioblastoma PDX to fractionated RT, with maximum efficacy when treatment started 24h prior to RT vs simultaneously (Log-rank Mantel-Cox test: p=0.0006 vs 0.0277). The integration of the treatment-mediated transcriptional patterns with differential sensibility to MDM2 antagonists and genomic landscape of the CSC panel provides a platform to identify targets for combination therapies, which is the most promising clinical application of the reactivation of wt-p53 in GBMs.

Radiation Oncology

Nagaraja T, **Datta I**, **Morosini N**, **Bartlett S**, Ayloo B, **Cabral G**, Avritt F, **Hasselbach L**, **Parasar P**, **De Carvalho A**, **Singh J**, **Knight R**, **Brown S**, **Ewing J**, **Noushmehr H**, and **Lee I**. IMAGING, HISTOLOGICAL AND MOLECULAR CHARACTERIZATION AND COMPARISON OF POST-ABLATION

RECURRENT TUMOR WITH THE PRIMARY TUMOR IN A PRECLINICAL GLIOBLASTOMA MODEL. *Neuro Oncol* 2023; 25:v301. Full Text

T. Nagaraja, Henry Ford Health, Detroit, MI, United States

Recurrent glioblastoma (rGBM) is highly aggressive and invasive. A reliable preclinical model that recapitulates these features is not presently available. The objective was to generate a preclinical rGBM model, characterize and compare its imaging, histological and molecular signatures in comparison to the primary tumor. Immune-suppressed, RNU/RNU female rats were implanted with U251N tumor cells in one brain hemisphere (n=33). Tumor progression in all rats was followed by longitudinal dynamic contrast enhanced-magnetic resonance imaging (DCE-MRI). In 24 rats the tumor was ablated under diffusion-weighted imaging (DWI)-guided laser interstitial thermal therapy (LITT) at post-implantation 2-weeks. Cohorts from twenty ablated rats were euthanized at post-LITT 24 h, 2- and 4-weeks and, along with 5 unablated controls, used for hematoxylin and eosin (H&E) and Ki67 staining. Tissues from 4 other unablated and 4 recurrent tumors at post-LITT 2-weeks were used for RNAseq. All the rats survived the LITT procedure. Unablated controls showed increased tumor burden by postimplantation 2 weeks and were euthanized. In the LITT group, MRI showed little tumor tissue at 24 h, evidence of recurrence at 2 weeks and significant tumor tissue at 4 weeks and matched with histological evidence for tumor recurrence. Compared to the primary tumor, H&E staining showed increased vascular hyperplasia, mitotic bodies and hypoxic regions with pseudopalisading necrosis in the recurrent tumor. Increased KI67 staining in recurrent tumors suggested higher rates of proliferation and evidence of infiltration into host tissue. Pathway analyses demonstrated differentially expressed genes in the canonical pathways of hypoxia-inducible factor-alpha (HIF-1α), nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) and OX40 signaling. The genes for the following functions were significantly affected: cell cycle, cellular movement and cell morphology. Reliable preclinical rGBM models are few. These data suggest that this model replicates the features of human rGBM and can be useful in testing putative anti-glioma therapies.

Research Administration

Sabbah H, **Gupta RC**, **Singh-Gupta V**, **Castle K**, and **Lanfear DE**. Mitochondrial function is abnormal in circulating blood monocytes of patients with chronic heart failure. *Eur Heart J* 2023; 44:1. Full Text

[Sabbah, H.; Gupta, R. C.; Singh-Gupta, V.; Castle, K.; Lanfear, D. E.] Henry Ford Hosp, Detroit, MI USA.

Rheumatology

Ibrahim H, and **Meysami A**. A Comprehensive Retrospective Analysis of Polymyalgia Rheumatica in Long COVID Patients at an Academic Medical Center in the Midwest. *Arthritis Rheumatol* 2023; 75:444-445. Full Text

[Ibrahim, Hanan] Henry Ford Hlth Syst HFHS, Detroit, MI USA. [Meysami, Alireza] Henry Ford Hlth, Detroit, MI USA.

Surgery

Fadel R, **Almajed MR**, **Parsons A**, **Kalsi J**, **Shadid AM**, **Maki M**, **Jones C**, **Williams C**, **Aronow H**, **Tanaka D**, **Nemeh H**, **Fuller B**, **Alqarqaz M**, **Koenig G**, **Villablanca P**, **Frisoli T**, **O'Neill B**, **Khandelwal A**, **Cowger J**, **Grafton G**, **Kim H**, **O'Neill W**, **Alaswad K**, and **Basir B**. TCT-302 Feasibility and Outcomes of a Cardiology-Based Extracorporeal Membrane Oxygenation Service. *J Am Coll Cardiol* 2023; 82(17):B120. Full Text

Background: There has been a significant increase in the use of veno-arterial extracorporeal membrane oxygenation (VA-ECMO). ECMO programs have typically been led by cardiothoracic surgery teams, and there is little evidence on alternative care models. Methods: We performed a retrospective analysis of patients treated with peripheral VA-ECMO at a tertiary care center from 2018 to 2022. The primary outcome was death while on ECMO or within 24 hours of decannulation. Results: A total of 244 patients were included in the analysis (median age 61 years; 28.7% female). Interventional cardiologists performed 91.8% of cannulations, and 84.4% of patients were managed primarily by a cardiology service

comprising interventional cardiologists, cardiac intensivists, or advanced heart failure cardiologists. The most common indications for ECMO were acute myocardial infarction (34.8%), decompensated heart failure (30.3%), and refractory VT/VF (10.2%). ECMO was utilized for peri-procedural arrest in 26.6% of patients. The median (IQR) pre-ECMO SAVE score was 0.0 (–4.0 to 3.0), and median (IQR) SOFA score was 13.0 (10.0 to 16.0). Forty-six percent of patients survived through decannulation; the majority of patients were decannulated percutaneously in the cardiac catheterization laboratory. There was no difference in survival following cannulation by a cardiac surgeon vs cardiologist (50% vs 45%; P = 0.90). Complications included arterial injury (3.7%), compartment syndrome (4.1%), cannulation site infection (1.2%), stroke (14.8%), AKI (52.5%), dialysis (22.5%), access site bleeding (16%), and need for blood transfusion (83.2%). Positive independent predictors of death while on ECMO or within 24 hours of decannulation included elevated initial serum lactate (OR per mmol/L increase: 1.13; 95% CI: 1.04-1.23; P < 0.01) and SOFA score (OR per 1 unit increase: 1.27; 95% CI: 1.15-1.40; P < 0.01), while SAVE score (OR per 1 unit increase: 0.92; 95% CI: 0.86-0.99; P = 0.03) and 8-hour lactate clearance (OR per % decrease: 0.98; 95% CI: 0.97-0.99; P < 0.01) were negative predictors of this outcome. Conclusion: The use of a cardiology-based ECMO service is feasible. As ECMO services and indications expand, the use of cardiology-based ECMO care may be practical for select centers. Categories: CORONARY: Hemodynamic Support and Cardiogenic Shock

Surgery
Hider A, Hassett KP, Pizzo CA, Finks JF, O'Neill SM, and **Varban OA**. Value Analysis of Improving Diabetes and Obesity on Total Episode Payment Outcomes after Common Surgical Procedures. *J Am Coll Surg* 2023; 237(5):S186-S187. Full Text

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Introduction: Total episode payments across surgical episodes of care provide healthcare systems with information on ways to reduce costs and optimize value when treating certain conditions. Although obesity and type 2 diabetes (T2D) are often associated with perioperative complications, the impact on total episode payments for common surgical procedures remains unclear.
Methods: The analysis included 90-day claims-based episodes of care for patients who underwent surgery between 1/1/2015 and 12/31/2021 for non-cancer colectomy, abdominal/groin hernia repair, hysterectomy, or total knee or hip replacement (total n=235,324). Patients with a diagnosis of obesity and T2D (n=20,510) were compared with patients without either diagnosis (N=214,814). Measures including 90-day price-standardized total episode payments, readmission payments, emergency room (ER) payments, and surgery length of stay (LOS) were calculated. Results: Patients with obesity and T2D had higher price-standardized 90-day total episode payments than the comparison group, regardless of procedure type. Obesity and T2D were also associated with significantly longer LOS, as well as higher rates of ER visits and readmissions (Figure 1). The impact of diabetes and obesity was greatest with hernia repair, with a total episode payment difference of $9,553. Hernia repair also had the largest between-group differences in rates of readmissions and ER visits, which were 8.7% and 6.6%, respectively. Conclusion: Obesity and diabetes has a significant impact on total episode payment costs for common surgical procedures and doubles the cost of hernia repair. Maximizing weight loss and inducing diabetes remission through intensive focused efforts, including metabolic surgery, should be considered before elective procedures.

Surgery
Ichkhanian Y, **Veracruz N**, **Al-Haddad M**, Albunni H, Schlachterman A, Gouda Z, Canakis A, Kim R, D'Souza L, Khashab M, **Nimri F**, **Ashraf T**, **Faisal MS**, **Jomaa D**, **Dababneh Y**, **Rehman S**, **Rizwan A**, **Singla S**, **Alsheik E**, **Ginnebaugh B**, **McFarlin K**, **Piraka C**, and **Zuchelli T**. Management of Patients After Failed Gastric Peroral Endoscopic Myotomy: A Multi-Center Study. *Am J Gastroenterol* 2023; 118(10):S1410-S1411. Full Text

[Ichkhanian, Yervant; Veracruz, Nicolette; Al-Haddad, Mohammad; Nimri, Faisal; Ashraf, Taha; Faisal, Muhammad Salman.; Jomaa, Diana; Dababneh, Yara; Rehman, Sheema; Rizwan, Aliza; Singla, Sumit; Alsheik, Eva; Ginnebaugh, Brian; McFarlin, Kellie; Piraka, Cyrus; Zuchelli, Tobias] Henry Ford Hosp,

Detroit, MI USA. [Albunni, Hashem] Indiana Univ, Detroit, MI USA. [Schlachterman, Alexander; Gouda, Zane] Univ Maryland, Baltimore, MD USA. [Canakis, Andrew; Kim, Raymond] Stony Brook Univ Hosp, Stony Brook, NY USA. [D'Souza, Lionel; Khashab, Mouen] Johns Hopkins Med, Baltimore, MD USA. System; University System of Maryland; University of Maryland Baltimore; State University of New York (SUNY) System; State University of New York (SUNY) Stony Brook; Stony Brook University Hospital; Johns Hopkins University; Johns Hopkins Medicine

Surgery
Jamali T, **Alvelo-Rivera M**, and **Elatrache M**. A Rare Case of Esophageal Obstruction After Rupture of an Esophageal Duplication Cyst. *Am J Gastroenterol* 2023; 118(10):S2187-S2188. Full Text

[Jamali, Taher] Henry Ford Hlth, Farmington Hills, MI USA. [Alvelo-Rivera, Miguel] Henry Ford Hlth, Detroit, MI USA. [Elatrache, Mazen] Henry Ford Hosp, Detroit, MI USA. System; Henry Ford Hospital

Surgery
Jamali T, **Nassif G**, **Kwon D**, and **Pompa R**. A Rare Case of Solid Pseudopapillary Tumor of the Pancreas in a Male Patient. *Am J Gastroenterol* 2023; 118(10):S1437-S1437. Full Text

[Jamali, Taher] Henry Ford Hlth, Farmington Hills, MI USA. [Nassif, Georges; Kwon, David] Henry Ford Hlth, Detroit, MI USA. [Pompa, Robert] Henry Ford Hosp, Detroit, MI USA. System; Henry Ford Hospital

Surgery
Manivannan A, Liapakis AM, Diehl AM, Verna E, Kumar V, **Salgia RJ**, **Wu T**, Lu M, Parikh ND, and **Jesse M**. INTERACTIONS BETWEEN RACE/ETHNICITY AND GENDER IN LIVER TRANSPLANTS: DO ACUITY CIRCLES MATTER? *Hepatology* 2023; 78:S277. Full Text

A. Manivannan, Henry Ford Health, New Haven, CT, United States

Background: Despite continued efforts, there are welldocumented disparities in liver transplantation (LT) from listing through post-transplant. National policies on allocation of deceased donor liver transplants (DDLT) aim to provide consistent and equitable access. However, the impacts of Acuity Circles (AC) and interactions between race and gender on delisting due to deterioration/death or receipt of DDLT have been minimally explored. Methods: Using data from the United Network for Organ Sharing (UNOS), we studied listed adults for DDLT from April 3, 2017, to October 4, 2022, a 60-month period (30 mo pre- and post-AC). Fine-Gray subdistribution hazard model was used to study AC impact on LT while delisting due to deterioration/ death was used as a competing risk. The model focused on AC indicator by race by gender interactions, as well as AC by hepatocellular carcinoma (HCC) diagnosis interactions. Results: 59,592 patients (30,202 pre-AC, 29,390 post-AC) were studied. No 3- way (AC X race X gender) interaction was detected, indicating effect of race and gender on LT was consistent pre- and post-AC periods. However, there were significant gender by race or AC by HCC interactions (Table 1): patients with HCC had greater chance for LT than non-HCC, though post-AC this effect was reduced. AC increased LT 25% in patients without HCC. Across gender, White, Black, and Hispanic men were more likely to receive transplant compared to their female counterparts. Within gender, Black and Hispanic women were less likely to receive transplant than White women, with no significant differences between White and Asian women. For men, there were no statistical difference in likelihood for transplant between White versus Black or Hispanic men, but Asian men had a lower likelihood for LT than White men. Additional significant predictors outlined in Table 1. Conclusion: Accounting for listing characteristics, AC did not significantly impact interactions between gender and race on receipt of LT. However, AC may have improved access to LT amongst those without HCC but may have diminished access amongst those with HCC post-AC. Regardless of AC, there were important gender-race interactions requiring closer examination, particularly where Black and Hispanic women appear disproportionately negatively impacted. The same patterns were not noted across male racial categories, suggesting future research and interventions should target those at greatest risk. (Table Presented).

Surgery

Miyake K, **Al-Juburi S**, **Young K**, **Chau LC**, **Kitajima T**, **Wickramaratne N**, **Nassar A**, **Yoshida A**, **Moonka D**, **Venkat D**, **Abouljoud MS**, and **Nagai S**. HIGHER INTRA-OPERATIVE PEAK LACTATE VALUE MAY BE ASSOCIATED WITH PROLONGED HEMODIALYSIS REQUIREMENT AFTER LIVER TRANSPLANT ALONE IN PATIENTS WITH PRE- TRANSPLANT KIDNEY DYSFUNCTION. *Hepatology* 2023; 78:S314-S315. Full Text

[Miyake, Katsunori; Al-Juburi, Saleh; Young, Kathleen; Chau, Lucy Ching; Kitajima, Toshihiro; Wickramaratne, Nikuwa; Nassar, Ahmed; Yoshida, Atsushi; Moonka, Dilip; Venkat, Deepak; Abouljoud, Marwan S.; Nagai, Shunji] Henry Ford Hosp, Detroit, MI USA.

Surgery

Youssef RM, **Obri M**, **Todter E**, **Salgia RJ**, and **Jesse M**. PSYCHOSOCIAL AND MEDICAL FACTORS ASSOCIATED WITH RECEIPT OF LIVER TRANSPLANT IN LISTED PATIENT WITH HEPATOCELLULAR CARCINOMA. *Hepatology* 2023; 78:S285. Full Text

R.M. Youssef, Henry Ford Health, United States

Background: Patients with hepatocellular carcinoma (HCC) are less likely to receive liver transplantation (LT) than patients without HCC. The aim of this study was to explore sociodemographic, psychosocial, and medical factors associated with progression to LT, versus delisting, in patients with HCC listed for LT. Methods: Prospectively maintained database from a single center tracking all patients diagnosed with HCC from 2005-2022. Amongst those listed for LT, the main outcome was receipt of transplant (versus delisting for any reason). Predictors included sociodemographic, psychosocial, and medical characteristics. Given the exploratory nature, predictors were included in the final multivariable logistic model if univariable logistic regression results approached significant ($p < 0.1$). Results: Among 341 patients listed with HCC; mean age 59.6 years (SD 6.8); 265 male (77.7%); racial composition was 246 White (72.1%), 50 Black (14.7%), and 45 “other” (13.2%). 261 (76.5%) underwent LT, 80 (23.5%) were delisted (any reason, majority due to disease progression/ medical deterioration). Variables included in the model were age at transplant listing, marital status, whether the patient underwent treatment for HCC, and histories of tobacco use, alcohol abuse, hepatic encephalopathy, diabetes, hypertension, and dyslipidemia. Final model presented in Table 1. Significant predictors of receipt of LT in the final model included younger age at transplant listing, no history of tobacco use, and no history of alcohol abuse. Conclusion: HCC patients are often delisted due to HCC disease progression and/or death while on the LT waitlist. Our data suggests that patients who are listed at a younger age, do not have a history of tobacco use, or of alcohol abuse are more likely to successfully receive LT. Also, contrary to hypotheses, race/ethnicity was not significant suggesting improved equity across these groups. (Table Presented).

Urology

Dominguez LBR, Medina IJ, Matamoros-Volante A, **Rambhatla A**, Mendez MGF, Villar L, Pérez ADG, Delgadillo D, Rosas IM, and Agarwal A. REPEATED ANTIOXIDANT SUPPLEMENTATION OF CULTURE MEDIA IMPROVES BLASTOCYST FORMATION IN HOMOLOGOUS SIBLING ZYGOTES FROM INFERTILE PATIENTS UNDER DIFFERENT O₂ CONCENTRATIONS. *Fertil Steril* 2023; 120(4):E213-E213. Full Text

[Ramirez Dominguez, Liliana Berenice] Citmer Reprod Med, Mexico City, EM, Mexico. [Jimenez Medina, Israel] CITMER Reprod Med, Mexico City, DE, Mexico. [Matamoros-Volante, Arturo] Inst Biotecnol, Cuernavaca, Mexico. [Rambhatla, Amarnath] Henry Ford Hlth Syst, Vattikuti Urol Inst, Dept Urol, Detroit, MI USA. [Figueroa Mendez, Maria Guadalupe; Garcia Perez, Alejandro Daniel; Delgadillo, Daniela] CITMER, Miguel Hidalgo, DF, Mexico. [Villar, Lina] Citmer, Reprod Med, Mexico City, DF, Mexico. [Maldonado Rosas, Israel] CITMER, Mexico City, DE, Mexico. [Agarwal, Ashok] Cleveland Clin, Cleveland, OH USA. Foundation

Urology

El Sharu H, **Jamil M**, Singh S, Cowles S, Liles DK, and Zweigle J. Mortality and Comorbidities of Covid-19 Patients with Immune Thrombocytopenic Purpura - a Review of the National Database 2019-2020. *Blood* 2023; 142:2595. Full Text

Introduction: Immune thrombocytopenic purpura (ITP) is a diagnosis of exclusion that is characterized by isolated thrombocytopenia with a generalized purpuric rash. If there is a known case for the ITP, it is referred to as secondary ITP. Secondary ITP may often be caused by drugs, systemic immunologic, or infectious diseases. Covid-19 is a disease caused by the SARS-CoV-2 virus, which caused a pandemic in 2020, affecting hundreds of millions of people worldwide. There have been several different hematologic conditions associated with this viral infection, including deep vein thromboses, pulmonary emboli, and many patients with ITP induced by Covid-19. With several case reports and case series available on these patients, the specifics behind the strength of the association, mortality of the patients, and their comorbidities have not been previously explored. Methods: Using the national inpatient sample from the years 2019-2020, we analyzed adult hospitalized patients with ITP and Covid-19 based on their International Classification of Diseases - 10 clinical modification codes. We calculated the odds ratios for patients with Covid-19 being diagnosed with ITP compared to other hospitalized patients. Additionally, we calculated the odds of several complications, treatments, as well as concurrent conditions in patients with Covid-19 and ITP. The complications measured were epistaxis or hemoptysis, intracranial hemorrhage (ICH), non-intracranial hemorrhage (nICH), deep vein thrombosis (DVT), pulmonary embolism (PE), and death. Treatments measured were transfusion with either red blood cells (RBC) or platelets. The concurrent conditions evaluated were systemic lupus erythematosus (SLE), hepatitis C and heparin-induced thrombocytopenia (HIT). Results Out of the 115,150 hospitalized patients with ITP included in the database, 0.02% of them were diagnosed with Covid-19. The odds of a patient with Covid-19 being diagnosed with ITP were lower than those for other hospitalized patients (OR=0.860 [0.787-0.941], p=0.001). The mean age for patients with ITP diagnosed with Covid-19 was 64.1 compared to 60.9 in patients without Covid-19 (p=0.001). Hospitalized patients with ITP who were also diagnosed with Covid-19 were at a higher risk of developing epistaxis (OR: 1.45 [1.01-2.07], p=0.042), pulmonary embolism (OR: 2.22 [1.35-3.66], p=0.002), and death (OR: 4.39 [3.33-5.80], p<0.001) compared to those without Covid-19. They were not at higher odds of developing a DVT (OR: 1.25 [0.798-1.97], p=0.325), ICH (OR: 0.158 [0.0160-1.56], 0.114) or nICH (OR: 1.03 [0.678-1.55], p=0.905). They were not significantly more or less likely to get transfused with RBC (OR: 0.816 [0.585-1.14], p=0.231) or platelets (OR: 1.14 [0.865-1.53], p=0.337). The ITP patients with concurrent Covid-19 were also not more likely to suffer from SLE (OR: 0.737 [0.453-1.20], p= 0.222), Hepatitis C (OR: 0.760 [0.392-1.47], 0.416), or HIT (OR: 1.16 [0.181-7.49], p=0.872). Conclusion Hospitalized patients with Covid-19 were at a lower risk of being diagnosed with concurrent ITP than other hospitalized Covid-19 patients. Those with ITP who also had Covid 19 had significantly higher odds of complication of bleeding with epistaxis or hemoptysis as well as a higher risk of pulmonary embolism and death. However, they were not at higher risk of hemorrhage elsewhere or DVT. They were not treated with transfusions differently and having SLE, hepatitis C or HIT did not place hospitalized patients with ITP at a higher risk of developing Covid-19.

Urology

El Sharu H, Zweigle J, **Jamil M**, Singh S, Cowles S, and Liles DK. Outcomes of Sarcoidosis on Patients with Sickle Cell Disease - a Review of the National Inpatient Database 2016-2020. *Blood* 2023; 142:1135. Full Text

Introduction: Sickle Cell Disease (SCD) is an inherited hemolytic disorder due to an autosomal recessive mutation affecting mainly African Americans. SCD can lead to various complications, including Sickle Cell Crisis (SCC), Acute Chest Syndrome (ACS), strokes, and different osseous complications. Notably, these complications can be provoked using steroids. Sarcoidosis is a multisystem inflammatory disorder that is characterized by the presence of bilateral hilar lymphadenopathy that is commonly treated with steroids. Unfortunately, it is also preferentially affecting African Americans. The complication rates in patients with both diseases have rarely been described. We aim to describe the effect of sarcoidosis on the mortality and complication rates of admitted patients with SCC. Methods: Using the National Inpatient Sample (NIS) 2016-2020, we analyzed adult SCC and ACS hospitalizations with and without sarcoidosis using International Classification of Diseases - 10 Clinical Modification (ICD-10-CM) codes. The primary

outcome was inpatient mortality. Secondary outcomes were inpatient morbidities, mean length of stay (LOS), and mean total hospital charge (THC). A multivariate logistic regression and linear regression analyses were used to adjust for potential confounders. Results: Out of 359655 patients hospitalized with SCC, only 4.6% had concomitant sarcoidosis. Of these, 70% were females, with a mean age of 38.4 compared to an average age of 32 in patients without sarcoidosis (p-value <0.05). The mean LOS for patients with sarcoidosis and SCC was 6.4 days, while it was 5.1 days for patients without sarcoidosis (p-value 0.001). While adjusting for common comorbidities and patients' characteristics, patients with SCC and sarcoidosis did not have a statistical mortality difference compared to patients without sarcoidosis [adjusted odds ratio (aOR): 2.3, CI: 0.4-14). On stratified analysis, patients with ACS and sarcoidosis had increased odds of mortality with an aOR of 6.68, CI: 1.1-39.7, and a p-value of 0.037. Moreover, amongst patients who had SCC, patients with concomitant sarcoidosis had a higher risk of acute coronary syndrome (aOR: 5.1, CI 1.24-21.0) and avascular necrosis (aOR: 1.57, CI: 1.12-2.20). There were no statistically significant differences in the odds of ischemic strokes, transient ischemic attacks, acute and chronic kidney disease, risk of intubation, pulmonary edema, osteoporosis, venous thrombosis, and THC. Figure 1 shows the Forrest plot for multivariate analysis of in-hospital morbidities when adjusted for patient demographics, comorbidities, and hospital characteristics. Conclusion: Patients admitted with ACS and sarcoidosis had higher odds of mortality. Patients with SCC and sarcoidosis also had higher odds of acute coronary syndrome, avascular necrosis, and mean LOS. Nevertheless, this has not impacted other inpatient comorbidity.

Urology

Jacob B, **Jamil M**, **Raslan S**, **Nasser Z**, **Springer K**, **Michael German A**, and **Kuriakose P**. Infusion Reactions with Alternative Therapies during the National Shortage of Iron Dextran. *Blood* 2023; 142:7338. Full Text

Introduction The national shortage of intravenous iron dextran has required patients to receive more alternative iron infusions, such as iron sucrose and sodium ferric gluconate/sucrose, since January 2023. While prior studies have evaluated rates of infusion reactions among some commonly used intravenous iron formulations, data is lacking among differing doses of iron formulations and especially in the setting of this iron dextran shortage. Clinicians at our institution generally observed more adverse reactions with alternative iron infusions during the national shortage of iron dextran compared to prior. Our study examines the infusion reactions of various iron therapies at differing doses and actions providers and patients took thereafter to assess the impact of the iron dextran national shortage on patients. Methods Patients were included who received iron infusions in three Henry Ford Hospital clinics in metropolitan Detroit, Michigan, from July 2022-June 2023 with the national iron dextran shortage impacting the health system since January 2023. Age, race, sex, reason for iron infusion, iron infusion formulation received, time of infusion, and dosing schedule of infusion were recorded for all participants. We assessed the symptoms experienced and actions taken for patients who had an infusion reaction. The number and type of infusion reactions between different iron infusion formulations and doses were then compared. Results Of the 880 unique patients assessed, 496 (56.4%) received iron dextran, iron sucrose, or sodium ferric gluconate/sucrose between July 2022 and December 2022 prior to the national iron dextran shortage and 384 (43.6%) patients had iron infusions between January 2023 and June 2023 during the shortage. Iron dextran accounted for most of the infusions (n= 356, 71.8%) prior to the shortage whereas iron sucrose was the majority (n=312, 81.3%) during the shortage. Prior to the national shortage, 30 iron infusions reactions occurred, with 18 (60%) associated with iron dextran, 9 (30%) with iron sucrose, and 3 (16.7%) with sodium ferric gluconate/sucrose. During the shortage, 44 reactions occurred, with 1 (2.27%) associated with iron dextran, 41 (93.1%) with iron sucrose, and 2 (4.54%) with sodium ferric gluconate/sucrose. The most reactions (n=41, 55.4%) occurred with iron sucrose at a dose of 500mg across the whole study period. Less reactions (n=9, 12.2%) were reported for iron sucrose at progressively lower doses, comparable to reactions with iron dextran at doses greater than 1000mg (n=8, 10.8%) and at lower doses of iron dextran (n=10, 13.5%). The most common reaction across all infusion types was nausea, vomiting, and/or diarrhea. After an iron infusion reaction, the infusion plan was then most commonly discontinued, with patients either switching to alternative iron infusion formulations, continuing the same infusion type with medications for symptoms, or continuing the same infusion type with lower dose and increased frequency. Conclusion More iron infusion reactions occurred after the national shortage of iron dextran since January 2023 in the setting of more frequent use of alternative iron

therapies. The most common infusion formulation associated with a reaction was iron sucrose at its higher recommended dose of 500mg, compared with iron dextran and sodium ferric gluconate/sucrose. Providers should be aware of these associated adverse reactions with the different doses of alternative formulations when recommending infusions for patients, and the need for preemptive intervention.

Urology

Jamil M, **Nasser Z**, **Jacob B**, **Mangal R**, and **Donthireddy V**. Efficacy of Direct Oral Anticoagulants Vs Warfarin Vs Low Molecular Weight Heparin in the Treatment of Acute Splanchnic Vein Thrombosis in Patients with Underlying Myeloproliferative Disorder. *Blood* 2023; 142:5533. Full Text

Introduction: Myeloproliferative neoplasms (MPNs) are hematopoietic stem cell disorders characterized by clonal proliferation of myeloid-lineage cells. Venous thrombosis poses a significant morbidity risk for MPN patients. The current recommended treatments for acute splanchnic vein thrombosis (SVT) are warfarin and low molecular weight heparin (LMWH). Direct oral anticoagulants (DOACs) are potential alternatives due to their predictable dose response and oral administration, but limited data exists for their use in acute SVTs. This retrospective study aims to assess the efficacy and outcomes of DOACs, LMWH, and warfarin in treating acute SVTs in patients with underlying MPN. Methods: We included patients of all ages with underlying myeloproliferative neoplasms and splanchnic vein thrombosis, with no underlying liver diseases, from Henry Ford Hospital Clinics in metropolitan Detroit, Michigan between 2013 and 2023. Patient data, which included age, gender, race, and BMI were recorded. The primary outcome was complete radiographic resolution (CRR) of the SVT, and secondary outcomes included recanalization, thrombosis progression, recurrent thrombosis, major bleeding, thrombocytopenia, and skin necrosis. The outcomes were compared between the three anticoagulant groups and patients using aspirin. Results: Among the 34 MPN patients with SVT, warfarin was prescribed most frequently (n=19), followed by enoxaparin (n=5) and DOACs (n=5). Although no significant differences were observed, warfarin showed the highest CRR rates (41.2%), while enoxaparin and DOACs had equal CRR rates (25%). DOACs showed recanalization rates similar to warfarin and higher than enoxaparin (44.4% and 47.1% vs. 20.0%, respectively). LMWH was associated with increased recurrent thrombosis rates (50.0%), while DOACs had a higher risk of major bleeding. All three anticoagulants had similar effects on thrombocytopenia and SVT progression. Aspirin use was linked to a higher risk of major bleeding (42.9%), but not using aspirin correlated with complete SVT resolution (30.8%), SVT progression (20.8%), recurrent thrombosis (29.2%), and thrombocytopenia (28.6%). Conclusions: Although limited by a small sample size, our study found no significant differences among the three anticoagulant groups. This contributes to establishing the role of DOACs in treating SVTs in patients with underlying MPN. Further studies with larger sample sizes are needed to explore the efficacy of DOACs compared to warfarin. Additionally, investigating the potential benefits of early thrombolysis in conjunction with anticoagulation for SVT patients with underlying MPN should be pursued, as the rates of complete resolution in these patients were low.

Urology

Wani K, **Gutta R**, **Mittal A**, **Jamil M**, **Springer K**, and **Kuriakose P**. Comparison of Maintenance Therapy Regimens of Patients Treated for Multiple Myeloma. *Blood* 2023; 142:6698. Full Text

Background: Despite significant progress in treatment modalities and improved survival and response rates in patients diagnosed with multiple myeloma (MM), it remains an incurable disease with a poor outcome, especially in high-risk groups. Though not all patients are eligible, autologous stem-cell transplantation (ASCT) remains an integral part of the treatment of patients with both newly diagnosed and relapsed MM. Regardless of whether patients receive a transplant, they do receive maintenance therapy, and recent evidence has demonstrated that maintenance therapies offer an advantage in progression free and overall survival. While Revlimid is the standard of care, data regarding the specifics of maintenance therapy in high-risk patients is limited and the overall impact of various regimens on survival needs to be further investigated. In our retrospective chart review we reviewed all adult patients with advanced MM within Henry Ford Cancer Institute in the last 10 years to determine the impact of maintenance therapy on progression free survival (PFS) and overall survival (OS). Methods: We conducted a retrospective chart review of adult patients with MM who underwent ASCT between January 1, 2012 to December 31, 2022. Those who received maintenance chemotherapy after transplant were included in the study. Patients who were lost to follow-up or who had largely incomplete records were

excluded. Data points including age, ethnicity, cytogenetic analysis, risk category, maintenance regimen after transplant, last chemotherapy regimen, last follow-up, and date of death (if applicable) were recorded. Maintenance chemotherapy regimens were recorded as Revlimid versus other. Patients were split into 2 categories based on risk - high risk and standard risk. Kaplan-Meier plots were used to illustrate overall survival and time to relapse between groups for various variables. Statistical significance was set at $p<0.05$ Results: 158 patients were included in the study of which 44 were considered high-risk based on cytogenetics, 106 were standard-risk and 8 were missing. Most of the patients (n=137, 87.3%) received Revlimid, while 20 (12.7%) received maintenance therapy other than Revlimid, and for 1 patient, the type of maintenance therapy was unknown. Within the high-risk group, no statistical significance in OS or PFS was found between patients that received Revlimid versus those that did not. Furthermore, there was no statistical significance in OS and PFS within high risk versus standard cytogenetic risk groups. Conclusions: We did not see a difference in outcome based on risk and believe all patients would derive equal benefit from maintenance therapy We also did not see a difference in outcome between high and standard risk patients, and for the high-risk subgroup, there was a separation in curves suggesting that maintenance therapy has benefit compared to no maintenance.

Urology

Wani K, **Gutta R**, **Mittal A**, **Jamil M**, **Springer K**, and **Kuriakose P**. Impact of Race on Progression-Free Survival and Overall Survival in Patients with Multiple Myeloma. *Blood* 2023; 142:6661. Full Text

Background: Multiple myeloma (MM) is a disorder of plasma cells. Management typically includes induction therapy, autologous stem-cell transplantation (ASCT) and maintenance therapy. Despite significant progress in treatment modalities and improved survival and response rates in patients diagnosed with MM, it remains an incurable disease with a poor outcome, especially in high-risk groups. Black patients have been shown to have a higher incidence of MM than white patients. Multiple studies have been done to examine racial disparities among white and black patients, specifically in overall survival (OS) and progression free survival (PFS). However, data has been overall inconclusive with some studies suggesting there is a difference in survival based on race, while other studies suggesting the opposite. Thus, racial disparities among white and black patients' needs to be further investigated. In our retrospective chart review we reviewed all adult patients with advanced MM within Henry Ford Cancer Institute in the last 10 years to determine the impact of maintenance therapy on PFS and overall survival OS. Methods: We conducted a retrospective chart review of adult patients with MM who underwent autologous stem cell transplantation (ASCT) between January 1, 2012 to December 31, 2022. Those who received maintenance chemotherapy after transplant were included in the study. Patients who were lost to follow-up or who had largely incomplete records were excluded. Data points including age, gender, race, date of transplant, maintenance chemotherapy regimen, last follow-up, and date of death (if applicable) were recorded. Kaplan-Meier plots were used to illustrate overall survival and time to relapse between various races. Statistical significance was set at $p<0.05$. Results: There were 158 patients included in the study. Of the 158 patients, 82 (51.9%) were male, and 76 (48.1%) were female. The average age of patients included was 61.66 + 9.30 years, spanning from 32 to 78 years old. There were 71 (44.9%) White patients, 76 (48.1%) Black patients, and 11 (7.0%) patients that were of another race. There was no statistical significance in PFS and OS between Black, White and Other race categories. Conclusions: We did not see a difference in outcome based on race and believe all patients would derive equal benefit from maintenance therapy. Further prospective studies are warranted to examine racial disparities in patients with multiple myeloma.