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HENRY FORD HEALTH

Henry Ford Health Publication List – May 2025

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 biomedical databases PubMed, Embase, Web of Science, CINAHL, and PsycINFO, as well as Google Books during the month, and then imported into EndNote for formatting. There are 329 unique citations listed this month, including 193 articles, 135 conference abstracts, and 1 book chapter.

Articles are listed first, followed by conference abstracts and books and book chapters. Due to various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health authors.

Click the "Full Text" link to view the articles to which Sladen Library provides access. If the full-text of the article is not available, you may request it through ILLiad or by calling us at (313) 916-2550. If you would like to be added to the monthly email distribution list to automatically receive a PDF of this bibliography, or you have any questions or comments, please contact smoore31@hfhs.org. If your published work has been missed, please use this form to notify us for inclusion on next month's list. All articles and abstracts listed here are deposited into Scholarly Commons, the Henry Ford Health institutional repository.

Articles

Conference Abstracts

Administration
Allergy and Immunology
Anesthesiology
Behavioral Health Services/Psychiatry/Neuropsychology
Cardiology/Cardiovascular Research
Clinical Quality and Safety
Dermatology
Diagnostic Radiology
Emergency Medicine
Family Medicine
Gastroenterology
Hematology-Oncology
Hospital Medicine
Infectious Diseases
Internal Medicine
Nephrology
Neurology
Obstetrics, Gynecology and Women's Health Services
Pathology and Laboratory Medicine
Pharmacy
Public Health Sciences
Pulmonary and Critical Care Medicine
Sleep Medicine
Surgery
Urology

Books and Book Chapters

Center for Health Policy and Health Services Research

Articles

Administration

Muma B, **Keteyian C**, **Kolde D**, **Drake S**, **George D**, **Foust M**, **Fried S**, **Elsberg J**, **Thomas S**, **Johnston L**, **Kulawczyk A**, Paculdo D, Cooney I, Peabody J, and Burgon T. Patient Simulation-Based Primary Care Training to Increase Evidence-Based COPD Care and Value-Based Success: Real-World Cost and Quality Impact Analysis. *Am J Med* 2025; Epub ahead of print. PMID: 40447064. Full Text

Henry Ford Physician Network; Detroit, MI; Henry Ford Health.
Detroit, MI; Henry Ford Health; Detroit, MI; Jackson Health Network.
Detroit, MI; Henry Ford Health.
Jackson, MI; QURE Healthcare.
Jackson, MI; QURE Healthcare; St Louis, MO, USA, University of California, San Francisco, CA.

Anesthesiology

Guerra-Londoño JJ, Moreno-Lopez SM, Gundre S, Jehanzeb A, Wong R, Cortes-Mejia N, Bejarano-Ramirez D, Mensah CKB, and Cata JP. Association between intravenous 5 % albumin administration and acute kidney injury after partial nephrectomy. A retrospective study. *J Clin Anesth* 2025; 104:111873. PMID: 40373496. Full Text

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BACKGROUND: Acute kidney injury (AKI) after partial nephrectomy is a frequent postoperative complication that can affect nearly half of patients, according to various studies. In the current study, we investigated the association of intraoperative administration of 5 % albumin, compared with crystalloids alone, with AKI after partial nephrectomy. METHODS: This single-center retrospective study included adult patients undergoing partial nephrectomy. The primary endpoint was AKI within 72 h after surgery using the KIDGO definition. Secondary endpoints were time-to-AKI, reoperations, AKI severity and length of hospital stay. We used propensity score-based nearest-neighbor methods balance the patient baseline characteristics. RESULTS: A total of 1688 patients were included in the analysis, with 809 receiving 5 % albumin and 879 in the control group. After matching, 729 patients received 5 % albumin, while 674 were controls. The incidence of acute kidney injury (AKI) was significantly higher in the 5 % albumin group (32.78 %) compared to the control group (25.51 %). Multivariate analysis revealed that receiving 5 % albumin was associated with a 32 % increased risk of developing AKI. Furthermore, the analysis indicated that this association was dose-dependent. CONCLUSION: Our study suggests that intraoperative administration of 5 % albumin may not be a risk factor for AKI after partial nephrectomy. Given the discrepancy between these results and previous studies, a future prospective randomized controlled trial is needed to confirm our findings.

Anesthesiology

Smith T, **Kheirabadi D**, Guo Y, Sun J, Pierce J, Bergmans RS, Boehnke KF, Schrepf A, Clauw D, Kaplan CM, and Arewasikporn A. Adverse childhood experiences and multisite pain among adolescents in the United States. *Pain Rep* 2025; 10(3):e1279. PMID: 40303901. Full Text

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INTRODUCTION: Childhood adversity can have a lasting negative impact throughout one's life. Youth with pain conditions consistently report a higher rate of adverse childhood experiences (ACEs) when compared with their healthy peers. Adolescents experiencing pain in more than 1 region tend to have greater symptom burden and reduced quality of life. Research on the association between ACEs and multisite pain in adolescents is sparse. OBJECTIVES: The objective of our study was to investigate the association between cumulative ACEs and self-report of multisite pain in early adolescence using data from the Adolescent Brain Cognitive Development study. METHODS: We used a 19-region body map to evaluate the presence of regional pain (1-2 regions) and multisite pain (≥3 regions). We analyzed data using multinominal logistic regression, adjusting for sociodemographic factors including pubertal status, sex, race/ethnicity, and income-to-needs ratio. RESULTS: We included a total of 7582 children aged 12 to 13 years, with 33.4%, 24.0%, 13.2%, and 8.6% reporting 1, 2, 3, and 4+ ACEs, respectively. Moreover, 30.7%, 24.2%, 15.2%, and 10.1% of children with multisite pain reported 1, 2, 3, and 4+ ACEs, respectively. Those with 4+ ACEs (adjusted odds ratio 1.62, 95% confidence interval 1.24-2.12) and 3 ACEs (adjusted odds ratio 1.44, 95% confidence interval 1.14-1.82) were more likely to report multisite pain compared with the children with no ACEs. CONCLUSION: We showed a potential dose-response relationship between cumulative ACEs and multisite pain, suggesting that the impact of ACEs on pain, particularly multisite pain, may emerge earlier than previously documented. Keywords: Adverse childhood experiences, Multisite pain, Adolescent pain.

Anesthesiology
Weinstein J, Ali H, Metrouh O, Sarwar A, **Mitchell JD**, Baribeau V, Wong VT, Matyal R, Palmer MR, MacLellan C, and Ahmed M. Hand Motion Analysis of Different Segments of a Procedure: Is One Segment Enough? *J Med Syst* 2025; 49(1):69. PMID: 40407939. Full Text

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PURPOSE: This study aims to examine if the hand motions of operators associated with certain parts of central venous access are more important than others in distinguishing between experts and non-experts. MATERIALS AND METHODS: Experts (n = 10) and Trainees (PGY2; n = 18) performed central venous access on a phantom 4 times each as their needle hand and ultrasound probe motions were tracked. Path length-time graphs were used to divide the procedure into three phases: (1) the access phase: visualizing the internal jugular vein on ultrasound and needle placement; (2) the wire phase: passing a wire through the needle; and (3) the confirmation phase: confirming the intravascular wire position and threading a dilator on the wire. Comparisons between trainees and experts were made for the complete trial, and each phase using Mann-Whitney U tests with Benjamini-Hochberg correction. Receiver Operating Characteristic analysis was performed to compare the performance of each phase in differentiating between experts and trainees. RESULTS: Motion data from 10 experts and 18 trainees was analyzed. Experts and trainees differed significantly for all the motion metrics ($p < 0.001$). A comparison of the phases showed that the access phase (AUC = 0.96; R2 = 0.79) and the wire phase (AUC = 0.95; R2 = 0.59) were able to distinguish between experts and trainees with an accuracy comparable to the complete trial (AUC = 0.94; R2 = 0.69). CONCLUSIONS: The access phase of simulated central venous access can best differentiate between experts and trainees. This sample of

hand motion performance may be able to simplify motion analysis of technical performance and obviate the need for recording hand motion for the entire procedure.

Anesthesiology
Wong R, Patel RG, Cortes-Mejia N, **Guerra-Londono JJ**, Huang H, Gundre S, Napa N, and Cata JP. Impact of intraoperative dexmedetomidine on clear cell renal cell carcinoma progression: a retrospective cohort study. *Br J Anaesth* 2025; Epub ahead of print. PMID: 40348672. Full Text

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BACKGROUND: Dexmedetomidine, an α-2 adrenoreceptor agonist, is commonly administered during cancer surgery as an adjuvant sedative because of its general anaesthetic agent-sparing effects. We investigated the association between ADRA2 gene expression and dexmedetomidine on oncological outcomes after surgery for clear cell renal cell carcinoma (RCC). METHODS: We conducted an in silico analysis using a publicly available database and a retrospective study in patients with clear cell RCC. The associations between ADRA2A expression and recurrence-free survival and overall survival were analysed. The same outcomes were investigated in a cohort of patients who underwent partial or total nephrectomy and received dexmedetomidine or not. A propensity score matching strategy was utilised to account for selection bias, and a multivariable analysis was performed to control for variables implicated in survival. RESULTS: Expression of the ADRA2A gene at the tumour level was not associated with recurrence-free survival; however, higher levels of expression were significantly associated with shorter overall survival. A total of 1766 patients with clear cell RCC were included in the retrospective study. Dexmedetomidine administration was not associated with higher rates of recurrence or mortality or with a significant impact on recurrence-free survival or overall survival. CONCLUSIONS: Intraoperative administration of dexmedetomidine was not associated with a significant impact on cancer progression and survival. The role of ADRA2A as a prognosis biomarker for clear cell RCC warrants further study.

Behavioral Health Services/Psychiatry/Neuropsychology
Prabhakar D. Advances in Psychiatry and Behavioral Health. *Adv Psychiatry Behav Health* 2025. PMID: Not assigned. Full Text

Cardiology/Cardiovascular Research
Alexandrou M, Strepkos D, Carvalho PEP, Mutlu D, Ser OS, Poommipanit P, Gorgulu S, Khelimskii D, Krestyaninov O, Ahmad Y, Jamil Y, **Alaswad K**, **Basir MB**, Azzalini L, Kearney KE, Khatri JJ, Young L, Ozdemir R, Uluganyan M, Raj LM, Kumar S, Mastrodemos OC, Rangan BV, Jalli S, Burke MN, Sandoval Y, and Brilakis ES. Dissection Techniques in Chronic Total Occlusion Percutaneous Coronary Intervention. *Catheter Cardiovasc Interv* 2025; Epub ahead of print. PMID: 40350793. Full Text

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BACKGROUND: There is limited data on dissection strategies in chronic total occlusion (CTO) percutaneous coronary intervention (PCI). AIMS: To study the differences in the baseline characteristics and procedural outcomes of antegrade CTO PCIs that used dissection strategies. METHODS: We performed a comparative analysis of antegrade dissection and re-entry CTO PCIs from the PROGRESS-CTO registry from 50 centers (2012-2024). Three dissection strategies were compared: (a) knuckle wiring: knuckle wire(s) without Carlino technique or CrossBoss catheter; (b) the CrossBoss technique: use of the CrossBoss catheter; and (c) the Carlino technique: use of the Carlino technique. In-stent CTO PCIs were excluded from the analysis. RESULTS: In total, 1575 (74.6%) cases used knuckle wiring, 427 (20.2%) the CrossBoss, and 110 (5.2%) the Carlino technique. Knuckle wiring was the most frequent strategy with increasing utilization over time ($p < 0.001$). The CrossBoss catheter was more common in lesions with lower J-CTO scores (CrossBoss: 2.91 vs. Knuckle wiring: 3.07 vs. Carlino: 3.18; $p = 0.015$), and was associated with higher technical success (CrossBoss: 84.0% vs. Knuckle wiring: 74.2% vs. Carlino: 64.2%; $p < 0.001$) and similar major adverse cardiac events rates, but lower perforation rates. Time to crossing was longer when Carlino was used (CrossBoss: 93 [70, 133] min vs. Knuckle wiring: 97 [63, 136] min vs. Carlino: 133 [84, 166] min, $p = 0.001$). Use of different types of knuckle wires (Pilot 200, Gladius Mongo, and Fielder XT) was associated with similar success rates. CONCLUSIONS: Knuckle wiring is the most commonly used antegrade dissection strategy. The CrossBoss catheter was used in less complex cases and was associated with higher success, whereas the opposite was true for the Carlino technique.

Cardiology/Cardiovascular Research

Alhuneafat L, Ghanem F, Brankovic M, Obeidat O, Pertuz GDR, Gutierrez A, **Jabri A**, Patel D, Bartos J, and Elliott A. Predictors of extracorporeal membrane oxygenation utilization and survival during cardiopulmonary resuscitation in out and in-hospital cardiac arrest. *Cardiovasc Revasc Med* 2025; Epub ahead of print. PMID: 40393867. Full Text

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INTRODUCTION: Extracorporeal membrane oxygenation during cardiopulmonary resuscitation (ECPR) has shown promise in managing both out-of-hospital cardiac arrest (OHCA) and in-hospital cardiac arrest (IHCA). METHODS: We analyzed hospital discharge records from the National Inpatient Sample of adult individuals who underwent ECPR between 2016 and 2020. Multivariable regression analyses were conducted to identify factors influencing ECPR utilization and survival. RESULTS: Among 1,585,960 patients (901,470 OHCA, 684,490 IHCA), ECPR utilization rates were 1 % for OHCA and 1.4 % for IHCA, with inpatient mortality rates of 52 % and 67 %, respectively. In OHCA, ECPR was more likely in patients from higher-income areas, those with Medicaid/private insurance, systolic heart failure, shockable rhythms, and Hispanic/other races but less likely in those over 65, with patients with history of atrial fibrillation, diabetes, cerebrovascular accident, or COPD. In IHCA, ECPR was more common in larger hospitals, higher-income areas, and those with private insurance but less frequent in Black patients, those over 65, or with prior cerebrovascular accidents, COPD, diabetes, or end-stage renal disease. In OHCA ECPR, Asian race (aOR: 2.31), diabetes (aOR: 1.29), and liver disease (aOR: 1.77) predicted mortality, while shockable rhythms (aOR: 0.75), systolic heart failure (aOR: 0.67), and treatment in southern states (aOR: 0.72) predicted survival. In IHCA ECPR, acute myocardial infarction (aOR: 0.73) and private insurance (aOR: 0.63) were associated with improved survival, whereas liver disease (aOR: 1.59) predicted higher mortality. CONCLUSION: We highlight the selective nature of ECPR utilization between OHCA and IHCA and the distinct survival predictors in each setting. Further research is needed to refine selection criteria and optimize patient outcomes.

Cardiology/Cardiovascular Research

Alhuneafat L, Ghanem F, Nandy S, Khan S, Puttur A, **Jabri A**, Haddad A, Ramu B, Sabol B, Schultz J, and Carlson S. Examining maternal and fetal outcomes across various subtypes of hypertension during pregnancy. *Int J Cardiol Cardiovasc Risk Prev* 2025; 25:200413. PMID: 40343146. Full Text

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INTRODUCTION: Hypertensive disorders of pregnancy (HDP) are a leading cause of maternal morbidity and mortality worldwide. It includes chronic hypertension (CH), gestational hypertension (GH), preeclampsia (PRE), and CH with superimposed preeclampsia (SPE).We aim to assess in-hospital maternal and fetal outcomes of women in each of these groups in comparison to normotensive controls. METHODS: Study sample included women in the National Inpatient Sample dataset from 2016 to 2020 who were categorized into the 4 groups of HDP as described above. They were compared to normotensive pregnancies for maternal and fetal outcomes using regression analysis after adjusting for age, race, C-section status, and comorbidities. RESULTS: The study dataset from October 2015-December 2020 included 19,089,780 delivery admissions with 2,771,809 (14.5 %) of patients affected by HDP. The HDP groups were distributed as follows: GH - 38 %, PRE - 32 %, SPE - 11 %, and CH - 19 %. Women with PRE, SPE, and CH had significantly higher rates of mortality, circulatory shock, peripartum cardiomyopathy, acute kidney injury, preterm labor, stillbirth, and cerebrovascular events as compared to normotensive patients, while GH did not. Specifically, maternal mortality was highest in the SPE group (adjusted odds ratio [aOR] 3.16), followed by PRE (aOR 2.91) and CH (aOR 2.42). Additionally, all HDP groups had higher rates of small for gestational age and significant bleeding as compared to normotensive patients. CONCLUSIONS: Pregnant patients with CH, PRE, and SPE experience higher rates of adverse maternal and fetal outcomes during their delivery admission when compared to normotensive patients. Understanding the graded risk differences across HDP subtypes may enable more tailored interventions, optimizing maternal and fetal outcomes for those at highest risk.

Cardiology/Cardiovascular Research

Bonnet G, Rommel KP, Falah B, Lansky AJ, Zhang Y, Schonning MJ, Redfors B, Burkhoff D, Cohen DJ, **Basir MB**, **O'Neill WW**, and Granada JF. Impact of Mean Blood Pressure Profiles in Percutaneous Left Ventricular Assist Device-Supported High-Risk Percutaneous Coronary Intervention: The PROTECT III Study. *J Am Heart Assoc* 2025; 14(10):e036367. PMID: 40371603. Full Text

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BACKGROUND: Percutaneous left ventricular assist devices are used prophylactically to prevent hypotension during high-risk percutaneous coronary intervention. However, the impact of preprocedural hemodynamic profiles on procedural and clinical outcomes in these patients is unknown. METHODS AND RESULTS: Patients from the central venous access device PROTECT III registry (NCT04136392) were

categorized according to preprocedural mean blood pressure (MBP). Procedural and in-hospital outcomes, including hypotensive episodes, need for prolonged percutaneous left ventricular assist device support, and in-hospital death, were compared between groups. We also assessed the relationship between preprocedural MBP and 90-day major adverse cardiovascular and cerebrovascular events, which included all-cause death, myocardial infarction, stroke/transient ischemic attack, and repeat revascularization, as well as with 1-year mortality. A total of 1159 patients underwent percutaneous left ventricular assist device-supported high-risk percutaneous coronary intervention and were stratified into 4 hemodynamic profiles of preprocedural MBP level: MBP>100 mm Hg (n=242), >90 to ≤100 mm Hg (n=264), >80 to ≤90 mm Hg (n=306), and ≤80 mm Hg (n=347). Lower preprocedural MBP was associated with baseline anemia, history of heart failure, left main disease, and transfer from another hospital. In-hospital and procedural adverse outcomes did not differ between the BP categories. However, 90-day major adverse cardiovascular and cerebrovascular events rates and 1-year mortality increased with decreasing baseline BP levels. The association between BP category and 1-year mortality remained significant after adjustment for other factors (hazard ratio [HR], 0.79 [95% CI, 0.71-0.88], P<0.001). CONCLUSIONS: In a real-world cohort undergoing high-risk percutaneous coronary intervention with percutaneous left ventricular assist device support, there was no association between hemodynamic status and in-hospital outcomes. Lower preprocedural BP was associated with higher rates of 90-day major adverse cardiovascular and cerebrovascular events and 1-year mortality. REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT04136392.

Cardiology/Cardiovascular Research

Doshi A, Upreti P, **Aggarwal V**, Poppas A, Soukas PA, Abbott JD, and Vallabhajosyula S. Socioeconomic Disparities in the Care of for High-Risk Pulmonary Embolism in the United States, 2016 to 2020. *Am J Cardiol* 2025; 250:61-69. PMID: 40348044. Full Text

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There are limited data on the impact of socioeconomic factors on the management and outcomes of high-risk acute pulmonary embolism (PE). Using the National Inpatient Sample (NIS) from 2016 to 2020, we identified adult (≥18 years) admissions with high-risk PE (defined as PE with one of: cardiogenic shock, vasopressor use, or cardiac arrest). Socioeconomic determinants included sex, race, insurance payer, and economic status. Outcomes of interest included in-hospital mortality, rates of mechanical circulatory support (MCS) and definitive PE interventions, hospitalization duration, and hospitalization costs. Among 21,521 high-risk PE hospitalizations (median age 65 years, 53% male, 64% white race), the socioeconomic variables remained stable during the 5-year period. MCS utilization was 4%, with lower rates of utilization in Medicare and Medicaid beneficiaries, uninsured admissions, and those from the lowest income quartile (all p <0.05). Racial minorities, those from lower economic status, and uninsured admissions received advanced PE interventions less frequently. There did not appear to be notable sex disparities in use of advanced PE therapies. Overall, in-hospital mortality was 50%, with higher adjusted in-hospital mortality in female, African American, Hispanic, uninsured, and economically disadvantaged individuals. In conclusion, significant inequities in in-hospital mortality, mechanical circulatory support, and definitive pulmonary embolism therapy utilization persist among high-risk PE hospitalizations in the United States based on sex, race, income, and insurance status.

Cardiology/Cardiovascular Research

El-Sabawi B, Barker CM, Absi T, Bommareddi S, Szerlip MI, Iyer V, Batchelor WB, **Villablanca PA**, Rihal CS, and Goel K. Lithotripsy-Facilitated or Conventional Percutaneous Mitral Balloon Valvuloplasty for Calcific Mitral Valve Disease: A Systematic Review. *J Soc Cardiovasc Angiogr Interv* 2025; 4(4):102582. PMID: 40308244. Full Text

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BACKGROUND: The efficacy of percutaneous mitral balloon valvuloplasty (PMBV) for mitral stenosis (MS) secondary to mitral annular calcification (MAC) is poorly understood. The purpose of this systematic review was to consolidate existing data on conventional and lithotripsy-facilitated PMBV in patients with calcific mitral valve disease, to better understand procedural outcomes. METHODS: We performed a systematic search of the literature published in PubMed and Scopus databases through May 2024. We included all studies that reported outcomes of conventional PMBV as a standalone therapy or lithotripsy-facilitated mitral intervention for calcific mitral valve disease. RESULTS: A total of 12 reports met the criteria for inclusion (8 lithotripsy and 4 conventional PMBV), including 4 case series and 8 case reports. Conventional PMBV (n = 44) procedural success in MAC was variable and associated with a limited reduction in mitral gradient in most patients. After conventional PMBV, 4 (9.1%) patients had moderate-to-severe mitral regurgitation (MR) or more, and 6 (13.6%) required mitral re-intervention. On the contrary, lithotripsy-facilitated PMBV for MAC (n = 40) led to hemodynamic improvement in most cases with a mean reduction of 5 to 8 mm Hg in mean mitral gradient. One case (2.5%) developed increased MR from baseline, and 1 (2.5%) required mitral reintervention. Outcomes beyond 3 months were lacking and precluded assessment on whether these improvements are sustained. CONCLUSIONS: This systematic review suggests that lithotripsy-facilitated PMBV for MAC-related MS is feasible and may offer favorable short-term outcomes compared with conventional PMBV alone. These findings highlight the need for larger, multicenter studies with longer follow-up.

Cardiology/Cardiovascular Research

Fadel RA, **Hofeld B**, **Aronow HD**, **Jabri A**, **Engel P**, **Koenig G**, **Memon M**, **Alqarqaz M**, **Alaswad K**, **Fuller B**, **Nakhle A**, **Aggarwal V**, **O'Neill B**, **Frisoli T**, **Basir MB**, **Kim H**, **O'Neill W**, and **Villablanca P**. Propensity matched analysis of single access technique for Impella-assisted unprotected left main percutaneous coronary intervention. *Cardiovasc Revasc Med* 2025; Epub ahead of print. PMID: 40436725. Full Text

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Structural Heart Disease, Henry Ford Hospital, Detroit, MI, United States of America.
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BACKGROUND: The single access for high-risk percutaneous coronary intervention (SHiPCI) technique is an intriguing alternative to traditional dual access Impella-assisted PCI, potentially reducing access-site complications. Current data is limited to retrospective case studies. OBJECTIVES: To analyze procedural complications and clinical outcomes of SHiPCI. METHODS: This single-center retrospective observational study evaluated consecutively admitted patients undergoing high-risk unprotected left main PCI (UPLM-PCI) from 2018 through 2023. Patients were grouped according to index strategy of single or dual access Impella-assisted UPLM-PCI, and propensity score matching without replacement was used to match patients 1:1. The primary outcome was a composite of all-cause in-hospital mortality, major bleeding, vascular access site complications, and blood transfusion. RESULTS: Six-hundred patients underwent

UPLM-PCI during the study period, and one hundred patients were matched (50 patients per group). There were no significant differences in baseline characteristics between the two groups. Up-front balloon tamponade assistance was higher in the dual access group (14 % vs 4.0 %, p = 0.027), and rate of successful hemostasis post-closure was lower (82 % vs 100 %, p = 0.001). The primary composite outcome occurred in 7 patients (14 %) in the single access group, compared to 16 patients (32 %) in the dual access group (p = 0.033). Patients in the dual-access group had higher rates of major bleeding (17 % vs 2 %, p = 0.014). CONCLUSIONS: SHiPCI compared to standard dual access for Impella-assisted UPLM-PCI demonstrated a lower rate lower rate of the composite outcome, driven primarily by a lower rate of major bleeding. Prospective randomized controlled trials are needed to delineate the efficacy and safety of SHiPCI.

Cardiology/Cardiovascular Research
Fang JX, **Giustino G**, **Frisoli TM**, **Lee JC**, and **Villablanca PA**. Lacerate and Macerate: The BASILICA-LLAMACORN/UNICORN Combination to Optimize Bioprosthetic Bileaflet Modification. *J Soc Cardiovasc Angiogr Interv* 2025; 4(5):102614. PMID: 40454276. Full Text

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National Heart Centre Singapore, Singapore.
Gagnon Cardiovascular Institute, Morristown Medical Center, Atlantic Health System, Morristown, New Jersey.

Cardiology/Cardiovascular Research
Fang JX, and **Villablanca PA**. Do Not BASILICA the New Valve. *JACC Case Rep* 2025; 30(13). PMID: Not assigned. Full Text

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Object: Bioprosthetic or native Aortic Scallop Intentional Laceration to prevent Iatrogenic Coronary Artery obstruction (BASILICA) is currently the standard technique for leaflet modification in transcatheter aortic valve replacement to overcome coronary obstruction. The technique involves traversal of the coronary cusp with a 0.014-inch coronary wire, snaring the wire, and then lacerating the leaflet with a denuded portion of the wire known as the flying V. The procedure requires careful planning and technical expertise. We report a new complication of BASILICA where prepositioning of a transcatheter heart valve (THV) before laceration accidentally damaged the THV. Key Steps: This complication originates from the inadvertent crossing of the straight-tip wire between the flying V and the aortic cusp when the flying V was not well apposed to the cusp. Prepositioning of the THV has become a variation of the procedure for patients with a high perceived risk of hemodynamic instability after BASILICA. This backfired, resulting in a complicated procedure. Potential Pitfalls: The exact position of the 0.014-inch wire and flying V might be difficult to visualize in patients with a large body habitus. Operators should check that the flying V is at the cusp level before crossing the aortic valve with a wire. During the initial delivery of the flying V to the cusp, care should be taken to avoid losing the wire in the guide. Multicenter data of BASILICA show that hemodynamic instability is uncommon in single-leaflet lacerations. Therefore, prepositioning of a THV before leaflet laceration is usually unnecessary and requires strong clinical justification if pursued Take-Home Messages: BASILICA is a complex procedure. Operator familiarity with potential pitfalls and appropriate bailout methods are necessary. Operators should ensure that the flying V is well apposed to the leaflet before crossing into the left ventricle with a wire to prepare for valve deployment.

Cardiology/Cardiovascular Research
Fleurestil M, Mohan A, Ergui I, Samaha J, Colombo R, Mitrani R, de Marchena E, **Villablanca P**, Wiley J, Chatzizisis YS, and Cox P. Outcomes of Left Atrial Appendage Occlusion in Hispanic/Latino Patients: Insights From the National Inpatient Sample. *Clin Cardiol* 2025; 48(5):e70152. PMID: 40365821. Full Text

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BACKGROUND: Left atrial appendage occlusion (LAAO) is an established therapy for stroke prevention in non-valvular atrial fibrillation (NVAF), but outcomes in Hispanic populations remain underexplored. OBJECTIVE: The objective of our study was to evaluate the inpatient outcomes of Hispanic patients undergoing LAAO as compared to non-Hispanic white patients. METHODS: We conducted a retrospective cohort study using the National Inpatient Sample (NIS). From 157 434 LAAO hospitalizations identified, 133 517 were non-Hispanic white and 6814 were Hispanic/Latino. The primary outcome was in-hospital mortality. RESULTS: Unadjusted odds in the Hispanic/Latino group were higher for mortality (OR 1.78, 95% CI 1.18-2.68, p 0.006), stroke (OR 1.64, 95% CI 1.26-2.14, p < 0.001), infectious complications (OR 3.89, 95% CI 3.03-4.99, p < 0.001), major bleeding (OR 1.22, 95% CI 1.11-1.33, p < 0.001), DVT/PE (OR 2.15, 95% CI 1.58-2.93, p < 0.001), and vascular complications (OR 1.81, 95% CI 0.53-0.93, p < 0.001). After adjusting for covariates and comorbidities, Hispanic/Latino patients had still greater odds of mortality (aOR 1.20, 95% CI 0.75-1.92, p 0.445), infectious complications (aOR 3.54, 95% CI 2.62-4.55, p < 0.001), and vascular complications (aOR 1.57, 95% CI 1.22-2.03, p < 0.001). Non-Hispanic white patients had higher adjusted odds of pericardial effusion/tamponade (aOR 0.64, 95% CI 0.52-0.95, p 0.03), while Hispanic/Latino patients also had higher adjusted odds of cardiac arrest (aOR 1.99, 95% CI 1.15-3.42, p 0.46). CONCLUSION: Hispanic/Latino patients undergoing LAAO experience higher odds of infectious and vascular complications compared to non-Hispanic white patients. These findings highlight the need to further investigate disparities in procedural outcomes.

Cardiology/Cardiovascular Research
Fram G, **Alrayes H**, **Lai LKL**, **Dawdy J**, **Zweig B**, **Parikh S**, **Alter J**, **Gonzalez PE**, **Villablanca P**, **O'Neill B**, **Lee J**, and **Frisoli T**. Finishing the Job: Utilization of Amulet Device for 2 Prior Incomplete Left Atrial Appendage Occlusion. *JACC Cardiovasc Interv* 2025; Epub ahead of print. PMID: 40338781. Full Text

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Cardiology/Cardiovascular Research
Fram G, **Alrayes H**, **Lai LKL**, **Dawdy J**, **Zweig B**, **Parikh S**, **Song T**, **Pantelic M**, **Alter J**, **Gonzalez PE**, **O'Neill B**, **Frisoli T**, **Villablanca P**, and **Lee J**. Fluoroscopy-Guided Intracardiac Echocardiography Navigation: A Novel Landmark-Based Imaging Technique for Transcatheter Tricuspid Valve Replacement. *J Soc Cardiovasc Angiogr Interv* 2025; 4(4):102613. PMID: 40308230. Full Text

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Cardiology/Cardiovascular Research
Giustino G, **Fadel RA**, **Jabri A**, **Cowger J**, **O'Neill B**, **Basir MB**, **Engel Gonzalez P**, **Frisoli T**, **Lee J**, Généreux P, **O'Neill WW**, and **Villablanca PA**. Left Atrial Veno-Arterial Extracorporeal Membrane Oxygenation In Valvular Cardiogenic Shock. *J Soc Cardiovasc Angiogr Interv* 2025; 4(5):102615. PMID: 40454278. Full Text

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BACKGROUND: Treatment of valvular cardiogenic shock (VCS) is challenging as the options for mechanical cardiocirculatory support are limited. Left atrial veno-arterial extracorporeal membrane oxygenation (LAVA-ECMO) is a mechanical cardiocirculatory support strategy that provides cardiocirculatory support and simultaneous left ventricular unloading, compared to traditional VA-ECMO. METHODS: This is a single-center retrospective analysis of patients with VCS who underwent LAVA-ECMO between 2018 and 2023. During LAVA-ECMO, the ECMO venous cannula is placed transeptally in the LA, therefore providing active biventricular unloading. RESULTS: A total of 18 patients who had VCS and underwent LAVA-ECMO cannulation were included. Among patients with VCS, 10 were related to the aortic valve (55.6%), 7 to the mitral valve (38.9%), and 1 to the tricuspid valve (5.6%). Four patients (22.2%) had multivalvular disease. The median age was 65 years, most were men (66.7%) and most were in Society for Cardiovascular Angiography & Interventions cardiogenic shock stage D or E (89%). LAVA-ECMO was associated with substantial improvement in hemodynamics, including lower right atrial pressure (-8 mm Hg; 95% CI, 7.0-9.5; P = .004), mean pulmonary artery systolic pressure (-18.5 mm Hg; 95% CI, 14.3-21.7; P = .026), pulmonary capillary wedge pressure (-14.5 mm Hg; 95% CI, 12.8-12.3; P = .003), and left ventricular end-diastolic pressure (-20.0 mm Hg; 95% CI, 16.5-21.0; P < .001). These effects were consistent across VCS types. There were no complications from transeptal cannulation. Survival to a transcatheter or surgical procedure was 69.1%, and survival to hospital discharge was 44.4%. CONCLUSIONS: LAVA-ECMO appears to be feasible, safe, and associated with improved hemodynamics in patients with VCS. Further research is needed to evaluate whether LAVA-ECMO as a bridge treatment strategy to intervention is beneficial in VCS.

Cardiology/Cardiovascular Research
Giustino G, Koulogiannis K, Blitz L, van Boxtel B, Cohen B, **Villablanca P**, Gillam L, Brown J, 3rd, Kipperman R, and Genereux P. First-in-human percutaneous transseptal Retrieval of Embolized TRanscatheter valve In the lEft VEntricle (RETRIEVE). *JACC Cardiovasc Interv* 2025; Epub ahead of print. PMID: 40338782. Full Text

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Cardiology/Cardiovascular Research
Giustino G, **Lee JC**, **O'Neill BP**, **Fang JX**, **Zweig B**, **Jabri A**, **Frisoli TM**, **Engel P**, **O'Neill WW**, and **Villablanca PA**. Percutaneous Paravalvular Leak Closure of the EVOQUE Transcatheter Tricuspid Valve Replacement System. *Struct Heart* 2025; 9(5). PMID: Not assigned. Full Text

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Cardiology/Cardiovascular Research
Gupta RC, **Szekely K**, **Zhang K**, **Lanfear DE**, and **Sabbah HN**. Evidence of Hyperacetylation of Mitochondrial Regulatory Proteins in Left Ventricular Myocardium of Dogs with Chronic Heart Failure. *Int J Mol Sci* 2025; 26(8). PMID: 40332514. Full Text

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Increased acetylation or "hyperacetylation" of mitochondrial (MITO) proteins can lead to abnormalities of the electron transport chain (ETC) and oxidative phosphorylation. In this study we examined the levels of proteins that regulate acetylation. Studies were performed in isolated MITO fractions from left ventricular (LV) myocardium of seven healthy normal (NL) dogs and seven dogs with coronary microembolization-induced heart failure (HF, LV ejection fraction ~35%). Protein levels of drivers of hyperacetylation, namely sirtuin-3 (Sirt-3), a MITO deacetylase, and CD38, a regulator of nicotinamide adenine dinucleotide (NAD(+)), were measured by Western blotting, and the bands were quantified in densitometric units (du). To assess MITO function, MITO components directly influenced by a hyperacetylation state, namely the

protein level of cytophillin-D (CyPD), a regulator of MITO permeability transition pore and MITO Complex-I activity, were also measured. Protein level of Sirt-3 and amount of NAD(+) were decreased in HF compared to NL dogs. Protein levels of CD38 and CyPD were increased in HF compared to NL dogs. Complex-I activity was decreased in HF compared to NL dogs. The results support the existence of a protein hyperacetylation state in mitochondria of failing LV myocardium compared to NL. This abnormality can contribute to MITO dysfunction as evidenced by reduced Complex-I activity and opening of MITO permeability pores.

Cardiology/Cardiovascular Research
Hanson ID, Bentley D, Naidu SS, and **Basir MB**. Response to Letter to the Editor Regarding the Article "Acute Myocardial Infarction and Stage E Shock: Insights From the RECOVER III Study". *J Soc Cardiovasc Angiogr Interv* 2025; 4(5):103599. PMID: 40454286. Full Text

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Cardiology/Cardiovascular Research
Jabri A, Kumar S, **Shadid AM**, Ramakrishna H, Giustino G, **Fadel RA**, **O'Neill B**, **Alqarqaz M**, **Basir MB**, **Engel-Gonzalez P**, **Frisoli T**, Genereux P, Bagur R, Jimenez-Rodriguez G, Hanson I, Abbas A, Dixon S, **O'Neill W**, and **Villablanca PA**. A Comprehensive Review of Left Atrial Venoarterial Extracorporeal Membrane Oxygenation. *J Cardiothorac Vasc Anesth* 2025; Epub ahead of print. PMID: 40404523. Full Text

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Cardiogenic shock (CS) in patients with structural heart disease (SHD) and severe valvular abnormalities poses unique challenges to traditional mechanical circulatory support (MCS) strategies, such as intra-aortic balloon pumps and ventricular assist devices. These devices may fail to address the complex interplay between ventricular unloading and systemic perfusion. Left atrial venoarterial extracorporeal membrane oxygenation (LAVA-ECMO) incorporating left atrial (LA) drainage into the ECMO circuit to reduce left ventricular (LV) preload, mitigate pulmonary congestion, and maintain systemic perfusion. This review explores the pathophysiologic principles and clinical applications associated with LAVA-ECMO. Studies have demonstrated its efficacy in managing CS due to severe valvular disease, biventricular failure, and complex hemodynamic profiles, such as those complicated by aortic regurgitation or ventricular septal defect. Although traditional venoarterial ECMO can incorporate LA drainage, LAVA-ECMO offers distinct advantages by actively unloading the left ventricle, thereby preventing such complications as LV distension and pulmonary edema. Clinical evidence suggests its role as a bridge to definitive interventions, including transcatheter and surgical valve replacements. Despite these benefits, challenges remain, including high in-hospital mortality and complications such as bleeding. LAVA-ECMO

represents a transformative advancement in MCS, offering superior hemodynamic stabilization and myocardial recovery for patients with refractory CS and severe valvular disease. Its ability to address LV unloading directly positions it as a pivotal tool in critical care and SHD management; however, significant gaps in evidence, particularly in long-term outcomes and optimal patient selection, underscore the need for further research.

Cardiology/Cardiovascular Research
Jabri A, Suri RM, and **Villablanca P**. Redo or Redon't? Mitral valve reoperation vs. first-time surgery outcomes: A nationwide study. *Int J Cardiol* 2025; 434:133353. PMID: 40324488. Full Text

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Cardiology/Cardiovascular Research
Lingamsetty SSP, Doma M, Kritya M, Thyagaturu H, Ubaid M, Jitta SR, Prajapati K, Ramadan A, Al-Shammari AS, Martignoni FV, Seto A, Shlofmitz E, **Basir MB**, Megaly MS, and Goldsweig AM. Mechanical outcomes of coronary stenting guided by intravascular ultrasound versus optical coherence tomography: A systematic review and meta-analysis with trial sequential analysis of randomized trials. *Int J Cardiol* 2025; 435:133387. PMID: 40373983. Full Text

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BACKGROUND: Intravascular imaging with intravascular ultrasound (IVUS) or optical coherence tomography (OCT) may guide stent sizing and placement during percutaneous coronary intervention (PCI). We compared IVUS- vs. OCT-guided PCI in terms of mechanical outcomes. METHODS: PubMed, Embase and Cochrane databases were systematically searched until December 2024 for randomized controlled trials (RCTs) comparing IVUS- vs. OCT-guided PCI. Random-effects models were used to estimate mean differences (MDs) and standard mean differences (SMDs) with 95 % confidence intervals (CIs). RESULTS: Six RCTs with 2696 patients were included; 1396 (49.6 %) underwent IVUS-guided PCI. The mean age was 65.1 ± 10.2 years. In the pooled analysis, the post-PCI minimum stent area (MSA) was significantly higher with IVUS-guided PCI than with OCT-guided PCI (MD 0.64 mm(2); 95 % CI 0.17-1.10; $p < 0.01$), and post-PCI mean diameter stenosis was significantly lower with IVUS (MD -1.05 %; 95 % CI -1.90 to -0.21; $p = 0.01$). There were no significant differences between groups in acute lumen gain, stent expansion index, malapposition, tissue protrusion, or edge dissection. In a subgroup analysis, IVUS-guided PCI yielded a greater MSA in studies that did not size vessels by measurement of the external elastic membrane. However, trial sequential analysis suggested that the RCTs to date have

not reached the required quantity of information to support definitive conclusions about MSA and mean diameter stenosis. CONCLUSION: This meta-analysis demonstrated that IVUS-guided PCI was associated with greater MSA and reduced diameter stenosis compared to OCT-guided PCI, with no difference in stent expansion index, more trials are required to confirm this hypothesis.

Cardiology/Cardiovascular Research
Luzum JA, Littleton SDR, Lopez-Medina AI, **Liu B**, **She R**, and **Lanfear DE**. The Beta-Blocker Pharmacogenetic Puzzle: More Pieces of Evidence for Pharmacodynamic Candidate Variants. *Clin Transl Sci* 2025; 18(5):e70239. PMID: 40285373. Full Text

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Previous pharmacogenetic findings for beta-blocker pharmacodynamic candidate genes (ADRB1, ADRB2, ADRA2C, GRK4, and GRK5) have been inconsistent. Therefore, the purpose of this study was to determine whether interactions of pharmacodynamic variants with beta-blocker exposure significantly associated with survival in patients with heart failure with reduced ejection (HFrEF). The 893 patients were 51% self-reported African American and 49% self-reported White race, 36% female, and 240 died (27%) over a median follow-up of 2.8 years. The primary outcome was all-cause mortality. Using Cox proportional hazards models with time-varying beta-blocker exposure and adjusted for clinical risk factors and ancestry, interactions of ADRB1 Arg389Gly, ADRB1 Ser49-Arg389Gly haplotype, ADRA2C Del(322-325), and GRK4 Ala486Val with beta-blocker exposure were significant before correction for multiple comparisons ($p < 0.1$), but only GRK4 Ala486Val remained significant in African Americans after correction for multiple comparisons using the adaptive Hochberg method ($p = 0.022$). Beta-blocker exposure only associated with a significant reduction in the risk of mortality in the African American HFrEF patients with the GRK4 Ala486/Ala486 genotype (HR = 0.44; 95% CI = 0.20-0.96; $p = 0.04$). In conclusion, the interaction of GRK4 Ala486Val with beta-blocker exposure significantly associated with survival in African American HFrEF patients. Larger sample sizes or meta-analyses are needed to have more statistical power to better assess beta-blocker pharmacogenetic interactions for ADRB1 Arg389Gly, ADRB1 Ser49-Arg389Gly haplotype, and ADRA2C Del(322-325) in the future.

Cardiology/Cardiovascular Research
Maini AS, Abu-Much A, Redfors B, Wollmuth JR, **Basir MB**, Faraz HA, Thompson JB, Schonning MJ, Falah B, Moses JW, and **O'Neill WW**. Outcomes Among Patients with Coronary Bifurcation Lesions Undergoing Impella-Supported High-Risk Percutaneous Coronary Intervention. *Am Heart J* 2025; Epub ahead of print. PMID: 40412495. Full Text

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BACKGROUND: Coronary bifurcation lesions (CBL) are associated with lower procedural success, worse post-procedural outcomes, and greater unplanned repeat revascularization. We sought to better understand the impact of Impella support in patients undergoing percutaneous coronary intervention (PCI) of CBLs. METHODS: We used data from the cVAD PROTECT III study (NCT04136392), an FDA-audited, single-arm study of patients undergoing high-risk PCI with Impella support, to examine the outcomes of patients undergoing PCI of CBLs. Patients with a Medina classification of 1.1.1, 1.0.1, or 0.1.1 were considered to have a true CBL, and were compared to patients with non-true CBLs and/or no CBLs. The primary outcome was the rate of CEC-adjudicated major adverse cardiac and cerebrovascular events (MACCE: composite of all-cause death, myocardial infarction, stroke/transient ischemic attack, and repeat revascularization) at 90 days. Cox proportional hazards regression models were adjusted for age, sex, left main disease, and triple vessel disease. RESULTS: Of 1044 patients, 523 had at least one true CBL treated. Baseline characteristics were comparable between groups except for age which was higher in patients with CBLs. Patients with CBLs had a significantly higher pre-PCI SYNTAX scores and number of treated lesions, more left main disease and triple vessel disease, and longer procedure duration. There was no difference in post-PCI SYNTAX score, PCI-related complications, or failure to achieve angiographic success. After adjustment for potential confounders, patients with CBLs had similar rates of 90-day MACCE. CONCLUSIONS: While patients with CBLs undergoing Impella-supported high-risk PCI had higher complexity, there were similar rates of PCI-related complications and 90-day MACCE. TRIAL REGISTRATION: Trial Name: The Global cVAD Study (cVAD), ClinicalTrial.gov Identifier: NCT04136392, URL:https://clinicaltrials.gov/ct2/show/NCT04136392?term=cvad&draw=2&rank=2.

Cardiology/Cardiovascular Research
Mannozzi J. Swimming-induced cardioprotection and cardiac remodeling are a multi-organ affair. *Am J Physiol Regul Integr Comp Physiol* 2025; 328(6):R700-r702. PMID: 40279210. Full Text

Division of Cardiovascular Medicine, Department of Medicine, Henry Ford Hospital, Henry Ford Health System, Detroit, Michigan, United States. ROR: https://ror.org/0193sb042

Cardiology/Cardiovascular Research
McDermott MM, Kadian-Dodov D, **Aronow HA**, Beckman JA, Bolden DM, Castro-Dominguez YS, Creager MA, Criqui MH, Goodney PP, Gornik HL, Hamburg NM, Leeper NJ, Olin JW, Ross E, and Bonaca MP. Research priorities for peripheral artery disease: A statement from the Society for Vascular Medicine. *Vasc Med* 2025; Epub ahead of print. PMID: 40310104. Full Text

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Lower-extremity peripheral artery disease (PAD) affects approximately 236 million people worldwide and at least eight million people in the United States (US). Despite availability of new therapies that prevent major adverse cardiovascular events (MACE), these and major adverse limb events (MALE) remain common and occur more frequently in people with PAD, either with or without coronary artery disease (CAD), compared to people with CAD who do not have PAD. The most effective therapies to prevent cardiovascular events are not identical in people with PAD and those with CAD. Walking impairment and

the risk of lower-extremity amputation are significantly greater in people with PAD compared to those without PAD. This report from the Society for Vascular Medicine (SVM) proposes and summarizes high-priority topics for scientific investigation in PAD, with the goal of improving health outcomes in people with PAD. To develop this report, a multidisciplinary team of scientists and clinicians reviewed literature, proposed high-priority topics for scientific investigation, and voted to rank the highest priority topics for scientific investigation. Priorities for clinical scientific investigation include: determine the current prevalence of PAD in the US by age, sex, race, and ethnicity; improve methods to diagnose PAD; develop new medical therapies to eliminate walking impairment; and improve implementation of established therapies to reduce rates of MACE and MALE in people with PAD. Priorities in basic science and translational science investigation include: developing animal models that closely resemble the vascular, skeletal muscle, and platelet pathology in patients with PAD and defining the genetic and epigenetic contributors to PAD and PAD-associated outcomes. Successful investigation of these research priorities will require more well-trained investigators focused on scientific investigation of PAD, greater and more efficient enrollment of diverse patients with PAD in randomized clinical trials, and increased research funding dedicated to PAD.

Cardiology/Cardiovascular Research
Rawlley B, **Gupta K**, Vaishnav PP, **Parikh SS**, Virani SS, Yandrapalli S, Weinberg A, and Chaudhuri D. Prevalence of Very-High HDL-C and Association with Incident Atherosclerotic Cardiovascular Disease and All-Cause Mortality. *Eur J Prev Cardiol* 2025; Epub ahead of print. PMID: 40366901. Full Text

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Cardiology/Cardiovascular Research
Vuppuluri N, **Makki T**, and **Zahwe F**. Successful Leadless Pacemaker Implantation Despite SVC Obstruction. *JACC Case Rep* 2025; 30(11):103364. PMID: 40409840. Full Text

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BACKGROUND: A 69-year-old male underwent implantation of a leadless pacemaker after a failed attempt to upgrade his single lead ICD in the setting of SVC obstruction. CASE SUMMARY: A 69-year-old male with ischemic cardiomyopathy status post single chamber ICD presented with fatigue. Device interrogation revealed increased RV pacing. Device upgrade was attempted; however, he was found to have a SVC obstruction. A leadless pacemaker was subsequently placed in the right atrium via femoral approach. DISCUSSION: Permanent leadless pacemakers provide a safe, less invasive alternative for patients with conditions that would have previously required complex interventions. Our case demonstrates the use of a leadless pacemaker in a patient with SVC obstruction and ESRD, offering lower infection risk and benefit of retrievability.

Center for Health Policy and Health Services Research
Braciszewski JM, Colby SM, Franklin MJ, Stout RL, Vose-O'Neal A, and Bock BC. Perspectives on a Technology-Based Smoking Cessation Intervention Among Youth Exiting Foster Care. *Child Youth Serv Rev* 2025; 173. PMID: 40463359. Full Text

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Youth in foster care are at increased risk for tobacco-related disease and burden, with very little research and access to evidence-based care. This vulnerable population is also less likely to be involved in the creation of systems and programs that impact their health and well-being. As part of the initial trial of a technology-based smoking cessation program specifically targeting youth exiting foster care, participants (n = 18) provided feedback on their experiences with the approach, including strengths, barriers to cessation, and suggestions for improvement. Results indicated that young people enjoyed their experience with the intervention, as it was both easy to use and provided much needed support in their journey to reduce cigarette use. Participants cited a lack of coping skills and having many family members and friends who smoke as significant impediments to quitting. Finally, respondents suggested a connection to a tobacco quitline, further support from former foster youth, and additional resources for handling comorbid mental health issues as needed adaptations to the intervention. Overall, technology-based smoking cessation may be a feasible and scalable approach to addressing tobacco-related health disparities among youth exiting foster care.

Center for Health Policy and Health Services Research
Malin KJ, **Vance AJ**, Moser SE, Zemlak J, Edwards C, White-Traut R, Koerner R, McGrath J, and McGlothen-Bell K. The impact of social determinants of health on infant and maternal health using a reproductive justice lens. *BMC Pregnancy Childbirth* 2025; 25(1):577. PMID: 40380315. Full Text

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BACKGROUND: Rates of preterm birth, low birth weight, and Neonatal Intensive Care Unit (NICU) admissions continue to rise in the United States (US). Social determinants of health (SDOH) are recognized as significant contributors to infant and maternal health, underscoring the need for use of research frameworks that incorporate SDOH concepts. The Restoring Our Own Through Transformation (ROOTT) theoretical framework is rooted in reproductive justice (i.e. reproductive rights and social justice-based framework) and emphasizes both structural and social determinants as root causes of health inequities. The impact of SDOH on maternal and infant mortality and morbidity can often be traced to structural determinants unique to the US, including slavery, Jim Crow laws, redlining, and the GI Bill. AIMS: Using data from the Pregnancy Risk Assessment Monitoring System (PRAMS) 8 database, we aimed to evaluate relationships between SDOH (as guided by the ROOTT Framework) and maternal and infant health outcomes. METHODS: Data were analyzed from 11 states that included the SDOH supplement in their PRAMS 8 data collection. We used bivariate analyses to examine relationships between SDOH measures guided by the ROOTT framework (e.g. abuse during pregnancy, access to prenatal care, housing stability and education) and maternal morbidity (i.e., gestational hypertension and gestational diabetes) and infant outcomes (i.e., preterm birth, NICU admission, breastfeeding). Pre-identified covariates were controlled for in the logistic and linear regression models. RESULTS: Preterm birth, NICU admission, breastfeeding, and maternal morbidities were significantly associated with SDOH measures linked to structural determinants in the US. Abuse during pregnancy, access to prenatal care, housing, and education were all significantly associated with poorer infant health outcomes in the final regression models. Women who received prenatal care beginning in the 3(rd) trimester were twice as likely to develop gestational hypertension. CONCLUSIONS: SDOHs rooted in structural determinants are important predictors of poorer maternal and infant health outcomes. Evaluating health outcomes using a reproductive justice framework reveals modifiable risk factors, including access to stable healthcare,

safety, and housing. Comprehensive healthcare provision must ensure early and consistent access to healthcare and resources for safety and housing stability to support maternal and infant health.

Center for Health Policy and Health Services Research
Pfeiffer PN, Abraham KM, Lapidos A, Vega E, Jagusch J, Garlick J, Pasiak S, Ganoczy D, Kim HM, **Ahmedani B**, Ilgen M, and King C. Peer Support Intervention for Suicide Prevention Among High-Risk Adults in Michigan: A Randomized Clinical Trial. *JAMA Netw Open* 2025; 8(5):e2510808. PMID: 40434775. Full Text

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IMPORTANCE: Innovative approaches to address interpersonal risk factors for suicide attempts and suicidal ideation may help reduce persistently elevated suicide rates in the US. OBJECTIVE: To determine whether Peers for Valued Living (PREVAIL), a posthospital peer support intervention, reduces suicide attempts and suicidal ideation among adults psychiatrically hospitalized for suicide risk. DESIGN, SETTING, AND PARTICIPANTS: This single-masked, randomized clinical trial recruited adult psychiatric inpatients aged 18 years or older from 3 Michigan-based facilities between June 22, 2018, and December 30, 2022. The study compared 3 months of the PREVAIL intervention plus enhanced usual care with enhanced usual care only, with 3 months of postintervention follow-up. INTERVENTION: One-on-one support from a peer specialist initiated during hospital admission and continued 3 months after discharge. MAIN OUTCOMES AND MEASURES: Suicide attempts were measured using the Columbia Suicide Severity Rating Scale, and suicidal ideation was measured using the Beck Scale for Suicidal Ideation at 3 and 6 months after randomization. RESULTS: Of 5310 patients screened, 455 were randomized using a minimization algorithm. A total of 229 participants were randomized to the PREVAIL peer mentorship arm (mean [SD] age, 32.4 [14.0] years, 134 women [58.5%]), and 226 were randomized to the enhanced usual care arm (mean [SD] age, 31.6 [13.5] years; 139 women [61.5%]). In the intention-to-treat sample with nonmissing data, the percentage of participants with any suicide attempt over 6 months (including participants who only completed 3-month follow-up assessments) was 17.2% (28 of 163) for enhanced usual care and 14.9% (24 of 161 with 2 deaths by suicide) for PREVAIL. Mean (SD) suicidal ideation scores were 4.3 (95% CI, 3.2-5.3) for enhanced usual care and 4.9 (95% CI, 3.7-6.1) for PREVAIL at 6 months. There were no statistically significant effects of the intervention for either outcome in the primary analyses. In post hoc analyses, the interaction between study arm and the COVID-19 pandemic was statistically significant. The enhanced usual care arm had a mean (SD) 6-month suicidal ideation score of 3.5 (6.1) before and 6.1 (7.4) after the pandemic vs the PREVAIL arm (mean [SD] scores, 5.0 [7.7] and 4.5 [6.6], respectively). There were 2 study-related adverse events, with 1 resulting in participant withdrawal from the intervention arm. CONCLUSIONS AND RELEVANCE: In this randomized clinical trial, the peer-delivered PREVAIL intervention up to 3 months after discharge did not significantly differ from enhanced usual care in terms of reducing subsequent suicide attempts or suicidal ideation. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT03373916.

Center for Health Policy and Health Services Research
Santarossa S, Austin B, Bell MA, **Henry SC**, Inclima A, Maddox H, Smith TG, **Copeland L**, **Murphy D**, **Redding A**, and **Loree A**. The Art of Resiliency: Patient Stories of Maternal Mental Health Experiences. *J Patient Cent Res Rev* 2025; 12(2):87-100. PMID: 40337189. Full Text

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Center for Health Policy and Health Services Research

Shuman CJ, Zhang X, Hall SV, Tilea A, Clark SJ, **Vance AJ**, Courant A, and Zivin K. Relationship between opioid use disorder during pregnancy, delivery-related outcomes, and healthcare utilization in Michigan Medicaid, 2012-2021. *J Subst Use Addict Treat* 2025; 175:209720. PMID: 40328372. Full Text

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INTRODUCTION: Pregnant individuals with opioid use disorder (OUD) deliver >20,000 infants annually in the United States, with serious health consequences for perinatal individuals and their infants. This study compares delivery-related outcomes and healthcare utilization among Michigan Medicaid-enrolled perinatal individuals with and without an OUD diagnosis. METHODS: We conducted a retrospective cohort study among Michigan Medicaid enrollees aged 15-44 who delivered a live infant between 2012 and 2021. RESULTS: The cohort included 218,890 deliveries among 170,002 individuals enrolled continuously in Michigan Medicaid for nine months before delivery and up to three months postpartum. Of those, 3.26 % had an OUD diagnosis during this analytic period. Perinatal individuals with OUD identified primarily as White (82.9 %), lived in urban areas (77.2 %), and had a lower income (68.6 %). Among individuals with OUD, 31 % had another behavioral health diagnosis and 55.1 % received a prescription for a psychotropic medication. Of those with OUD, 47.4 % received a prescription for medication for OUD. Deliveries with OUD versus without OUD had a lower probability of cesarean delivery (aOR = 0.89) but higher odds of preterm delivery (aOR = 1.31). Those with OUD had higher likelihood of ambulatory (aOR = 1.99), ED/observational (aOR = 1.19), psychotherapy (aOR = 5.48), and substance use disorder care (aOR = 27.05) visits than those without OUD. CONCLUSIONS: Medicaid-enrolled perinatal individuals in Michigan with OUD had higher rates of preterm birth and healthcare utilization compared to those without OUD. Clinicians and policymakers should target early detection and tailored, coordinated treatment to better address the needs of these individuals.

Center for Health Policy and Health Services Research

Teotia A, and Beltran-Silva F. Hidden Wounds: Exploring Racial and Gender Disparities in the Impact of Mass Shooting Events on Suicide Risk Among U.S. High School Students. *J Interpers Violence* 2025; Epub ahead of print. PMID: 40353529. Full Text

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This study examines the impact of mass shooting events (MSEs) on youth suicide-related behaviors in schools, focusing on heterogeneity across age, race, and gender. Suicide is the second leading cause of death among adolescents and has increased by 63% in the last two decades. Using individual-level data from the Youth Risk Behavior Surveillance System (YRBS) and state-level data from the Gun Violence Archive (GVA) from 2013 to 2019, a difference-in-differences approach is employed to analyze the impact of MSEs on suicide consideration, suicide planning, suicide attempt, and injury from attempted suicide among high school students. Our findings indicate that MSEs lead to a significant increase in the likelihood of suicide attempts (5.1 pp) and injury from suicide (1.9 pp). We particularly observe NH-Black students show a dramatic increase in all measured behaviors, indicating a heightened vulnerability. Notable variations by race and gender suggest that targeted strategies and policies are necessary in addressing students' suicide risk following MSEs. Our findings also reveal lagged effects, demonstrating that the behavioral impacts of MSEs persist over a year, highlighting the importance of investigating longer-term consequences. Strategies targeting the progression from suicide ideation to suicide attempts are particularly crucial to effectively mitigate the long-lasting and detrimental impact that exposure to MSEs can have on youth mental health and well-being.

Center for Individualized and Genomic Medicine Research

Luzum JA, Littleton SDR, Lopez-Medina AI, **Liu B**, **She R**, and **Lanfear DE**. The Beta-Blocker Pharmacogenetic Puzzle: More Pieces of Evidence for Pharmacodynamic Candidate Variants. *Clin Transl Sci* 2025; 18(5):e70239. PMID: 40285373. Full Text

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Previous pharmacogenetic findings for beta-blocker pharmacodynamic candidate genes (ADRB1, ADRB2, ADRA2C, GRK4, and GRK5) have been inconsistent. Therefore, the purpose of this study was to determine whether interactions of pharmacodynamic variants with beta-blocker exposure significantly associated with survival in patients with heart failure with reduced ejection (HFrEF). The 893 patients were 51% self-reported African American and 49% self-reported White race, 36% female, and 240 died (27%) over a median follow-up of 2.8 years. The primary outcome was all-cause mortality. Using Cox proportional hazards models with time-varying beta-blocker exposure and adjusted for clinical risk factors and ancestry, interactions of ADRB1 Arg389Gly, ADRB1 Ser49-Arg389Gly haplotype, ADRA2C Del(322-325), and GRK4 Ala486Val with beta-blocker exposure were significant before correction for multiple comparisons ($p < 0.1$), but only GRK4 Ala486Val remained significant in African Americans after correction for multiple comparisons using the adaptive Hochberg method ($p = 0.022$). Beta-blocker exposure only associated with a significant reduction in the risk of mortality in the African American HFrEF patients with the GRK4 Ala486/Ala486 genotype (HR = 0.44; 95% CI = 0.20-0.96; $p = 0.04$). In conclusion, the interaction of GRK4 Ala486Val with beta-blocker exposure significantly associated with survival in African American HFrEF patients. Larger sample sizes or meta-analyses are needed to have more statistical power to better assess beta-blocker pharmacogenetic interactions for ADRB1 Arg389Gly, ADRB1 Ser49-Arg389Gly haplotype, and ADRA2C Del(322-325) in the future.

Dermatology

Bissonnette R, **Gold LS**, Kircik L, Simpson EL, Eichenfield LF, Browning J, Hebert AA, Alexis AF, Soong W, Piscitelli SC, Tallman AM, Rubenstein DS, Brown PM, and Silverberg JI. Skin Clearance, Duration of Treatment-free Interval, and Safety of Tapinarof Cream 1% Once Daily: Results from ADORING 3, a 48-week Phase 3 Open-label Extension Trial in Adults and Children Down to 2 Years of Age with Atopic Dermatitis. *J Am Acad Dermatol* 2025; Epub ahead of print. PMID: 40383273. Full Text

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BACKGROUND: In two pivotal phase 3 trials, tapinarof demonstrated significant efficacy and was well tolerated in patients down to age 2 years with atopic dermatitis. OBJECTIVE: Assess skin clearance rates, duration of treatment-free intervals, and safety of tapinarof in a phase 3 open-label extension trial. METHODS: Patients from the ADORING 1 and 2 pivotal phase 3 trials, a 4-week maximal usage pharmacokinetics trial, and tapinarof-naive patients received tapinarof for up to 48 weeks. Treatment was based on Validated Investigator Global Assessment for Atopic Dermatitis™ (vIGA-AD™) score. Patients with vIGA-AD™≥1 received tapinarof until vIGA-AD™=0. Patients achieving vIGA-AD™=0 discontinued tapinarof and were monitored for treatment-free interval. Patients with vIGA-AD™≥2 were re-treated until vIGA-AD™=0. RESULTS: 728 patients enrolled. Overall, 51.9% achieved vIGA-AD™=0, and 81.6% achieved vIGA-AD™=0 or 1 at least once. After first achieving complete clearance and discontinuing treatment, the mean first treatment-free interval was 79.8 consecutive days. Tapinarof was well tolerated, with no new safety signals. Most-frequent adverse events were folliculitis (12.1%), nasopharyngitis (6.9%), and upper respiratory tract infection (6.9%). LIMITATIONS: Open-label; treatment-free interval potentially underestimated. CONCLUSION: Tapinarof was well tolerated and resulted in high skin clearance rates that were maintained off-therapy and consistent safety in patients down to age 2 years.

Dermatology

Duponselle J, Herbelet S, Delbaere L, De Schryver Z, Terwee CB, Wolkerstorfer A, Seneschal J, Spuls P, Garg A, **Hamzavi I**, Speeckaert R, and van Geel N. Quality Analysis of Measurement Properties of Patient-Reported Outcome Measures for Vitiligo and of the Studies Assessing Them: A Systematic Review. *Pigment Cell Melanoma Res* 2025; 38(3):e70014. PMID: 40259443. Full Text

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Evaluating measurement properties (MPs) of Patient Reported Outcome Measures (PROMs) in vitiligo is essential for evidence-based recommendations and identifying research gaps. This study assesses the quality of PROMs used in vitiligo. A systematic search of PubMed, Embase, and the Cochrane Library (up to 20 February 2024) included studies on PROM analysis or development, excluding those validating other tools. Quality assessments followed the COSMIN guidelines. PROMs with the highest number MPs rated sufficient (supported by moderate/high Quality of Evidence [QoE]) were reported per construct category, and information related to content validity specifically was provided. Forty articles on 24 PROMs (=161 MP studies) were analyzed. In the QoL group, the VIT, VLQI, VIP-FS, and ViPPO had the highest

number of MPs rated sufficient (n = 3). For severity-related constructs, the Self-Assessment Vitiligo Extent Score (SA-VES) had the most MPs rated sufficient (n = 3). For treatment-related PROMs, the BMQ had the highest number MPs rated sufficient (n = 2). Content validity was limitedly assessed in 12 different PROMs. Comprehensive MP assessment and further validation of vitiligo PROMs are necessary to make definitive conclusions. These systematic reviews are registered at PROSPERO (CRD42020216338). Only English publications were included, which may limit the scope. Additionally, systematic searches conducted by different reviewers in consecutive updates may introduce subjectivity.

Dermatology
Eichenfield LF, **Stein Gold LF**, Simpson EL, Zaenglein AL, Armstrong AW, Tollefson MM, Soong W, Lee LW, Devani AR, Forman SB, Siri DD, Kallender H, Angel B, Li Q, Chen X, and Paller AS. Efficacy and Safety of Ruxolitinib Cream in Children Aged 2 to 11 Years With Atopic Dermatitis: Results From TRuE-AD3, a Phase 3, Randomized Double-Blind Study. *J Am Acad Dermatol* 2025; Epub ahead of print. PMID: 40378883. Full Text

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Dermatology
Gold M, Lain T, Harper JC, Baldwin H, Guenin E, and **Stein Gold L**. Efficacy and Safety of Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Gel: Post Hoc Analysis by Baseline Disease Severity. *Dermatol Ther (Heidelb)* 2025; 15(7):1867-1882. PMID: 40377868. Full Text

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INTRODUCTION: Clindamycin phosphate (CLIN) 1.2%/adapalene (ADAP) 0.15%/benzoyl peroxide (BPO) 3.1% gel (CAB) is the only triple-combination topical approved for acne. These post hoc analyses assessed efficacy and safety of CAB gel compared with component dyads and branded ADAP 0.3%/BPO 2.5% gel in participants stratified by baseline acne severity. METHODS: Data were pooled from two phase 2 and two phase 3 12-week studies. Participants were randomized to once-daily CAB or vehicle; one phase 2 study included dyad combinations of CAB active ingredients (ADAP/BPO, CLIN/BPO, and CLIN/ADAP) and the other included a head-to-head comparison with branded ADAP 0.3%/BPO 2.5%. Assessments included percent changes from baseline in inflammatory/noninflammatory lesions (IL/NIL) and treatment success (≥ 2-grade reduction from baseline in Evaluator's Global Severity Score [EGSS] and clear/almost clear skin). Treatment-emergent adverse events (TEAEs) and cutaneous safety/tolerability were assessed. RESULTS: At week 12, IL reductions in moderate participants (EGSS = 3; n = 1557) were significantly greater with CAB vs vehicle, dyads, and branded ADAP/BPO

(77.1% vs 54.1%, 64.4-69.4%, and 72.8%, respectively; P < 0.05, all). IL reductions in severe participants (EGSS = 4; n = 230) were significantly greater with CAB vs vehicle, ADAP/BPO, and CLIN/BPO (74.5% vs 44.4%, 63.9%, and 61.3%; P < 0.05, all), and similar to CLIN/ADAP and branded ADAP/BPO (73.7%/75.4%). IL reductions were greater than NIL. Moderate participants achieved greater treatment success rates with CAB vs vehicle, dyads, or branded ADAP/BPO (53.9% vs 19.5%, 31.5-35.3%, and 38.1%; P ≤ 0.001, all); only CAB- and CLIN/ADAP-treated severe participants had significantly greater rates vs vehicle (30.9% and 34.0% vs 9.0%; P < 0.05). Most TEAEs were of mild to moderate severity. All mean cutaneous safety/tolerability scores were ≤ 1 (1 = mild). CONCLUSIONS: CAB demonstrated superior efficacy to three dyads and branded ADAP 0.3%/BPO 2.5% in moderate acne participants, and generally numerically greater efficacy in severe acne participants. To our knowledge, these analyses include data from the only double-blind, vehicle-controlled, head-to-head study. TRIAL REGISTRATION: ClinicalTrials.gov identifier NCT03170388, NCT04892706, NCT04214639, and NCT04214652.

Dermatology

Grimes P, **Hamzavi IH**, Bibeau K, Harris JE, van Geel N, Parsad D, Gardner J, Valle Y, Tlhong Matewa G, Gao J, Ren H, and Ezzedine K. Mental Health and Psychosocial Burden Among Patients with Skin of Color Living with Vitiligo: Findings from the Global VALIANT Study. *Dermatol Ther (Heidelb)* 2025; 15(7):1931-1939. PMID: 40325321. Full Text

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INTRODUCTION: Factors associated with vitiligo burden in patients with darker skin (Fitzpatrick skin types IV-VI) are not fully understood. This analysis of patients in the global VALIANT study examined the quality of life (QoL) and psychosocial health among patients with vitiligo by skin type. METHODS: Participants from 17 countries were surveyed regarding their clinical characteristics, everyday experiences with vitiligo, impact of vitiligo on daily activities, emotional well-being, and mental health. RESULTS: Of 3541 surveyed patients, 40.8% (n = 1445) had darker skin versus 59.2% (n = 2096) with fairer skin (types I-III). Patients with darker skin had greater median disease extent than those with fairer skin (6.6% vs 2.5%; P < 0.0001). Mean Vitiligo Impact Patient scale scores were higher among patients with darker skin (31.2 vs 24.5; P < 0.0001); daily activities and emotional well-being were significantly more impacted among patients with darker skin. Among individual skin types, patients with types V and VI expressed considerably higher rates of burden versus all other skin types in all assessments. Interestingly, among patients with fairer skin, those with skin type I reported higher rates of burden than those with skin types II and III. CONCLUSION: Patients with darker skin, particularly skin types V and VI, were more impacted in their daily lives, emotional well-being, and mental health than those with fairer skin, suggesting that a disproportionate need for strategies to improve QoL and mental health burden exists among patients with vitiligo who have skin of color. Vitiligo is a disease that causes white patches to appear on the skin. The study described here analyzed whether vitiligo is more difficult for people with darker skin. To answer this question, the authors used data from a large patient survey called the VALIANT study. Over 3000 people living with vitiligo from 17 countries responded to the survey, and close to half had darker skin. People with darker skin tended to report that larger areas of their body were covered in white patches, suggesting that people with fairer skin may underestimate the extent of their vitiligo. In addition, people with darker skin reported a worse effect on their daily life than those with fairer skin; were more likely to be discouraged and worried about their disease spreading; and were more likely to feel that their vitiligo affected what clothes they wore or what activities they participated in. People with darker skin reported more difficulty with their careers and were more likely to be anxious or depressed.

Even among people with darker skin (three types), effects of vitiligo were worst among those with the darkest skin. These results show that vitiligo is a difficult disease for all people living with vitiligo, but the burden is most amplified among people with darker skin.

Dermatology
Halezeroğlu Y, Chiang BM, **Adame S**, Chattopadhyay A, Ma Y, Barry J, and Abuabara K. Atopic dermatitis is a risk factor for total joint arthroplasty surgical site infections. *J Eur Acad Dermatol Venereol* 2025; Epub ahead of print. PMID: 40407295. Full Text

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Dermatology
Parajuli N, **Subedi K**, **Solone XK**, **Jiang A**, **Zhou L**, and **Mi QS**. Epigenetic Control of Alveolar Macrophages: Impact on Lung Health and Disease. *Cells* 2025; 14(9). PMID: 40358164. Full Text

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Alveolar macrophages (AMs) are immune cells located in the alveoli-the tiny air sacs in the lungs where gas exchange occurs. Their functions are regulated by various epigenetic mechanisms, which are essential for both healthy lung function and disease development. In the lung's microenvironment, AMs play critical roles in immune surveillance, pathogen clearance, and tissue repair. This review examines how epigenetic regulation influences AM functions and their involvement in lung diseases. Key mechanisms, such as DNA methylation, histone modifications, and non-coding RNAs, regulate gene expression in response to environmental signals. In healthy lungs, these modifications enable AMs to quickly respond to inhaled threats. However, when these processes malfunction, they could contribute to diseases such as pulmonary fibrosis, COPD, and pulmonary hypertension. By exploring how epigenetic changes affect AM polarization, plasticity, and immune responses, we can gain deeper insights into their role in lung diseases and open new avenues for treating and preventing respiratory conditions. Ultimately, understanding the epigenetic mechanisms within AMs enhances our knowledge of lung immunology and offers potential for innovative interventions to restore lung health and prevent respiratory diseases.

Dermatology
Parajuli N, **Wang Q**, **Wang J**, **Yin C**, **Subedi K**, **Ge J**, **Yu Q**, **Khalasawi N**, **Jiang A**, **Mi QS**, and **Zhou L**. MicroRNA-17-92 regulate skin Langerhans cell embryonic development through targeting cell proliferation pathways. *J Invest Dermatol* 2025; Epub ahead of print. PMID: 40409677. Full Text

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Dermatology
Richmond A, Ray L, Truong-Balderas K, Almukhtar R, Minkis K, Eshaq M, Kuemmet T, Joo J, Desai S, Lucas R, Wambier C, **Boucher A**, Kang B, Levin Y, Wyles S, and Alam M. Pearls for dermatology resident education in cosmetic and laser procedures. *Dermatol Online J* 2025; 31(2). PMID: Not assigned. Full Text

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Comprehensive education in cosmetic and laser procedures is fundamental during dermatology residency to meet the demand for cosmetic medical procedures and effectively treat a myriad of complex dermatological conditions. This article highlights the importance of structured learning to provide step-wise opportunities for proficiency throughout residency. Although reading assignments and didactic sessions create a solid foundation, focused workshops, resident cosmetic clinics, and offsite electives serve as important experiences for residents to practice hands-on skills. This article provides guidance for curriculum development and establishing hands-on procedural learning. Additionally, the importance of joining professional societies to receive unique training as well as mentorship is highlighted. Having a structured and comprehensive cosmetic curriculum will equip dermatology residents with the toolkit to successfully care for diverse patient needs effectively and safely.

Dermatology
Roszell K, and **Mohammad TF**. The Role of Sunscreen in Protection from Melanoma. *Dermatol Clin* 2025. PMID: Not assigned. Full Text

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Dermatology
Stein Gold L, Eyerich K, Merola JF, Torres J, Coates LC, and Allegretti JR. Oral Peptide Therapeutics as an Emerging Treatment Modality in Immune-Mediated Inflammatory Diseases: A Narrative Review. *Adv Ther* 2025; Epub ahead of print. PMID: 40439953. Full Text

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Immune-mediated inflammatory diseases (IMIDs), such as psoriasis, psoriatic arthritis, and inflammatory bowel disease, encompass a heterogenous group of conditions associated with chronic inflammation.

Systemic treatments for patients with IMIDs include parenterally delivered monoclonal antibodies (mAbs) that disrupt specific cytokine and cytokine receptor binding interactions, and orally delivered small molecules that inhibit certain enzymes involved in the regulation of inflammatory signaling. Many patients prefer oral alternatives to injectables, but currently available oral advanced therapies are less effective than mAbs and/or have tolerability concerns. Thus, an unmet need exists for additional oral treatment options for patients with IMIDs. Therapeutic peptides can be designed to possess characteristics that provide both the target selectivity typically associated with parenterally delivered mAbs and an oral route of administration. Oral peptide therapeutics are an area of intense research in several therapeutic areas, and, although some oral peptides are available for certain indications, such as diabetes, there are currently no targeted oral peptides available for the treatment of patients with IMIDs. Icotrokinra (JNJ-77242113), which is currently in development to treat patients with various IMIDs, is the first targeted oral peptide designed to selectively inhibit interleukin (IL)-23 signaling by blocking the IL-23 receptor on human immune cells. In a phase 2b study in adults with moderate-to-severe psoriasis, icotrokinra showed a significant dose-response effect versus placebo, and a tolerable safety profile at Week 16. Sustained skin clearance and no safety signals were observed through Week 52 in the extension study to the phase 2b study. Ongoing phase 2 and phase 3 clinical studies in patients with psoriasis, psoriatic arthritis, and ulcerative colitis will provide data to inform the therapeutic potential of icotrokinra to address the unmet need in these diseases.

Dermatology
Valle Y, Arenas Soto CM, Kassymkhanova AA, Ocampo-Candiani J, Gondokaryono SP, Binić I, Thuong NV, Cunha PR, Hercogová J, Gao XH, Parsad D, **Lim HW**, Lotti T, and Sigova J. World vitiligo day: a model for grassroots medical activism and pharmaceutical innovation. *Front Med (Lausanne)* 2025; 12:1571422. PMID: 40303368. Full Text

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Dermatology
Veenstra J, **Boothby-Shoemaker W**, and **Friedman BJ**. Response to "Appropriate Statistical Methods to Assess Cross-Study Diagnostic 23-Gene Expression Profile Test Performance for Cutaneous Melanocytic Neoplasms". *Am J Dermatopathol* 2025; 47(6):497-498. PMID: 40314646. Full Text

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Dermatology
Veenstra J, **Ozog D**, and **Stephens A**. Response to Barbieri, "Response to Veenstra et al's 'Benzoyl peroxide acne treatment shows no significant association with benzene-related cancers: A multicenter retrospective analysis'". *J Am Acad Dermatol* 2025; Epub ahead of print. PMID: 40228660. Full Text

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Dermatology
Young KZ, **Kolli SS**, **Kwa MC**, and **McHargue C**. Fluoroscopic radiation-induced skin reactions: radiation dermatitis and radiation-induced morphea. *Dermatol Online J* 2025; 31(2). PMID: Not assigned. Full Text

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Given the rise of radiation based medical procedures, cutaneous radiation reactions are increasing in frequency. Diagnosis of fluoroscopic radiation-related cutaneous injuries are challenging, as patients are often unaware of or cannot recall radiation exposure. It is important to maintain clinical suspicion of radiation-induced skin injuries in patients with persistent morpheaform areas and localized areas of dermatitis or ulceration. Several cutaneous radiation-induced injuries have overlapping clinical presentations. Histopathology may be required to help differentiate between these distinct disorders. Treatment of cutaneous radiation reactions may vary, dictated by a variety of factors, including the disease process, the severity of the lesions, and the presence of comorbidities. Herein, we present two cases to highlight the spectrum of fluoroscopic radiation-induced cutaneous injuries.

Dermatology
Ziglar J, **Mohammad TF**, Gilaberte Y, and **Lim HW**. Sunscreens: Updates on Sunscreen Filters and Formulations. *Photodermatol Photoimmunol Photomed* 2025; 41(3):e70026. PMID: 40371942. Full Text

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BACKGROUND/PURPOSE: Sunscreens are a critical component of photoprotection, shielding the skin from the harmful effects of solar radiation. However, current sunscreens have limitations, including insufficient filters with long-wavelength ultraviolet A (UVA) and visible light (VL) coverage. This review briefly discusses the mechanisms of sunscreen filters, newly developed filters that improve broad-spectrum protection, and examines recent advances in sunscreen formulations that enhance efficacy. METHODS: A targeted literature review was conducted using databases such as Pubmed to identify recent studies published on advancements in sunscreen filters. RESULTS: Recent developments include novel filters with extended UVA and VL coverage. Additives such as antioxidants and anti-inflammatory agents are also being integrated to bolster skin protection. CONCLUSION: Although traditional sunscreens have limitations, ongoing innovations in filter development and formulation science are progressively addressing existing gaps in photoprotection.

Diagnostic Radiology
Eldaya RW, Parsons MS, Hutchins TA, Avery R, Burns J, **Griffith B**, Hassankhani A, Khan MA, Ng H, Raizman NM, Reitman C, Shah VN, Sliker C, Soliman H, Timpone VM, Tomaszewski CA, Yahyavi-Firouz-Abadi N, and Policeni B. ACR Appropriateness Criteria® Cervical Pain or Cervical Radiculopathy: 2024 Update. *J Am Coll Radiol* 2025; 22(5s):S136-s162. PMID: 40409873. Full Text

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Panel Vice-Chair, University of Utah Health, Salt Lake City, Utah.
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Cervical spine pain is one of the most common reasons for seeking medical care as it ranks in the top 5 causes of global years lost to disability. The economic burden of cervical pain is also significant. Imaging is at the center of diagnosis of cervical pain and its causes. However, different symptoms and potential causes of cervical pain require different initial imaging to maximize the benefit of diagnostic usefulness of imaging. In this document we address different cervical pain variants with detailed assessment of the strengths and weaknesses of different modalities for addressing each specific variant. The American College of Radiology Appropriateness Criteria are evidence-based guidelines for specific clinical conditions that are reviewed annually by a multidisciplinary expert panel. The guideline development and revision process support the systematic analysis of the medical literature from peer reviewed journals. Established methodology principles such as Grading of Recommendations Assessment, Development, and Evaluation or GRADE are adapted to evaluate the evidence. The RAND/UCLA Appropriateness Method User Manual provides the methodology to determine the appropriateness of imaging and treatment procedures for specific clinical scenarios. In those instances where peer reviewed literature is lacking or equivocal, experts may be the primary evidentiary source available to formulate a recommendation.

Diagnostic Radiology
Gregg A, **Sly M**, **Lin M**, **Oluborode B**, **McFarlin K**, and **Arnold G**. Small Bowel Obstruction Secondary to Coiling of Gastric Electrical Stimulator Leads: A Rare Complication of Gastroparesis Management. *Radiol Case Rep* 2025; 20(8):4066-4070. PMID: Not assigned. Full Text

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Gastroparesis is a syndrome marked by delayed gastric emptying without mechanical obstruction, and surgical interventions such as gastric electrical stimulation (GES) are typically considered after conservative treatments fail. We present the case of a 53-year-old woman with idiopathic gastroparesis who had undergone GES placement 13 years prior and presented with three days of nausea, vomiting, and abdominal pain. CT imaging revealed a high-grade mechanical small bowel obstruction due to interval coiling and migration of the GES leads, which was confirmed intraoperatively; the patient underwent enterolysis, lead explantation, and placement of a new GES system. This case highlights a rare but serious complication of GES, with only three similar cases previously reported, and underscores the importance of recognizing lead migration as a potential cause of bowel obstruction. Clinicians, especially radiologists and surgeons, should closely assess for changes in lead position on imaging in symptomatic patients with implanted devices, as early diagnosis and intervention are critical to preventing severe outcomes such as bowel ischemia.

Diagnostic Radiology
Hassankhani A, Freeman CW, Banks J, Parsons MS, Wessell DE, Hutchins TA, Lenchik L, Burns J, Eldaya RW, **Griffith B**, Hickey SM, Khan MA, Lawrence B, Paisley TS, Reitman C, Ropper AE, Shah VN, Steenburg SD, Timpone VM, Yahyavi-Firouz-Abadi N, Chang EY, and Policeni B. ACR Appropriateness Criteria® Acute Spinal Trauma: 2024 Update. *J Am Coll Radiol* 2025; 22(5s):S48-s66. PMID: 40409895. Full Text

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Due to its wide spectrum of injury patterns, imaging of acute blunt spine trauma can present many challenges. CT is generally the first-line imaging modality, as it is fast, accurate, and easily accessible. Choice of appropriate imaging is important, as overuse of imaging is associated with prolonged emergency visits and unnecessary hospital admission, potentially leading to iatrogenic injuries and an increase in economic burden. In contrast, failure to identify injuries can have severe consequences. The American College of Radiology Appropriateness Criteria are evidence-based guidelines for specific clinical conditions that are reviewed annually by a multidisciplinary expert panel. The guideline development and revision process support the systematic analysis of the medical literature from peer reviewed journals. Established methodology principles such as Grading of Recommendations Assessment, Development, and Evaluation or GRADE are adapted to evaluate the evidence. The RAND/UCLA Appropriateness Method User Manual provides the methodology to determine the appropriateness of imaging and treatment procedures for specific clinical scenarios. In those instances where peer reviewed literature is lacking or equivocal, experts may be the primary evidentiary source available to formulate a recommendation.

Diagnostic Radiology
Khan S, **Klochko CL**, Cooper S, **Franz B**, **Wolf L**, Alessio A, and Soliman SB. Skeletal Muscle Ultrasound Radiomics and Machine Learning for the Earlier Detection of Type 2 Diabetes Mellitus. *J Med Ultrasound* 2025; 33(2):116-124. PMID: Not assigned. Full Text

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Background: Studies have demonstrated that a qualitatively and quantitatively assessed hyperechoic deltoid muscle on ultrasound (US) was accurate for the earlier detection of type 2 diabetes (T2D). We aim to demonstrate the utility of automated skeletal muscle US radiomics and machine learning for the earlier detection of T2D and prediabetes (PreD) as a supplement to traditional hemoglobin A1c (HbA1c) testing. Methods: A sample of 1191 patients who underwent shoulder US was collected with five cohorts: 171 “normal” (without T2D), 69 “screening” (negative pre-US, but positive HbA1c post-US), 190 “risk” (negative, but clinically high-risk and referred for HbA1c), 365 with “PreD” (pre-US), and 396 with “diabetes” (pre-US). Analysis was performed on deltoid muscle US images. Automatic detection identified the deltoid region of interest. Radiomics features, race, age, and body mass index were input to a gradient-boosted decision tree model to predict if the patient was either low-risk or moderate/high-risk for T2D. Results: Combining selected radiomics and clinical features resulted in a mean area under the receiver operating characteristic (AUROC) of 0.86 with 71% sensitivity and 96% specificity. In a subgroup of only patients with obesity, combining radiomics and clinical features achieved an AUROC of 0.92 with 82% sensitivity and 95% specificity. Conclusion: US radiomics and machine learning yielded promising results for the detection of T2D using skeletal muscle. Given the increasing use of shoulder US and the increasingly high number of undiagnosed patients with T2D, skeletal muscle US and radiomics analysis has the potential to serve as a supplemental noninvasive screening tool for the opportunistic earlier detection of T2D and PreD.

Diagnostic Radiology

Oravec D, **Yadav RN**, **Cushman T**, **Flynn MJ**, **Divine GW**, **Rao SD**, and **Yeni YN**. Osteoporosis screening in the mammography setting via digital wrist tomosynthesis. *Osteoporos Int* 2025; Epub ahead of print. PMID: 40341965. Full Text

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Adherence to osteoporosis screening guidelines could be considerably higher if offered at the time of routine mammography using the same imaging modality. We found that forearm density measurements using a breast imaging system provides density information with excellent diagnostic capability for osteoporosis and osteopenia status determined by hip and spine DXA. PURPOSE: Adherence to osteoporosis screening guidelines via bone mineral density (BMD) measurements with dual-energy x-ray absorptiometry (DXA) is low. Since adherence to breast cancer screening is quite high, it was suggested that the rate of osteoporosis screening can be improved if wrist imaging were performed at the time of breast screening using the very same equipment. METHODS: Digital wrist tomosynthesis (DWT) imaging was performed in 150 women using a 3D mammography system and BMD was measured from both 3D tomosynthesis and synthesized 2D images. In addition, standard DXA based BMD measurements were performed at the hip, spine, and forearm sites. We examined the extent to which DWT-derived ultradistal radius BMD correlates with DXA based BMD measurements, evaluated DWT measurement precision errors, and determined the accuracy of DWT in diagnosing low bone mass and osteoporosis in vivo. RESULTS: DWT BMD strongly correlated with DXA-derived ultradistal radius BMD (R2 up to 0.814) and discriminated osteoporosis (AUC up to 0.978) and osteopenia (AUC up to 0.938) by ultradistal T-score with low in vivo precision errors (0.91-2.3%). BMD derived from 3D DWT BMD performed comparably to forearm DXA BMD in the diagnosis of osteopenia (AUC up to 0.916) and osteoporosis (AUC up to 0.946) determined by hip and spine DXA. CONCLUSIONS: DWT can be readily implemented in mammography settings with similar diagnostic accuracy to DXA, has the potential to increase adherence to osteoporosis screening recommendations, and offers a convenient means to measure bone density within the highly accessible breast screening environment.

Emergency Medicine

Durell K, and **Hooley A**. Utility of Combining a Simulation-Based Method with Lecture for Retinopathy Training in Emergency Medicine Residency. *Spartan Med Res J* 2025; 10(1):1-11. PMID: 40352135. Full Text

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INTRODUCTION: Funduscopic examination is a critical skill for diagnosing eye-related pathologies but has witnessed a decline in proficiency over recent decades. Simulation-based training is proposed as a solution to enhance emergency medicine residents' funduscopic examination skills. We hypothesized that a combination of lecture and simulation would improve residents' diagnostic abilities, with senior residents potentially outperforming junior counterparts. METHODS: This study aimed to assess the effectiveness of simulation-based training in improving the funduscopic examination skills of emergency medicine residents and whether factors such as seniority or prior ophthalmology rotation influenced the results. Residents participated in a 10-question image-based exam, with alternating pairs viewing images and answering questions. Simulation equipment, including digital eye examination retinopathy trainers, was utilized for the study. A lecture covering possible answers was provided, followed by a second round of testing. RESULTS: A total of 20 participants in this pilot study took both the pre- and post-lecture tests. Test scores significantly improved after supplemental education, indicating the effectiveness of simulation-based training in enhancing funduscopic diagnostic skills. Interestingly, resident year and prior completion of an ophthalmology rotation did not significantly impact test scores, underscoring the importance of supplemental education. Notably, participants demonstrated high accuracy in identifying Normal Fundus and several specific pathologies post-training. CONCLUSION: Simulation-based training, supplemented by lectures, offers a promising avenue for improving funduscopic examination proficiency among emergency medicine residents. This study's findings highlight the potential for standardized training methods to benefit residents across different levels of experience. Future research could explore the long-term retention of these skills and their translation into clinical practice. In an era where technological advancements are reshaping medical education, simulation-based training offers a promising avenue for ensuring that essential clinical skills are not lost but rather strengthened among medical professionals.

Emergency Medicine

Owda D, Mensah MO, Yang D, Canavan ME, Gross CP, and Chaudhry SI. Salary Differences by Gender, Race, and Ethnicity Among Assistant Professors at US Medical Schools. *JAMA Netw Open* 2025; 8(5):e259583. PMID: 40366659. Full Text

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IMPORTANCE: Salary inequities by gender are well documented in medicine, but there is limited understanding of racial and ethnic disparities or how these intersect with gender across clinical specialties. OBJECTIVE: To determine whether salaries for assistant professors at US medical schools differ by gender, race and ethnicity, and gender-race-ethnicity intersections across clinical specialties.

DESIGN, SETTING, AND PARTICIPANTS: This cross-sectional study of medical school assistant professor faculty salary data assessed 19 clinical specialties by gender, race and ethnicity, and gender-race-ethnicity intersections. Aggregated data were obtained from the Association of American Medical Colleges Faculty Salary Report for 2022 to 2023 for assistant professors at 153 US medical schools. EXPOSURES: Gender, race and ethnicity, and gender-race-ethnicity. MAIN OUTCOMES AND MEASURES: Median annual salary and salary ratios were calculated for assistant professors across gender, race and ethnicity, and at their intersections for the 2022-2023 academic year. Salary ratios compared women with men, Asian and underrepresented in medicine (URIM) faculty to White faculty, and various gender-race-ethnicity subgroups to White men. RESULTS: In this cross-sectional study of 45 906 assistant professor faculty members from 19 clinical specialties in 2022 and 2023, there were 23 538 (51%) men and 22 368 (49%) women, with a racial and ethnic composition of 10 294 (27%) Asian, 4543 (12%) URIM, and 23 781 (62%) White. Across all specialties, women (median annual salary, $266 450; salary ratio, $0.81:$1.00) earned less than men (annual median salary, $330 000). Asian (median annual salary, $291 360; salary ratio, $0.97:$1.00) and URIM (median annual salary, $278 010; salary ratio, $0.93:$1.00) physicians were paid less than White physicians (median annual salary, $300 000). Intersectional analyses showed that URIM women were paid the least (median annual salary, $259 570; salary ratio, $0.78:$1.00) compared with White men (median annual salary, $333 800). CONCLUSIONS AND RELEVANCE: This cross-sectional study of assistant professor faculty across 19 clinical specialties found salary disparities, with Asian and URIM, both men and women, receiving lower pay than White men. These findings suggest the need to address salary inequities in academia using an intersectional approach that considers both gender and race and ethnicity.

Emergency Medicine

Ratwani A, Grosu HB, Husnain SMN, Sanchez TM, Yermakhanova G, Pannu J, **Debiane LG**, DePew Z, Yarmus L, Maldonado F, Lentz RJ, Rickman OB, Feller-Kopman D, Arain MH, New H, Chen H, Chen SC, Ost DE, Dana F, Rezai Gharai L, Parker M, Lee PM, Khemasuwan D, Shepherd RW, Rahman NM, and Shojaee S. Post-thoracentesis Ultrasound vs. Chest X-ray for the Evaluation of Effusion Evacuation and Lung Re-Expansion, A Multicenter Study. *Ann Am Thorac Soc* 2025; Epub ahead of print. PMID: 40439529. Full Text

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INTRODUCTION: Post-thoracentesis chest radiography (CXR) is often used to evaluate the degree of residual fluid post-thoracentesis. Whether post-drainage ultrasound exam is comparable to CXR in the evaluation of pleural space evacuation is unknown. RESEARCH QUESTION: How do post-thoracentesis ultrasound and CXR compare in assessing the effectiveness of pleural space evacuation? METHODS: In this prospective, multicenter study, patients with free-flowing pleural effusions with minimal to no septations requiring thoracentesis were recruited. Post-thoracentesis ultrasound was performed immediately post-procedure; CXR was performed within 4-hours post-procedure. The primary outcome was agreement on complete pleural space evacuation between ultrasound and CXR. Complete pleural space evacuation was defined as the absence of pleural fluid on anterior, mid-axillary, and posterior ultrasound views and lack of costophrenic angle blunting on CXR. Interobserver reliability was assessed via independent image reviews by two pulmonologists and two radiologists blinded to patient/procedure data, with disagreements resolved by a third reviewer. RESULTS: Of the 147 patients enrolled (February/2021 - May/2022), 145 were included in the final analysis. The median age was 64 years (56-75), and malignancy was the most frequent effusion etiology (n=49). The lung was considered trapped in 50% (n=73). A total of 826 ultrasound images were collected for blind review. The Gwet's Agreement Coefficient 1 (AC1) assessing complete pleural evacuation between ultrasound and CXR was 0.93 (95% CI: 0.83-1.00). When assessing agreement based on the pre-specified criteria of effusion size (small vs large), a substantial level of agreement was observed between ultrasound and CXR, indicated by a kappa of 0.64 (95% CI: 0.51-0.77). There was a strong agreement (kappa= 0.81 (95% CI: 0.71-0.90)) between proceduralist and blind ultrasound reviewers regarding complete pleural space evacuation. CONCLUSION: Post-thoracentesis ultrasound is an equally effective alternative to CXR in evaluating pleural space evacuation in simple pleural effusions.

Emergency Medicine

Roeckner AR, Lin ER, Hinrichs R, Harnett NG, Lebois LAM, van Rooij SJH, Ely TD, Jovanovic T, Murty VP, Bruce SE, House SL, Beaudoin FL, An X, Neylan TC, Clifford GD, Linnstaedt SD, Germine LT, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Hendry PL, Sheikh S, Jones CW, Punches BE, Swor RA, Hudak LA, Pascual JL, Seamon MJ, Datner EM, Pearson C, Peak DA, Merchant RC, Domeier RM, Rathlev NK, O'Neil BJ, Sergot P, Sanchez LD, Joormann J, Sheridan JF, Harte SE, Koenen KC, Kessler RC, McLean SA, Ressler KJ, and Stevens JS. Sequential decreases in basolateral amygdala response to threat predict failure to recover from PTSD. *Neuropsychopharmacology* 2025; Epub ahead of print. PMID: 40319171. Full Text

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Amygdala hyperreactivity early-post trauma has been a demonstrable neurobiological correlate of future posttraumautic stress disorder (PTSD). The basolateral amygdala (BLA) particularly is vital for fear memory and threat processing, but BLA functional dynamics following a traumatic event are unexplored. BLA reactivity to threat may be a trait that can predict PTSD and persist over time. Alternatively, BLA

responsivity to threat cues may change over time and be related to PTSD severity. As part of a larger, multisite study, AURORA, participants 18-75 years old were enrolled in an emergency department (ED) within 72 h of a traumatic event (N = 304, 199 female). At 2-weeks and 6-months post-trauma, PTSD symptoms, BLA responses to threat (fearful>neutral faces), and functional connectivity (FC) during fMRI were assessed. Generalizability of findings was assessed in an external replication sample of ED patients (n = 33). Two weeks post-trauma right BLA reactivity positively predicted later PTSD severity. However, left BLA reactivity to threat at 6 months post-trauma was negatively associated with PTSD severity at that timepoint (ΔPseudo-R(2) = 0.04, IRR = 0.38, p < 0.001). In addition, a decrease in BLA reactivity from 2-weeks to 6-months predicted greater PTSD severity at 6 months (ΔPseudo-R(2) = 0.03, IRR = 0.58, p < 0.001). This replicated in the external sample. A reduction in left BLA FC with the dorsal attention network predicted increased PTSD severity over time. These findings support a shift in BLA function within the first 6 months post-trauma that predicts PTSD pathology and stand in contrast to prior conceptualizations of amygdala hyperreactivity as a trait-like PTSD risk factor.

Emergency Medicine

Vizer L, Pierce J, Ji Y, Bucher MA, Liu M, Ungar L, Giorgi S, Xing Z, House SL, Beaudoin FL, Stevens JS, Neylan TC, Clifford GD, Jovanovic T, Linnstaedt SD, Zeng D, Germine LT, Bollen KA, Rauch SL, Haran JP, Storrow AB, **Lewandowski C**, Musey PI, Jr., Hendry PL, Sheikh S, Jones CW, Punches BE, Hudak LA, Pascual JL, Seamon MJ, Harris E, Pearson C, Peak DA, Merchant RC, Domeier RM, O'Neil BJ, Sergot P, Sanchez LD, Bruce SE, Harte SE, Kessler RC, Koenen KC, McLean SA, and An X. Smartphone language features may help identify adverse post-traumatic neuropsychiatric sequelae and their trajectories. *NPP Digit Psychiatry Neurosci* 2025; 3(1):8. PMID: 40406207. Full Text

Language features may reflect underlying cognitive and emotional processes following a traumatic event that portend clinical outcomes. The authors sought to determine whether language features from usual smartphone use were markers associated with concurrent posttraumatic symptoms and worsening or improving posttraumatic symptoms over time following a traumatic exposure. This investigation was a secondary analysis of the Advancing Understanding of RecOvery afteR traumA study, a longitudinal study of traumatic outcomes among survivors recruited from 33 emergency departments across the United States. Adverse posttraumatic sequelae were assessed over the six months following the initial traumatic exposure. Language features were extracted from usual smartphone use in a specialized app. Bivariate linear mixed models were used to identify and validate language features that are markers associated with posttraumatic symptoms. Participants were 1744 trauma survivors, with a mean age of 39 [SD = 13] years old, and 56% were female. Fourteen language features were associated with severity level of posttraumatic symptoms at specific timepoints (cross-sectional markers) and five features were associated with change in severity level of posttraumatic symptoms (longitudinal markers). References to the body and health or illness were predictive of worsening pain, somatic, and thinking/concentration/fatigue symptom severity over time. An increase in references to others was associated with improvement in somatic symptom severity over time and increases in expressions of causation or cognitive processes were associated with improvement in pain symptom severity over time. Language features derived from usual smartphone use can convey important information about health, functioning, and recovery following a traumatic event. Clinicians might utilize such information to determine who may experience a high symptom burden or risk of worsening posttraumatic symptoms. Via usual smartphone use following trauma exposure, this study identified language markers associated with patient-reported severity and change in severity for multiple symptoms. Using language markers as a proxy for the status of and changes in specific symptoms supports efficient remote health status monitoring and can provide clinicians with valuable real-time insights into health, functioning, and recovery. These insights can be leveraged to guide targeted interventions tailored to individual trauma survivors.

Endocrinology and Metabolism

Dupenloup P, Guan G, Aleppo G, Bergenstal RM, Hood K, **Kruger D**, McArthur T, Olson B, Oser S, Oser T, Weinstock RS, Gal RL, Kollman C, and Scheinker D. Assessing the Financial Sustainability of a Virtual Clinic Providing Comprehensive Diabetes Care. *J Diabetes Sci Technol* 2025; Epub ahead of print. PMID: 40357670. Full Text

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INTRODUCTION: The Virtual Diabetes Specialty Clinic (VDiSC) study demonstrated the feasibility of providing comprehensive diabetes care entirely virtually by combining virtual visits with continuous glucose monitoring support and remote patient monitoring (RPM). However, the financial sustainability of this model remains uncertain. METHODS: We developed a financial model to estimate the variable costs and revenues of virtual diabetes care, using visit data from the 234 VDiSC participants with type 1 or type 2 diabetes. Data included virtual visits with certified diabetes care and education specialists (CDCES), endocrinologists, and behavioral health services (BHS). The model estimated care utilization, variable costs, reimbursement revenue, gross profit, and gross profit margin per member, per month (PMPM) for privately insured, publicly insured, and overall clinic populations (75% privately insured). We performed two-way sensitivity analyses on key parameters. RESULTS: Gross profit and gross profit margin PMPM (95% confidence interval) were estimated at $-4 ($-14.00 to $5.68) and -4% (-3% to -6%) for publicly insured patients; $267.26 ($256.59-$277.93) and 73% (58%-88%) for privately insured patients; and $199.41 ($58.43-$340.39) and 67% (32%-102%) for the overall clinic. Profits were primarily driven by CDCES visits and RPM. Results were sensitive to insurance mix, cost-to-charge ratio, and commercial-to-Medicare price ratio. CONCLUSIONS: Virtual diabetes care can be financially viable, although profitability relies on privately insured patients. The analysis excluded fixed costs of clinic infrastructure, and securing reimbursement may be challenging in practice. The financial model is adaptable to various care settings and can serve as a planning tool for virtual diabetes clinics.

Endocrinology and Metabolism

Oravec D, **Yadav RN**, **Cushman T**, **Flynn MJ**, **Divine GW**, **Rao SD**, and **Yeni YN**. Osteoporosis screening in the mammography setting via digital wrist tomosynthesis. *Osteoporos Int* 2025; Epub ahead of print. PMID: 40341965. Full Text

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Adherence to osteoporosis screening guidelines could be considerably higher if offered at the time of routine mammography using the same imaging modality. We found that forearm density measurements using a breast imaging system provides density information with excellent diagnostic capability for osteoporosis and osteopenia status determined by hip and spine DXA. PURPOSE: Adherence to osteoporosis screening guidelines via bone mineral density (BMD) measurements with dual-energy x-ray absorptiometry (DXA) is low. Since adherence to breast cancer screening is quite high, it was suggested that the rate of osteoporosis screening can be improved if wrist imaging were performed at the time of breast screening using the very same equipment. METHODS: Digital wrist tomosynthesis (DWT) imaging

was performed in 150 women using a 3D mammography system and BMD was measured from both 3D tomosynthesis and synthesized 2D images. In addition, standard DXA based BMD measurements were performed at the hip, spine, and forearm sites. We examined the extent to which DWT-derived ultradistal radius BMD correlates with DXA based BMD measurements, evaluated DWT measurement precision errors, and determined the accuracy of DWT in diagnosing low bone mass and osteoporosis in vivo. RESULTS: DWT BMD strongly correlated with DXA-derived ultradistal radius BMD (R2 up to 0.814) and discriminated osteoporosis (AUC up to 0.978) and osteopenia (AUC up to 0.938) by ultradistal T-score with low in vivo precision errors (0.91-2.3%). BMD derived from 3D DWT BMD performed comparably to forearm DXA BMD in the diagnosis of osteopenia (AUC up to 0.916) and osteoporosis (AUC up to 0.946) determined by hip and spine DXA. CONCLUSIONS: DWT can be readily implemented in mammography settings with similar diagnostic accuracy to DXA, has the potential to increase adherence to osteoporosis screening recommendations, and offers a convenient means to measure bone density within the highly accessible breast screening environment.

Endocrinology and Metabolism

Rao SD. Grading Pseudo Fractures. *Calcif Tissue Int* 2025; 116(1):74. PMID: 40366410. Full Text

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Family Medicine

Veve MP, **Arena CJ**, **Kenney RM**, **Church BM**, **Fried ST**, and **Shallal AB**. Things I wish I knew when implementing an ambulatory antimicrobial stewardship program at an urban health system: lessons learned and future directions. *Antimicrob Steward Healthc Epidemiol* 2025; 5(1):e109. PMID: 40391168. Full Text

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Gastroenterology

Abusuliman M, **Jamali T**, and **Zuchelli TE**. Advances in gastrointestinal endoscopy: A comprehensive review of innovations in cancer diagnosis and management. *World J Gastrointest Endosc* 2025; 17(5):105468. PMID: 40438719. Full Text

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The field of gastroenterology has experienced revolutionary advances over the past years, as flexible endoscopes have become widely accessible. In addition to enabling faster, less invasive, and more affordable treatment, flexible endoscopes have greatly improved the detection and endoscopic screening of malignancies and prevented many cancer-related deaths. The development and clinical application of new diagnostic endoscopic technologies, such as magnification endoscopy, narrow-band imaging, endoscopic ultrasound with biopsy, and more recently, artificial intelligence enhanced technologies, have made the recognition and detection of various neoplasms and sub-epithelial tumors more possible. This review demonstrates the latest advancements in endoscopic procedures, techniques, and devices applied in the diagnosis and management of gastrointestinal cancer.

Gastroenterology
Abusuliman M, Milgrom Y, **Mellinger J**, and Parker R. Management of alcohol use disorder in alcohol-related liver disease. *Frontline Gastroenterol* 2025. PMID: Not assigned. Full Text

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Alcohol-related liver disease (ArLD) is a leading cause of liver-related morbidity and mortality worldwide and is fundamentally connected to alcohol use disorder (AUD). ArLD develops in a subset of heavy drinkers, with progression from steatosis to cirrhosis. Despite the proven benefits of AUD treatment in halting ArLD progression, fewer than 20% of patients with AUD and ArLD receive treatment, and less than 2% are prescribed pharmacotherapy. Hepatology and gastroenterology practitioners are often not confident to manage coexistent AUD and ArLD. This article examines the relationship between AUD and ArLD, evaluates treatment options and highlights the role of integrated care in improving outcomes. Medical addiction therapy significantly reduces binge drinking, hospitalisations and the risk of hepatic decompensation. Several pharmacotherapies are viable in ArLD, but require specific consideration of hepatotoxicity, renal excretion and central nervous system effects. Psychotherapy is associated with lower rates of hepatic decompensation and improved liver-related outcomes. Integrated care models that embed AUD treatment within liver clinics improve engagement, abstinence rates and clinical outcomes compared with standard referrals. AUD treatment is fundamental in ArLD management. Increased use of pharmacological and psychological therapies, alongside integrated care models, may improve patient outcomes and reduce the burden of ArLD. Further research is needed to optimise treatment strategies in this high-risk population.

Gastroenterology
Ahsan BU, **Jin M**, **Theisen BK**, **Singla S**, **Chitale D**, **Shaw B**, **Azordegan N**, **Xu Z**, **Schultz D**, and **Zhang Z**. Comparison of fluorescence in situ hybridization and cytology for the accurate detection of malignant biliary strictures, with emphasis on unusual results. *J Am Soc Cytopathol* 2025; Epub ahead of print. PMID: 40345927. Full Text

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INTRODUCTION: Biliary brushing cytology is the standard diagnostic approach for evaluating biliary strictures, but it has low sensitivity and a high rate of atypical diagnoses. Fluorescence in situ hybridization (FISH) has become an increasingly valuable adjunct to cytology. Therefore, the aim of this retrospective quality improvement study was to evaluate the relative diagnostic performance of traditional cytology and FISH for correctly determining malignant versus benign biliary strictures from biliary brushing samples and to evaluate whether adding FISH to the diagnostic pipeline improves diagnostic accuracy over relying on cytology alone. MATERIALS AND METHODS: We conducted a retrospective study of biliary brushing and FISH results in patients evaluated for biliary strictures between April 2019 and March 2023. RESULTS: A total of 228 specimens were retrieved. For cytology results: 151 negative, 55 atypical, 6 suspicious, and 16 positive. For FISH results: 105 negative, 71 equivocal, and 52 positive. When calculating performance measures, cytology atypical and FISH equivocal were excluded; cytology suspicious was considered positive. The sensitivity and specificity of cytology were 45.8% and 100%, respectively. The sensitivity and specificity of FISH were 84.2% and 96.0%, respectively. CONCLUSIONS: Our findings indicate that FISH exhibits considerably higher diagnostic sensitivity than routine cytology in identifying malignant biliary strictures. Furthermore, combining cytology with FISH may provide a more comprehensive diagnostic approach, reducing the likelihood of false-negative results. However, positive and equivocal FISH results should be interpreted carefully and considered alongside more specific cytology findings to minimize the risk of false-positive diagnoses.

Gastroenterology

Anwar MT, Shahzil M, Arif TB, Khaqan MA, Co EL, Hasan F, Tarar R, Naeem H, Farooq S, Jaan A, **Chaudhary AJ**, Jahagirdar V, and **Salgia R**. MMF Is an Effective and Safer Treatment Options for Treatment-Naïve Patients With Autoimmune Hepatitis Compared to Azathioprine: A Systematic Review and Meta-Analysis. *J Dig Dis* 2025; Epub ahead of print. PMID: 40386905. Full Text

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OBJECTIVES: Autoimmune Hepatitis (AIH) is a chronic inflammatory liver disease with significant morbidity and mortality if untreated. Current first-line treatment involves corticosteroids and azathioprine (AZA), which are effective but are associated with significant adverse effects and treatment intolerance. Mycophenolate mofetil (MMF), an immunosuppressive agent with a potentially better safety profile, has emerged as an alternative. This meta-analysis evaluated the efficacy and safety of MMF compared to AZA in treatment-naïve AIH patients. METHODS: We conducted a systematic review and meta-analysis in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines. Databases were searched for articles published up to May 2024. Statistical analysis was performed using RevMan, employing a random-effects model. RESULTS: Five studies involving 621 patients were included. MMF showed significantly higher rates of complete biochemical response compared to AZA (odds ratio [OR] 3.64, 95% confidence interval [CI] 2.07-6.40, $p < 0.00001$) and lower non-response rates (OR 0.45, 95% CI 0.24-0.85, $p = 0.01$). Corticosteroid withdrawal rates were also higher in the MMF group (OR 2.89, 95% CI 1.69-4.94, $p = 0.0001$). Relapse rate and cumulative prednisolone dose were comparable between the two groups. MMF demonstrated a better safety profile, with significantly lower rates of gastrointestinal symptoms (OR 0.46, 95% CI 0.27-0.79, $p = 0.005$). CONCLUSIONS: MMF shows superior efficacy and tolerability compared to AZA in treatment-naïve AIH patients and may serve as a preferred first-line therapy, offering improved patient adherence and clinical outcomes. Further randomized controlled trials are warranted to confirm these findings.

Gastroenterology

Arif TB, Ali SH, Bhojwani KD, Sadiq M, Siddiqui AA, Ur-Rahman A, **Khan MZ**, Hasan F, and Shahzil M. Global prevalence and risk factors of irritable bowel syndrome from 2006 to 2024 using the Rome III and IV criteria: a meta-analysis. *Eur J Gastroenterol Hepatol* 2025; Epub ahead of print. PMID: 40359286. Full Text

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Functional gastrointestinal disorders impact 40% of the global population, with irritable bowel syndrome (IBS) standing out due to its complexity, quality-of-life effects, and economic impact. Our meta-analysis explored the global prevalence of IBS, considering diagnostic criteria, subtypes, sampling methods, geographical variations, and risk factors. The literature search used databases like PubMed and Cochrane Library, focusing on IBS studies from 2006 to June 2024. Eligibility criteria included studies on individuals aged ≥18, based on Rome III/IV criteria, using random or convenience sampling. Data on IBS prevalence, subtypes, and sampling methods were extracted, and statistical analysis was performed using Open MetaAnalyst and the review manager. The study reviewed 96 articles on IBS prevalence using Rome III and IV criteria across 52 countries, revealing a global prevalence of 14.1%. Prevalence varied by subtype: IBS-C (26.1%), IBS-D (26.5%), IBS-M (31.4%), and IBS-U (8.3%). IBS-D was more prevalent under Rome III (26.2%), while IBS-C was more common under Rome IV (34.2%). First-world countries like the UK, China, and Japan had the highest prevalence. Females [odds ratios (OR): 1.49], stress (OR: 2.47), anxiety (OR: 2.93), and depression (OR: 2.24) were significantly more prevalent in IBS patients, while no significant differences were found in smoking, alcohol use, or education levels. This meta-analysis reveals regional and subtype variations in IBS prevalence, with psychological factors significantly impacting its development. The influence of sampling techniques and Rome III/IV criteria on prevalence estimates highlights the need for a multidisciplinary treatment approach, with important implications for IBS management.

Gastroenterology
Brown K. Update on the Management of Cholestatic Pruritus. *Gastroenterol Hepatol (N Y)* 2025; 21(5):315-317. PMID: 40416922. Full Text

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Gastroenterology
Chaudhary AJ, **Faisal MS**, Sohail A, Baldwin H, **Harris K**, Shahzil M, **Faisal MS**, **Toiv A**, **Mullins K**, and **Suresh S**. Endocuff-Assisted Colonoscopy for Identifying Sessile Serrated Polyps and Adenomas During Routine Colorectal Cancer Screening: A Retrospective Cohort Study. *JGH Open* 2025; 9(5):e70173. PMID: 40375857. Full Text

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BACKGROUND AND AIMS: Polyps located in less accessible areas of the colon, such as inner curves of flexures, are often difficult to visualize. Colonoscope attachments such as the Endocuff have been developed to improve the visualization of these polyps. We aimed to assess the utility of Endocuff-assisted colonoscopy (EAC) in the detection of tubular adenomas and sessile serrated polyps (SSP) compared to conventional colonoscopy during routine colorectal cancer screening. PATIENTS AND METHODS: This retrospective cohort study included patients who underwent colorectal cancer screening with either conventional colonoscopy or EAC between November 2022 and March 2023. The primary outcomes were SSP and tubular adenoma detection rates. Secondary outcomes included total procedure time, cecal intubation time, and ileal intubation rates. RESULTS: Of the 435 patients included, 189 (43%) underwent EAC, and 246 (57%) underwent conventional colonoscopy. The mean ± standard deviation number of polyps detected was 1.7 ± 2.2, the mean procedure time was 18.7 ± 7.5 min, and the mean cecal intubation time was 4.4 ± 3.3 min, with no significant differences between groups. A smaller proportion of patients in the EAC group had successful ileal intubation (14% vs. 55%; $p < 0.01$). The tubular adenoma detection rate was similar between EAC and conventional colonoscopy (41% vs. 39%; $p = 0.70$), but the SSP detection rate was significantly higher with EAC (16% vs. 8.5%; $p < 0.01$). CONCLUSION: EAC may enhance the detection of difficult-to-visualize SSPs during screening

colonoscopies without affecting overall procedure time. However, physicians should consider the examination indication when selecting EAC, as ileal intubation may be more challenging.

Gastroenterology
Dean R, Yazdanfar M, Zepeda J, Levy C, Lammert C, Pratt D, **Gordon SC**, Forman L, Assis DN, McGirr A, McLaughlin M, Mukherjee S, Gungabissoon U, and Bowlus CL. Treatment of pruritus in primary sclerosing cholangitis: Analysis of the consortium for autoimmune liver disease registry. *Hepatol Commun* 2025; 9(5). PMID: 40366147. Full Text

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BACKGROUND: Cholestasis from primary sclerosing cholangitis (PSC) frequently causes pruritus. However, the prevalence of pruritus and its management have not been well studied. Investigating the Cholestatic Pruritus of Primary Sclerosing Cholangitis (ItCh-PSC) includes a retrospective medical record review to determine the prevalence, severity, and treatment patterns of pruritus. METHODS: Data was collected at 5 academic medical centers in the United States. Medical records were searched for the terms "itch" and "pruritus" and data abstracted related to itch severity, number of encounters, and treatment. RESULTS: Among 724 patients with PSC, 359 (50%) of patients had a documented history of pruritus, including 40%, 39%, and 21% with mild, moderate, or severe itch. Itch was less common in those with small ducts compared to large duct PSC (p=0.02) and more frequent in those of Hispanic versus non-Hispanic ethnicity (p=0.001). Compared to patients with mild itch, patients with moderate or severe itch were younger, and had more elevated liver biochemistries, more encounters with itch, and more frequently prescribed 2 or more anti-pruritic medications. Bile acid-binding resins were prescribed in 36%, hydroxyzine in 23%, rifampin in 11%, and fenofibrate in 4% of patients with any itch. The prevalence and severity of pruritus were not affected by cirrhosis, hepatic decompensation, or inflammatory bowel disease. CONCLUSION: Itch is common in patients with PSC and is often associated with multiple prescriptions of antipruritic agents. Effective treatments for pruritus in patients with PSC remain an unmet need.

Gastroenterology
Diaz LA, Ajmera V, Arab JP, Huang DQ, Hsu C, Lee BP, Louvet A, Thiele M, Tavaglione F, Tincopa M, Pose E, Adams LA, Alazawi W, Arrese M, Bataller R, Duseja A, Liangpunsakul S, Lucey MR, Mathurin P, **Mellinger J**, Nakajima A, Ratziu V, Reau N, Rinella ME, Thursz M, Wai-Sun Wong V, Kamath PS, and Loomba R. An Expert Consensus Delphi Panel in Metabolic Dysfunction- and Alcohol-associated Liver Disease: Opportunities and Challenges in Clinical Practice. *Clin Gastroenterol Hepatol* 2025; Epub ahead of print. PMID: 40315973. Full Text

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BACKGROUND & AIMS: Metabolic dysfunction- and alcohol-associated liver disease (MetALD) is a recently defined entity for individuals with liver steatosis, metabolic dysfunction, and increased alcohol intake. However, the current definition of MetALD poses multiple challenges in clinical practice and research. In this Delphi consensus, we provide practical recommendations for the clinical assessment and management of MetALD to address current clinical challenges in MetALD. METHODS: We used a modified Delphi process, including 2 surveys involving a panel of 28 experts from 10 countries spanning 4 continents. We predefined consensus as requiring an ≥80% agreement. RESULTS: The panel reached consensus on 29 statements. Recommendations emphasize the importance of a comprehensive assessment of patients with presumed MetALD, including the quantification of alcohol intake using validated questionnaires and the use of objective biomarkers of alcohol use, such as phosphatidylethanol. The need to reassess metabolic risk factors and liver disease after a period of alcohol abstinence was highlighted to distinguish the primary driver of liver injury. Noninvasive tests were recommended to assess liver disease severity, whereas routine liver biopsy was deemed unnecessary unless other diagnoses were suspected. Comprehensive management strategies should involve multidisciplinary care focusing on lifestyle modifications, alcohol reduction or cessation, weight loss, and exercise. Finally, the panel identified significant gaps in knowledge, advocating for standardized research protocols, longitudinal studies, exploration of pathophysiological mechanisms to inform precision medicine approaches, and the validation of quantitative alcohol biomarkers for identifying MetALD. CONCLUSIONS: This Delphi consensus provides clear recommendations for the clinical assessment and management of MetALD, addressing the unique challenges posed by this condition.

Gastroenterology

Kabir K, **LeRoy DI**, Liyanaarachchi B, Shams Z, and **Singla V**. Humor me with calcium: a case report of humoral hypercalcemia of malignancy secondary to cholangiocarcinoma. *J Gastrointest Oncol* 2025; 16(2):719-725. PMID: 40386597. Full Text

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BACKGROUND: Humoral hypercalcemia of malignancy (HHM) is a rare presentation of cholangiocarcinoma, with few reports in prior literature. HHM is due to the production of parathyroid hormone related peptide (PTHrP) from malignant tissues leading to hypercalcemia, often hard to control. Currently, HHM due to cholangiocarcinoma has been associated with poor prognosis and therapies utilized to manage HHM have not been shown to increase survival. Furthermore, biomarkers such as cytokeratin-7 (CK7) have been shown to correlate with worse prognosis in cholangiocarcinoma. While surgical treatment can be curative for cholangiocarcinoma, current nonsurgical treatment options for HHM due to cholangiocarcinoma have not been associated with improved prognosis. CASE DESCRIPTION: We present a rare case of HHM secondary to cholangiocarcinoma. This case presents a rare case of HHM due to cholangiocarcinoma with an atypical presentation in a 55-year-old female. This patient presented with abdominal swelling and severe hypercalcemia prompting evaluation for a possible gastrointestinal source and was found to have HHM due to cholangiocarcinoma. She was treated for her hypercalcemia medically, however due to the extent of her disease she was unable to undergo surgery. Chemotherapy was not considered during her initial presentation as she originally had a malignancy of unknown primary. Ultimately, shortly after her initial presentation, the patient passed at another hospitalization 36 days after her initial presentation. CONCLUSIONS: HHM rarely presents in cholangiocarcinoma, and of the reported cases, it is often associated with poor prognosis. Given the complexity of these cases, a multi-disciplinary approach is necessary for optimal management of these patients. The ability to risk-stratify patients with unique presentations such as this is crucial for accurate diagnosis and potential treatment. HHM in cholangiocarcinoma is poorly studied due to its rarity; however, given the prognosis of this syndrome, further research is essential for earlier detection and better treatments.

Gastroenterology

Khan HH, **Kumar S**, and **Lyons H**. Practices of North American pediatric gastroenterologists in the management of celiac disease-A survey study. *JPGN Rep* 2025; 6(2):137-145. PMID: 40386323. Full Text

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Celiac disease (CD) is a common autoimmune disorder characterized by an immune-mediated reaction to gluten. We conducted a survey study of the pediatric gastroenterology list server to assess the practices of North American pediatric gastroenterologists in the management of CD. Overall, 160 out of 2400 respondents participated in the study, of which 52.5% of the respondents were females and 72.5% were practicing in university hospitals. Overall, respondents were practicing in adherence to the latest guidelines, except only 36% were screening for hepatitis B virus immunization at diagnosis on most of the visits, and 25% were utilizing human leukocyte antigens typing on most visits if serologies were negative. In addition, female respondents screened for vitamin D deficiency more often than males with a p value < 0.05.

Gastroenterology
Kochhar GS, Dziegielewski C, **Schairer JN**, and Cross RK. Role of Endoscopy in Inflammatory Bowel Disease: What Every Gastroenterologist Should Know. *Am J Gastroenterol* 2025; Epub ahead of print. PMID: 40298226. Full Text

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Endoscopy plays a pivotal role in managing inflammatory bowel disease (IBD). The role of endoscopy has evolved over the years, from diagnostic to surveillance to now doing therapeutic procedures to manage patients with IBD. From the initial diagnostic endoscopy, describing the extent and severity of the disease is an essential step in differentiating between Crohn's disease and ulcerative colitis. Patients with IBD frequently undergo surgeries, and understanding various postoperative configurations and performing endoscopy in postoperative patients can pose a challenge. A thorough understanding of the same can help us to assess disease activity and manage our patients. The purpose of this review was to provide an overview of the role of endoscopy in the management of IBD and to examine various anatomical variations in patients postoperatively.

Gastroenterology
Pohl H, Rex DK, Barber J, Moyer MT, Elmunzer BJ, Rastogi A, Gordon SR, Zolotarevsky E, Levenick JM, Aslanian HR, **Elatrache M**, von Renteln D, Wallace MB, Brahmbhatt B, Keswani RN, Kumta NA, Pleskow DK, Smith ZL, Abu Ghanimeh MK, Simmer S, Sanaei O, Mackenzie TA, and **Piraka C**. Cold snare endoscopic resection for large colon polyps: a randomised trial. *Gut* 2025; Epub ahead of print. PMID: 40393701. Full Text

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Gastroenterology and Hepatology, Mayo Clinic's Campus in Florida, Jacksonville, Florida, USA.
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BACKGROUND: Complications of endoscopic mucosal resection (EMR) of large colorectal polyps remain a concern. OBJECTIVE: We aimed to compare safety and efficacy of cold EMR (without electrocautery) to hot EMR (with electrocautery) of large colorectal polyps. DESIGN: In this multicentre randomised trial, patients with any large (≥20 mm) non-pedunculated colon polyp were assigned to cold or hot EMR (primary intervention), and to submucosal injection with a viscous or non-viscous solution (secondary intervention) following a 2×2 design. The primary outcome was the rate of severe adverse events (SAEs). The secondary outcome was polyp recurrence. In this study, we report results of the primary intervention. RESULTS: 660 patients were randomised and analysed. An SAE was observed in 2.1% of patients in the cold EMR group and in 4.3% in the hot EMR group (p=0.10) (per protocol analysis 1.4 vs 5.0%, p=0.017) with fewer perforations following cold EMR (0%) compared with hot EMR (1.6%, p=0.028). Postprocedure bleeding did not differ (1.5% vs 2.2%, p=0.57). The effect of cold resection was independent of the type of submucosal injection solution, polyp size or antithrombotic medications. Recurrence was detected in 27.6% and 13.6% in the cold and hot EMR groups, respectively (p<0.001). Recurrence was not significantly different for 20-29 mm polyps (18.6% vs 13.4%, p=0.24) and for sessile serrated polyps (14.1% vs 8.5%, p=0.33). CONCLUSION: Universal application of cold EMR did not significantly lower SAEs (unless cold EMR could be completed) and doubled the recurrence rate compared with hot EMR. TRIAL REGISTRATION DETAILS: ClinicalTrials.gov, number: NCT03865537.

Gastroenterology
Saleem A, **Jamali T**, and **Gueorguieva I**. Mucosal Schwann Cell Hamartoma of the Appendix: Expanding the Differential for Gastrointestinal Bleeding. *ACG Case Rep J* 2025; 12(5):e01708. PMID: 40401048. Full Text

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Mucosal Schwann cell hamartomas (MSCH) are rare benign tumors typically found in the colorectal region. We present the case of an 87-year-old man with a history of mucosa-associated lymphoid tissue lymphoma who developed symptomatic gastrointestinal bleeding due to an appendiceal MSCH. The patient's ongoing melena and anemia led to further evaluation. Subsequent colonoscopy revealed active bleeding from the appendiceal orifice with hemostasis achieved using epinephrine injection. A laparoscopic appendectomy confirmed MSCH through histopathology and immunohistochemical staining. Given its rarity, this case underscores the importance of considering MSCH in unexplained gastrointestinal bleeding and demonstrates its potential to be a symptomatically significant entity.

Gastroenterology
Singal AG, Yang JD, Jalal PK, **Salgia R**, Mehta N, Hoteit MA, Kao K, Daher D, El Dahan KS, Hernandez P, Nayak A, Kim N, Pham S, Gamez J, Troost JP, and Parikh ND. Patient-Perceived Risk of Hepatocellular Carcinoma and Net Benefit of Surveillance: A Multicenter Survey Study. *Am J Gastroenterol* 2025; Epub ahead of print. PMID: 40267274. Full Text

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INTRODUCTION: Hepatocellular carcinoma (HCC) surveillance is underused in clinical practice, and few contemporary data have assessed patients' perceptions of surveillance effectiveness and net benefit. METHODS: We conducted a survey study among adult patients with cirrhosis at 7 health systems in the United States. The survey was based on validated measures, when available, and assessed patient

knowledge about HCC surveillance, attitudes regarding surveillance benefits and harms, perceived HCC risk, and trust in their doctors. RESULTS: Respondents (n = 665; median age 60; 46.5% female) were knowledgeable about HCC surveillance, with no significant differences across sociodemographic groups; however, approximately 1 in 5 patients had knowledge gaps about the need and benefit of surveillance. Over three fourths of patients believed that surveillance improves early HCC detection (80.3%) and survival (77.9%). While 74.0% of patients reported that doctors had discussed surveillance benefits, only 54.2% recalled a discussion about potential harms. Patients placed greater importance on surveillance benefits, but expressed harms should be measured when assessing the net benefit of surveillance programs. Based on a pictogram depicting current estimates for surveillance benefits and harms, 93.2% of patients chose to undergo surveillance, with no significant differences by race, perceived surveillance benefits, or fear of dying from HCC. Study limitations include response and nonresponse biases, which may result in an overestimation of reported surveillance benefits and patient acceptance. DISCUSSION: Most patients with cirrhosis followed at academic health systems have high knowledge about HCC surveillance, believe that it is beneficial, and express interest in undergoing surveillance after being counseled about the benefits and harms.

Global Health Initiative

Agbedinu K, **Antwi S**, Aduse-Poku L, Akakpo PK, **Larrious-Lartey H**, Ofori Aboah V, Mensah S, Nyarko V, Amponsah-Manu F, Nsaful J, Dampson R, Nortey M, Aja I, Sheriff M, Dokurugu MA, Affram N, Mremi A, Mwakyembe T, **Kamita M**, **Kaljee L**, and **Jiagge E**. A Scoping Review on Barriers to Cancer Diagnosis and Care in Low- and Middle-Income Countries. *Cancer Epidemiol Biomarkers Prev* 2025; Epub ahead of print. PMID: 40304503. Full Text

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Korle Bu Teaching Hospital, Ghana.
Eastern Regional Hospital, Ghana.
Korle Bu Teaching Hospital, Accra, Ghana.
Pathologists Without Borders, Ghana.
Cape Coast Teaching Hospital, Cape Coast, Central, Ghana.
Tamale Teaching Hospital, Ghana.
Tamale Teaching Hospital, Tamale, Ghana.
Ho Teaching Hospital, Ghana.
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Cancer remains a significant global health challenge, with low- and middle-income countries (LMICs) disproportionately burdened by high mortality rates despite a lower overall incidence. Barriers to timely diagnosis and care exacerbate these disparities. This scoping review synthesize existing literature on barriers for women in LMICs following the Joanna Briggs Institute methodology and PRISMA-ScR guidelines. Studies on women in LMICs reporting barriers to accessing care for breast, colorectal, lung, cervix uteri, thyroid, corpus uteri, and stomach cancers were included. 29 studies involving 7,031 participants were included. The most common barriers included financial challenges (65.5%), geographical obstacles (34.5%), health system limitations (55.2%), and low health literacy (51.7%). Patients experienced significant delays, averaging 7.4 months from symptom onset to diagnosis and 4.9 months from diagnosis to treatment initiation. Structural issues such as limited diagnostic services, inadequate healthcare infrastructure, and healthcare provider shortages were widespread. Addressing the multifaceted barriers to cancer care in LMICs requires comprehensive strategies, including increasing financial support, decentralizing care services, improving healthcare infrastructure, and enhancing education for patients and providers. Policymakers and stakeholders should prioritize investments in

cancer care to reduce disparities and improve outcomes. These findings will inform strategies for improving cancer care in low-resource settings globally.

Graduate Medical Education
Sankari A, Aldwaikat A, Habra M, Salloum A, Zeineddine S, Pandya N, Martin JL, and Badr MS. Comorbid sleep disorders among individuals with spinal cord injury. *J Clin Sleep Med* 2025; Epub ahead of print. PMID: 40353318. Full Text

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STUDY OBJECTIVES: To determine the rate of sleep-disordered breathing (SDB) in individuals with spinal cord injury (SCI). and its types (central and obstructive, and combined (COSA) and to assess the response to treatment using positive airway pressure (PAP) (defined as an apnea-hypopnea index (AHI) of less than 5 events per hour on initial PAP titration) in individuals with SCI. METHODS: Individuals with SCI who underwent a full night of diagnostic polysomnography (PSG) from to 2010-2024 to determine the type of SDB and its severity using the AHI and central apnea index (CAI). The inclusion criteria were individuals with chronic SCI at low cervical or thoracic (at C4-T6 levels). who are not mechanically ventilated or had tracheostomies. "Central sleep apnea (CSA)" is diagnosed with an AHI of 5+ events/h and a CAI of at least 50% of the AHI. "Obstructive sleep apnea (OSA) only" is identified by an AHI of 5+ events/h and a CAI of less than 5 events/h. COSA is characterized by an AHI of 5+ events/h, with a CAI over 5 events/h but under 50% of the total AHI. The positive response to PAP therapy was based on the AHI level of less than 5 events/h after initiating PAP treatment and based on remote monitoring data. RESULTS: Among the 81 individuals who met the inclusion criteria, 12 patients (15%) were diagnosed with COSA, 4 patients (5%) presented with CSA only, 56 patients (69%) had OSA, and 8 patients (10%) exhibited no SDB. In a subset of participants (N=51) hypopneas were classified as obstructive or central events based on American Academy of Sleep Medicine (AASM) definition and revealed that approximately one-third (32%) had central or COSA, 63% had OSA, and 6% did not have SDB on PSG. A total of 35 (47%) individuals diagnosed with SDB underwent PAP titration and were prescribed PAP. Twenty (27%) individuals received PAP treatment, and only 17 (23%) continued their use for the initial three months. Only 11 patients (15%) demonstrated responsiveness to PAP on day 90 (AHI<5 during therapy). CONCLUSIONS: SDB is extremely common in individuals with SCI. The efficacy of PAP therapy is suboptimal, and adherence rates decline significantly over time.

Hematology-Oncology
Abu Omar Y, Sullivan E, Schulte R, **Pichardo R**, and Rothberg MB. White Blood Counts of Hospitalized Patients Without Infection, Malignancy, or Immune Dysfunction. *South Med J* 2025; 118(5):287-292. PMID: 40316273. Full Text

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OBJECTIVES: An elevated white blood cell (WBC) count may indicate malignancy, infection, and immune dysfunction. In diagnosing these conditions, physicians generally evaluate laboratory results compared with reference ranges based on healthy populations. Reference ranges for hospitalized patients are lacking. This study aims to define a normal reference range for WBC count in hospitalized patients without malignancy, infection, or immune dysfunction. METHODS: This was a retrospective cross-sectional study of nonsurgical patients hospitalized from 2017 to 2018 in the Cleveland Clinic Health System without malignancy, infection, or immunological dysfunction. WBC count, absolute neutrophil

count, and absolute lymphocyte count were collected. We calculated means, standard deviations, and the reference range for each variable. RESULTS: A total of 46,419 patients had WBC counts. Mean WBC count was 8.0 (standard deviation 3.31, reference range 1.6-14.5). In a multivariable linear regression, mean WBC count decreased with age, Black race relative to White race, and congestive heart failure. Body mass index, diabetes mellitus, chronic kidney disease, chronic obstructive pulmonary disease, and steroid use were associated with higher WBC count. In total, 13.5% of patients in this cohort had WBC counts above the "normal" threshold of 11. CONCLUSIONS: Among hospitalized patients without infection, malignancy, or immune dysfunction, the normal range for WBC count was 1.6 to 14.5 × 10(9) WBCs/L. Age, race, body mass index, steroid use, and several comorbidities were associated with WBC count variation from the reference levels established based on healthy populations. Physicians should be cautious when interpreting WBC counts between 11 and 14.5 × 10(9) WBCs/L, which appear to represent normal values in the hospital.

Hematology-Oncology

Agbedinu K, **Antwi S**, Aduse-Poku L, Akakpo PK, **Larrious-Lartey H**, Ofori Aboah V, Mensah S, Nyarko V, Amponsah-Manu F, Nsaful J, Dampson R, Nortey M, Aja I, Sheriff M, Dokurugu MA, Affram N, Mremi A, Mwakyembe T, **Kamita M**, **Kaljee L**, and **Jiagge E**. A Scoping Review on Barriers to Cancer Diagnosis and Care in Low- and Middle-Income Countries. *Cancer Epidemiol Biomarkers Prev* 2025; Epub ahead of print. PMID: 40304503. Full Text

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Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.
Korle Bu Teaching Hospital, Ghana.
Eastern Regional Hospital, Ghana.
Korle Bu Teaching Hospital, Accra, Ghana.
Pathologists Without Borders, Ghana.
Cape Coast Teaching Hospital, Cape Coast, Central, Ghana.
Tamale Teaching Hospital, Ghana.
Tamale Teaching Hospital, Tamale, Ghana.
Ho Teaching Hospital, Ghana.
KCMC University, Moshi, Kilimanjaro, Tanzania.
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Henry Ford Hospital, Detroit, Michigan, United States.

Cancer remains a significant global health challenge, with low- and middle-income countries (LMICs) disproportionately burdened by high mortality rates despite a lower overall incidence. Barriers to timely diagnosis and care exacerbate these disparities. This scoping review synthesize existing literature on barriers for women in LMICs following the Joanna Briggs Institute methodology and PRISMA-ScR guidelines. Studies on women in LMICs reporting barriers to accessing care for breast, colorectal, lung, cervix uteri, thyroid, corpus uteri, and stomach cancers were included. 29 studies involving 7,031 participants were included. The most common barriers included financial challenges (65.5%), geographical obstacles (34.5%), health system limitations (55.2%), and low health literacy (51.7%). Patients experienced significant delays, averaging 7.4 months from symptom onset to diagnosis and 4.9 months from diagnosis to treatment initiation. Structural issues such as limited diagnostic services, inadequate healthcare infrastructure, and healthcare provider shortages were widespread. Addressing the multifaceted barriers to cancer care in LMICs requires comprehensive strategies, including increasing financial support, decentralizing care services, improving healthcare infrastructure, and enhancing education for patients and providers. Policymakers and stakeholders should prioritize investments in cancer care to reduce disparities and improve outcomes. These findings will inform strategies for improving cancer care in low-resource settings globally.

Hematology-Oncology

Azar I, Khan HY, Bannoura SF, Gandhi N, Uddin MH, Nagasaka M, Gong J, Nazha B, Choucair K, Vojjala N, Khushman MM, Soares HP, El-Deiry WS, **Philip PA**, El-Rayes B, Chen H, Lou E, Muqbil I, Farrell AP, Swensen J, Oberley MJ, Nabhan C, Goel S, Shields AF, Mohammad RM, Pasche BC, and Azmi AS. Molecular Characterization and Clinical Outcomes of Pancreatic Neuroendocrine Neoplasms Harboring PAK4-NAMPT Alterations. *JCO Oncol Adv* 2025; 2(1):e2400032. PMID: 40330142. Full Text

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PURPOSE: The mammalian target of rapamycin (mTOR) inhibitor everolimus is US Food and Drug Administration-approved for advanced pancreatic neuroendocrine neoplasms (pNENs), yet resistance is common, necessitating the identification of resistance mechanisms for effective treatment strategies. Previous studies suggest that targeting the aberrant expression of mTOR regulators p21-activated kinase 4 (PAK4) and nicotinamide phosphoribosyl transferase (NAMPT) sensitizes pNENs to everolimus. In this study, we queried a large real-world data set of pNENs, characterizing the molecular and immune landscapes, as well as the clinical outcomes associated with aberrant PAK4 and NAMPT expression. METHODS: Two-hundred and ninety-four pNEN cases were analyzed using next-generation sequencing and whole-exome/whole-transcriptome sequencing. We stratified patients into clusters on the basis of median cutoff. RESULTS: High expression of genes activated in response to mTOR activation was found in NAMPT-high and PAK4-high groups. Enrichment of PI3K/AKT/mTOR and glycolysis pathways was observed in these tumors. Higher mutation rates in multiple endocrine neoplasia type 1, alpha thalassemia/mental retardation syndrome X-linked, TSC2, SETD2, and CCNE1 were observed in high NAMPT and PAK4 clusters. Immune analysis revealed enrichment in inflammatory response pathways, IL2/STAT5 signaling, and immune checkpoint genes. Increased neutrophils, natural killer cells, and macrophages were found in PAK4-high/NAMPT-high tumors. Analysis of real-world patient data revealed that high PAK4 (P = .0428) or NAMPT (P = .0002) expression individually correlated with lower overall survival in all neuroendocrine neoplasms (NEN) cohorts, while the combined high expression of both was associated with the worst outcomes (P = .0002). Similar trends were observed in pancreatic NEN cohorts. CONCLUSION: Our study demonstrates that PAK4-high/NAMPT-high pNENs are associated with distinct molecular and immune profiles. Further investigation is warranted to determine if dual PAK4 and NAMPT blockade enhances the efficacy of immunotherapeutics.

Hematology-Oncology

Babiker HM, Picozzi V, Chandana SR, Melichar B, Kasi A, Gang J, Gallego J, Bullock A, Chunyi H, Wyrwicz L, Hitre E, Osipov A, de la Fouchardiere C, Ales I, Dragovich T, Lee W, Feeney K, **Philip P**, Ueno M, Van Cutsem E, Seufferlein T, and Macarulla T. Tumor Treating Fields With Gemcitabine and Nab-Paclitaxel for Locally Advanced Pancreatic Adenocarcinoma: Randomized, Open-Label, Pivotal Phase III PANOVA-3 Study. *J Clin Oncol* 2025; Epub ahead of print. PMID: 40448572. Full Text

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PURPOSE: Tumor treating fields (TTFields) use alternating electric fields to disrupt cancer cell proliferation. Feasibility of TTFields therapy with gemcitabine/nab-paclitaxel was previously demonstrated in patients with advanced pancreatic adenocarcinoma. PANOVA-3 was designed to confirm safety and efficacy of TTFields in patients with unresectable locally advanced pancreatic adenocarcinoma (LA-PAC). METHODS: In this global phase III trial, 571 patients with newly diagnosed LA-PAC were randomly assigned to receive gemcitabine 1,000 mg/m(2) and nab-paclitaxel 125 mg/m(2) by intravenous infusion once a day on days 1, 8, and 15 of a 28-day cycle with or without TTFields. The primary end point was overall survival (OS). Secondary end points included progression-free survival (PFS), local PFS, pain-free survival, and overall response rate (ORR). Distant PFS was analyzed post hoc. RESULTS: OS was significantly prolonged using TTFields with gemcitabine/nab-paclitaxel versus gemcitabine/nab-paclitaxel (median, 16.2 months [95% CI, 15.0 to 18.0] v 14.2 months [95% CI, 12.8 to 15.4]; hazard ratio [HR], 0.82 [95% CI, 0.68 to 0.99]; P = .039). PFS, local PFS, and ORR were not improved. Pain-free survival was significantly prolonged with TTFields with gemcitabine/nab-paclitaxel (median, 15.2 months [95% CI, 10.3 to 22.8] v 9.1 months [95% CI, 7.4 to 12.7]; HR, 0.74 [95% CI, 0.56 to 0.97]; P = .027), as was distant PFS (median, 13.9 months [95% CI, 12.2 to 16.8] v 11.5 months [95% CI, 10.4 to 12.9]; HR, 0.74 [95% CI, 0.57 to 0.96]; P = .022). Device-related skin adverse events (AEs) were experienced by 76.3% of patients. Most device-related skin AEs were mild to moderate, with 7.7% of patients reporting a grade 3 AE. CONCLUSION: This study demonstrated significant OS, pain-free survival, and distant PFS benefits for TTFields with gemcitabine/nab-paclitaxel versus gemcitabine/nab-paclitaxel in patients with unresectable LA-PAC, with no additive systemic toxicity.

Hematology-Oncology

Bowen AM, Cloud A, Fadly S, Gennette R, Hector-Word Z, **Hirth J**, Kier Y, **Kostoff D**, **Kuriakose P**, Malhotra B, Nourkeyhani H, Rana J, DeVries K, Mackler E, Winsted S, Voisine E, and Griggs JJ. Increasing Olanzapine Prescribing for Patients Undergoing Highly Emetogenic Chemotherapy. *JAMA Netw Open* 2025; 8(5):e2510392. PMID: 40397444. Full Text

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IMPORTANCE: Olanzapine as part of a 4-drug antiemetic regimen is highly effective at preventing nausea and vomiting in patients receiving highly emetogenic chemotherapy (HEC). National prescribing rates of olanzapine in eligible patients have, however, remained persistently low. OBJECTIVE: To describe efforts to increase the guideline-concordant use of olanzapine in patients receiving HEC in a statewide oncology collaborative. DESIGN, SETTING, AND PARTICIPANTS: The Michigan Oncology Quality Consortium (MOQC) is a collaborative of Michigan-based oncology practices whose mission is to advance the care of patients with cancer and their caregivers through comprehensive, patient- and practice-led quality improvement initiatives. Participants were patients receiving HEC at 38 MOQC member practices during an initiative from 2019 to 2023 to improve guideline-concordant inclusion of olanzapine as part of a 4-drug antiemetic regimen in HEC prophylaxis. INTERVENTIONS: Interventions included performance audit and feedback to practices along with peer comparison, learning collaboratives of practices, education by experts at collaborative meetings, creation of patient-facing materials, and the addition of value-based reimbursement beginning in 2021. Measure performance was assessed using the American Society of Clinical Oncology's Quality Oncology Practice Initiative. MAIN OUTCOMES AND MEASURES: Proportion of patients receiving olanzapine for the first cycle of HEC as part of a 4-drug antiemetic regimen for chemotherapy-induced nausea and vomiting. RESULTS: Between 2019 and 2024, data were manually collected from the medical records of 8662 patients treated with HEC at 38 medical oncology practices at 71 sites across the state. Individual patient-level demographic data are not available from the QOPI database. For patients from years 2021 through 2024, the median (IQR) age was 62 (52-69) years; 4434 were female (65.5%); 814 were Black or African American (12.0%), 121 were Hispanic or Latino (1.8%), and 5385 were White (79.7%). The use of olanzapine as part of a 4-drug antiemetic increased from 7.2% in 2019 to 63.4% in 2024 ($\chi 21 = 553.61$; $P < .001$). CONCLUSIONS AND RELEVANCE: In this quality improvement study of olanzapine prescribing in eligible patients, MOQC deployed quality improvement methods to increase the prescribing of olanzapine as part of a 4-drug regimen in patients receiving HEC, well above both the baseline and national levels of prescribing. This work suggests that efforts to improve patient care can be effective across diverse practice types, locations, and sizes in a statewide collaborative. Ongoing efforts include supporting change in those practices with low rates of prescribing and demonstrating the importance of this work for patient outcomes.

Hematology-Oncology

Connell B, **Hwang C**, Folefac E, Lawlor C, Koethe B, and Mathew P. Dose-Dense Docetaxel and Radium-223 in Bone-Dominant Metastatic Castration-Resistant Prostate Cancer. *Clin Genitourin Cancer* 2025;102368. Epub ahead of print. PMID: 40383703. Full Text

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BACKGROUND: Disease progression in castration-resistant prostate cancer (CRPC) remains bone-dominant and docetaxel-responsive. Docetaxel and radium-223 would be a logical combination but myelosuppression is dose-limiting. Dose-dense schedules of docetaxel have comparable activity to bolus dosing with mitigated myelosuppression. We hypothesized that dose-dense docetaxel with standard radium-223 would be a feasible, safe and effective combination in bone-dominant metastatic CRPC. METHODS: Subjects had progressive bone-predominant CRPC. Design was dose escalation plus expansion with 28-day cycles. Docetaxel was given every 2 weeks in a 4-week lead-in, then with Radium-223 every 4 weeks up to 6 cycles. Dose-levels (DL) included 1: docetaxel 40 mg/m(2); 1a: docetaxel 40 mg/m(2) with G-CSF on Day 16, 2a: docetaxel 50 mg/m(2) with G-CSF on Day 16. The maximum tolerated dose (MTD) was defined as the highest (DL) of docetaxel achieved without dose-limiting toxicity (DLT). Markers of safety and efficacy were annotated. RESULTS: Forty-three subjects were enrolled

(NCT03737370). The patient population included 21% black, 9% Asians, 93% had prior intensified hormonal therapy, 67% had bone pain, and 76% had ≥ 4 bone metastases. Seven patients dropped out during the 4-week docetaxel lead in. Neutropenia at DL 1 limited combination therapy. No (DLT) occurred at DL 1a (n = 6) or DL 2a (n = 5). Twenty-two patients were enrolled to an expansion cohort with docetaxel 50 mg/m(2) with G-CSF on Day 16 (DL 2a), the designated MTD. Among 35 patients treated with the combination, there were no febrile neutropenia events. One patient had dose-limiting Grade 3 anemia. PSA50 response was 51.4% and PSA90 was 25.7%. Median progression-free survival was 11.7 months, and median overall survival was 20.1 months. CONCLUSIONS: A lead-in cycle and a dose-dense schedule of docetaxel with G-CSF enabled the combination with radium-223 in standard dose-intensities with minimal hematological toxicity. The regimen will likely combine logically and safely with hormone-intensification for study in high-risk/high-volume castration-sensitive metastatic disease.

Hematology-Oncology

Gadgeel SM, Fajardo O, Barlesi F, Eun Kim J, Kurzrock R, Thomas DM, Jagtiani R, Noe J, Schwemmers S, and Nikolaidis C. Real-world characteristics and survival outcomes of patients with metastatic ALK fusion-positive solid tumors treated with standard-of-care therapies. *Oncologist* 2025; 30(5). PMID: 40338218. Full Text

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BACKGROUND: Anaplastic lymphoma kinase (ALK) fusions can be found in different solid tumors. This study aims to describe the clinical characteristics and investigate survival outcomes of patients with ALK fusion-positive solid tumors (excluding non-small cell lung cancer [NSCLC]) treated with standard-of-care therapies in a real-world setting. PATIENTS AND METHODS: Data for patients with metastatic solid tumors (excluding NSCLC) who had ≥1 Foundation Medicine comprehensive genomic profiling (CGP) test between January 1, 2011 and September 30, 2023, were obtained from a nationwide (US-based) de-identified multi-tumor clinico-genomic database. Patients with ALK wild-type (ALK-WT) tumors were matched with patients with ALK fusion-positive tumors (4:1 ratio) using pre-specified baseline characteristics. Two models were used to analyze survival outcomes: Model 1 used the CGP report date as the index date; Model 2 used the date of metastatic diagnosis as the index date (including adjustment for immortal time bias). RESULTS: Overall, 22 and 88 patients were included in the ALK fusion-positive and ALK-WT cohorts, respectively. Co-alterations were rare in the ALK fusion-positive cohort. Median overall survival was consistently lower in patients with ALK fusion-positive tumors compared with patients with ALK-WT tumors, across all analyses (hazard ratios between 1.8 and 2.0). CONCLUSION: Data from this study suggest that ALK fusions have a negative prognostic effect in metastatic solid tumors and highlight the need for further investigation of ALK inhibitors in the tumor-agnostic setting.

Hematology-Oncology
Hullfish H, Kistner-Griffin E, Maurer S, Balliet W, Vanderlan J, **Slavin-Spenny O**, Padgett L, Rush A, Johnson B, McLeod T, Starr EJ, Ruggiero KJ, Sterba KR, and Graboyes EM. Efficacy of a Brief Cognitive Behavioral Treatment Across Body Image Distress Domains: Secondary Outcomes of the BRIGHT Randomized Clinical Trial. *JAMA Otolaryngol Head Neck Surg* 2025; Epub ahead of print. PMID: 40367345. Full Text

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This secondary analysis of a randomized clinical trial evaluates whether a brief, tailored cognitive behavioral treatment program is effective across multiple domains of head and neck cancer–related body image distress.

Hematology-Oncology
Lam VK, and **Gadgeel SM**. A Response to the Letter to the Editor: “Can We Refine Criteria for the First-Line Treatment for Patients With Advanced ALK-Positive NSCLC in the Real World?”. *J Thorac Oncol* 2025; 20(6):e73. PMID: Not assigned. Full Text

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Hematology-Oncology
Othón-Martínez D, **Peña-Muñoz SV**, Riojas Barret M, Vidales-Lopez GG, Sánchez Guzmán JM, and Kwapisz L. EXPRESS: Cardiovascular Disease in Inflammatory Bowel Disease Pathophysiology and Risk Factors: A Review. *J Investig Med* 2025; Epub ahead of print. PMID: 40415193. Full Text

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Inflammatory Bowel Disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic systemic immune dysregulated disorders affecting the gastrointestinal tract that often have extraintestinal manifestations. Limited data exists on the cardiovascular (CV) implications of IBD, but a higher prevalence of cardiovascular disease (CVD) has been observed compared to the general population, resulting in increased mortality risk. Although IBD's etiology remains unclear, research has shown that it involves a complex interplay between factors such as enteric neural activity, inflammatory mediators, microbiome imbalance, intestinal barrier dysfunction, and environmental stressors. This proinflammatory environment in IBD may contribute significantly to the development of CVD, including myocarditis, pericarditis, thromboembolism, arrhythmia, and heart failure. Furthermore, certain IBD-specific medications have been associated with either the development or worsening of CVD. Despite this potential risk to CV health, drugs like anti-integrins, amino-salicylates, corticosteroids, immunomodulators, and advanced therapies including biologics have proven effective for managing and achieving remission in patients with IBD. This literature review analyzes existing data on IBD's pathophysiology and its potential effect on CVD development and progression, along with examining IBD drugs linked to CV health risks and those with less harmful cardiac involvement.

Hematology-Oncology
Simone CB, 2nd, Amini A, **Chetty IJ**, Choi JI, Chun SG, Donington J, Edelman MJ, Higgins KA, Kestin LL, Mohindra P, **Movsas B**, Rodrigues GB, Rosenzweig KE, **Rybkin, II**, Shepherd AF, Slotman BJ, Wolf A, and Chang JY. American Radium Society Appropriate Use Criteria Systematic Review and Guidelines on Reirradiation for Non-Small Cell Lung Cancer Executive Summary. *Int J Radiat Oncol Biol Phys* 2025; Epub ahead of print. PMID: 40185207. Full Text

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Definitive thoracic reirradiation can improve outcomes for select patients with non-small cell lung cancer (NSCLC) with locoregional recurrences. To date, there is a lack of systematic reviews on safety or efficacy of NSCLC reirradiation and dedicated guidelines. This American Radium Society Appropriate Use Criteria Systematic Review and Guidelines provide practical guidance on thoracic reirradiation safety and efficacy and recommends consensus of strategy, techniques, and composite dose constraints to minimize risks of high-grade/fatal toxicities. Preferred Reporting Items for Systematic Reviews and Meta-Analyses systematic review assessed all studies published through May 2020 evaluating toxicities, local control and/or survival for NSCLC thoracic reirradiation. Of 251 articles, 52 remained after exclusions (3 prospective) and formed the basis for recommendations on the role of concurrent chemotherapy, factors associated with toxicities, and optimal reirradiation modalities and dose-fractionation schemas. Stereotactic body radiation therapy improves conformality/dose escalation and is optimal for primary-alone failures, but caution is needed for central lesions. Concurrent chemotherapy with definitive reirradiation improves outcomes in nodal recurrences but adds toxicity and should be individualized. Hyperfractionated reirradiation may reduce long-term toxicities, although data are limited. Intensity modulated reirradiation is recommended over 3D conformal reirradiation. Particle therapy may further reduce toxicities and enable safer dose escalation. Acute esophagitis/pneumonitis and late pulmonary/cardiac/esophageal/brachial plexus toxicities are dose limiting for reirradiation. Recommended reirradiation composite dose constraints (2 Gy equivalents): esophagus V60 <40%, maximum point dose (Dmax) < 100 Gy; lung V20 <40%; heart V40 <50%; aorta/great vessels Dmax < 120 Gy; trachea/proximal bronchial tree Dmax < 110 Gy; spinal cord Dmax < 57 Gy; brachial plexus Dmax < 85 Gy. Personalized thoracic reirradiation approaches and consensus dose constraints for thoracic reirradiation are recommended and serve as the basis for ongoing Reirradiation Collaborative Group and NRG Oncology initiatives. As very few prospective and small retrospective studies formed the basis for generating the dose constraint recommended in this report, further prospective studies are needed to strengthen and improve these guidelines.

Hematology-Oncology
Tamr A, **Shahid MA**, **Wollner I**, and **Theisen B**. Delayed Presentation of Metastatic Solid Pseudopapillary Epithelial Neoplasm in a Pregnant Woman: A Case Report. *Cureus* 2025; 17(4):e82454. PMID: 40385926. Full Text

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Solid pseudopapillary epithelial neoplasm (SPEN) is a rare, low-grade malignant pancreatic tumor usually found incidentally on imaging, most commonly in young women. Its association with women suggests that hormones may play a significant role in tumor pathogenesis. Surgical resection is the mainstay of treatment in all stages of disease, and few other treatment options have been thoroughly explored. This case demonstrates the unique therapeutic challenges involved in the management of a pregnant woman with new liver metastasis and significant disease burden following remote resection of the primary SPEN tumor. The patient was treated with chemotherapy, radiation, and hormone therapy, followed by hepatic trisegmentectomy without recurrence during surveillance. This case presents a unique therapeutic approach to a situation where no established treatment guidelines exist.

Hematology-Oncology
Valle LF, Jiang T, Rosenbloom A, Zaorsky NG, **Hwang C**, Solanki A, Dickstein D, Mitin T, Schroeder T, Potters L, Lloyd S, Showalter T, Bagshaw HP, Jeffrey Karnes R, Hoffman KE, Nguyen PL, and Kishan AU. American Radium Society Appropriate Use Criteria for the Workup and Treatment of Local Intraprostatic Recurrence of Prostate Cancer Following Definitive Radiotherapy. *Eur Urol Oncol* 2025; 8(3):796-804. PMID: 39307608. Full Text

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BACKGROUND AND OBJECTIVE: Local intraprostatic radiorecurrence of prostate cancer (IPR-PC) can be associated with an aggressive natural history and impact long-term disease-specific survival. While appropriate local salvage intervention can be curative, best practices for workup and local salvage of intraprostatic recurrence are poorly defined. The American Radium Society (ARS) Genitourinary Appropriate Use Criteria Committee sought to develop evidence-based recommendations to address this gap. METHODS: PubMed and Embase were searched to retrieve a comprehensive set of relevant peer-reviewed articles on four topics relevant to the workup and treatment of IPR-PC. The literature was evaluated and summarized by three investigators, and clinical variants were created for each of the four topics. The ARS Genitourinary AUC multidisciplinary expert panel voted on the most appropriate procedures for each variant, and a modified Delphi approach was used to summarize recommendations. KEY FINDINGS AND LIMITATIONS: The panel concluded that radiographic staging via prostate-specific membrane antigen positron emission tomography (PSMA PET) and multiparametric magnetic resonance imaging should be performed to exclude patients with metastatic disease and identify the local extent of radiorecurrence. Biopsy is required before local salvage to avoid excessive toxicity in patients whose radiographic recurrence represents a treatment effect. Consideration of local salvage is preferred in lieu

of noncurative hormonal manipulation alone, although shared decision-making is critical. Salvage reirradiation approaches are recommended to limit toxicity. Hormonal therapy may be beneficial for radiosensitization when radiotherapeutic salvage is pursued, but only of short duration, and classic androgen deprivation therapies are preferred over novel hormonal agents. Focal salvage should be pursued when confidence in focal recurrence can be confirmed via multiple radiographic and tissue sampling modalities, although the toxicity associated with whole-gland salvage appears to be very tolerable. Several radiotherapeutic salvage regimens exist, most of which can be carried out in six or fewer fractions. The data informing this guideline are limited to individuals initially treated with conventionally fractionated external beam radiotherapy and with workup for recurrence before the PSMA PET era. CONCLUSIONS AND CLINICAL IMPLICATIONS: This consensus guideline provides evidence-based guidance on the appropriate procedures for workup and treatment of IPR-PC. Prospective evidence to enrich these guidelines is eagerly anticipated. PATIENT SUMMARY: We summarize evidence for the best workup and treatment for patients with local recurrence of prostate cancer after radiotherapy. A panel of experts evaluated previous studies and voted on the procedures that should be performed and those that should be avoided. This guideline is a useful tool for helping doctors to discuss the best treatment options that maximize the chance of cure while minimizing side effects.

Hematology-Oncology

Vojjala N, Prabhu R, Liyanage JS, Modi DK, Yang J, Kin A, Woldie I, **Alavi A**, and Singh V. Real world analysis of long-term eff icacy of isovolemic red cell exchange in sickle cell disease: a single center experience. *Blood Transfus* 2025; Epub ahead of print. PMID: 40423587. Full Text

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Hospital Medicine

Sherwood JR, **Parsons A**, **Al Jammala H**, and **Kaatz S**. Perioperative Management of Oral Anticoagulation in Patients with Venous Thromboembolism. *Med Clin North Am* 2025. PMID: Not assigned. Full Text

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Hypertension and Vascular Research

Crocetti L, Giovannoni MP, **Pavlov TS**, **Ivanov V**, Melani F, and Guerrini G. Synthesis of 3-Carboxy-6-sulfamoylquinolones and Mefloquine-Based Compounds as Panx1 Blockers: Molecular Docking, Electrophysiological and Cell Culture Studies. *Molecules* 2025; 30(10). PMID: 40430343. Full Text

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The membrane channel protein Panx1 is a promising therapeutic target since its involvement was demonstrated in a variety of pathologies such as neuropathic pain, ischemic stroke and cancer. As a continuation of our previous work in this field, we report here the synthesis and biological evaluation of two classes of compounds as Panx1 blockers: 3-carboxy-6-sulphonamidoquinolone derivatives and new Mefloquine analogs. The series of 3-carboxy-6-sulphonamidoquinolones gave interesting results, affording powerful Panx1 channel blockers with 73.2 < I% < 100 at 50 µM. In particular, 12f was a more potent Panx1 blocker than the reference compound CBX (IC(50) = 2.7 µM versus IC(50) = 7.1 µM), and

its profile was further investigated in a cell culture model of polycystic kidney disease. Finally, interesting results have been highlighted by new molecular modeling studies.

Infectious Diseases
Arena CJ, **Abed A**, **Kenney RM**, **Suleyman G**, **Shallal A**, Davis SL, and **Veve MP**. Retrospective cohort study of oral switch versus intravenous antibiotics for carbapenem-resistant enterobacterales and Pseudomonas aeruginosa infections on hospital discharge. *Pharmacotherapy* 2025; 45(5):244-250. PMID: 40345979. Full Text

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OBJECTIVES: To compare outcomes of oral switch versus intravenous antibiotics for the treatment of carbapenem-resistant Enterobacterales (CRE) and Pseudomonas aeruginosa (CRPA) infections at hospital discharge. METHODS: Institutional review board approved, retrospective cohort of adults infected with CRE or CRPA who received oral switch or intravenous antibiotics at hospital discharge from January 1, 2017, to April 30, 2024. Patients were included if they were eligible for oral switch and infected with an isolate susceptible to one or more oral antibiotics; non-bacteremic urinary tract infections were excluded. The primary outcome was 30-day clinical success at end of therapy, defined as lack of infection-related hospitalization, infection-related recurrence, or change/escalation of therapy. Secondary outcomes included hospital length of stay (LOS) and 30-day all-cause mortality from end of therapy. RESULTS: Fifty-five patients were included; 51% received oral switch antibiotics and 49% received intravenous antibiotics. Thirty-three percent of patients had CRE, 67% had CRPA, and 38% of cultures were polymicrobial. The most common infection types were pneumonia (33%), intra-abdominal (26%), and bone/joint (22%). The median (interquartile range [IQR]) duration of outpatient therapy was 12 (6-25) days versus 20 (4-34) days for the oral switch and intravenous antibiotic groups, respectively (p = 0.341). 30-day clinical success was 61% in the oral switch and 48% in the intravenous antibiotic groups (p = 0.349); the median (IQR) hospital LOS for the oral switch and intravenous antibiotic groups was 14 (9-25) days and 16 (9-49) days, respectively (p = 0.165); 30-day mortality was 4% in the oral switch group and 15% in the intravenous antibiotic group (p = 0.193). CONCLUSION: A limited sample of patients who received oral switch antibiotics had similar outcomes to intravenous outpatient treatment of carbapenem-resistant organisms, with a shorter hospital LOS.

Infectious Diseases
Bhargava A, **Szpunar S**, and **Saravolatz L**. The prognostic nutritional index as a risk factor for severe COVID-19 infection among hospitalized patients: A multicenter historical cohort study. *Am J Med Sci* 2025; Epub ahead of print. PMID: 40320145. Full Text

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INTRODUCTION: Malnutrition is a critical prognostic factor in COVID-19, affecting up to 50 % of hospitalized patients and increasing their mortality risk tenfold compared to well-nourished patients. The prognostic nutritional index (PNI) assesses nutritional and immune status and can help gauge the severity of COVID-19. OBJECTIVE: To evaluate whether PNI was independently associated with the severity of COVID-19 infection among hospitalized patients in the United States. METHODS: This study was a

historical cohort study of adult patients with COVID-19 hospitalized in five hospitals in southeast Michigan. Data collected from the electronic medical record were analyzed using SPSS v. 29.0, and a p-value <0.05 was considered statistically significant. RESULTS: Data were included on 286 patients, with a mean age of 58.7 ± 17.5 years, 53.5 % (153/286) female, and 48.3 % (138/286) black/African American. The most common comorbidities were hypertension (62.9 %), obesity (54.2 %) and type 2 diabetes mellitus (32.1 %). Of the 286 patients, 144 (50.3) had severe/ critical disease. Patients with severe COVID-19 had significantly lower mean PNI levels than those with mild to moderate disease (35.1 ± 5.2 vs 37.7 ± 6.4, p < 0.001). After controlling for smoking status, vaccination status, race, and home steroid use, PNI remained an independent predictor for severe/ critical COVID-19 (OR=0.92, p < 0.001). CONCLUSIONS: This study demonstrated that PNI is an independent predictor of severe COVID-19. The PNI score can be easily calculated from routine blood tests for every patient and helps risk stratify hospitalized COVID-19 patients. Additional research is needed to confirm these results.

Infectious Diseases

Rashid I, Unger NR, Willis C, Dhippayom T, Ramgopal M, Sherman EM, **Yared N**, Safran R, Swiatlo E, Weinberg AR, Navadeh S, Schmutz HW, and Chaiyakunapruk N. Comparison of treatment-emergent resistance-associated mutations and discontinuation due to adverse events among integrase strand transfer inhibitor-based single-tablet regimens and cabotegravir + rilpivirine for the treatment of virologically suppressed people with HIV: A systematic literature review and network meta-analysis. *HIV Med* 2025; Epub ahead of print. PMID: 40426337. Full Text

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OBJECTIVE: This study evaluated rates of treatment-emergent resistance-associated mutations (TE-RAMs) and discontinuation due to adverse events (DC-AEs) across integrase strand transfer inhibitor (INSTI)-based single-tablet regimens and injectable cabotegravir + rilpivirine (CAB + RPV) in virologically suppressed people with HIV. METHODS: A systematic literature review was conducted for phase 2-4 randomized controlled trials with ≥48 weeks of follow-up involving virologically suppressed people with HIV aged ≥12 years and published January 2003-March 2024. A random-effects network meta-analysis estimated comparative rates of TE-RAMs and DC-AEs among regimens at 48 weeks. Risk of bias and strength of evidence were assessed using Cochrane RoB and CINeMA, respectively. RESULTS: Fourteen (7509 participants) and nine (4656 participants) studies were included in the TE-RAMs and DC-AEs analyses, respectively. No significant differences in rates of TE-RAMs were observed; risk ratios (RRs) for TE-RAMs for bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF), dolutegravir/abacavir/lamivudine (DTG/ABC/3TC) and CAB + RPV every 4 weeks (Q4W) versus CAB + RPV every 8 weeks (Q8W) were 0.22 (95% CI, 0.02-2.04), 0.22 (95% CI, 0.00-19.85) and 0.40 (95% CI, 0.14-1.09). Compared with CAB + RPV Q4W and Q8W, DC-AEs were significantly lower with B/F/TAF (RR, 0.15 [95% CI, 0.03-0.75] and RR, 0.16 [95% CI, 0.04-0.67], respectively) and DTG/ABC/3TC (RR, 0.05 [95% CI, 0.01-0.48] and RR, 0.05 [95% CI, 0.01-0.46], respectively). CONCLUSIONS: In virologically suppressed people with HIV, switching to CAB + RPV Q8W yielded a non-significant increased risk of TE-RAMs compared with INSTI-based 2- and 3-drug regimens and CAB + RPV Q4W. Both CAB + RPV Q4W and Q8W had significantly higher risks of DC-AEs than B/F/TAF and DTG/ABC/3TC. Findings highlight the importance of considering both resistance and tolerability when switching regimens.

Infectious Diseases
Veve MP, **Arena CJ**, **Kenney RM**, **Church BM**, **Fried ST**, and **Shallal AB**. Things I wish I knew when implementing an ambulatory antimicrobial stewardship program at an urban health system: lessons learned and future directions. *Antimicrob Steward Healthc Epidemiol* 2025; 5(1):e109. PMID: 40391168. Full Text

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Internal Medicine
Abu-Zahra A, Haque MZ, **Saleem A**, Hussain A, and Nipu F. FIP1L1-PDGFRA Positive Chronic Eosinophilic Leukemia Presenting With Vestibular Neuritis. *Clin Case Rep* 2025; 13(6):e70554. PMID: 40454332. Full Text

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Myeloproliferative neoplasms are disorders of stem cells that result in excessive proliferation of one or more myeloid progenitors. We report a rare finding of chronic eosinophilic leukemia with a rearrangement of the PDGFRA gene in a 53-year-old male patient presenting with symptoms suggestive of vestibular neuritis.

Internal Medicine
Abusuliman M, **Jamali T**, and **Zuchelli TE**. Advances in gastrointestinal endoscopy: A comprehensive review of innovations in cancer diagnosis and management. *World J Gastrointest Endosc* 2025; 17(5):105468. PMID: 40438719. Full Text

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The field of gastroenterology has experienced revolutionary advances over the past years, as flexible endoscopes have become widely accessible. In addition to enabling faster, less invasive, and more affordable treatment, flexible endoscopes have greatly improved the detection and endoscopic screening of malignancies and prevented many cancer-related deaths. The development and clinical application of new diagnostic endoscopic technologies, such as magnification endoscopy, narrow-band imaging, endoscopic ultrasound with biopsy, and more recently, artificial intelligence enhanced technologies, have made the recognition and detection of various neoplasms and sub-epithelial tumors more possible. This review demonstrates the latest advancements in endoscopic procedures, techniques, and devices applied in the diagnosis and management of gastrointestinal cancer.

Internal Medicine
Abusuliman M, Milgrom Y, **Mellinger J**, and Parker R. Management of alcohol use disorder in alcohol-related liver disease. *Frontline Gastroenterol* 2025. PMID: Not assigned. Full Text

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Alcohol-related liver disease (ArLD) is a leading cause of liver-related morbidity and mortality worldwide and is fundamentally connected to alcohol use disorder (AUD). ArLD develops in a subset of heavy

drinkers, with progression from steatosis to cirrhosis. Despite the proven benefits of AUD treatment in halting ArLD progression, fewer than 20% of patients with AUD and ArLD receive treatment, and less than 2% are prescribed pharmacotherapy. Hepatology and gastroenterology practitioners are often not confident to manage coexistent AUD and ArLD. This article examines the relationship between AUD and ArLD, evaluates treatment options and highlights the role of integrated care in improving outcomes. Medical addiction therapy significantly reduces binge drinking, hospitalisations and the risk of hepatic decompensation. Several pharmacotherapies are viable in ArLD, but require specific consideration of hepatotoxicity, renal excretion and central nervous system effects. Psychotherapy is associated with lower rates of hepatic decompensation and improved liver-related outcomes. Integrated care models that embed AUD treatment within liver clinics improve engagement, abstinence rates and clinical outcomes compared with standard referrals. AUD treatment is fundamental in ArLD management. Increased use of pharmacological and psychological therapies, alongside integrated care models, may improve patient outcomes and reduce the burden of ArLD. Further research is needed to optimise treatment strategies in this high-risk population.

Internal Medicine

Anwar MT, Shahzil M, Arif TB, Khaqan MA, Co EL, Hasan F, Tarar R, Naeem H, Farooq S, Jaan A, **Chaudhary AJ**, Jahagirdar V, and **Salgia R**. MMF Is an Effective and Safer Treatment Options for Treatment-Naïve Patients With Autoimmune Hepatitis Compared to Azathioprine: A Systematic Review and Meta-Analysis. *J Dig Dis* 2025; Epub ahead of print. PMID: 40386905. Full Text

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Department of Internal Medicine, Cooper University Hospital, Camden, New Jersey, USA.
Department of Medicine, King Edward Medical University, Lahore, Pakistan.
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OBJECTIVES: Autoimmune Hepatitis (AIH) is a chronic inflammatory liver disease with significant morbidity and mortality if untreated. Current first-line treatment involves corticosteroids and azathioprine (AZA), which are effective but are associated with significant adverse effects and treatment intolerance. Mycophenolate mofetil (MMF), an immunosuppressive agent with a potentially better safety profile, has emerged as an alternative. This meta-analysis evaluated the efficacy and safety of MMF compared to AZA in treatment-naïve AIH patients. METHODS: We conducted a systematic review and meta-analysis in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines. Databases were searched for articles published up to May 2024. Statistical analysis was performed using RevMan, employing a random-effects model. RESULTS: Five studies involving 621 patients were included. MMF showed significantly higher rates of complete biochemical response compared to AZA (odds ratio [OR] 3.64, 95% confidence interval [CI] 2.07-6.40, $p < 0.00001$) and lower non-response rates (OR 0.45, 95% CI 0.24-0.85, $p = 0.01$). Corticosteroid withdrawal rates were also higher in the MMF group (OR 2.89, 95% CI 1.69-4.94, $p = 0.0001$). Relapse rate and cumulative prednisolone dose were comparable between the two groups. MMF demonstrated a better safety profile, with significantly lower rates of gastrointestinal symptoms (OR 0.46, 95% CI 0.27-0.79, $p = 0.005$). CONCLUSIONS: MMF shows superior efficacy and tolerability compared to AZA in treatment-naïve AIH patients and may serve as a preferred first-line therapy, offering improved patient adherence and clinical outcomes. Further randomized controlled trials are warranted to confirm these findings.

Internal Medicine

Baqal O, Karikalan SA, Hasabo EA, **Tareen H**, Futela P, Qasba RK, Shafqat A, Qasba RK, Hayes SN, Tweet MS, El Masry HZ, Lee KS, Shen WK, and Sorajja D. In-hospital and long-term outcomes in spontaneous coronary artery dissection with concurrent cardiac arrest: Systematic review and meta-analysis. *Heart Rhythm O2* 2025. PMID: Not assigned. Full Text

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Background: Our understanding of factors predisposing patients with spontaneous coronary artery dissection (SCAD) to worse outcomes, such as concurrent sudden cardiac arrest (CA) and secondary prevention of sudden cardiac death in those patients, is limited. Objective: We conducted the largest systematic review of studies assessing clinical outcomes in SCAD with concurrent CA. Methods: This study was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. PubMed, Cochrane, and Scopus were searched using relevant search terms including “Spontaneous Coronary Artery Dissection,” “Ventricular Tachycardia,” “Ventricular Fibrillation,” “Sudden Cardiac Death,” and “Cardiac Arrest.” The search was conducted from database inception to January 2025. Results: Out of 269 studies that underwent screening, 10 were included (n = 3978). In-hospital mortality, postdischarge mortality, recurrent myocardial infarction (MI) and recurrent SCAD occurred in 20%, 3%, 12%, and 9% of patients with SCAD and CA, respectively. When compared with patients with SCAD without CA, patients with SCAD and CA were at significantly higher risk of in-hospital mortality (risk ratio [RR] 6.7, 95% confidence interval [CI] 4.5–10.1, P < .00001), postdischarge mortality (RR = 5.9, 95% CI 1.7–19.9, P = .005), recurrent MI (RR = 3.3, 95% CI 2.0–5.4, P < .00001), and recurrent SCAD (RR = 1.9, 95% CI 1.1–3.3, P = .02). Out of a pooled 35 implanted cardiac defibrillators (ICDs) and wearable cardiac defibrillators (WCDs), there was only 1 appropriate and 1 inappropriate defibrillator discharge recorded over the follow-up period. Conclusion: SCAD with concurrent CA is associated with worse in-hospital and long-term outcomes, although long-term rate of administered defibrillator therapies was low, supporting a conservative approach.

Internal Medicine

Bhargava A, **Szpunar S**, and **Saravolatz L**. The prognostic nutritional index as a risk factor for severe COVID-19 infection among hospitalized patients: A multicenter historical cohort study. *Am J Med Sci* 2025; Epub ahead of print. PMID: 40320145. Full Text

Department of Internal Medicine, Wayne State University, Detroit, MI, USA; Division of Infectious Disease, Department of Internal Medicine, Henry Ford Health - St John Hospital, Detroit, MI, USA; Thomas Mackey Center for Infectious Disease Research, Henry Ford Health - St John Hospital, Detroit, MI, USA. Electronic address: Abharga1@hfhs.org.
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INTRODUCTION: Malnutrition is a critical prognostic factor in COVID-19, affecting up to 50 % of hospitalized patients and increasing their mortality risk tenfold compared to well-nourished patients. The prognostic nutritional index (PNI) assesses nutritional and immune status and can help gauge the severity of COVID-19. OBJECTIVE: To evaluate whether PNI was independently associated with the severity of COVID-19 infection among hospitalized patients in the United States. METHODS: This study was a historical cohort study of adult patients with COVID-19 hospitalized in five hospitals in southeast Michigan. Data collected from the electronic medical record were analyzed using SPSS v. 29.0, and a p-value <0.05 was considered statistically significant. RESULTS: Data were included on 286 patients, with a mean age of 58.7 ± 17.5 years, 53.5 % (153/286) female, and 48.3 % (138/286) black/African American. The most common comorbidities were hypertension (62.9 %), obesity (54.2 %) and type 2 diabetes mellitus (32.1 %). Of the 286 patients, 144 (50.3) had severe/ critical disease. Patients with severe COVID-19 had significantly lower mean PNI levels than those with mild to moderate disease (35.1

± 5.2 vs 37.7 ± 6.4, p < 0.001). After controlling for smoking status, vaccination status, race, and home steroid use, PNI remained an independent predictor for severe/ critical COVID-19 (OR=0.92, p < 0.001). CONCLUSIONS: This study demonstrated that PNI is an independent predictor of severe COVID-19. The PNI score can be easily calculated from routine blood tests for every patient and helps risk stratify hospitalized COVID-19 patients. Additional research is needed to confirm these results.

Internal Medicine

Campbell LA, Ammon JP, Kombathula R, **Muhammad N**, and Jackson CD. New atrial fibrillation guideline: Modify risk, control rhythm, prevent progression. *Cleve Clin J Med* 2025; 92(5):291-296. PMID: 40312119. Full Text

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The latest (2023) guideline on atrial fibrillation from the American College of Cardiology, American Heart Association, American College of Chest Physicians, and Heart Rhythm Society introduces a new staging system for the disease, emphasizes risk-factor modification, prioritizes rhythm control over rate control, and clarifies which patients should be considered for catheter ablation. It also delves deeper than earlier guidelines into calculations of risk of thrombosis when deciding whether to start anticoagulant therapy.

Internal Medicine

Chaudhary AJ, **Faisal MS**, Sohail A, Baldwin H, **Harris K**, Shahzil M, **Faisal MS**, **Toiv A**, **Mullins K**, and **Suresh S**. Endocuff-Assisted Colonoscopy for Identifying Sessile Serrated Polyps and Adenomas During Routine Colorectal Cancer Screening: A Retrospective Cohort Study. *JGH Open* 2025; 9(5):e70173. PMID: 40375857. Full Text

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BACKGROUND AND AIMS: Polyps located in less accessible areas of the colon, such as inner curves of flexures, are often difficult to visualize. Colonoscope attachments such as the Endocuff have been developed to improve the visualization of these polyps. We aimed to assess the utility of Endocuff-assisted colonoscopy (EAC) in the detection of tubular adenomas and sessile serrated polyps (SSP) compared to conventional colonoscopy during routine colorectal cancer screening. PATIENTS AND METHODS: This retrospective cohort study included patients who underwent colorectal cancer screening with either conventional colonoscopy or EAC between November 2022 and March 2023. The primary outcomes were SSP and tubular adenoma detection rates. Secondary outcomes included total procedure time, cecal intubation time, and ileal intubation rates. RESULTS: Of the 435 patients included, 189 (43%) underwent EAC, and 246 (57%) underwent conventional colonoscopy. The mean ± standard deviation number of polyps detected was 1.7 ± 2.2, the mean procedure time was 18.7 ± 7.5 min, and the mean cecal intubation time was 4.4 ± 3.3 min, with no significant differences between groups. A smaller proportion of patients in the EAC group had successful ileal intubation (14% vs. 55%; p < 0.01). The tubular adenoma detection rate was similar between EAC and conventional colonoscopy (41% vs. 39%; p = 0.70), but the SSP detection rate was significantly higher with EAC (16% vs. 8.5%; p < 0.01). CONCLUSION: EAC may enhance the detection of difficult-to-visualize SSPs during screening colonoscopies without affecting overall procedure time. However, physicians should consider the examination indication when selecting EAC, as ileal intubation may be more challenging.

Internal Medicine
Draelos ZD, Ghannoum M, Stein Gold L, Harper JC, Baldwin H, Guenin E, and Tanghetti EA. Clindamycin Phosphate 1.2%/Adapalene 0.15%/ Benzoyl Peroxide 3.1% for Acne: Results From A 6-Month Open-Label Study. *J Drugs Dermatol* 2025; 24(5):516-523. PMID: 40327582. Full Text

BACKGROUND: Treatment of acne may require many months of treatment before maximal benefits are observed, and acne sequelae (eg, scarring, dyspigmentation) can persist long after lesion resolution. In 12-week clinical trials, triple-combination clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel (CAB) demonstrated efficacy and tolerability in the treatment of moderate to severe acne. This study assessed CAB long-term efficacy/tolerability and reductions in acne scarring/dyspigmentation. METHODS: This 24-week, single-center, open-label study assessed once-daily CAB in participants (N=25) aged ≥12 years with moderate acne (Investigator’s Global Assessment [IGA] score=3). Endpoints included change from baseline in IGA score, inflammatory/noninflammatory lesions, skin appearance (dryness, postinflammatory hyperpigmentation [PIH], and postinflammatory erythema [PIE]), and scarring. Tolerability parameters (itching, burning, redness, swelling) and adverse events were assessed. At baseline and week 24, participants’ foreheads were swabbed to assess Cutibacterium acnes. Results: At week 24, 68% of participants achieved treatment success (≥2-grade IGA score reduction from baseline and clear/almost clear skin), and significant inflammatory/noninflammatory lesion reductions from baseline were observed (89%; 70%; P<0.001, both). Decreases from baseline in investigator- and participant-assessed PIH (77%; 82%) and PIE (84%; 88%) and investigator-assessed scarring severity (33%) were statistically significant (P≤0.001, all). There were no significant increases in skin dryness or any tolerability parameter, and no adverse events occurred. C. acnes assessment indicated no development of antibiotic resistance with long-term CAB treatment. Conclusions: With 24 weeks of once-daily use, CAB was efficacious, well-tolerated, and significantly improved acne-related scarring and dyspigmentation. These results support the long-term use of CAB in the topical treatment of acne. Citation: Draelos ZD, Ghannoum M, Stein Gold L, et al. Clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% for acne: results from a six-month open-label study. J Drugs Dermatol. 2025;24(5):516-523. doi:10.36849/JDD.9018.

Internal Medicine
Drallmeier M, Ranspach L, and Elias G. Leukemia Cutis With Concomitant Seborrheic Keratosis as the Presenting Symptom of Chronic Lymphocytic Leukemia: A Case Report. *Cureus* 2025; 17(4):e82433. PMID: 40385890. Full Text

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Leukemia cutis is a term used to describe a dermatologic manifestation of hematologic malignancies. It represents a wide range of identifiable cutaneous lesions that result from the infiltration of neoplastic leukocytes in patients with leukemia or lymphoma. We report a case involving an initial solitary lesion without systemic symptoms, but a biopsy revealed a seborrheic keratosis in the epidermis with lymphoid infiltration in the dermis. Flow cytometry studies confirmed a B-cell chronic lymphocytic leukemia, and an additional investigation with fluorescence in situ hybridization demonstrated a chromosomal deletion in the long arm of chromosome 13 at position 14, indicating a favorable prognosis. The patient was referred to a hematologist, who determined that no pharmacologic treatment was necessary at that time. The patient continues to follow up for monitoring of his disease.

Internal Medicine
Elfert K, **Abusuliman M**, Elbenawi H, Abosheaishaa H, Beran A, Mohamed M, Nassar M, Krafft M, and Elhanafi SE. Impact of antithrombotic medications on postprocedural outcomes of percutaneous endoscopic gastrostomy: a US Collaborative Network study. *Eur J Gastroenterol Hepatol* 2025; Epub ahead of print. PMID: 40359274. Full Text

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BACKGROUND AND AIMS: Percutaneous endoscopic gastrostomy (PEG) is an essential procedure for patients who require long-term enteral nutrition but are unable to eat orally. However, it carries a risk of bleeding, particularly in patients on anticoagulation or dual antiplatelet therapy (DAPT). This study aimed to assess the bleeding risk associated with continuing anticoagulation or DAPT during PEG placement. METHODS: Using the TriNetX US Collaborative Network Database, we analyzed four cohorts: patients on anticoagulants, patients not on anticoagulants, patients on DAPT, and patients on aspirin (ASP), focusing on gastrostomy-related bleeding within 7 and 30 days, along with secondary outcomes such as mortality and the need for blood transfusion or endoscopic reintervention. RESULTS: Our analysis showed no statistically significant difference in the 7-day bleeding risk between the anticoagulant and no anticoagulant groups. However, a higher 30-day bleeding risk was observed in the anticoagulant group (0.9 vs. 0.4%, P = 0.007). There was no significant difference in the incidence of severe bleeding events requiring endoscopic intervention or blood transfusion. In addition, the difference in the bleeding risk between the DAPT and ASP groups was not statistically significant within 7 and 30 days. CONCLUSION: These findings suggest that while anticoagulant use increases the risk of minor post-PEG bleeding, it does not lead to a higher incidence of severe bleeding. Additionally, the continuation of DAPT was not associated with statistically significant increase in bleeding risk. This study provides valuable insights into the management of antithrombotic therapy in patients undergoing PEG.

Internal Medicine

Fadel RA, **Hofeld B**, **Aronow HD**, **Jabri A**, **Engel P**, **Koenig G**, **Memon M**, **Alqarqaz M**, **Alaswad K**, **Fuller B**, **Nakhle A**, **Aggarwal V**, **O'Neill B**, **Frisoli T**, **Basir MB**, **Kim H**, **O'Neill W**, and **Villablanca P**. Propensity matched analysis of single access technique for Impella-assisted unprotected left main percutaneous coronary intervention. *Cardiovasc Revasc Med* 2025; Epub ahead of print. PMID: 40436725. Full Text

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BACKGROUND: The single access for high-risk percutaneous coronary intervention (SHiPCI) technique is an intriguing alternative to traditional dual access Impella-assisted PCI, potentially reducing access-site complications. Current data is limited to retrospective case studies. OBJECTIVES: To analyze procedural complications and clinical outcomes of SHiPCI. METHODS: This single-center retrospective observational study evaluated consecutively admitted patients undergoing high-risk unprotected left main PCI (UPLM-PCI) from 2018 through 2023. Patients were grouped according to index strategy of single or dual access Impella-assisted UPLM-PCI, and propensity score matching without replacement was used to match patients 1:1. The primary outcome was a composite of all-cause in-hospital mortality, major bleeding, vascular access site complications, and blood transfusion. RESULTS: Six-hundred patients underwent UPLM-PCI during the study period, and one hundred patients were matched (50 patients per group). There were no significant differences in baseline characteristics between the two groups. Up-front balloon tamponade assistance was higher in the dual access group (14 % vs 4.0 %, p = 0.027), and rate of successful hemostasis post-closure was lower (82 % vs 100 %, p = 0.001). The primary composite

outcome occurred in 7 patients (14 %) in the single access group, compared to 16 patients (32 %) in the dual access group (p = 0.033). Patients in the dual-access group had higher rates of major bleeding (17 % vs 2 %, p = 0.014). CONCLUSIONS: SHiPCI compared to standard dual access for Impella-assisted UPLM-PCI demonstrated a lower rate lower rate of the composite outcome, driven primarily by a lower rate of major bleeding. Prospective randomized controlled trials are needed to delineate the efficacy and safety of SHiPCI.

Internal Medicine
Kabir K, **LeRoy DI**, Liyanaarachchi B, Shams Z, and **Singla V**. Humor me with calcium: a case report of humoral hypercalcemia of malignancy secondary to cholangiocarcinoma. *J Gastrointest Oncol* 2025; 16(2):719-725. PMID: 40386597. Full Text

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BACKGROUND: Humoral hypercalcemia of malignancy (HHM) is a rare presentation of cholangiocarcinoma, with few reports in prior literature. HHM is due to the production of parathyroid hormone related peptide (PTHrP) from malignant tissues leading to hypercalcemia, often hard to control. Currently, HHM due to cholangiocarcinoma has been associated with poor prognosis and therapies utilized to manage HHM have not been shown to increase survival. Furthermore, biomarkers such as cytokeratin-7 (CK7) have been shown to correlate with worse prognosis in cholangiocarcinoma. While surgical treatment can be curative for cholangiocarcinoma, current nonsurgical treatment options for HHM due to cholangiocarcinoma have not been associated with improved prognosis. CASE DESCRIPTION: We present a rare case of HHM secondary to cholangiocarcinoma. This case presents a rare case of HHM due to cholangiocarcinoma with an atypical presentation in a 55-year-old female. This patient presented with abdominal swelling and severe hypercalcemia prompting evaluation for a possible gastrointestinal source and was found to have HHM due to cholangiocarcinoma. She was treated for her hypercalcemia medically, however due to the extent of her disease she was unable to undergo surgery. Chemotherapy was not considered during her initial presentation as she originally had a malignancy of unknown primary. Ultimately, shortly after her initial presentation, the patient passed at another hospitalization 36 days after her initial presentation. CONCLUSIONS: HHM rarely presents in cholangiocarcinoma, and of the reported cases, it is often associated with poor prognosis. Given the complexity of these cases, a multi-disciplinary approach is necessary for optimal management of these patients. The ability to risk-stratify patients with unique presentations such as this is crucial for accurate diagnosis and potential treatment. HHM in cholangiocarcinoma is poorly studied due to its rarity; however, given the prognosis of this syndrome, further research is essential for earlier detection and better treatments.

Internal Medicine
Mazhar Z, Tareen MK, and **Qureshi MA**. Unilateral access in TF-TAVR: Promising innovation, but rigor and generalizability await validation, a letter to editor. *Int J Cardiol* 2025; 433:133314. PMID: 40300699. Full Text

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Internal Medicine
Muma B, **Keteyian C**, **Kolde D**, **Drake S**, **George D**, **Foust M**, **Fried S**, **Elsberg J**, **Thomas S**, **Johnston L**, **Kulawczyk A**, Paculdo D, Cooney I, Peabody J, and Burgon T. Patient Simulation-Based Primary Care Training to Increase Evidence-Based COPD Care and Value-Based Success: Real-World Cost and Quality Impact Analysis. *Am J Med* 2025; Epub ahead of print. PMID: 40447064. Full Text

Henry Ford Physician Network; Detroit, MI; Henry Ford Health.
Detroit, MI; Henry Ford Health; Detroit, MI; Jackson Health Network.
Detroit, MI; Henry Ford Health.
Jackson, MI; QURE Healthcare.
Jackson, MI; QURE Healthcare; St Louis, MO, USA, University of California, San Francisco, CA.

Internal Medicine
Nieto LM, **Martinez J**, Narvaez SI, Ko D, Kim DH, Vega KJ, and Chawla S. Glucagon-Like Peptide-1 Receptor Agonists Use Does Not Increase the Risk for Acute Pancreatitis and Is Associated with Lower Complications in Patients with Type 2 Diabetes Who Develop Acute Pancreatitis: A Multi-Center Analysis. *Am J Gastroenterol* 2025; Epub ahead of print. PMID: 40358430. Full Text

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BACKGROUND: Type 2 Diabetes Mellitus (T2DM) can lead to structural pancreatic changes potentially predisposing to Acute Pancreatitis (AP), increasing morbidity and mortality. Scarce data exists on the outcomes of AP in T2DM patients who are taking Glucagon-like peptide-1 receptor agonists (GLP-1 RAs). The study aim was to evaluate AP outcome and all-cause mortality in T2DM patients using GLP-1 RAs. METHODS: A retrospective cohort study was performed using population-based data from the TriNetX platform. T2DM patients receiving GLP-1 RAs drugs (semaglutide, liraglutide, dulaglutide and tirzepatide) between January 1, 2015, and October 31, 2023 were included. This patient cohort was matched with T2DM patients who did not receive GLP-1 RAs according to age, demographics, comorbidities, and medication by using 1:1 propensity matching. To avoid confounding, etiologies of AP including alcohol-induced, trauma, biliary, class Ia drug-induced, hypertriglyceridemia, and post-ERCP were excluded from both cohorts. Primary outcomes were risk of developing AP, need for parenteral nutrition, systemic complications (sepsis, systemic inflammatory response syndrome, shock, mechanical ventilation, acute kidney injury (AKI)) and local pancreatic complications. The secondary outcome was all-cause mortality. Cox proportional hazards models were used to estimate hazard ratios (HRs). RESULTS: A total of 740,370 patients with T2DM were identified with 29,423 on GLP -1 RAs; 20,459 out of those 29,423 (mean [SD] age, 58.1 [11.9] years; 10,190 [49.85%] female) were matched with 20,459 individuals (mean [SD] age, 57.5 [13.9] years; 10,301 [50.35%] female) who did not take GLP-1 RAs. The GLP-1 RAs group had lower risk of complicated pancreatitis (HR, 0.32; 95% CI, 0.14-0.74), parenteral nutrition needs (HR, 0.28; 95% CI, 0.09-0.83), sepsis (HR, 0.71; 95% CI, 0.59-0.84), AKI (HR, 0.54; 95% CI, 0.49-0.60), shock (HR, 0.52; 95% CI, 0.36-0.75) and mechanical ventilation support during admission (HR, 0.23; 95% CI, 0.16-0.33) compared with the non- GLP-1 RAs group. Also, all-cause mortality was decreased in the GLP-1 agonist group compared to the non-GLP-1 agonist group (HR, 0.45; 95% CI, 0.41-0.49). Important to note that the GLP-1 RAs group had a tendency of lower risk of uncomplicated pancreatitis (HR, 0.71; 95% CI, 0.49-1.01) but without statistically significant result. No difference was found between the groups in risk of developing SIRS if it occurs. CONCLUSION: GLP-1 RAs use does not increase AP risk, is associated with lower complications in those who developed AP and linked with lower all-cause mortality in T2DM patients. Prospective studies are needed to determine the mechanisms behind these findings.

Internal Medicine
Rackerby N, Ahn C, Ball BD, Samant S, Bernstein JS, and Bernstein JA. Evolving paradigms of treatment of allergic and nonallergic rhinitis. *Ann Allergy Asthma Immunol* 2025; Epub ahead of print. PMID: 40245980. Full Text

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Allergic rhinitis (AR) is a prevalent disease affecting approximately 15% of the US population, which is approximately 50 million individuals. More broadly, it is estimated that 400 to 500 million people worldwide experience AR. Not surprisingly, AR has a significant impact on quality of life due to increased fatigue, cognitive impairment, sleep disturbances, presenteeism or absenteeism, and impairment of performance, which all contribute to an increased cost burden to the medical system. Recent studies have identified social determinants of health including income level, age of migration from rural to urban areas or to high-income countries, and access to health care as important factors associated with the prevalence of allergic diseases. However, up to 25% of individuals have non-AR triggered by mechanical, osmotic, and chemical irritants, and 50% have mixed rhinitis characterized by allergic and nonallergic triggers. Uncontrolled chronic rhinitis subtypes have all been associated with asthma, eczema, chronic or recurrent sinusitis, cough, and both tension and migraine headaches. This review will address AR and non-AR with a focus on evolving treatments in adults.

Internal Medicine
Saleem A, **Jamali T**, and **Gueorguieva I**. Mucosal Schwann Cell Hamartoma of the Appendix: Expanding the Differential for Gastrointestinal Bleeding. *ACG Case Rep J* 2025; 12(5):e01708. PMID: 40401048. Full Text

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Mucosal Schwann cell hamartomas (MSCH) are rare benign tumors typically found in the colorectal region. We present the case of an 87-year-old man with a history of mucosa-associated lymphoid tissue lymphoma who developed symptomatic gastrointestinal bleeding due to an appendiceal MSCH. The patient's ongoing melena and anemia led to further evaluation. Subsequent colonoscopy revealed active bleeding from the appendiceal orifice with hemostasis achieved using epinephrine injection. A laparoscopic appendectomy confirmed MSCH through histopathology and immunohistochemical staining. Given its rarity, this case underscores the importance of considering MSCH in unexplained gastrointestinal bleeding and demonstrates its potential to be a symptomatically significant entity.

Internal Medicine
Shahzil M, Kashif TB, Jamil Z, Khaqan MA, Munir L, Amjad Z, **Faisal MS**, **Chaudhary AJ**, Ali H, Khan S, and Enofe I. Assessing the effectiveness of texture and color enhancement imaging versus white-light endoscopy in detecting gastrointestinal lesions: A systematic review and meta-analysis. *DEN Open* 2026; 6(1):e70128. PMID: 40313348. Full Text

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INTRODUCTION: Gastrointestinal cancers account for 26% of cancer incidence and 35% of cancer-related deaths globally. Early detection is crucial but often limited by white light endoscopy (WLE), which misses subtle lesions. Texture and color enhancement imaging (TXI), introduced in 2020, enhances

texture, brightness, and color, addressing WLE's limitations. This meta-analysis evaluates TXI's effectiveness compared to WLE in gastrointestinal lesion lesion detection. METHODS: A systematic review and meta-analysis were conducted per Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Searches of CENTRAL, PubMed, Embase, and Web of Science identified randomized controlled trials and observational studies comparing TXI with WLE. Outcomes included lesion detection rates, color differentiation, and visibility scores. The risk of bias was assessed using the Cochrane ROB 2.0 tool and Newcastle-Ottawa tools, and evidence certainty was evaluated using Grading of Recommendations Assessment, Development, and Evaluation. RESULTS: Seventeen studies with 16,634 participants were included. TXI significantly improved color differentiation (mean difference: 3.31, 95% confidence interval [CI]: 2.49-4.13), visibility scores (mean difference: 0.50, 95% CI: 0.36-0.64), and lesion detection rates (odds ratio [OR]: 1.84, 95% CI: 1.52-2.22) compared to WLE. Subgroup analyses confirmed TXI's advantages across pharyngeal, esophageal, gastric, and colorectal lesions. TXI also enhanced adenoma detection rates (OR: 1.66, 95% CI: 1.31-2.12) and mean adenoma detection per procedure (mean difference: 0.48, 95% CI: 0.25-0.70). CONCLUSION: TXI improves gastriontestinal lesion lesion detection by enhancing visualization and color differentiation, addressing key limitations of WLE. These findings support its integration into routine endoscopy, with further research needed to compare TXI with other modalities and explore its potential in real-time lesion detection.

Internal Medicine
Sherwood JR, **Parsons A**, **Al Jammala H**, and **Kaatz S**. Perioperative Management of Oral Anticoagulation in Patients with Venous Thromboembolism. *Med Clin North Am* 2025. PMID: Not assigned. Full Text

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Internal Medicine
Tamr A, **Shahid MA**, **Wollner I**, and **Theisen B**. Delayed Presentation of Metastatic Solid Pseudopapillary Epithelial Neoplasm in a Pregnant Woman: A Case Report. *Cureus* 2025; 17(4):e82454. PMID: 40385926. Full Text

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Solid pseudopapillary epithelial neoplasm (SPEN) is a rare, low-grade malignant pancreatic tumor usually found incidentally on imaging, most commonly in young women. Its association with women suggests that hormones may play a significant role in tumor pathogenesis. Surgical resection is the mainstay of treatment in all stages of disease, and few other treatment options have been thoroughly explored. This case demonstrates the unique therapeutic challenges involved in the management of a pregnant woman with new liver metastasis and significant disease burden following remote resection of the primary SPEN tumor. The patient was treated with chemotherapy, radiation, and hormone therapy, followed by hepatic trisegmentectomy without recurrence during surveillance. This case presents a unique therapeutic approach to a situation where no established treatment guidelines exist.

Internal Medicine
Tareen MK, Mazhar Z, **Qureshi MA**, and Asghar S. Letter to the editor: Intracoronary adenosine compared with adrenaline and verapamil in the treatment of no-reflow phenomenon following primary PCI in STEMI patients. *Int J Cardiol* 2025; 434:133357. PMID: 40334948. Full Text

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Internal Medicine

Wang J, Kaufhold R, Wang T, Rajpurkar A, Shapiro J, **Garrett S**, Hameed M, and Bohm L. Participant Perceptions of Using Research Mentorship to Create a Pipeline Program for Premedical Students Underrepresented in Medicine. *Med Sci Educ* 2025; 35(2):619-624. PMID: 40352994. Full Text

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The Medical Mentorship Program (MMP) at the University of Michigan was established to use research as a vehicle to mentor undergraduate students from backgrounds underrepresented in medicine (URiM). Eleven undergraduate students were paired with a medical student mentor and faculty principal investigator to lead a research project and participate in educational sessions. We found that 100% of undergraduates agreed that the program increased their interest in medicine. Additionally, 83.4% of medical students and 100% of faculty agreed they gained valuable mentorship experience. In conclusion, MMP provided URiM undergraduate students with valuable research, mentorship, networking, and medical exposure. SUPPLEMENTARY INFORMATION: The online version contains supplementary material available at 10.1007/s40670-025-02312-z.

Internal Medicine

Winder GS, Arab JP, Goswami Banerjee A, **Bryce K**, Fipps DC, Hussain F, Im G, Omary L, Patel AA, **Patel S**, Rubman S, Serper M, Shenoy A, Suzuki J, Zimbrean P, **Brown K**, **Abouljoud M**, and **Mellinger JL**. From embedded interprofessional clinics to expanded alcohol-associated liver disease programs. *Liver Transpl* 2025; Epub ahead of print. PMID: 40359009. Full Text

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Hazardous alcohol use remains a major contributor to acute and chronic liver disease, while alcohol-associated liver disease (ALD) is a leading indication for liver transplantation. In recent years, embedded, interprofessional ALD clinics have improved access to alcohol use disorder care within hepatology and liver transplantation, but more work is needed to meet this challenge. The literature is lacking regarding scaling procedures to provide services for increasingly large ill patient populations. This article begins to fill this gap by describing "expanded ALD care": broad, innovative, longitudinal, interprofessional care delivery strategies surpassing standalone clinics. Drawing from analogous patient populations served by collaborative models in primary care and comprehensive eating disorder treatment, the expanded ALD care framework proposes practical strategies toward specific innovations: equipoise between biomedical and psychosocial care elements, increased clinician number and reach, long-term patient relationships, harm reduction and palliative care, outreach to external agencies and clinicians, and enhanced support for patients and families. The article also defines attributes of innovative healthcare systems that support expanded ALD care.

Nephrology

Kobashigawa J, Levitsky J, Singh N, Khush K, Pinney S, Aby E, Afzal A, Adey D, Bhalla A, Doshi M, Farouk S, Fox A, Hall S, Kittleson M, King L, Kuo A, Levine D, Manla Y, Modaresi J, Mufti A, Anand PM, Nurok M, Norvell J, Parikh N, Pillai A, Pradhan F, Ramsey A, **Samaniego-Picota M**, Poojary-Hohman I, Samra M, Sawinski D, Schlendorf K, Sweet S, Tanriover B, Virmani S, and Bloom RD. Recommendations to Overcome Barriers to Transplant Fellowship Training: A Report from the American Society of Transplantation Fellows Task Force. *Am J Transplant* 2025; Epub ahead of print. PMID: 40373877. Full Text

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With the expansion of solid organ transplantation activities in the US, there is a critical need for more transplant care providers and trainees to sustain and advance the field of transplantation. However, there has been a pending shortage of trainees pursuing transplant fellowship training in the U.S. in recent years. To address this issue, the American Society of Transplantation (AST) organized the Fellows' Task Force, including representatives of all four major organs from various AST communities of practice, to understand the drivers of this pending shortage and develop strategies to increase interest in transplant specialization. The task force identified four areas of focus, including early & sustained exposure to transplant medicine, awareness through education, flexible fellowships & pathways to transplant, and work/life resources. Based on these focus areas, the task force developed recommendations and action items, which were compiled into a report to be implemented by individuals, institutions, communities of practice (work groups), and societies such as the AST. We hope that this report will be the first step in overcoming barriers and concerns to encourage the pursuit of specialization in transplantation in the US.

Neurology

Agarwal U, Hamilton K, **Ali A**, and Mathew PG. The use of onabotulinum toxin type A and other neurotoxins for the treatment of chronic migraine: An American Headache Society survey study. *Clin Neurol Neurosurg* 2025; 254:108960. PMID: 40373455. Full Text

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PURPOSE: OnabotA is the only US Food and Drug Administration-approved neurotoxin for chronic migraine prevention; however, non-onabotA toxins may be equally effective. Few studies have explored clinician practices and patient outcomes with non-onabotA neurotoxins. Our study aimed to generate a statistical snapshot of clinician perspectives and treatment practices regarding onabotulinum toxin A (onabotA) and other neurotoxins for chronic migraine and comorbid conditions. METHODS: A 15-question survey was distributed online to clinician members of the American Headache Society (AHS) assessing clinical practices using onabotA and non-onabotA toxins for chronic migraine and comorbid conditions, and descriptive analysis was performed. RESULTS: 168 respondents (162 from the United States and 6 from Canada) completed the survey (response rate 10.1 % [168/1665]). Of 48 respondents (28 % of total) using non-onabotA toxins for chronic migraine, 27 (16 %) used incobotulinum toxin A; 23 (14 %) used abobotulinum toxin A; and 12 (7 %) used rimabotulinum toxin B. Non-onabotA toxins were predominantly used due to administration/payor imposed issues (19/48; 40 %) and cost (18/48 [38 %]). Most clinicians using non-onabotA toxins reported similar efficacy to onabotA (32/48; 67 %), while fewer reported better efficacy (9/48 [19 %]) or worse efficacy (7/48 [15 %]) than onabotA. Many respondents (114/168 [68 %]) had used neurotoxins for chronic migraine in addition to other comorbid conditions, including temporomandibular joint disorders (95/114 [83 %]) and cervical dystonia (64/114 [56 %]). CONCLUSION: While non-onabotA toxins are used less frequently for chronic migraine, they may have similar efficacy as onabotA and are used off-label in clinical practice due to administrative/payor issues or cost.

Neurology

Arguedas A, Schneck D, Cui E, Xenopoulos-Oddsson A, **Arcila-Londono X**, Lunetta C, Wymer J, Olney N, Gwathmey K, Ajroud-Driss S, Hayat G, Heiman-Patterson T, Cerri F, Fournier C, Glass J, Sherman A, Walk D, and Fiecas M. Risk prediction for ALS using semi-competing risk models with applications to the ALS Natural History Consortium dataset. *Amyotroph Lateral Scler Frontotemporal Degener* 2025;1-8. Epub ahead of print. PMID: 40366870. Full Text

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Background and objectives: Important landmarks in progression of amyotrophic lateral sclerosis (ALS) can occur prior to death. Predictive models for the risk of these events can assist in clinical trial design and personal planning. We propose a predictive model, using a semi-competing risks modeling approach, for five important disease progression landmarks in ALS. Methods: Data on 1508 participants from the ALS Natural History Consortium (ALS NHC) were used, including baseline characteristics and the ALS Functional Rating Scale-Revised (ALSFRS-R) score collected at clinic visits. A semi-competing risks modeling approach was used to study the time to disease progression landmarks, accounting for the possibility of death. Specifically, time to gastrostomy, use of noninvasive ventilation (NIV), continuous use of NIV, loss of speech, and loss of ambulation were chosen and modeled individually. To measure the predictive capabilities of the model, the integrated Brier score was computed for each model using cross-validation for the NHC data. Data from Emory University were used for external validation of the models. Results: We present model results using gastrostomy as the intermediate outcome. Similar trends in disease progression groups were found across all model pathways. Diagnostic delay, age, and site of onset were the most important covariates. Predictive metrics in both internal and external validation are presented across all models and for different pathways. Conclusion: Semi-competing risks modeling is a flexible approach to studying disease progression. The models have good predictive capabilities across different outcomes and pathways. These are replicated in the external validation dataset.

Neurology
Gross WL, Swanson SJ, **Helfand AI**, Pillay SB, Humphries CJ, Raghavan M, Mueller WM, Carlson CE, Conant LL, Busch RM, Lowe M, Tivarus ME, Drane DL, Jacobs M, Morgan VL, Allendorfer JB, Szaflarski JP, Bonilha L, Bookheimer S, Grabowski T, Vannest J, and Binder JR. Predicting memory decline from left temporal lobe epilepsy surgery using preoperative fMRI: a multicenter study. *Neuroimage Clin* 2025; 46:103804. PMID: 40424645. Full Text

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OBJECTIVE: While fMRI language laterality has been used to predict verbal memory after epilepsy surgery, supporting evidence is not yet definitive. The FMRI in Anterior Temporal Epilepsy Surgery (FATES) project was a prospective observational cohort study at 10 US epilepsy centers, performed to determine whether a multivariable model including fMRI language laterality can predict verbal memory outcome 6 months after left temporal lobe epilepsy surgery. METHODS: This analysis includes 70 adults who underwent left temporal lobe epilepsy surgeries including hippocampal resection for treatment of epilepsy. Patients completed standard protocols, including preoperative fMRI language mapping with a semantic decision versus tone decision (SDTD) task contrast and preoperative and postoperative verbal memory assessment. Five memory measures, obtained from the Selective Reminding Test, Rey Auditory Verbal Learning Test, and Wechsler Memory Scale, were selected to cover a range of episodic memory tasks including word list learning, delayed list recall, and story recall. Multiple linear regression was performed using the preoperative memory score, duration of epilepsy, age at epilepsy onset, age at surgery, hippocampal sclerosis status, and fMRI SDTD laterality index (LI) as predictor variables for 6-month postoperative verbal memory change. RESULTS: Across different memory measures, decline (defined using Reliable Change Index) was seen in 8%-28% of patients. Changes on all five memory measures were significantly correlated with preoperative score, epilepsy duration, and fMRI SDTD LI. Variance explained by linear regression models for each test ranged from 34%-41%, with fMRI LI independently accounting for 7%-25% of the total variance (all $p < 0.05$). Cross-validation accuracy for predicting change scores in independent held-back samples ranged from 0.54-0.75 standard deviations of the preoperative sample. SIGNIFICANCE: We demonstrate that models incorporating fMRI language LIs from a semantic decision task trained to predict verbal memory decline after left temporal lobe surgery provide meaningful information to help inform patients of the risk associated with left temporal lobe surgery and are practical to implement in different hospital settings. This confirms previous limited evidence that fMRI-based preoperative language protocols can be used to predict verbal episodic memory outcome after left temporal lobe epilepsy surgery.

Neurology
Reidy M, Khan M, Mills EA, Wu Q, Garton J, Draayer DE, **Zahoor I**, **Giri S**, Axtell RC, and Mao-Draayer Y. New Frontiers in Multiple Sclerosis Treatment: From Targeting Costimulatory Molecules to Bispecific Antibodies. *Int J Mol Sci* 2025; 26(8). PMID: 40332536. Full Text

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Multiple sclerosis (MS) is an autoimmune demyelinating disease of the central nervous system. The therapeutic landscape for MS has evolved significantly since the 1990s, with the development of more than 20 different disease-modifying therapies (DMTs). These therapies effectively manage relapses and inflammation, but most have failed to meaningfully prevent disease progression. While classically understood as a T cell-mediated condition, the most effective DMTs in slowing progression also target B cells. Novel classes of MS therapies in development, including anti-CD40L monoclonal antibodies, CD19 chimeric antigen receptor (CAR) T cells, and Bruton's tyrosine kinase (BTK) inhibitors show greater capacity to target and eliminate B cells in the brain/CNS, as well as impacting T-cell and innate immune compartments. These approaches may help tackle the disease at its immunopathological core, addressing both peripheral and central immune responses that drive MS progression. Another emerging therapeutic strategy is to use bispecific antibodies, which have the potential for dual-targeting various disease aspects such as immune activation and neurodegeneration. As such, the next generation of MS therapies may be the first to reduce both inflammatory demyelination and disease progression in a clinically meaningful way. Their ability to target specific immune cell populations while minimizing broad immune suppression could also lead to better safety profiles. Here, we explore the biological rationale,

advantages, limitations, and clinical progress of these emerging immunotherapies for relapsing-remitting and progressive forms of MS.

Neurology
Sharaf J, and **Ali A**. Cluster headache vs. labor: A comparative perspective on acute pain during and after delivery. *Headache* 2025; Epub ahead of print. PMID: 40444682. Full Text

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Neurology
Shen Y, **Zhang L**, **Ding G**, **Boyd E**, **Kaur J**, **Li Q**, Haacke EM, Hu J, and **Jiang Q**. Vascular Contribution to Cerebral Waste Clearance Affected by Aging or Diabetes. *Diagnostics (Basel)* 2025; 15(8). PMID: 40310437. Full Text

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Background: The brain's vascular system has recently been shown to provide an important efflux pathway for cerebral waste clearance (CWC). However, little is known about the influence of aging or diabetes on the CWC. The aim of the current study is to investigate the vasculature contribution to CWC under aging and diabetic conditions. Methods: Male Wistar rats under aging and diabetic conditions were evaluated using dynamic intra-cisterna superparamagnetic iron oxide-enhanced susceptibility-weighted imaging (SPIO-SWI). Theoretical analysis of the expected signal intensity using SPIO-SWI was compared with the corresponding dynamic in vivo images. Quantitative susceptibility mapping (QSM) was used to evaluate the iron-based tracer concentration in the venous system. Results: Our data demonstrated that the theoretical analysis predicted the dynamic changes in the signal intensity after SPIO infusion. The distinct hyperintense signals due to the lower concentration of the SPIO over time in cerebrospinal fluid (CSF) and meningeal lymphatic (ML) vessels likely represented the CWC through various efflux pathways, including cerebral vascular and ML vessels. The QSM analysis further revealed reduced CWC from the vasculature in both the aged and diabetic groups compared to the younger group. Conclusions: Our results demonstrated that SPIO-SWI can quantitatively evaluate the CWC efflux contributions from cerebral vascular vessels under aging or diabetic conditions.

Neurology
Shneider NA, Harms MB, Korobeynikov VA, Rifai OM, Hoover BN, Harrington EA, Aziz-Zaman S, Singleton J, Jamil A, Madan VR, Lee I, Andrews JA, Smiley RM, Alam MM, Black LE, Shin M, Watts JK, Walk D, **Newman D**, Pascuzzi RM, Weber M, Neuwirth C, Da Cruz S, Soriano A, Lane R, Henry S, Mathews J, Jafar-Nejad P, Norris D, Rigo F, Brown RH, Miller S, Crean R, and Bennett CF. Antisense oligonucleotide jacifusen for FUS-ALS: an investigator-initiated, multicentre, open-label case series. *Lancet* 2025; Epub ahead of print. PMID: 40414239. Full Text

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VIB-KU Leuven Center for Brain and Disease Research, Department of Neurosciences, KU Leuven and Leuven Brain Institute, Leuven, Belgium.
Ionis Pharmaceuticals, Carlsbad, CA, USA.

BACKGROUND: Pathogenic variants of fused in sarcoma (FUS) cause amyotrophic lateral sclerosis (FUS-ALS), with evidence of gain of function. Jacifusen is an antisense oligonucleotide targeting FUS pre-mRNA, previously shown to delay neurodegeneration in a mouse model and potentially slow functional decline in a first-in-human study. Here, we sought to further evaluate use of jacifusen as a treatment for FUS-ALS. METHODS: This expanded access programme was conducted through a series of single-patient investigational new drug applications at five sites (four hospitals in the USA and one in Switzerland). Participants carried a FUS variant and had clinical evidence of motor neuron disease onset or electrophysiological abnormalities, if not a diagnosis of ALS. Participants were ineligible if chronically ventilated with tracheostomy. Enrolled sequentially, participants received serial intrathecal injections of jacifusen over 2·8-33·9 months. Based on multiple ascending doses of jacifusen (from 20 mg to 120 mg), successive protocols were modified as safety and other data were acquired, with the last participants enrolled receiving 120 mg doses monthly from the start of their treatment. Safety was assessed using the Common Terminology Criteria for Adverse Events version 4.0 and standard cerebrospinal fluid (CSF) metrics. Concentration of neurofilament light chain (NfL) in CSF was used as a biomarker of axonal injury and neurodegeneration, and the ALS Functional Rating Scale-Revised (ALSFRS-R) score was used as an overall measure of motor function. Biochemical analysis and immunohistochemical staining were done on post-mortem CNS tissues to quantify FUS protein expression and assess the burden of FUS pathology. FINDINGS: Between June 11, 2019, and June 2, 2023, we recruited 12 participants (median age 26 years [range 16-45]; seven [58%] were female and five [42%] were male) into the expanded access programme. Transient elevations in cell counts or total protein concentration in CSF (six [50%] participants) were unrelated to treatment duration. The most common adverse events were back pain (six [50%]), headache (four [33%]), nausea (three [25%]), and post-lumbar puncture headache (three [25%]). Two participant deaths were recorded during the programme, both thought to be unrelated to the investigational drug. The concentration of NfL in CSF was reduced by up to 82·8% after 6 months of treatment. Although most participants had continued functional decline (as measured by ALSFRS-R) after starting treatment with jacifusen, one showed unprecedented, objective functional recovery after 10 months, and another remained asymptomatic, with documented improvement in electromyographic abnormalities. Biochemical and immunohistochemical analysis of CNS tissue samples from four participants showed reduced FUS protein levels and an apparent decrease in the burden of FUS pathology. INTERPRETATION: The findings suggest the safety and possible efficacy of jacifusen for treating FUS-ALS. The efficacy of jacifusen is being further evaluated in an ongoing clinical trial. FUNDING: ALS Association, Project ALS, Ionis Pharmaceuticals, Tow Foundation, Nancy D Perlman and Thomas D Klingenstein Innovation Fund for Neurodegenerative Disease, National Institutes of Health, Angel Fund for ALS Research, Cellucci Fund for ALS Research, Max Rosenfeld ALS Fund, University of Minnesota, and the Muscular Dystrophy Association.

Neurology

Wang M, **Wang W**, **Chopp M**, **Zhang ZG**, and **Zhang Y**. Therapeutic and diagnostic potential of extracellular vesicle (EV)-mediated intercellular transfer of mitochondria and mitochondrial components. *J Cereb Blood Flow Metab* 2025; Epub ahead of print. PMID: 40367392. Full Text

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Extracellular vesicles (EVs) facilitate the transfer of biological materials between cells throughout the body. Mitochondria, membrane-bound organelles present in the cytoplasm of nearly all eukaryotic cells, are vital for energy production and cellular homeostasis. Recent studies highlight the critical role of the transport of diverse mitochondrial content, such as mitochondrial DNA (mt-DNA), mitochondrial RNA (mt-RNA), mitochondrial proteins (mt-Prots), and intact mitochondria by small EVs (<200 nm) and large EVs (>200 nm) to recipient cells, where these cargos contribute to cellular and mitochondrial homeostasis. The interplay between EVs and mitochondrial components has significant implications for health,

metabolic regulation, and potential as biomarkers. Despite advancements, the mechanisms governing EV-mitochondria crosstalk and the regulatory effect of mitochondrial EVs remain poorly understood. This review explores the roles of EVs and their mitochondrial cargos in health and disease, examines potential mechanisms underlying their interactions, and emphasizes the therapeutic potential of EVs for neurological and systemic conditions associated with mitochondrial dysfunction.

Obstetrics, Gynecology and Women's Health Services

Bacal V, Li A, Shapiro H, **Rana U**, Zwingerman R, Avery L, Palermo A, Philipoppolous E, and Chan C. A systematic review and meta-analysis of the diagnostic accuracy after preimplantation genetic testing for aneuploidy. *PLoS One* 2025; 20(5):e0321859. PMID: 40367147. Full Text

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OBJECTIVE: Aneuploidy accounts for many pregnancy failures and congenital anomalies. Preimplantation genetic testing for aneuploidy (PGT-A) is a screening test applied to embryos created from in vitro fertilization to diminish the chance of an aneuploid conception. The rate of misdiagnosis for both false aneuploidy (false positive) and false euploidy (false negative) test results is unknown. The objective of this study was to determine the rate of misclassification of both aneuploidy and euploidy after PGT-A. DATA SOURCES: We conducted a systematic review and meta-analysis. We searched Medline, Embase, Cochrane Central, CINAHL and WHO Clinical Trials Registry from inception until April 10, 2024. The protocol was registered in International Prospective Register of Systematic Reviews (PROSPERO CRD 42020219074). METHODS OF STUDY SELECTION: We included studies that conducted either a pre-clinical validation of the genetic platform for PGT-A using a cell line, studies that compared the embryo biopsy results to those from the whole dissected embryo or its inner cell mass (WE/ICM), and studies that compared the biopsy results to prenatal or postnatal genetic testing. TABULATION, INTEGRATION, AND RESULTS: Two independent reviewers extracted true and false positives and negatives comparing biopsy results to the reference standard (known karyotype, WE/ICM, pregnancy outcome). For preclinical studies, the main outcome was the positive and negative predictive values. Misdiagnosis rate was the outcome for pregnancy outcome studies. The electronic search yielded 6674 citations, of which 109 were included. For WE/ICM studies (n=40), PPV was 89.2% (95% CI 83.1-94.0) and NPV was 94.2% (95% CI 91.1-96.7, I2=42%) for aneuploid and euploid embryos, respectively. The PPV for mosaic embryos of either a confirmatory mosaic or aneuploid result was 52.8% (95% CI 37.9-67.5). For pregnancy outcome studies (n=43), the misdiagnosis rate after euploid embryo transfer was 0.2% (95% CI 0.0-0.7%, I2=65%). However, the rate for mosaic transfer, with a confirmatory euploid pregnancy outcome, was 21.7% (95% CI: 9.6-36.9, I2=95%). CONCLUSION: The accuracy of an aneuploid result from PGT-A is excellent and can be relied upon as a screening tool for embryos to avoid aneuploid pregnancies. Similarly, the misdiagnosis rate after euploid embryo transfer is less than 1%. However, there is a significant limitation in the accuracy of mosaic embryos.

Obstetrics, Gynecology and Women's Health Services

Daviskiba S, **Irshad M**, **Katz S**, and **Swain M**. Elective fertility preservation among graduate medical trainees: a survey study of perceived barriers and the impact of employer-sponsored financial benefits. *J Assist Reprod Genet* 2025; Epub ahead of print. PMID: 40447955. Full Text

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PURPOSE: To assess the impact of employer-provided financial support on graduate medical trainees' decision to pursue fertility preservation and to identify perceived barriers to participation in fertility preservation. METHODS: An anonymous online survey study addressing perspectives surrounding participation in elective fertility preservation while in training was distributed in August 2024 to residents and fellows in graduate medical programs across the United States. RESULTS: Of 306 medical trainee respondents, 202 (67.1%) had intentionally delayed childbearing due to their medical training. There were 66.4% (n = 200) who reported that their sex/gender impacted their interest in fertility preservation, including 87% (n = 172) of whom had been assigned female at birth. High costs and time constraints of training were the most commonly cited factors (63.1%) negatively impacting the decision to participate in elective fertility preservation. Employer financial support was reported by 32.9% (n = 99) as a factor that would make them more likely to pursue fertility preservation. Trainees who worked an average of 60 to > 80 hours per week had the highest rate of reported intentional delay in childbearing, and the time constraints of training negatively impacted their interest in fertility preservation. Only 24% knew whether coverage for fertility services was mandated in their state, 25.2% were unfamiliar with fertility preservation, and 35.3% did not know how to access fertility services. CONCLUSION: Medical trainees face significant financial and structural barriers to accessing fertility preservation. Widespread financial benefits and systemic changes in training programs may improve the feasibility of fertility preservation for graduate medical trainees.

Obstetrics, Gynecology and Women's Health Services

Kalmbach DA, Ong JC, **Cheng P**, **Reffi AN**, Swanson LM, **Hirata M**, **Seymour GM**, **Castelan-Cuamatzi AS**, **Jennings MB**, **Pitts DS**, Roth A, **Roth T**, and **Drake CL**. A randomized controlled trial of telemedicine CBTI and PUMAS for prenatal insomnia: Reducing nocturnal cognitive arousal is a treatment mechanism for alleviating insomnia and depression during pregnancy. *Sleep Med* 2025; 133:106570. PMID: 40413907. Full Text

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OBJECTIVE: Insomnia is common in pregnancy and fuels perinatal depression (PND). Cognitive-behavioral therapy for insomnia (CBTI) is effective during pregnancy, but unresolved cognitive arousal limits treatment outcomes. Enhancing reduction of cognitive arousal may improve patient outcomes. This randomized controlled trial (RCT) evaluated the effectiveness of CBTI and Perinatal Understanding of Mindful Awareness for Sleep (PUMAS, which combines mindfulness with behavioral sleep strategies) on insomnia, depression, and nocturnal cognitive arousal relative to sleep hygiene education (SHE). METHODS: A single-site, three-arm RCT of N = 64 pregnant women with clinically significant insomnia symptoms who received CBTI, PUMAS, or SHE. Active treatment was delivered via six weekly telemedicine video sessions. Outcomes included the insomnia severity index (ISI), Edinburgh postnatal depression scale (EPDS), and the pre-sleep arousal scale's cognitive factor (PSASC; nocturnal cognitive arousal). RESULTS: Over 95 % of active therapy patients completed ≥4 sessions, indicating high engagement. CBTI (ΔISI = -11.20 ± 6.93; 65.0 % insomnia remission) and PUMAS (ΔISI = -11.05 ± 3.84; 81.8 % insomnia remission) significantly alleviated insomnia relative to SHE (ΔISI = -4.50 ± 1.71; 13.6 % remission), which was replicated in women with comorbid OSA. PUMAS produced large reductions in PND and nocturnal cognitive arousal relative to SHE, whereas CBTI did not. Mediation analyses supported reducing cognitive arousal as a key mechanism by which PUMAS alleviated insomnia and PND. CONCLUSIONS: CBTI and PUMAS are effective for prenatal insomnia, even in women with comorbid OSA. PUMAS may be especially beneficial for pregnant women presenting with PND and/or

high cognitive arousal (including perinatal rumination and worry), whereas CBTI may yield more modest benefits for these non-sleep outcomes.

Obstetrics, Gynecology and Women's Health Services

Vilkins A, Nherera L, Searle R, and Welsh T. Comparison of the effectiveness of two prophylactic single-use negative pressure wound therapy devices in reducing surgical site complications after cesarean delivery: insights from a large US claims database. *Wounds* 2025; 37(4):152-157. PMID: 40368390. Full Text

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BACKGROUND: Single-use negative pressure wound therapy (sNPWT) has emerged as a promising intervention for patients at high risk of surgical site complications (SSCs) after a cesarean delivery. However, the available studies primarily compare negative pressure wound therapy to standard dressings rather than evaluating differences between negative pressure wound therapy devices or pressure settings. OBJECTIVE: To compare the effectiveness of 2 commonly used sNPWT devices, a -80 mm Hg device and a -125 mm Hg device, in reducing the risk of SSCs following cesarean delivery. MATERIALS AND METHODS: Real-world data were obtained from a large claims database in the United States from January 2017 through June 2022. Adult patients who had an inpatient encounter in which the -80 mm Hg device or the -125 mm Hg device was used after a cesarean delivery were included. Propensity score matching was used to balance the cohorts. Study end points included incidence of overall surgical site infection (SSI), superficial SSI, dehiscence, seroma, hematoma, deep SSI, length of stay (LOS), and costs. RESULTS: The study included 5332 cases in each group. Overall SSI, superficial SSI, dehiscence, seroma, and costs were significantly lower with the -80 mm Hg device compared with the -125 mm Hg device ($P \leq .05$). No differences between the 2 devices were observed for hematoma, deep SSI, and LOS ($P > .05$). CONCLUSION: Of the 2 commonly used sNPWT devices, use of the -80 mm Hg device was associated with a lower likelihood of developing overall SSI, superficial SSI, dehiscence, and seroma, and was associated with lower costs after cesarean delivery compared with the -125 mm Hg device. There were nonsignificant differences in LOS, deep SSI, and hematoma. Further studies are required to confirm these findings.

Ophthalmology and Eye Care Services

Carey NL, DuPuis DT, Lin G, Flores E, Mitchell J, **Darnley-Fisch D**, **Imami N**, Heisler M, Resnicow K, McHaney-Conner P, Priester A, MacKenzie C, and Newman-Casey PA. Glaucoma Patient Perspectives on Effective Coaching for Self-Management. *J Glaucoma* 2025; Epub ahead of print. PMID: 40387429. Full Text

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PRECIS: In semi-structured exit interviews, participants in a personalized glaucoma coaching program reported improved self-efficacy in managing their disease. Coaching was frequently cited as catalyst to enhancing medication adherence, emphasizing its role in team-based care. PURPOSE: To assess patients' experience with coaching to motivate improved adherence to glaucoma self-management. METHODS AND MATERIALS: Participants in the Support, Educate, Empower (SEE) personalized glaucoma coaching program completed exit interviews after participating in a six-month coaching program. Interviews were audio-recorded and transcribed verbatim. Transcripts were analyzed using interpretivist grounded theory. Thematic saturation was reached after coding 30 interviews; 32 were

included. Themes were identified, a codebook was generated, and two researchers coded the transcripts (NLC, DTD) and a third adjudicated any disagreements (EF). Main outcomes measures were defined as themes and the number of participants who expressed a theme. RESULTS: Of the 32 participants interviewed in this study, 59% (n=19) identified as male, 41% (n=13) identified as female, 50% (n=16) identified as Black, 34% (n=11) identified as White, 6% (n=2) identified as Asian. Major themes surrounding coaching included how coaching promoted change in eye drop use, knowledge learned from the coach, feeling accountable to the coach, the coach being accessible, how coaches demonstrated empathy, how the coach collaborated to help people develop a sense of control and efficacy over glaucoma self-management, and how coaches built rapport. Additional themes were program satisfaction, fear of vision loss as a motivator to improve glaucoma self-management, and constructive feedback for the program. CONCLUSION: This qualitative assessment of the SEE personalized glaucoma coaching program demonstrated that high-quality coaching and rapport building may help patients with previously low medication adherence feel more motivated and in control of their glaucoma.

Ophthalmology and Eye Care Services

Trivedi V, You Q, Lee PSY, Im J, Tran DV, Me R, Benenati B, Gregory A, **Le K**, and Lin X. EFFICACY OF SPLIT-THICKNESS THIN AMNIOTIC MEMBRANE GRAFT FOR CLOSURE OF REFRACTORY OR LARGE MACULAR HOLES. *Retina* 2025; 45(5):833-838. PMID: 39805138. Full Text

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PURPOSE: To assess the effectiveness of split-thickness amniotic membrane grafts in achieving closure of refractory or large macular holes (MH). METHODS: This retrospective study reviewed data from patients who underwent surgical repair of MHs using split-thickness amniotic membrane grafts between January 2019 and December 2023. Key parameters, including best-corrected visual acuity and MH size, were evaluated both preoperatively and postoperatively. RESULTS: The study included 13 patients (nine females; mean age 63.5 years). Before surgery, the median best-corrected visual acuity was 1.30 ± 0.56 logarithmic measure of angle of resolution (approximate Snellen equivalent: 20/400) and the median MH size measured 717 ± 246.6 μ m. After an average follow-up period of 28 months, the median best-corrected visual acuity improved significantly to 1.00 ± 0.52 logarithmic measure of angle of resolution (P < 0.05) (approximate Snellen equivalent: 20/200). All MHs were successfully closed, and no intraoperative complications were observed. CONCLUSION: Split-thickness amniotic membrane grafting is a safe and reliable option for closing refractory or large MHs, resulting in significant improvements in best-corrected visual acuity and successful hole closure. Compared with full-thickness grafts, split-thickness amniotic membrane grafts offer advantages such as increased flexibility in placement and ease of removal post-closure, due to their thinner and more pliable nature, which facilitates easier handling and positioning within the MH.

Orthopedics/Bone and Joint Center

Abusuliman M, Milgrom Y, **Mellinger J**, and Parker R. Management of alcohol use disorder in alcohol-related liver disease. *Frontline Gastroenterol* 2025. PMID: Not assigned. Full Text

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Alcohol-related liver disease (ArLD) is a leading cause of liver-related morbidity and mortality worldwide and is fundamentally connected to alcohol use disorder (AUD). ArLD develops in a subset of heavy drinkers, with progression from steatosis to cirrhosis. Despite the proven benefits of AUD treatment in halting ArLD progression, fewer than 20% of patients with AUD and ArLD receive treatment, and less than 2% are prescribed pharmacotherapy. Hepatology and gastroenterology practitioners are often not confident to manage coexistent AUD and ArLD. This article examines the relationship between AUD and ArLD, evaluates treatment options and highlights the role of integrated care in improving outcomes. Medical addiction therapy significantly reduces binge drinking, hospitalisations and the risk of hepatic decompensation. Several pharmacotherapies are viable in ArLD, but require specific consideration of

hepatotoxicity, renal excretion and central nervous system effects. Psychotherapy is associated with lower rates of hepatic decompensation and improved liver-related outcomes. Integrated care models that embed AUD treatment within liver clinics improve engagement, abstinence rates and clinical outcomes compared with standard referrals. AUD treatment is fundamental in ArLD management. Increased use of pharmacological and psychological therapies, alongside integrated care models, may improve patient outcomes and reduce the burden of ArLD. Further research is needed to optimise treatment strategies in this high-risk population.

Orthopedics/Bone and Joint Center

Baes T, **Gaudiani M**, and **Moutzouros V**. Medial Portal Placement for ACL Femoral Tunnel Drilling With an Over-the-Top Guide: Concepts and Technique. *Video J Sports Med* 2025; 5(3). PMID: 40444171. Full Text

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BACKGROUND: The rate of graft failure after anterior cruciate ligament (ACL) reconstruction ranges from 3% to 22%. Surgeons must mitigate risks of failure by limiting technical errors. Femoral tunnel malposition has been cited as the most common technical error associated with ACL reconstruction. As such, techniques for femoral tunnel drilling have evolved to ensure placement of the tunnel within the anatomic footprint of the native ACL. If using an over-the-top guide, the placement of the medial portal becomes critical to ensure safe and accurate drilling. INDICATIONS: The purpose of this video is to highlight key concepts related to the proper placement of the medial portal during ACL reconstruction when using an over-the-top guide and low-profile reamer. TECHNIQUE DESCRIPTION: A skin marking for the planned medial portal is made approximately 1.5 to 2 cm medial to the patellar tendon while palpating the joint line. After standard bone-patella tendon-bone (BTB) autograft harvest and anterolateral portal establishment, the medial portal is created under direct visualization, utilizing an 18-gauge spinal needle to ensure proper trajectory for over-the-top femoral tunnel drilling. After the tibial tunnel is prepared, the over-the-top guide is inserted via the medial portal and hooked onto the back wall. The knee is then hyperflexed and the beath pin is advanced out the lateral thigh. The low-profile reamer is advanced over the wire and reamed to the desired tunnel depth. The back wall integrity is confirmed and the prepared autograft is then passed and secured via interference screw fixation. RESULTS: This technique provides a consistent and reproducible method of femoral tunnel placement in the anatomic footprint of the ACL without damaging the medial femoral condyle. We can also instrument through the same portal to treat meniscal pathology without necessitating an accessory medial portal. DISCUSSION/CONCLUSION: Appropriate medial portal placement for femoral tunnel drilling with an over-the-top guide is critical for safe, reproducible, and consistent tunnel location. PATIENT CONSENT DISCLOSURE STATEMENT: The author(s) attests that consent has been obtained from any patient(s) appearing in this publication. If the individual may be identifiable, the author(s) has included a statement of release or other written form of approval from the patient(s) with this submission for publication.

Orthopedics/Bone and Joint Center

Baker KC, Fleischer M, Newton MD, Galasso L, Cavinatto L, Weisz KM, Hartner S, Maerz T, Lammlin L, **Baker EA**, Allen AA, and Bedi A. Pharmacologic Mobilization and Chemokine-Directed Recruitment of Mesenchymal Stromal Cells to the Surgically Repaired Rotator Cuff. *Am J Sports Med* 2025; Epub ahead of print. PMID: 40444728. Full Text

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BACKGROUND: Mesenchymal stromal cell (MSC) techniques represent a promising method to enhance the surgical repair of rotator cuff tears. To eliminate the resource-intensive process of cell isolation and culture expansion, a method to recruit endogenous MSCs was investigated in an established rat model of rotator cuff repair. HYPOTHESIS: MSCs can be pharmacologically mobilized from the peripheral blood and recruited to the operative rotator cuff to enhance tendon-bone healing. STUDY DESIGN: Controlled laboratory study. METHODS: The rat model of supraspinatus tendon detachment and acute surgical repair was used to compare the ability of 3 different chemokines (SDF-1β, MIP-3α, and MCP-1) to recruit optically labeled MSCs to the operative shoulder from circulation. Additional experimentation was undertaken to assess the effects of pharmacological MSC mobilization using a combination of a β(3) adrenoreceptor agonist (BRL37344) and a CXCR4 antagonist (AMD3100) on chemokine-directed recruitment to the shoulder. Finally, the effects of this therapeutic strategy on tendon-bone healing were assessed. RESULTS: MCP-1-loaded hydrogels recruited the greatest number of MSCs from circulation. MCP-1-driven MSC recruitment was significantly enhanced by a regimen of subcutaneous BRL37344 and AMD3100. Postmortem micro-computed tomography imaging performed at a 6-week endpoint revealed that local MCP-1 delivery was associated with significant reductions in trabecular spacing and apparent mineral density, and a significant increase in trabecular number, while pharmacological MSC mobilization had no significant effects. MCP-1 delivery was associated with a lower tendon cross-sectional area and a significant increase in percent relaxation (P = .006). Pharmacological MSC mobilization was associated with significantly increased peak stress (P = .039), significantly increased elastic modulus (P = .037), and a nonsignificant increase in both equilibrium stress (P = .057) and ultimate stress (P = .058). Local MCP-1 delivery was associated with significant improvements in tenocyte morphology. CONCLUSION: Endogenous MSCs can be pharmacologically mobilized into peripheral blood and recruited to the site of rotator cuff repair via local delivery of MCP-1. This therapeutic strategy was associated with improvements in the static and dynamic mechanical properties of the tendon-bone interface. CLINICAL RELEVANCE: The healing of rotator cuff repairs represents an ongoing clinical challenge in orthopaedic surgery. This study demonstrates a method to use endogenous MSCs to enhance healing of the rotator cuff.

Orthopedics/Bone and Joint Center
Best J, **Timoteo T**, **Geers B**, Ayad M, Mathijs E, Warren J, Bernacki K, Arnoczky S, and **Bishai SK**. Failure of dermal allograft remodeling and integration after superior capsular reconstruction for an irreparable rotator cuff tear: a case study 70 months postimplantation. *JSES Int* 2025. PMID: Not assigned. Full Text

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Orthopedics/Bone and Joint Center
Comfort SM, Ray LJ, Harley JD, Kleinsmith RM, Puckett HD, **Braman JP**, Harrison AK, and Rao AJ. Improved patient outcomes and range of motion following primary and revision reverse total shoulder arthroplasty utilizing a custom glenoid implant for glenoid deficiency. *Semin Arthroplasty* 2025. PMID: Not assigned. Full Text

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Background: Glenoid bone loss in the primary and revision setting of reverse total shoulder arthroplasty (rTSA) creates the challenge of sufficient glenoid component positioning and fixation and is at risk of early mechanical failure and aseptic baseplate loosening. The purpose of this study was to evaluate clinical outcomes of primary and revision rTSA utilizing a custom glenoid implant for treatment of glenoid bone deficiency. Methods: Patients who underwent rTSA with a Comprehensive Vault Reconstruction System (VRS) (Zimmer Biomet, Warsaw, IN, USA) custom glenoid implant in the primary or revision setting performed by 2 orthopedic surgeons between April 2016 and October 2023 were included. Demographic, prior surgical history, preoperative assessment, radiographic parameters, intraoperative procedures, and complication data were collected. Preoperative and postoperative range of motion and Single

Assessment Numeric Evaluation (SANE) scores were compared and minimal clinically important difference was calculated for shoulder forward flexion (aFF), shoulder external rotation (aER), and SANE scores. Results: Fifty-two shoulders (50 patients) met the inclusion criteria with 49 shoulders (47 patients) (94%) completing follow-up at mean 15.3 ± 21.0 months (range: 3-91 months). Mean age was 67 ± 13 with 25 females (51%). There were 16 (33%) primary and 33 (67%) revision rTSAs. There was significant improvement from preoperative to postoperative aFF (n = 45, 79 ± 35 to 118 ± 36, P < .001), aER (n = 42, 18 ± 24 to 29 ± 21, P = .02), and SANE score (n = 34, 32 ± 22 to 69 ± 23, P < .001). Minimal clinically important difference was calculated to be 69% for aFF, 67% for aER, and 79% for SANE. Two shoulders (4%) required revision surgery. Conclusion: At mean follow-up of 15.3 months, rTSA with VRS custom glenoid implants for the treatment of glenoid bone deficiency in the primary and revision setting demonstrated improved patient-reported-outcomes and range of motion with low complication rate.

Orthopedics/Bone and Joint Center

Hodson N, **Raja H**, Hallstrom B, Hughes RE, Zheng H, and **Charters M**. Achieving the Centers for Medicare and Medicaid Services Defined Substantial Clinical Benefit Following Total Knee Arthroplasty and Total Hip Arthroplasty in the Michigan Arthroplasty Registry Collaborative Quality Initiative. *J Arthroplasty* 2025; Epub ahead of print. PMID: 40368074. Full Text

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INTRODUCTION: The Centers for Medicare & Medicaid Services (CMS) mandates patient-reported outcome measure (PROM) reporting for inpatient total hip arthroplasty (THA) and total knee arthroplasty (TKA) starting July 1, 2024, requiring preoperative (zero to 90 days) and postoperative (300 to 425 days) scores for ≥ 50% of claims. Substantial clinical benefit (SCB) is defined as a 22-point Hip dysfunction and Osteoarthritis Outcome Score for Joint Replacement (HOOS-JR) improvement for THA and a 20-point Knee injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS-JR) improvement for TKA, with a CMS-defined goal for hospitals to achieve SCB for ≥ 60% of patients. The purpose of this study was to assess the Michigan Arthroplasty Registry Collaborative Quality Initiative (MARCQI) sites' readiness to meet these CMS PROM collection requirements and their success in achieving SCB thresholds. METHODS: We analyzed 8,826 THAs and 12,210 TKAs performed between January 1, 2022, and June 30, 2022, in MARCQI. Matched pre- and postoperative PROMs and SCB rates were assessed across 81 sites. RESULTS: Only 22.1% of the patients who underwent THA and 22.7% of the patients who underwent TKA had matched PROMs, and 7.4% of sites met CMS thresholds for collection. However, 90% of sites with matched PROMs met the SCB threshold. CONCLUSION: For a statewide registry in Michigan, few sites met CMS collection requirements, but most achieved SCB targets. These findings reflect the experience of a diverse group of MARCQI sites and may not be generalizable to other states or institutions.

Orthopedics/Bone and Joint Center

James CL, **Sanii R**, **Kasto J**, **Zhu K**, Burdick G, Fathima B, **Rahman T**, and **Muh S**. The Perception of Residency Experiences Among Orthopaedic Surgery Residents in the United States Differs by Race and Gender. *Cureus* 2025; 17(4):e81670. PMID: 40322420. Full Text

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INTRODUCTION: Women and racial minorities remain underrepresented in orthopaedic surgery. While there is extensive research into the recruitment of these groups into the field, as well as more recent research regarding their representation in academic medicine and research, there is limited data on their experiences during residency. The purpose of this study is to assess the perceptions of orthopaedic surgery residents regarding their experiences during residency. METHODS: In mid-2022, a voluntary survey was sent to 2,122 orthopaedic surgery residents addressing mentorship, access to opportunities,

and "fit" within their residency programs. Responses were compared by race and gender, with 345 responses received, yielding a response rate of 16.3%. RESULTS: Compared to male and Caucasian residents, female and underrepresented in medicine (URM) residents reported feeling less satisfied with the training they received, felt less supported, and perceived greater difficulty for women and minorities in being promoted within orthopaedics. Female residents also reported having less mentorship, receiving less recognition for their accomplishments, and being less satisfied with their career choice than male residents. CONCLUSIONS: The results of this study highlight the need to improve equity and inclusion within orthopaedic surgery residencies in order to continue advancing diversity in the field.

Orthopedics/Bone and Joint Center

Markel DC, **Bou-Akl T**, **Wu B**, **Pawlitz P**, Yu X, Chen L, Shi T, and **Ren W**. In Vivo Cell Migration and Growth Within Electrospun Porous Nanofibrous Scaffolds with Different Pore Sizes in a Mouse Pouch Model. *J Funct Biomater* 2025; 16(5). PMID: 40422845. Full Text

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Cellular infiltration into traditional electrospun nanofibers (NFs) is limited due to their dense structures. We were able to obtain polycaprolactone (PCL) NFs with variable and defined pore sizes and thicknesses by using a customized programmed NF collector that controls the moving speed during electrospinning. NFs obtained by this method were tested in vitro and have shown better cell proliferation within the NFs with larger pore sizes. This study investigated in vivo host cell migration and neovascularization within implanted porous PCL NF discs using a mouse pouch model. Four types of PCL NFs were prepared and classified based on the electrospinning speed: NF-zero (static control), NF-low (0.085 mm/min), NF-mid (0.158 mm/min) and NF-high (0.232 mm/min) groups. With the increase in the speed, we observed an increase in the pore area; NF-zero (11.6 ± 6.2 μm(2)), NF-low (37.4 ± 28.6 μm(2)), NF-mid (67.6 ± 54.8 μm(2)), and NF-high (292.3 ± 286.5 μm(2)) groups. The NFs were implanted into air pouches of BALB/cJ mice. Mice without NFs served as control. Animals were sacrificed at 7 and 28 days after the implantation. Pouch tissues with implanted NFs were collected for histology (n = three per group and time point). The efficiency of the tissue penetration into PCL NF sheets was closely linked to the pore size and area. NFs with the highest pore area had more efficient tissue migration and new blood vessel formation compared to those with a smaller pore area. No newly formed blood vessels were observed in NF-zero sheets up to 28 days. We believe that a porous NF scaffold with a controllable pore size and thickness has great potential for tissue repair/regeneration and for other healthcare applications.

Orthopedics/Bone and Joint Center

Oravec D, **Yadav RN**, **Cushman T**, **Flynn MJ**, **Divine GW**, **Rao SD**, and **Yeni YN**. Osteoporosis screening in the mammography setting via digital wrist tomosynthesis. *Osteoporos Int* 2025; Epub ahead of print. PMID: 40341965. Full Text

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Adherence to osteoporosis screening guidelines could be considerably higher if offered at the time of routine mammography using the same imaging modality. We found that forearm density measurements using a breast imaging system provides density information with excellent diagnostic capability for

osteoporosis and osteopenia status determined by hip and spine DXA. PURPOSE: Adherence to osteoporosis screening guidelines via bone mineral density (BMD) measurements with dual-energy x-ray absorptiometry (DXA) is low. Since adherence to breast cancer screening is quite high, it was suggested that the rate of osteoporosis screening can be improved if wrist imaging were performed at the time of breast screening using the very same equipment. METHODS: Digital wrist tomosynthesis (DWT) imaging was performed in 150 women using a 3D mammography system and BMD was measured from both 3D tomosynthesis and synthesized 2D images. In addition, standard DXA based BMD measurements were performed at the hip, spine, and forearm sites. We examined the extent to which DWT-derived ultradistal radius BMD correlates with DXA based BMD measurements, evaluated DWT measurement precision errors, and determined the accuracy of DWT in diagnosing low bone mass and osteoporosis in vivo. RESULTS: DWT BMD strongly correlated with DXA-derived ultradistal radius BMD (R2 up to 0.814) and discriminated osteoporosis (AUC up to 0.978) and osteopenia (AUC up to 0.938) by ultradistal T-score with low in vivo precision errors (0.91-2.3%). BMD derived from 3D DWT BMD performed comparably to forearm DXA BMD in the diagnosis of osteopenia (AUC up to 0.916) and osteoporosis (AUC up to 0.946) determined by hip and spine DXA. CONCLUSIONS: DWT can be readily implemented in mammography settings with similar diagnostic accuracy to DXA, has the potential to increase adherence to osteoporosis screening recommendations, and offers a convenient means to measure bone density within the highly accessible breast screening environment.

Orthopedics/Bone and Joint Center
Roberts JB, Rockel JS, Mulders R, Capellini TD, Appleton CT, Phanstiel DH, Lories R, Geurts J, **Ali SA**, Bhutani N, Stone L, Cruz-Almeida Y, Jurisica I, Boer CG, Ramos YFM, Rice SJ, and Kapoor M. From mechanism to medicine: The progress and potential of epigenetics in osteoarthritis. *Osteoarthr Cartil Open* 2025; 7(3). PMID: Not assigned. Full Text

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Objective: Osteoarthritis (OA) is a chronic, degenerative disease of the articular joints. The disease presents an enormous clinical and economic burden globally, due in part to the lack of disease modifying therapies. For over a decade, OA researchers have been working to determine epigenetic mechanisms underlying the disease to better understand pathology, identify biomarkers of progression, and pinpoint novel targets for therapeutic intervention. Design: This article presents a summary of the 3rd International Workshop on the Epigenetics of Osteoarthritis held in Toronto, Ontario, Canada, in September 2024. The purpose of this meeting was to gather the international community to discuss the status of OA epigenetic research and share expertise on innovative techniques for future. Results: Since the two previous meetings, there has been increasing adoption of advanced single-cell and spatial sequencing technologies and bioinfomatic analyses. Furthermore, investigations of multiple joint tissues has highlighted the shifting paradigm from OA as a cartilage centric disease to the consideration of all joint tissues. Conclusions: The workshop provided a unique opportunity for early-career researchers to expand their network, and for all participants to discuss new or improved approaches to advance the field, including international consortia and data sharing. The highlights and outcomes from this OA epigenetics workshop are described in this report.

Orthopedics/Bone and Joint Center
Ziedas A, **Miller A**, **Biddle E**, **Laker M**, **Michaelson J**, **Frush T**, and **Markel DC**. Manual vs robotic patellofemoral arthroplasty outcomes: A Michigan arthroplasty registry collaborative quality initiative-based study. *J Orthop* 2025; 64:217-221. PMID: Not assigned. Full Text

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Background: Historically, all patellofemoral arthroplasty (PFA) was performed manually. Recently, robotic-assisted PFA has gained popularity. The purpose of this study was to determine whether a robotic-assisted technique influenced outcomes and revision rates. We hypothesized that robotic-assisted PFA

would have improved 90-day complication and revision rates. Methods: A single center's data from the Michigan Arthroplasty Registry Collaborative Quality Initiative (MARCQI) was queried for all primary PFAs from January 2014 to December 2022. Manual and robotic cohorts were compared for revisions and 90-day complications, including emergency visits, readmissions, and returns to the operating room (OR). Chi-square and Fisher's exact tests were used for categorical data and t-tests for continuous data. Results: Among 75 PFAs (mean age 53.0 ± 12.9 years, 78% women), 19 were manual and 56 robotic. Manual PFA experienced more 90-day complications (31% vs 10%, p = 0.0321) and a longer mean length of stay (30.9 ± 14.4 vs 20.6 ± 17.7 h, p = 0.03). No significant differences existed in age, BMI, gender, race, surgical time, 30-day complications, or revision rate. Manual PFA had no revisions, while 5% of robotic PFAs were revised for osteoarthritis progression, with a mean conversion time of 4.5 ± 2.7 years. Five-year cumulative percent revision (CPR) for all PFAs was 7.37%. Logistical regression showed manual PFA patients were more likely to experience 90-day complications (OR 3.84, p = 0.04). Conclusions: Manual PFA were prone to more 90-day complications and longer hospital stays compared to robotic PFA, which may minimize complications without affecting revision rates. Importantly, the PFA revision rate herein exceeded MARCQI-reported rates for unicompartmental and total knee arthroplasty.

Orthopedics/Bone and Joint Center
Ziedas AC, **Michaelson J**, **Knesek D**, **Laker M**, **Frush T**, and **Markel DC**. Cemented and Cementless Robotic-Assisted versus Manual Total Knee Arthroplasty Outcomes: A Single Center Michigan Arthroplasty Registry Collaborative Quality Initiative-Based Study. *J Arthroplasty* 2025; Epub ahead of print. PMID: 40280209. Full Text

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BACKGROUND: The purpose of our study was to determine whether a difference existed between cemented and cementless robotic-assisted total knee arthroplasty (RA-TKA) and manual TKA with regard to revision rates and 90-day outcomes. We hypothesized these techniques would have similar results. METHODS: A single center's data from the Michigan Arthroplasty Registry Collaborative Quality Initiative were queried for all primary TKAs from January 2012 to July 2023. The RA-TKA and manual cohorts were compared for revisions and 90-day complications, including emergency department (ED) visits, readmissions, and returns to the operating room Chi-square and Fisher's exact tests were used for categorical data, and t-tests for continuous data. Of the 7,417 cemented TKAs (mean age 67 ± 9.6 years, 70% women), 273 were RA-TKA and 7,144 were manual. Of the 2,407 cementless TKAs (mean age 65 ± 8.6 years, 53% women), 730 were RA-TKA and 1,677 were manual. RESULTS: Cemented RA-TKA had more periprosthetic joint infection revisions, more 90-day ED visits, and readmissions for wound complications compared to cemented manual TKA. Cementless RA-TKA had more 90-day readmissions for wound complications, while manual TKA had more 90-day ED visits for postoperative pain. Cemented and cementless RA-TKA had longer surgical time, shorter length of stay, and shorter time to revision. There were 283 revisions performed on cemented manual TKA (nine RA-TKAs, 3.2%, 274 manual, 3.8%, (P = 0.87)). There were 56 revisions performed on cementless knees (13 RA-TKAs, 1.7%, 43 manual 2.5% (P = 0.303)). Cumulative percent revision at 5 years was 3.9% for cemented RA-TKA, 3.5% for cemented manual TKA, 1.8% for cementless RA-TKA, and 2.8% for cementless manual TKA. CONCLUSIONS: Both RA-TKA and manual TKA have similar revision rates, while RA-TKA had more wound complications. Cementless RA-TKA may be beneficial in reducing postoperative pain.

Orthopedics/Bone and Joint Center
Zingas N, Munley J, O'Toole RV, and Manson TT. Functional Outcomes for Elderly Patients After ORIF for Distal Femur Fractures Are Similar to Outcomes for Patients After Primary Total Knee Arthroplasty. *Orthopedics* 2025; 48(3):e124-e130. PMID: 40239051. Full Text

BACKGROUND: The long-term clinical outcomes after open reduction and internal fixation (ORIF) for distal femoral fractures, both native and peri-prosthetic, are not yet well established in the literature. MATERIALS AND METHODS: We used the clinically validated Western Ontario and McMaster Universities Arthritis Index (WOMAC) score to make the functional outcomes after ORIF comparable with the well-characterized results achieved after total knee arthroplasty (TKA) for osteoarthritis. After long-term clinical follow-up and prospectively collected WOMAC scores were obtained, pain, stiffness, and

function were evaluated for 68 elderly patients with distal femur fractures (34 periprosthetic, 34 native; median follow-up time, 2.43 years). RESULTS: Although pain and stiffness scores were significantly lower than those achieved after TKA, functional and total WOMAC scores were similar. Pain and function continued to improve with greater time to follow-up. Although 32% (22/68) of patients had a return to the operating room (3 for infection, 11 for nonunion, and 7 for implant prominence), total WOMAC scores at long-term follow-up were not different for the patients who returned to the operating room. Although stiffness may persist for some patients, the functional outcomes after this procedure are similar to outcomes for patients after primary TKA. The rate of fracture-related re-operations was 32%, but was not associated with poor clinical outcomes. CONCLUSION: The 91% rate of good to excellent outcomes seen in our cohort suggests ORIF is likely to provide a favorable result for distal femur fractures, both native and periprosthetic, among elderly patients. [Orthopedics. 2025;48(3):e124-e130.].

Otolaryngology – Head and Neck Surgery

Craig JR, and Saibene AM. Diagnosing odontogenic sinusitis and avoiding the trap of maxillary sinus mucosal thickening on computed tomography: A clinical report. *J Prosthet Dent* 2025; Epub ahead of print. PMID: 40340185. Full Text

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Odontogenic sinusitis (ODS) refers to bacterial maxillary sinusitis caused by infectious maxillary dental pathology or dental procedures. ODS is the most common cause of unilateral sinusitis and a common cause of extrasinus infectious complications, including orbital and brain abscesses. While managing ODS has been highly successful, the greatest challenge can be recognizing and confirming the diagnosis. Diagnosing ODS requires confirming infectious maxillary dental pathology with appropriate examination and imaging and, very importantly, infectious sinusitis through nasal endoscopy. Sinus computed tomography is an important complimentary diagnostic method of confirming the location(s) of sinus disease but can be misleading if done without nasal endoscopy. Critical to note, clinicians must distinguish purulent ODS from maxillary sinus mucosal thickening (MSMT) seen on computed tomography, a reactive mucosal inflammation (mucositis) commonly seen with maxillary dental disease or dental treatment. MSMT is usually not infectious and, therefore, not usually ODS. The clinical scenario presented highlights the devastating progression from MSMT to ODS and ultimately a fatal brain abscess, all which had gone undetected for years. Recognizing and managing ODS requires increased ODS awareness and coordinated care between dental providers and otolaryngologists. Such interdisciplinary care will optimize outcomes for patients with ODS and may help prevent catastrophic complications.

Otolaryngology – Head and Neck Surgery

Gao MZ, Omer TM, Miller KM, Simpson MC, Bukatko AR, Gedion K, **Adjei Boakye E**, Kost KM, Dickinson JA, Varvares MA, and Osazuwa-Peters N. Thyroid Cancer Incidence and Trends in United States and Canadian Pediatric, Adolescent, and Young Adults. *Cancers (Basel)* 2025; 17(9). PMID: 40361355. Full Text

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BACKGROUND/OBJECTIVES: Thyroid cancer incidence has risen in both the United States and Canada, despite differing healthcare systems. While overdiagnosis likely partly explains this trend in adults, its impact on younger populations is unclear. We used the North American Association of Central Cancer Registries, which included 133,808 thyroid cancer cases from the United States and Canada, to assess incidence trends among pediatric, adolescent, and young adult (PAYA) populations. METHODS: Age-adjusted incidence rates (AAIR) per 100,000 person-years (PY) were compared using rate ratios (RR), stratified by sex, age, race/ethnicity (United States only), and histology. Joinpoint regression estimated annual percentage changes (APC) and average APCs (AAPC) in AAIRs. From 1995 to 2014, thyroid cancer incidence increased by 137%. Significant increases occurred across all age groups (0-14, 15-24, 25-34, 35-39 years). The rate increase was highest for papillary thyroid cancer (AAPC = 5.50, 95% CI 5.06, 5.94), and among individuals aged 35-39 years (AAPC = 5.99, 95% CI 4.84, 7.15). Of racial/ethnic groups in the United States, non-Hispanic White individuals had the highest AAIR (6.22 per 100,000 PY). Mortality has changed minimally. CONCLUSIONS: Over the past two decades, thyroid cancer incidence has increased in individuals under 40. While evidence suggests that overdiagnosis primarily accounts for this trend, other contributing factors cannot be ruled out. Further research and surveillance of the drivers of increased incidence are critical.

Otolaryngology – Head and Neck Surgery
Grewal JS, Bouzaher MH, Namin AW, Wang W, and Ducic Y. Trapezius Myocutaneous Flap Reconstruction for the Head and Neck. *J Craniofac Surg* 2025; Epub ahead of print. PMID: 40299788.
Full Text

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INTRODUCTION: The trapezius myocutaneous flap is a valuable option for reconstructing defects in the head and neck region requiring a sizeable skin paddle. This study assessed surgical outcomes of the trapezius myocutaneous flap in head and neck reconstruction, specifically focusing on defects of the lateral temporal bone, lateral neck, and scalp or posterior midline neck. METHODS: This retrospective study analyzed patients grouped by site of defect within the head and neck. Subgroup analysis was performed. RESULTS: Overall rates of complication for the lateral temporal bone and lateral neck were 14.5% and 21.1%, respectively. The odds of complications in the scalp and midline posterior neck site were significantly higher (2.94 times higher) than in patients with a temporal bone defect site (odds ratio=2.94, P=0.027). CONCLUSIONS: The trapezius flap is useful when reconstructing the lateral temporal bone and lateral neck defects, likely due to a more favorable arc of rotation.

Otolaryngology – Head and Neck Surgery
Kuan EC, Talati V, Patel JA, Nguyen TV, Abiri A, Pang JC, Goshtasbi K, Liu L, **Craig JR**, Papagiannopoulos P, Phillips KM, Tajudeen BA, Adappa ND, Palmer JN, Sedaghat AR, Wang EW, Anand V, Batra PS, Bergsneider M, Bernal-Sprekelsen M, Bleier BS, Cappabianca P, Carrau RL, Casiano RR, Castelnuovo P, Cavallo LM, Cohen MA, Dallan I, Eloy JA, El-Sayed IH, Evans JJ,

Fernandez-Miranda JC, Ferrari M, Froelich S, Gardner PA, Georgalas C, Gray ST, Hanna EY, Harvey RJ, Hong SD, Hwang PH, Kelly DF, Kong DS, Lan MY, Lee JYK, Levine CG, Liu JK, Locatelli D, Meço C, McKean EL, Nicolai P, Nyquist GG, Omura K, Passeri T, Patel ZM, Celda MP, Neto CP, Rabinowitz MR, Rabinowitz MR, Raza SM, Recinos PF, Rosen MR, Sargi ZB, Schlosser RJ, Schwartz TH, Sindwani R, Snyderman CH, Stamm AC, Thorp BD, Turri-Zanoni M, Wang MB, Wang WH, Witterick IJ, Won TB, Woodworth BA, Wormald PJ, Zada G, and Su SY. Expert Strategies: Skull Base Reconstruction-Global Perspectives, Insights, and Algorithms through a MixedMethods Approach. *Int Forum Allergy Rhinol* 2025;e23596. Epub ahead of print. PMID: 40371737. Full Text

OBJECTIVE: There is limited consensus on endoscopic skull base surgery (ESBS) reconstruction principles. This study aims to generate comprehensive themes regarding ESBS reconstruction by pooling the experiences of ESBS experts, with comparison to a literature review of current published evidence. METHODS: Structured qualitative interviews of ESBS experts regarding postoperative management and reconstruction of various defect locations were conducted. RESULTS: A total of 68 experts comprising 40 academic teams across 13 countries with an average of 18 years of ESBS experience were included. We propose 10 stepwise algorithms for common skull base reconstruction scenarios based on these expert interviews. When available, the nasoseptal flap is used for all high_flow cerebrospinal leak defects. Multilayered reconstruction is favored at all anatomical subsites with increasing number of layers for increasing defect size and complexity. Heterogeneity exists in terms of inlay technique and materials, free grafting versus various pedicled flap options for low-flow defects or in the absence of a nasal septum, nasal packing, tissue sealant, lumbar drain use, and postoperative management. Commonalities and discrepancies between experts were summarized. CONCLUSION: Skull base reconstruction and post-ESBS management is highly complex with a wide variety of practice patterns and expert strategies. Further research of higher quality evidence is warranted to identify optimal management patterns, though the current work aims to inform surgeons on these controversial areas by drawing from numerous experiences.

Otolaryngology – Head and Neck Surgery

Mason W, Mackie H, **Kulawczyk A**, **Jin J**, and **Craig JR**. Unilateral Clear Thin Rhinorrhea: How Often Is It a Cerebrospinal Fluid Leak? *Ann Otol Rhinol Laryngol* 2025; Epub ahead of print. PMID: 40370059. Full Text

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OBJECTIVES: Determine frequencies of conditions causing unilateral clear thin rhinorrhea (UCTR), and assess whether certain clinical features are associated with CSF rhinorrhea. METHODS: This was a retrospective review identifying all patients presenting with UCTR to one rhinologist over a 6-year period. The conditions causing UCTR were recorded, and the following demographic or clinical variables were collected when available: body-mass index (BMI, kg/m2), gender, age, race, and self-reported drainage volume (whether the UCTR dripped out the nose and could be collected, or it felt like a wet nostril with intermittent running down lip that was unlikely to be collectable). RESULTS: Of 3,041 patients, 146 were identified with at least UCTR (4.8%). Mean age was 56.2 ± 17.6 years, and 65.8% were female. Amongst UCTR, nonallergic rhinitis (NAR) was the most common cause (45%), followed by CSF rhinorrhea (30%). On multivariate analysis, the following were significantly positively associated with CSF rhinorrhea: BMI≥30 (OR=4.95), ages 45-54 years (OR=3.67) and 55-64 years (OR=4.15), and self-reported UCTR dripping with collectability (OR=5.96)). CONCLUSIONS: NAR was the most common cause of UCTR, representing nearly 50% of cases. However, CSF rhinorrhea still represented 30% of cases, reinforcing that UCTR should be worked up for CSF rhinorrhea, ideally with B2-Tf testing. BMI ≥30, ages 45-64 years, and patient-reported higher volume UCTR were positively associated with CSF rhinorrhea. If B2-Tf testing is negative or unobtainable, or clinical suspicion for CSF leak is low, clinicians can consider starting medical therapy for rhinitis or rhinosinusitis before pursuing further invasive CSF confirmatory testing.

Otolaryngology – Head and Neck Surgery

Samadi P, Sheykhhasan M, Omer I, Ullah A, Zarea A, Toomajian V, Khan MUA, Ertas D, **Jones LR**, **Levin AM**, Hasan A, Contag CH, Ertas YN, and Ashammakhi N. Regeneration of cartilage defects using engineered extracellular vesicles. *Biofabrication* 2025; Epub ahead of print. PMID: 40403758. Full Text

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In recent years, the number of adults with diagnosed cartilage defects has increased significantly, and various modes of treatment have been sought. However, traditional cartilage repair strategies have been proven inefficient, with limited success. Recently, regenerative treatment options have become more routinely used for specific indications, but they still have major limitations. Cell-derived extracellular vesicles (EVs) are becoming increasingly attractive for regenerative purposes because they provide several regenerative factors. In addition, they can be engineered to function as delivery agents for proteins, nucleic acids, and other molecules. Recently, EVs were explored for cartilage tissue engineering, with varying results. Unlike other cell-based therapies, this approach will lead to the avoidance of problems associated with immunogenic reactions against allogenic cells and easier approval of the therapy by regulatory bodies, which is expected to stimulate wider clinical application. Because of its broad interest and importance, this review was developed to discuss published works, their outcomes, and limitations and outline future research directions.

Otolaryngology – Head and Neck Surgery

Siddiqui RF, **Al-Antary N**, **Gilbert M**, **Fakhoury L**, Vu M, **Siddiqui F**, and **Adjei Boakye E**. Knowledge of Head and Neck Cancer Risk Factors and Symptoms: A Cross-Sectional Survey Among Arab Americans. *J Immigr Minor Health* 2025; Epub ahead of print. PMID: 40407986. Full Text

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We examined head and neck cancer (HNC) risk factors and symptoms knowledge among Arab Americans in Michigan. A survey of 295 adult Arab Americans (≥ 18 years) was conducted between March and July 2023. Knowledge of HNC risk factors and symptoms were assessed using 10 and 14 questions, respectively. For each question, we asked, "Do you know that the following can be risk factors/symptoms of HNC?" and respondents chose "yes," "no," or "don't know/not sure." Regarding risk factors- tobacco smoking and chewing were the most recognized risk factors, identified by 78.9% and 72.8%, respectively. Less than half identified human papillomavirus (HPV) (40.6%) as risk factor. Regarding symptom knowledge, only 40-50% identified the most common HNC symptoms: nonhealing ulcers (41%), dysphagia or odynophagia (51.4%), and voice changes (48.6%); while 60.6% identified swelling or lump in neck/throat. Approximately, half of the respondents recognized persistent mass or lesion on the tongue (53.3%) and bleeding in the mouth/throat (50.3%) as symptoms of HNC. Education level, household income, and number of sexual partners were associated with knowledge regarding some common symptoms of HNC. While there is higher knowledge about tobacco as a risk factor for HNC, knowledge about HPV as a risk factor is very low. Similarly, knowledge about HNC symptoms is suboptimal in the Arab American community. Findings support the development of interventions for this community to help improve HNC knowledge and related health outcomes.

Otolaryngology – Head and Neck Surgery
Singer MC, and Terris DJ. Potential Disadvantages of the Modified Miami Criteria. *JAMA Otolaryngol Head Neck Surg* 2025; Epub ahead of print. PMID: 40402508. Full Text

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Otolaryngology – Head and Neck Surgery
Witek ME, Ward MC, Bakst R, Chandra RA, **Chang SS**, Choi KY, Galloway T, Hanna GJ, Hu KS, Robbins J, Shukla ME, **Siddiqui F**, Takiar V, Walker GV, Fu Y, and Margalit DN. Paranasal Sinus and Nasal Cavity Cancers: Systematic Review and Executive Summary of the American Radium Society Appropriate Use Criteria. *Head Neck* 2025; Epub ahead of print. PMID: 40344605. Full Text

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Tumors of the paranasal sinus and nasal cavity (PNS/NC) are rare and exhibit diverse histology, anatomic subsite, and malignant potential. Early-stage disease is typically managed with surgery, and locally advanced disease is treated with a combination of surgery, radiotherapy, and chemotherapy.

Clinical decision-making is commonly guided by limited retrospective evidence. To address this limitation, we performed a systematic review to inform evidence-based consensus for the management of common clinical scenarios, including the potential roles of radiation and systemic therapy to promote structural preservation, elective neck management, and radiation technique considerations. A librarian-mediated literature search identified 39 studies of adult patients with PNS/NC tumors treated with curative intent that met the study inclusion criteria. Search results were reported using the preferred reporting items for systematic reviews and meta-analyses (PRISMA) methodology. A modified-Delphi process was used to guide consensus for the appropriate use of various management strategies. Strong consensus existed for the appropriateness of primary surgery for early-stage disease, approaches to locally advanced disease with minimal periorbital fat invasion, and the use of induction chemotherapy with response-directed local therapy. Consensus regarding nodal treatment and the use of proton therapy in the adjuvant setting was less robust. The rarity and diversity of PNS/NC tumors limit randomized phase III trials to guide management. As such, this systematic review and appropriate-use consensus statements provide clinical guidance for the management of this challenging disease spectrum.

Pathology and Laboratory Medicine

Ahsan BU, **Jin M**, **Theisen BK**, **Singla S**, **Chitale D**, **Shaw B**, **Azordegan N**, **Xu Z**, **Schultz D**, and **Zhang Z**. Comparison of fluorescence in situ hybridization and cytology for the accurate detection of malignant biliary strictures, with emphasis on unusual results. *J Am Soc Cytopathol* 2025; Epub ahead of print. PMID: 40345927. Full Text

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INTRODUCTION: Biliary brushing cytology is the standard diagnostic approach for evaluating biliary strictures, but it has low sensitivity and a high rate of atypical diagnoses. Fluorescence in situ hybridization (FISH) has become an increasingly valuable adjunct to cytology. Therefore, the aim of this retrospective quality improvement study was to evaluate the relative diagnostic performance of traditional cytology and FISH for correctly determining malignant versus benign biliary strictures from biliary brushing samples and to evaluate whether adding FISH to the diagnostic pipeline improves diagnostic accuracy over relying on cytology alone. MATERIALS AND METHODS: We conducted a retrospective study of biliary brushing and FISH results in patients evaluated for biliary strictures between April 2019 and March 2023. RESULTS: A total of 228 specimens were retrieved. For cytology results: 151 negative, 55 atypical, 6 suspicious, and 16 positive. For FISH results: 105 negative, 71 equivocal, and 52 positive. When calculating performance measures, cytology atypical and FISH equivocal were excluded; cytology suspicious was considered positive. The sensitivity and specificity of cytology were 45.8% and 100%, respectively. The sensitivity and specificity of FISH were 84.2% and 96.0%, respectively. CONCLUSIONS: Our findings indicate that FISH exhibits considerably higher diagnostic sensitivity than routine cytology in identifying malignant biliary strictures. Furthermore, combining cytology with FISH may provide a more comprehensive diagnostic approach, reducing the likelihood of false-negative results. However, positive and equivocal FISH results should be interpreted carefully and considered alongside more specific cytology findings to minimize the risk of false-positive diagnoses.

Pathology and Laboratory Medicine

Alruwaii ZI, **Gokturk Ozcan G**, **Hassan O**, Cheng L, and Al-Obaidy KI. Genomic profiling of urological malignancies using tissue-based next generation sequencing. *Urol Oncol* 2025; Epub ahead of print. PMID: 40410007. Full Text

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Advances in understanding genomic drivers of human malignancies have evolved from morphologic evaluations to in-depth DNA and RNA analyses and gene expression profiling. In urologic malignancies, these molecular diagnostics are integral to patient management, aiding pathological diagnosis, providing prognostic and predictive relevance, and identifying therapeutic options for advanced diseases. For instance, renal cell carcinoma frequently harbors alterations in VHL, PBRM1, and BAP1, influencing therapeutic responses, while urothelial carcinoma is characterized by FGFR3 mutations and TERT promoter alterations, which have implications for targeted therapy. Prostate cancer commonly involves TMPRSS2-ERG fusions and BRCA2 mutations, affecting treatment strategies, and penile squamous cell carcinoma follows distinct HPV-dependent and HPV-independent pathways, with mutations in TP53 and CDKN2A genes. These advances in molecular pathology have deepened our understanding of these complex diseases and facilitated the introduction of novel targeted therapies. While these advances promise improved diagnosis, prognosis, and treatment options, many questions remain regarding the variable patient responses within the same histologic types. Addressing these will enable optimal management strategies and the development of personalized treatments targeting specific molecular alterations to improve patient outcomes.

Pathology and Laboratory Medicine
Liu J, Zhi X, **Fang X**, Li W, Zhao W, Liu M, Lai E, Fang W, Wang J, Zheng Y, Zou J, Fu Q, Cui W, and Zhang K. The Application of Microfluidic Chips in Primary Urological Cancer: Recent Advances and Future Perspectives. *Smart Med* 2025; 4(2):e70010. PMID: 40390767. Full Text

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The research of primary urological cancers, including bladder cancer (BCa), prostate cancer (PCa), and renal cancer (RCa), has developed rapidly. Microfluidic technology provides a good variety of benefits compared to the heterogeneity of animal models and potential ethical issues of human study. Microfluidic technology and its application with cell culture (e.g., organ-on-a-chip, OOC) are extensively used in urological cancer studies in preclinical and clinical settings. The application has provided diagnostic and therapeutic benefits for patients with urological diseases, especially by evaluating biomarkers for urinary malignancies. In this review, we go through the applications of OOC in BCa, Pca and Rca, and discuss

the prospects of reducing the cost and improving the repeatability and amicability of the intelligent integration of urinary system organ chips.

Pathology and Laboratory Medicine

Nourbakshs M, Du L, Acosta AM, Alaghehbandan R, Amin A, Amin MB, Aron M, Berney D, Brimo F, Chan E, Cheng L, Colecchia M, Dhillon J, Downes MR, Evans AJ, Harik LR, **Hassan O**, Haider A, Humphrey PA, Jha S, Kandukuri S, Kao CS, Kaushal S, Khani F, Kryvenko ON, Kweldam C, Lal P, Lobo A, Maclean F, Magi-Galluzzi C, Mehra R, Miyamoto H, Mohanty SK, Montironi R, Nesi G, Netto GJ, Nguyen JK, Nourieh M, Osunkoya AO, Paner GP, Sangoi AR, Shah RB, Srigley JR, Tretiakova M, Troncoso P, Trpkov K, Van Der Kwast TH, Zhang M, Zynger DL, Williamson SR, and Giannico GA. Current practices in prostate pathology reporting: results from a survey of genitourinary and general pathologists. *Histopathology* 2025; Epub ahead of print. PMID: 40364451. Full Text

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AIMS: Standardizing pathology reporting protocols through peer consensus review is critical for the best quality of care metrics. Reporting heterogeneity due to discrepancies among professional societies and practice patterns may lead to heterogeneous management and treatment approaches. This issue prompted a multi-institutional survey of pathologists to address potential similarities or differences in trends and practice patterns in prostate pathology reporting worldwide. METHODS AND RESULTS: A REDCap survey was distributed among 175 pathologists worldwide, recruited through invitations and social media. The response rate among invited pathologists was 83%. The practice locations were as follows: North America (USA, Canada, and Mexico, 62%), Europe (17%), Australia/New Zealand (3%), Central/South America (2%), Asia (13%), and Africa (2%). Most pathologists practiced for <5 years (28%). A genitourinary (GU) pathology fellowship was completed by 37%, 58% practiced in a subspecialized setting, and 43% in academia. Reporting includes (63%) or subtracts (37%) intervening benign tissue. Both Gleason score and Grade Groups (GG)s were reported by 96% of responders, whereas 94% report percent pattern 4 (%4). Aggregate grading and volume estimation in undesignated cores with different grades in the same jar are reported by 73% and 54% for systematic biopsies, and 83% and 62% for targeted biopsies, respectively. Cribriform morphology was reported by 81%. For presumed intraductal carcinoma (IDC), 89% use basal cell markers when isolated (iIDC), 82% with GG1 cancer, and 37% with ≥GG2. iIDC or IDC associated with GG1 or with ≥GG2 was not graded by 90%, 78%, and 70%, respectively. In radical prostatectomies, 90% report %4, but only 53% report it if the overall grade is ≥7. A tumour with Gleason 3 + 3 = 6 and <5% pattern 4 was graded as GG2 by 64%. A <5% cutoff for defining tertiary pattern was used by 74%, and 80% report >5% pattern 4 or 5 as a secondary pattern. Grading was assigned based on the dominant nodule by 59%. Finally, reporting practices were significantly associated with demographic characteristics. CONCLUSIONS: Although most issues are agreed upon, significant discordance is identified among societies and pathologists in different practice settings. We hope this survey will serve as the basis for future studies and new collaborative approaches to more standardized reporting practices.

Pathology and Laboratory Medicine
Tamr A, **Shahid MA**, **Wollner I**, and **Theisen B**. Delayed Presentation of Metastatic Solid Pseudopapillary Epithelial Neoplasm in a Pregnant Woman: A Case Report. *Cureus* 2025; 17(4):e82454. PMID: 40385926. Full Text

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Solid pseudopapillary epithelial neoplasm (SPEN) is a rare, low-grade malignant pancreatic tumor usually found incidentally on imaging, most commonly in young women. Its association with women suggests that hormones may play a significant role in tumor pathogenesis. Surgical resection is the mainstay of treatment in all stages of disease, and few other treatment options have been thoroughly explored. This case demonstrates the unique therapeutic challenges involved in the management of a pregnant woman with new liver metastasis and significant disease burden following remote resection of the primary SPEN tumor. The patient was treated with chemotherapy, radiation, and hormone therapy, followed by hepatic trisegmentectomy without recurrence during surveillance. This case presents a unique therapeutic approach to a situation where no established treatment guidelines exist.

Pathology and Laboratory Medicine
Unsihuay D, Wang P, Milone M, Thakrar A, and Perrone J. Performance of a Xylazine Test Strip in Urine Biospecimens. *J Addict Med* 2025. PMID: Not assigned. Full Text

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Objective: Herein, we evaluate the performance of xylazine test strips (XTS) in urine samples. XTS is used for community drug checking (powders and liquids) but lacks regulatory approval for human specimen testing. Methods: We obtained n=85 human urine specimens from a toxicology laboratory in Philadelphia, originally submitted for qualitative mass spectrometry (MS) expanded drug analysis. Residual urine was tested for xylazine using XTS (BTNX Inc.), and results were then compared against the MS method. Synthetic urine spiked with xylazine standards was used to determine the XTS cutoff. An external quantitative MS method was used to investigate potential mismatches. Results: Of n = 85 human urine specimens, XTS demonstrated 86% sensitivity and 93% specificity using a XTS cutoff of 750 ng/mL established with synthetic urine samples. Six false negatives (14%) among 43 qualitative MS-positive samples were observed, primarily due to XTS's lower sensitivity. Among 3 false positives (7%) observed in 42 qualitative MS-negative samples, lidocaine likely causes the interference. Interestingly, some XTS-positive samples were found to have xylazine concentration lower than 750 ng/mL using quantitative MS, suggesting cross-reactivity with unknown metabolites or analogs. Conclusions: XTS requires further refinement to achieve lab-quality performance, with a focus on improving sensitivity and minimizing false positives caused by nonspecific interactions with urine components. Further research is necessary to optimize their design, establish accurate detection thresholds, supporting clinical decision-making, and obtain regulatory validation.

Pathology and Laboratory Medicine

Wen T, Boyden SE, Hocutt CM, Lewis RG, Baldwin EE, Vagher J, Andrews A, Nicholas TJ, Chapin A, Fan EM, Botto LD, Bayrak-Toydemir P, Mao R, and Meznarich JA. Identification of 2 novel noncoding variants in patients with Diamond-Blackfan anemia syndrome by whole genome sequencing. *Blood Adv* 2025; 9(10):2443-2452. PMID: 40029997. Full Text

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Diamond-Blackfan anemia syndrome (DBAS) is a rare congenital disorder with variable penetrance and expressivity and is characterized by pure red cell aplasia that typically manifests as early-onset chronic macrocytic or normocytic anemia and is often associated with other congenital anomalies. DBAS is etiologically heterogeneous with >20 known DBAS-associated genes that encode small and large ribosomal protein subunits and an inheritance pattern that is largely autosomal dominant or sporadic. We report 2 DBAS cases with previous negative genetic testing, which included targeted gene panels, karyotype analysis, chromosome breakage analysis, and whole exome sequencing. Although clinical whole genome sequencing (WGS) was initially negative, in-depth reanalysis identified 2 novel noncoding variants in the RPS gene family, namely a maternally inherited splicing variant at the end of the first noncoding exon in RPS7 (NM_001011.4, c.-19G>C) in family 1 and a deep intronic de novo variant in RPS19 (NM_001022.4, c.172+350C>T) in family 2. In family 1, several maternal relatives were identified who shared the same variant through cascade testing; clinically, they exhibited variable degrees of anemia and elevated erythrocyte adenosine deaminase activity, a marker for DBAS. RNA sequencing analysis demonstrated deleterious functional consequences for both noncoding variants. In case 1, hematopoietic stem cell transplant with an unaffected matched sibling donor who did not carry the variant successfully cured the congenital anemia. This study identified novel noncoding variants and underscores the clinical utility of WGS in accelerating diagnosis and improving care for rare genetic disorders, particularly when timely treatment decisions are critically important.

Pediatrics

Elliott MR, Kerver JM, Drew A, Watson K, Kornatowski B, Norman GS, Copeland GE, Leissou E, Ridenour T, Kruger-Ndiaye S, Ma T, Ruden D, **Barone C**, Keating DP, Sokol RJ, **Johnson CC**, and Paneth N. Obtaining a Probability Sample of a Pregnancy Cohort of Births: A Review of the Problem and a Practical Solution. *Am J Epidemiol* 2025; Epub ahead of print. PMID: 40407221. Full Text

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The Michigan Archive for Research on Child Health (MARCH) study produced a probability sample of Michigan births between 2017 and 2023, with data collection beginning at first prenatal visit and continuing up to age 4. Birth certificate data were used to create a sampling frame of hospitals and associated obstetric clinics, from which a probability-proportional-size sample of 10 hospitals was drawn. Close to 100 pregnancies were then recruited in clinics serving each sampled hospital, yielding a probability sample of 1,021 births. This sample was supplemented with 109 births from a certainty selection of a Flint, MI hospital, for a total sample of 1,130. The resulting response rate was high, with 100% of sampled hospitals and 65% of sampled clinics participating. Comparing the resulting sample with all 2017-2023 Michigan births showed close correspondence with respect to birth outcomes (birthweight, gestational age, Apgar scores, gestational diabetes) and mothers' demographics (age, race, education, marital status), with underrepresentation of Hispanic ethnicity and overrepresentation of reported smoking. Given the recent failures of two major prospective birth cohorts (the US National Childrens' Study and the UK Life Study), our work shows a way forward for representative pre- and post-natal studies of births.

Pediatrics

Khan HH, **Kumar S**, and **Lyons H**. Practices of North American pediatric gastroenterologists in the management of celiac disease-A survey study. *JPGN Rep* 2025; 6(2):137-145. PMID: 40386323. Full Text

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Celiac disease (CD) is a common autoimmune disorder characterized by an immune-mediated reaction to gluten. We conducted a survey study of the pediatric gastroenterology list server to assess the practices of North American pediatric gastroenterologists in the management of CD. Overall, 160 out of 2400 respondents participated in the study, of which 52.5% of the respondents were females and 72.5% were practicing in university hospitals. Overall, respondents were practicing in adherence to the latest guidelines, except only 36% were screening for hepatitis B virus immunization at diagnosis on most of the visits, and 25% were utilizing human leukocyte antigens typing on most visits if serologies were negative.

In addition, female respondents screened for vitamin D deficiency more often than males with a p value < 0.05.

Pharmacy

Arena CJ, **Abed A**, **Kenney RM**, **Suleyman G**, **Shallal A**, Davis SL, and **Veve MP**. Retrospective cohort study of oral switch versus intravenous antibiotics for carbapenem-resistant enterobacterales and Pseudomonas aeruginosa infections on hospital discharge. *Pharmacotherapy* 2025; 45(5):244-250. PMID: 40345979. Full Text

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OBJECTIVES: To compare outcomes of oral switch versus intravenous antibiotics for the treatment of carbapenem-resistant Enterobacterales (CRE) and Pseudomonas aeruginosa (CRPA) infections at hospital discharge. METHODS: Institutional review board approved, retrospective cohort of adults infected with CRE or CRPA who received oral switch or intravenous antibiotics at hospital discharge from January 1, 2017, to April 30, 2024. Patients were included if they were eligible for oral switch and infected with an isolate susceptible to one or more oral antibiotics; non-bacteremic urinary tract infections were excluded. The primary outcome was 30-day clinical success at end of therapy, defined as lack of infection-related hospitalization, infection-related recurrence, or change/escalation of therapy. Secondary outcomes included hospital length of stay (LOS) and 30-day all-cause mortality from end of therapy. RESULTS: Fifty-five patients were included; 51% received oral switch antibiotics and 49% received intravenous antibiotics. Thirty-three percent of patients had CRE, 67% had CRPA, and 38% of cultures were polymicrobial. The most common infection types were pneumonia (33%), intra-abdominal (26%), and bone/joint (22%). The median (interquartile range [IQR]) duration of outpatient therapy was 12 (6-25) days versus 20 (4-34) days for the oral switch and intravenous antibiotic groups, respectively (p = 0.341). 30-day clinical success was 61% in the oral switch and 48% in the intravenous antibiotic groups (p = 0.349); the median (IQR) hospital LOS for the oral switch and intravenous antibiotic groups was 14 (9-25) days and 16 (9-49) days, respectively (p = 0.165); 30-day mortality was 4% in the oral switch group and 15% in the intravenous antibiotic group (p = 0.193). CONCLUSION: A limited sample of patients who received oral switch antibiotics had similar outcomes to intravenous outpatient treatment of carbapenem-resistant organisms, with a shorter hospital LOS.

Pharmacy

Goodhart AL, Adelman M, Mondiello T, and **Martirosov AL**. Choose your own adventure: Perception of gamification in continuing pharmacy education. *Curr Pharm Teach Learn* 2025; 17(9):102384. PMID: 40412193. Full Text

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BACKGROUND: Literature detailing the implementation of gamification strategies, including 'choose your own adventure' (CYOA) patient cases, in continuing professional development within the pharmacy profession is limited. CYOA-style activities have had positive impacts on student cohorts. This report details attendees' perceptions of a continuing pharmacy education presentation at a national pharmacy conference that utilized gamification for content delivery. EDUCATIONAL ACTIVITY: An educational session was developed to use gamification to teach important concepts in the management of asthma.

Presenters worked together to create 'choose your own adventure' (CYOA) activities as the gamification style for the session. Learning intentions were set for both cases based on important clinical considerations for pharmacists. A mixed methods approach was utilized to provide a descriptive evaluation of the CYOA educational session based on attendees' feedback. A survey was developed by the session moderators and distributed to attendees at the end of the session. A qualitative analysis was also conducted to analyze open-ended response questions within the end of session survey and the standardized session evaluation. EVALUATION FINDINGS: A total of 227 evaluations were submitted. Ninety-eight percent of respondents agreed or strongly agreed they would recommend the activity to a friend or colleague and were satisfied with the educational content and format of the activity. ANALYSIS OF EDUCATIONAL ACTIVITY: Incorporating gamification techniques, such as CYOA, into continuing pharmacy education presents a valuable opportunity for practitioners.

Pharmacy

Papamanolis IC, Stornelli N, **Everson N**, Ahmad Z, Kamrada M, Lockhart ER, and McDaniel L. Partial Courses of Fidaxomicin Followed by Oral Vancomycin and the Effect on Recurrence of Clostridioides difficile Infections. *Ann Pharmacother* 2025; Epub ahead of print. PMID: 40326081. Full Text

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BACKGROUND: Clostridioides difficile infection (CDI) causes a significant national health care burden. Literature has demonstrated lower rates of CDI recurrence with fidaxomicin compared with oral vancomycin. However, patients are sometimes switched to oral vancomycin before completing a fidaxomicin course. OBJECTIVE: The objective of this study is to evaluate rates of CDI recurrence in full courses of fidaxomicin versus partial courses of fidaxomicin followed by a switch to oral vancomycin. METHODS: In this single-center, retrospective, cohort study of adults with CDI, patients were screened for inclusion if they received either a full 10-day course of fidaxomicin or partial course of fidaxomicin followed by a switch to oral vancomycin. The primary outcome was the rate of CDI recurrence within 30 days after completion of initial therapy determined by a positive CDI test and initiation of treatment. RESULTS: Ninety-nine patients received a full course of fidaxomicin, and 95 patients received a partial course of fidaxomicin followed by oral vancomycin. Mean age was lower in the full course group compared with the partial course (65.3 years vs 71.5 years, $P < 0.002$). Clostridioides difficile infection recurrence occurred in 5.1% of the full course group and 7.4% of the partial therapy group ($P = 0.503$) at 30 days and 13.1% versus 14.7% ($P = 0.747$) at 90 days. Clostridioides difficile infection-related readmissions at 30 days were similar in the full course and partial course groups (7.1% vs 4.2%, $P = 0.389$). CONCLUSION AND RELEVANCE: Partial courses of fidaxomicin followed by oral vancomycin had similar 30-day CDI recurrence compared with full course fidaxomicin.

Pharmacy

Veve MP, **Arena CJ**, **Kenney RM**, **Church BM**, **Fried ST**, and **Shallal AB**. Things I wish I knew when implementing an ambulatory antimicrobial stewardship program at an urban health system: lessons learned and future directions. *Antimicrob Steward Healthc Epidemiol* 2025; 5(1):e109. PMID: 40391168. Full Text

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Public Health Sciences

Akubire JA, and **Smucker BJ**. A comparison of supersaturated designs and orthogonal arrays. *J Stat Comput Simul* 2025; 95(9):1928-1943. PMID: Not assigned. Full Text

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The purpose of a screening experiment is to accurately and cost-efficiently identify the few most influential factors from among the many studied. Two types of screening experiments use orthogonal arrays (OAs) and supersaturated designs (SSDs), respectively. The first requires the number of runs n to be a multiple of 4 and greater than the number of factors k, while the second is a bolder approach wherein n

Public Health Sciences

Bertini A, **Stephens A**, **Finocchiaro A**, **Silvia V**, **Arjun D**, Elnaz G, **Nicholas C**, Lughezzani G, Buffi N, Di Trapani E, Ficarra V, Briganti A, Salonia A, Montorsi F, Sood A, **Rogers C**, and **Abdollah F**. Association of Area of Deprivation Index With Active Surveillance (AS) Utilization and Adherence to as Guidelines: Results From a Contemporary North American Cohort. *Prostate* 2025; Epub ahead of print. PMID: 40326515. Full Text

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BACKGROUND: Active Surveillance (AS) for Prostate Cancer (PCa) requires regular follow-up, raising concerns that socioeconomic barriers may result in underutilization or decreased adherence to AS guidelines. We examined the relationship between socioeconomic factors, measured by the Area Deprivation Index (ADI), and AS habits in a contemporary North American cohort. METHODS: We included all the patients aged ≤ 75 years and diagnosed with low (ISUP GG = 1, PSA ≤ 10 ng/mL and cT1N0M0) and intermediate risk (ISUP GG = 2, PSA 10-20 ng/mL or cT2N0M0) PCa at Henry Ford Health (HFH) between 1995 and 2023. An ADI score was assigned to each patient based on their residential census block group, ranked as a percentile of deprivation relative to the national level. The higher the ADI, the more the area has a socioeconomic disadvantage. Logistic regression analysis tested the impact of ADI on AS utilization and adherence to AS guidelines. Only patients who underwent at least 1 PSA test per year and at least 1 biopsy every 4 years were considered as "adherent to guidelines". RESULTS: Our final cohort consisted of 4376 patients eligible for AS, 919 of whom actually underwent AS. Older patients (66 vs. 62 years, $p < 0.0001$) and those diagnosed in more recent years (2017 vs. 2010, $p < 0.0001$) had higher probability to undergo AS. Moreover, patients in the AS group more likely to be NHB (36% vs. 25%, $p < 0.0001$), had higher ADI score (61 vs. 55, $p < 0.0001$), more comorbidities according to Charlson Comorbidity Index (CCI) score, (19.5%% vs. 13.8%, $p < 0.0001$) and higher probability to harbor low risk PCa (65.7% vs. 26.6%, $p < 0.0001$), compared to patients who underwent active treatment. Among the 919 patients in AS, only 410 were "adherent to guidelines". Patients following guidelines were more likely to be NHW (64.1% vs. 52.8%, $p < 0.003$), and had lower ADI percentile (55.5 vs. 66, $p < 0.0003$). Furthermore, AS patients managed according to the prevailing guidelines received more PSAs tests (1.8 vs. 0.8, $p < 0.0001$) and prostate biopsies (0.3 vs. 0.0, $p < 0.0001$) per year, thus reporting both higher upgrading rates during AS (35.6% vs. 23%, $p < 0.0001$)

and an increased probability to undergo active treatment (48% vs. 27%, p < 0.0001). At MVA, patients with a higher ADI score reported higher probability to undergo AS (OR: 1.06, 95% CI: 1.02-1.10, p = 0.004), but at the same time they were less likely to follow AS' guidelines (OR: 0.94, 95% CI: 0.89-0.99, p = 0.02). CONCLUSIONS: Patients in the most deprived areas had a higher likelihood of undergoing AS but were more prone to receive guideline-discordant care. This should be taken into consideration by physicians when recommending AS for those men living in the least advantaged neighborhoods. Our study highlights the need for targeted community reforms to enhance proper and informed AS utilization among socioeconomically disadvantaged populations.

Public Health Sciences

Bowles EJA, Gao H, Fleckenstein LE, Bravo P, Nash MG, Comstock B, **Neslund-Dudas C**, Mou J, and Kessler LG. Accuracy of self-reported exam indications for breast cancer screening. *JNCI Cancer Spectr* 2025; 9(3). PMID: 40323589. Full Text

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We validated updated National Health Interview Survey questions on mammography indications compared with electronic health records (EHRs). We asked 244 Kaiser Permanente Washington members ages 40-74 years and eligible for breast cancer screening to self-report their most recent mammogram reason by using a series of new hierarchical yes/no questions. We first asked if they had the mammogram because of a health problem, then as a follow-up test, and last for screening. We compared self-reported reasons with 2 EHR datasets: procedure/diagnostic codes and radiologist-defined indications. Self-reported exams for a health problem had 89.2% agreement with codes and 92.2% agreement with radiologist-defined indications. Self-reported exams for follow-up had 87.5% agreement with codes and 89.3% agreement with radiologist-defined indications. Self-reported exams for screening had 91.4% agreement with codes and 95.7% agreement with radiologist-defined indications. Self-reported mammogram indications have good agreement with procedure/diagnostic codes and radiologist-reported indications, when asked using this novel hierarchical approach.

Public Health Sciences

Craig JR, and Saibene AM. Diagnosing odontogenic sinusitis and avoiding the trap of maxillary sinus mucosal thickening on computed tomography: A clinical report. *J Prosthet Dent* 2025; Epub ahead of print. PMID: 40340185. Full Text

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Odontogenic sinusitis (ODS) refers to bacterial maxillary sinusitis caused by infectious maxillary dental pathology or dental procedures. ODS is the most common cause of unilateral sinusitis and a common cause of extrasinus infectious complications, including orbital and brain abscesses. While managing ODS has been highly successful, the greatest challenge can be recognizing and confirming the diagnosis. Diagnosing ODS requires confirming infectious maxillary dental pathology with appropriate examination and imaging and, very importantly, infectious sinusitis through nasal endoscopy. Sinus computed tomography is an important complimentary diagnostic method of confirming the location(s) of sinus disease but can be misleading if done without nasal endoscopy. Critical to note, clinicians must distinguish purulent ODS from maxillary sinus mucosal thickening (MSMT) seen on computed tomography, a reactive mucosal inflammation (mucositis) commonly seen with maxillary dental disease or

dental treatment. MSMT is usually not infectious and, therefore, not usually ODS. The clinical scenario presented highlights the devastating progression from MSMT to ODS and ultimately a fatal brain abscess, all which had gone undetected for years. Recognizing and managing ODS requires increased ODS awareness and coordinated care between dental providers and otolaryngologists. Such interdisciplinary care will optimize outcomes for patients with ODS and may help prevent catastrophic complications.

Public Health Sciences
dos Santos NR, **Bah HAF**, Gomes EA, Jr., Martinez VO, Costa DO, Pires EM, and Menezes JA. Pre and postnatal exposure to glyphosate-based herbicides and potential neurodevelopmental outcomes: a systematic review of animal and epidemiological studies. *Toxicol Res* 2025:20. PMID: Not assigned. Full Text

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Emerging evidence indicates potential adverse effects on infant neurodevelopment from exposure to glyphosate during prenatal and postnatal periods. This systematic review examines the scientific literature to explore links between prenatal/postnatal glyphosate exposure and neurodevelopmental abnormalities in humans and non-humans. Twenty-five original articles were reviewed, focusing on the following descriptors: glyphosate-based herbicides, pre and postnatal exposure, and neurodevelopmental outcomes. Risk of bias assessment was conducted to quality of studies. Experimental studies commonly used tests such as open field and novel object recognition, while epidemiological studies relied on medical records for diagnoses of conditions like depression and autism-like behavior. Surprisingly, only one experimental study directly measured glyphosate levels, and one of the epidemiological studies included a biomarker measure. In rodents, GLY exposure was associated to impaired cognition, motor function, memory, as well as ASD and anxiety-like behavior. In fish models, impairment of swimming activity was predominant. Overall, findings suggest possible associations between glyphosate exposure and neurodevelopmental deficits, emphasizing the need for further research to comprehend the extent of glyphosate's impact on developmental functioning.

Public Health Sciences
Douglas CM, Newell M, Goruk S, Courneya KS, **Ghosh S**, Joy AA, Munhoz J, and Field CJ. Exploratory outcomes of the DHA WIN randomized controlled trial: Supplementing women with docosahexaenoic acid did not reduce the impact of neoadjuvant breast cancer chemotherapy on quality of life or exercise behaviour. *PLoS One* 2025; 20(5):e0322178. PMID: 40315249. Full Text

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Supplementation of omega-3 (n-3) polyunsaturated fatty acids has been associated with reduced side effects and improved quality of life (QoL) in breast cancer patients receiving chemotherapy. The current study reports secondary outcomes from the DHA WIN randomized controlled trial which was designed to evaluate docosahexaenoic acid (DHA) supplementation (4.4 g/day) in conjunction with six cycles of neoadjuvant chemotherapy (NAC) (3 weeks/cycle) in women with non-metastatic breast cancer (n = 49).

The objective of the current study was to assess the effects of DHA supplementation on QoL and exercise behaviour in women undergoing NAC for breast cancer. Self-administered questionnaires were used to measure QoL and exercise behaviour before starting chemotherapy (baseline), before each chemotherapy cycle (exercise), and after completing chemotherapy. DHA supplementation did not significantly affect QoL, aerobic exercise volume or resistance training frequency during treatment. However, mean aerobic exercise volume was significantly lower at week 12 (-53.5 minutes/week; 95% CI, -100.5 to -6.3; p = 0.02) and week 18 (-70.8 minutes/week; 95% CI, -123.0 to -18.6; p = 0.01) compared to baseline. Mean resistance training frequency was lower at week 12 (-0.57 times/week; 95% CI, -1.0 to -0.13; p = 0.02) compared to baseline. Meeting exercise guidelines during chemotherapy was not associated with better QoL. In the current exploratory study, QoL and exercise decreased during treatment regardless of DHA supplementation, highlighting the need for supportive care and potential therapies that may mitigate these declines in breast cancer patients receiving NAC. Adequately powered studies are needed to determine if DHA supplementation improves these two indices of health. The trial is registered at ClinicalTrials.gov (NCT03831178).

Public Health Sciences

Elliott MR, Kerver JM, Drew A, Watson K, Kornatowski B, Norman GS, Copeland GE, Leissou E, Ridenour T, Kruger-Ndiaye S, Ma T, Ruden D, **Barone C**, Keating DP, Sokol RJ, **Johnson CC**, and Paneth N. Obtaining a Probability Sample of a Pregnancy Cohort of Births: A Review of the Problem and a Practical Solution. *Am J Epidemiol* 2025; Epub ahead of print. PMID: 40407221. Full Text

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The Michigan Archive for Research on Child Health (MARCH) study produced a probability sample of Michigan births between 2017 and 2023, with data collection beginning at first prenatal visit and continuing up to age 4. Birth certificate data were used to create a sampling frame of hospitals and associated obstetric clinics, from which a probability-proportional-size sample of 10 hospitals was drawn. Close to 100 pregnancies were then recruited in clinics serving each sampled hospital, yielding a probability sample of 1,021 births. This sample was supplemented with 109 births from a certainty selection of a Flint, MI hospital, for a total sample of 1,130. The resulting response rate was high, with 100% of sampled hospitals and 65% of sampled clinics participating. Comparing the resulting sample with all 2017-2023 Michigan births showed close correspondence with respect to birth outcomes (birthweight, gestational age, Apgar scores, gestational diabetes) and mothers' demographics (age, race, education, marital status), with underrepresentation of Hispanic ethnicity and overrepresentation of reported smoking. Given the recent failures of two major prospective birth cohorts (the US National Childrens' Study and the UK Life Study), our work shows a way forward for representative pre- and post-natal studies of births.

Public Health Sciences

Finocchiaro A, **Chiarelli G**, **Stephens A**, **Viganó S**, **Bertini A**, **Cusmano N**, Guivatchian E, **Dinesh A**, Ficarra V, Sorce G, Briganti A, Montorsi F, Salonia A, Lughezzani G, Buffi N, Sood A, **Rogers C**, and **Abdollah F**. Active Surveillance for Prostate Cancer in "Real-World" Setting: Exploring Racial Disparities. *J Racial Ethn Health Disparities* 2025; Epub ahead of print. PMID: 40425976. Full Text

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INTRODUCTION AND OBJECTIVES: Active surveillance (AS) is a safe management strategy for low-risk prostate cancer (PCa), but limited "real-world" data exist outside trial cohorts. This study investigates racial disparities in progression to treatment, upgrading, and prostate cancer-specific mortality (PCSM) in a real-world AS population, aiming to improve healthcare quality. METHODS: We retrospectively analyzed data from the Henry Ford Health System (1995-2023) for men diagnosed with PCa (Gleason Grade ≤ 2, ≤ cT2c, N0-M0, PSA ≤ 20 ng/ml, age < 76 years) and enrolled in AS with ≥ 1 post-diagnosis PSA or biopsy and ≥ 1 year follow-up. Non-Hispanic Blacks (NHBs) and Non-Hispanic Whites (NHWs) were included. Surveillance adequacy was defined as ≥ 1 PSA/year and ≥ 1 biopsy every 4 years. Competing-risk cumulative incidence and regression assessed disparities in progression to treatment, upgrading, and PCSM. RESULTS: Among 864 patients (38% NHBs, 62% NHWs), NHBs presented with more advanced disease, including higher rates of GG2 (29% vs. 18%, $p < 0.001$) and intermediate-risk PCa (39% vs. 32%, $p = 0.04$). Surveillance adequacy was lower in NHBs (38% vs. 50%, $p < 0.001$). NHBs progressed to treatment more frequently (45% vs. 36%, $p < 0.001$), with a 1.46-fold higher risk (95% CI: 1.14-1.87, $p = 0.003$). NHBs had no higher odds of upgrading but showed higher 10-year PCSM (5.6% vs. 1.4%) and 5.9-fold higher odds of PCSM (95% CI: 1.38-25.37, $p = 0.01$). CONCLUSIONS: NHBs under AS face more advanced disease, lower follow-up adequacy, higher progression to treatment, and elevated PCSM odds. Targeted strategies are needed to address these disparities and improve equitable PCa care.

Public Health Sciences

Gao MZ, Omer TM, Miller KM, Simpson MC, Bukatko AR, Gedion K, **Adjei Boakye E**, Kost KM, Dickinson JA, Varvares MA, and Osazuwa-Peters N. Thyroid Cancer Incidence and Trends in United States and Canadian Pediatric, Adolescent, and Young Adults. *Cancers (Basel)* 2025; 17(9). PMID: 40361355. Full Text

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BACKGROUND/OBJECTIVES: Thyroid cancer incidence has risen in both the United States and Canada, despite differing healthcare systems. While overdiagnosis likely partly explains this trend in adults, its impact on younger populations is unclear. We used the North American Association of Central Cancer Registries, which included 133,808 thyroid cancer cases from the United States and Canada, to assess incidence trends among pediatric, adolescent, and young adult (PAYA) populations. METHODS: Age-adjusted incidence rates (AAIR) per 100,000 person-years (PY) were compared using rate ratios (RR), stratified by sex, age, race/ethnicity (United States only), and histology. Joinpoint regression estimated annual percentage changes (APC) and average APCs (AAPC) in AAIRs. From 1995 to 2014, thyroid cancer incidence increased by 137%. Significant increases occurred across all age groups (0-14, 15-24, 25-34, 35-39 years). The rate increase was highest for papillary thyroid cancer (AAPC = 5.50, 95% CI 5.06, 5.94), and among individuals aged 35-39 years (AAPC = 5.99, 95% CI 4.84, 7.15). Of racial/ethnic groups in the United States, non-Hispanic White individuals had the highest AAIR (6.22 per 100,000 PY). Mortality has changed minimally. CONCLUSIONS: Over the past two decades, thyroid cancer incidence has increased in individuals under 40. While evidence suggests that overdiagnosis primarily accounts for this trend, other contributing factors cannot be ruled out. Further research and surveillance of the drivers of increased incidence are critical.

Public Health Sciences

Luzum JA, Littleton SDR, Lopez-Medina AI, **Liu B**, **She R**, and **Lanfear DE**. The Beta-Blocker Pharmacogenetic Puzzle: More Pieces of Evidence for Pharmacodynamic Candidate Variants. *Clin Transl Sci* 2025; 18(5):e70239. PMID: 40285373. Full Text

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Previous pharmacogenetic findings for beta-blocker pharmacodynamic candidate genes (ADRB1, ADRB2, ADRA2C, GRK4, and GRK5) have been inconsistent. Therefore, the purpose of this study was to determine whether interactions of pharmacodynamic variants with beta-blocker exposure significantly associated with survival in patients with heart failure with reduced ejection (HFrEF). The 893 patients were 51% self-reported African American and 49% self-reported White race, 36% female, and 240 died (27%) over a median follow-up of 2.8 years. The primary outcome was all-cause mortality. Using Cox proportional hazards models with time-varying beta-blocker exposure and adjusted for clinical risk factors and ancestry, interactions of ADRB1 Arg389Gly, ADRB1 Ser49-Arg389Gly haplotype, ADRA2C Del(322-325), and GRK4 Ala486Val with beta-blocker exposure were significant before correction for multiple comparisons ($p < 0.1$), but only GRK4 Ala486Val remained significant in African Americans after correction for multiple comparisons using the adaptive Hochberg method ($p = 0.022$). Beta-blocker exposure only associated with a significant reduction in the risk of mortality in the African American HFrEF patients with the GRK4 Ala486/Ala486 genotype (HR = 0.44; 95% CI = 0.20-0.96; $p = 0.04$). In

conclusion, the interaction of GRK4 Ala486Val with beta-blocker exposure significantly associated with survival in African American HFrEF patients. Larger sample sizes or meta-analyses are needed to have more statistical power to better assess beta-blocker pharmacogenetic interactions for ADRB1 Arg389Gly, ADRB1 Ser49-Arg389Gly haplotype, and ADRA2C Del(322-325) in the future.

Public Health Sciences

Mason W, Mackie H, **Kulawczyk A**, **Jin J**, and **Craig JR**. Unilateral Clear Thin Rhinorrhea: How Often Is It a Cerebrospinal Fluid Leak? *Ann Otol Rhinol Laryngol* 2025; Epub ahead of print. PMID: 40370059. Full Text

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OBJECTIVES: Determine frequencies of conditions causing unilateral clear thin rhinorrhea (UCTR), and assess whether certain clinical features are associated with CSF rhinorrhea. METHODS: This was a retrospective review identifying all patients presenting with UCTR to one rhinologist over a 6-year period. The conditions causing UCTR were recorded, and the following demographic or clinical variables were collected when available: body-mass index (BMI, kg/m2), gender, age, race, and self-reported drainage volume (whether the UCTR dripped out the nose and could be collected, or it felt like a wet nostril with intermittent running down lip that was unlikely to be collectable). RESULTS: Of 3,041 patients, 146 were identified with at least UCTR (4.8%). Mean age was 56.2 ± 17.6 years, and 65.8% were female. Amongst UCTR, nonallergic rhinitis (NAR) was the most common cause (45%), followed by CSF rhinorrhea (30%). On multivariate analysis, the following were significantly positively associated with CSF rhinorrhea: BMI≥30 (OR=4.95), ages 45-54 years (OR=3.67) and 55-64 years (OR=4.15), and self-reported UCTR dripping with collectability (OR=5.96)). CONCLUSIONS: NAR was the most common cause of UCTR, representing nearly 50% of cases. However, CSF rhinorrhea still represented 30% of cases, reinforcing that UCTR should be worked up for CSF rhinorrhea, ideally with B2-Tf testing. BMI ≥30, ages 45-64 years, and patient-reported higher volume UCTR were positively associated with CSF rhinorrhea. If B2-Tf testing is negative or unobtainable, or clinical suspicion for CSF leak is low, clinicians can consider starting medical therapy for rhinitis or rhinosinusitis before pursuing further invasive CSF confirmatory testing.

Public Health Sciences

Morgan S, Raza Shah SH, Comstock SS, Goodrich JM, Liang D, Tan Y, McKee K, Ruden D, **Sitarik AR**, **Cassidy-Bushrow AE**, Dunlop AL, and Petriello MC. Prenatal PFAS exposure and outcomes related to maternal gut microbiome composition in later pregnancy. *Environ Res* 2025; 279(Pt 1):121709. PMID: 40311903. Full Text

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The composition of the gut microbiome is dependent on factors including diet, lifestyle, and exposure to environmental chemicals, and has implications for human health. Per- and polyfluoroalkyl substances (PFAS), a class of man-made chemicals that have nonstick and flame-retardant properties may impact on gut microbiome composition. Our objective was to elucidate links between PFAS and maternal gut microbiome composition in two geographically diverse sites of the Environmental Influences on Child Health Outcomes program. The present analysis includes participants in the Atlanta African American Maternal Child Cohort; ATL AA and a predominately non-Hispanic White subsample of the Michigan Archive for Research on Child Health Cohort; MARCH with serum or plasma PFAS concentrations measured in early or late pregnancy and 16s rRNA sequencing from maternal gut microbiome samples available primarily in later pregnancy (2nd-3rd trimester). Linear regression models tested associations between prenatal PFAS levels (separately for the 1st/3rd trimesters) and measures of alpha diversity, bacterial composition differences, and differential taxonomic abundance. Bayesian Kernel Machine Regression and Elastic net regression mixture modeling were also incorporated. In both cohorts, multiple PFAS were significantly associated with the relative abundance of specific microbiome taxa even after adjustment for covariates including maternal diet, age, race, BMI, and smoking; A total of 16 significant family-level associations were identified for ATL AA (e.g., PFOA with Clostridiaceae; natural log fold change = 0.94) and 13 significant family-level associations identified for MARCH e.g., PFOS with Desulfovibrionaceae; natural log fold change = -1.53 (p(FDR)<0.05), but similarities between cohorts were lacking. Mixture analyses did not identify interactive or combined effects but did provide modest evidence of inclusion of individual PFAS in beta diversity models in both cohorts. In 2 distinct cohorts, there were significant associations between prenatal PFAS and the relative abundance of several bacterial taxa, but these differences were cohort-specific. This work suggests that PFAS may modulate the gut microbiome during pregnancy.

Public Health Sciences

Munhoz J, Newell M, Goruk S, **Ghosh S**, Patel D, Joy AA, Bigras G, Mazurak V, Courneya KS, Hemmings DG, and Field CJ. Docosahexaenoic acid (DHA) supplementation attenuates changes in the concentration, phenotype, and response of immune peripheral blood cells in breast cancer patients undergoing neoadjuvant therapy. Secondary findings from the DHA-WIN trial. *Breast Cancer Res* 2025; 27(1):91. PMID: 40405290. Full Text

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BACKGROUND: Breast cancer neoadjuvant therapy may negatively impact the immune system. As a secondary outcome of the docosahexaenoic acid (DHA) for women with breast cancer in the neoadjuvant setting (DHA-WIN trial), we sought to assess the effects of an intervention with DHA on parameters of immune function of women undergoing neoadjuvant therapy. METHODS: Women with early-stage breast cancer in the neoadjuvant setting were recruited for the DHA-WIN trial and randomly assigned to receive either 4.4 g/day of DHA or a placebo for 18 weeks in conjunction with their neoadjuvant chemotherapy for breast cancer. Venous blood was collected to isolate peripheral blood mononuclear cells. Immune parameters were assessed by measuring white blood cell concentration, flow cytometry, and cytokines concentration after mitogen-stimulated immune response. RESULTS: In the placebo group the proportion of T cells (CD3 +), and functionally active monocytes (CD14 + HLA-DR +) was reduced at the last cycle of chemotherapy (15 weeks) but remained constant in the DHA group (P interaction < 0.05). The neutrophil-

to-lymphocyte ratio (NLR) was maintained in the DHA group but increased in the placebo at the end of chemotherapy (P-interaction = 0.02). An increase in this ratio was associated with lower chance of achieving pathological complete response (OR = 0.32, 95% CI [0.14,0.16], P = 0.01). After 15 weeks of therapy, the DHA-supplemented group had higher concentrations of stimulated cytokines IL-4, IL-10, and the T helper type 1 cytokine IFN-γ after phytohemagglutinin (PHA) challenge, and higher concentrations of TNF-α and IFN-γ cytokines after lipopolysaccharide exposure (P < 0.05). CONCLUSION: Supplementing DHA during breast cancer neoadjuvant chemotherapy improved systemic immune function by attenuating changes in blood cell concentrations, preventing depletion of immune cells, and enhancing ex vivo cytokine secretion after stimulation.

Public Health Sciences

Niu Z, Ako AA, Geiger SD, Howe CG, Perng W, Singh R, Karagas MR, Elliott AJ, **Cassidy-Bushrow A**, Camargo CA, Sanderson K, McEvoy CT, Oken E, Dabelea D, Hartert TV, Carter B, Stroustrup A, Lampland A, O'Connor TG, Gogcu S, Hudak ML, Shorey-Kendrick LE, Zhao Q, Ni Y, VanWormer J, Ferrara A, Hedderson M, Zhu Y, Alshawabkeh A, Cordero J, Koinis-Mitchell D, Carnell S, Breton CV, Bastain TM, and Farzan SF. Maternal Cardiometabolic Risk Factors in Pregnancy and Offspring Blood Pressure at Age 2 to 18 Years. *JAMA Netw Open* 2025; 8(5):e259205. PMID: 40338548. Full Text

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IMPORTANCE: Higher blood pressure in early life may signal cardiovascular disease over the life course, but determinants of blood pressure in early life are poorly understood. OBJECTIVE: To examine the association of maternal cardiometabolic risk factors during pregnancy with offspring blood pressure from age 2 to 18 years and explore whether the association is modified by offspring sex and race and ethnicity. DESIGN, SETTING, AND PARTICIPANTS: This cohort study analyzed data from the Environmental Influences on Child Health Outcomes program between January 1, 1994, and March 31, 2023. Three common maternal cardiometabolic risk factors during pregnancy were examined: prepregnancy obesity, gestational diabetes, and hypertensive disorders of pregnancy (HDP). EXPOSURE: Maternal cardiometabolic risk factors were retrieved and harmonized from medical records and questionnaires. MAIN OUTCOMES AND MEASURES: Offspring systolic blood pressure (SBP) and diastolic blood pressure (DBP) percentiles adjusted for age, sex, and height were calculated. RESULTS: Among 12 480 mother-offspring pairs (mean [SD] maternal age during pregnancy, 29.9 [6.4] years; 856 of 12 303 identifying as Asian [7.0%]; 1908 as Black [15.5%]; 2305 as Hispanic [18.7%]; 6522 as White [52.3%], and 712 as other [5.8%] race and ethnicity), at least 1 maternal cardiometabolic risk factor was present in 5537 (44.4%), with prepregnancy obesity being the most prevalent (3072 [24.6%]), followed by HDP (1693 [13.6%]) and gestational diabetes (805 [6.5%]). Offspring born to mothers with any cardiometabolic risk factors had higher SBP (4.88 percentile points; 95% CI, 3.97-5.82 percentile points) and higher DBP (1.90 percentile points; 95% CI, 1.15-2.64 percentile points) at their first blood pressure measurement, after adjusting for potential confounders, compared with their counterparts without any risk factors. Hypertensive disorders of pregnancy, alone or with either prepregnancy obesity or gestational diabetes, was significantly associated with higher offspring blood pressure. These associations were generally more significant among female compared with male offspring and among Black compared with other racial and ethnic groups. Among 6015 offspring who had 2 or more blood pressure measures, maternal cardiometabolic risk factors were associated with an increased rate of blood pressure change from age 2 to 18 years (SBP percentile, 0.5 [95% CI, 0.2-0.8] per year; DBP percentile, 0.7 [95% CI 0.5-1.0] per year). CONCLUSIONS AND RELEVANCE: These findings suggest that protecting pregnant individuals from cardiometabolic risk factors may promote healthier blood pressure in the next generation.

Public Health Sciences

Oravec D, **Yadav RN**, **Cushman T**, **Flynn MJ**, **Divine GW**, **Rao SD**, and **Yeni YN**. Osteoporosis screening in the mammography setting via digital wrist tomosynthesis. *Osteoporos Int* 2025; Epub ahead of print. PMID: 40341965. Full Text

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Adherence to osteoporosis screening guidelines could be considerably higher if offered at the time of routine mammography using the same imaging modality. We found that forearm density measurements using a breast imaging system provides density information with excellent diagnostic capability for osteoporosis and osteopenia status determined by hip and spine DXA. PURPOSE: Adherence to osteoporosis screening guidelines via bone mineral density (BMD) measurements with dual-energy x-ray absorptiometry (DXA) is low. Since adherence to breast cancer screening is quite high, it was suggested that the rate of osteoporosis screening can be improved if wrist imaging were performed at the time of breast screening using the very same equipment. METHODS: Digital wrist tomosynthesis (DWT) imaging was performed in 150 women using a 3D mammography system and BMD was measured from both 3D

tomosynthesis and synthesized 2D images. In addition, standard DXA based BMD measurements were performed at the hip, spine, and forearm sites. We examined the extent to which DWT-derived ultradistal radius BMD correlates with DXA based BMD measurements, evaluated DWT measurement precision errors, and determined the accuracy of DWT in diagnosing low bone mass and osteoporosis in vivo. RESULTS: DWT BMD strongly correlated with DXA-derived ultradistal radius BMD (R2 up to 0.814) and discriminated osteoporosis (AUC up to 0.978) and osteopenia (AUC up to 0.938) by ultradistal T-score with low in vivo precision errors (0.91-2.3%). BMD derived from 3D DWT BMD performed comparably to forearm DXA BMD in the diagnosis of osteopenia (AUC up to 0.916) and osteoporosis (AUC up to 0.946) determined by hip and spine DXA. CONCLUSIONS: DWT can be readily implemented in mammography settings with similar diagnostic accuracy to DXA, has the potential to increase adherence to osteoporosis screening recommendations, and offers a convenient means to measure bone density within the highly accessible breast screening environment.

Public Health Sciences

Samadi P, Sheykhhasan M, Omer I, Ullah A, Zarea A, Toomajian V, Khan MUA, Ertas D, **Jones LR**, **Levin AM**, Hasan A, Contag CH, Ertas YN, and Ashammakhi N. Regeneration of cartilage defects using engineered extracellular vesicles. *Biofabrication* 2025; Epub ahead of print. PMID: 40403758. Full Text

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In recent years, the number of adults with diagnosed cartilage defects has increased significantly, and various modes of treatment have been sought. However, traditional cartilage repair strategies have been proven inefficient, with limited success. Recently, regenerative treatment options have become more routinely used for specific indications, but they still have major limitations. Cell-derived extracellular vesicles (EVs) are becoming increasingly attractive for regenerative purposes because they provide several regenerative factors. In addition, they can be engineered to function as delivery agents for proteins, nucleic acids, and other molecules. Recently, EVs were explored for cartilage tissue engineering, with varying results. Unlike other cell-based therapies, this approach will lead to the avoidance of problems associated with immunogenic reactions against allogenic cells and easier approval of the therapy by regulatory bodies, which is expected to stimulate wider clinical application. Because of its broad interest and importance, this review was developed to discuss published works, their outcomes, and limitations and outline future research directions.

Public Health Sciences

Santarossa S, Austin B, Bell MA, **Henry SC**, Inclima A, Maddox H, Smith TG, **Copeland L**, **Murphy D**, **Redding A**, and **Loree A**. The Art of Resiliency: Patient Stories of Maternal Mental Health Experiences. *J Patient Cent Res Rev* 2025; 12(2):87-100. PMID: 40337189. Full Text

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Public Health Sciences

Siddiqui RF, **Al-Antary N**, **Gilbert M**, **Fakhoury L**, Vu M, **Siddiqui F**, and **Adjei Boakye E**. Knowledge of Head and Neck Cancer Risk Factors and Symptoms: A Cross-Sectional Survey Among Arab Americans. *J Immigr Minor Health* 2025; Epub ahead of print. PMID: 40407986. Full Text

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We examined head and neck cancer (HNC) risk factors and symptoms knowledge among Arab Americans in Michigan. A survey of 295 adult Arab Americans (≥ 18 years) was conducted between March and July 2023. Knowledge of HNC risk factors and symptoms were assessed using 10 and 14 questions, respectively. For each question, we asked, "Do you know that the following can be risk factors/symptoms of HNC?" and respondents chose "yes," "no," or "don't know/not sure." Regarding risk factors- tobacco smoking and chewing were the most recognized risk factors, identified by 78.9% and 72.8%, respectively. Less than half identified human papillomavirus (HPV) (40.6%) as risk factor. Regarding symptom knowledge, only 40-50% identified the most common HNC symptoms: nonhealing ulcers (41%), dysphagia or odynophagia (51.4%), and voice changes (48.6%); while 60.6% identified swelling or lump in neck/throat. Approximately, half of the respondents recognized persistent mass or lesion on the tongue (53.3%) and bleeding in the mouth/throat (50.3%) as symptoms of HNC. Education level, household income, and number of sexual partners were associated with knowledge regarding some common symptoms of HNC. While there is higher knowledge about tobacco as a risk factor for HNC, knowledge about HPV as a risk factor is very low. Similarly, knowledge about HNC symptoms is suboptimal in the Arab American community. Findings support the development of interventions for this community to help improve HNC knowledge and related health outcomes.

Public Health Sciences

Stallrich JW, Young K, Weese ML, **Smucker BJ**, and Edwards DJ. An optimal design framework for lasso sign recovery. *J R Stat Soc Series B Stat Methodol* 2025:24. PMID: Not assigned. Full Text

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Supersaturated designs investigate more factors than there are runs and are often constructed under a criterion measuring a design's proximity to an unattainable orthogonal design. The most popular analysis identifies active factors by inspecting the solution path of a penalized estimator, such as the lasso. Recent criteria encouraging positive correlations between factors have been shown to produce designs with more definitive solution paths so long as the active factors have positive effects. Two open problems affecting the understanding and practicality of supersaturated designs are: (1) do optimal designs under existing criteria maximize support recovery probability across an estimator's solution path and (2) why do designs with positively correlated columns produce more definitive solution paths when the active factors have positive sign effects? To answer these questions, we develop criteria maximizing the lasso's sign recovery probability. We prove that an orthogonal design is an ideal structure when the signs of the active factors are unknown, and a design with constant, small, positive correlations is ideal when the signs are assumed known. A computationally efficient design search algorithm is proposed that first filters through optimal designs under new heuristic criteria to select the one that maximizes the lasso sign recovery probability.

Public Health Sciences
Veenstra J, **Boothby-Shoemaker W**, and **Friedman BJ**. Response to "Appropriate Statistical Methods to Assess Cross-Study Diagnostic 23-Gene Expression Profile Test Performance for Cutaneous Melanocytic Neoplasms". *Am J Dermatopathol* 2025; 47(6):497-498. PMID: 40314646. Full Text

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Public Health Sciences
Wiley MM, Radziszewski M, Khatri B, Joachims ML, Tessneer KL, Stolarczyk AM, Yao S, Li J, Pritchett-Frazee C, Johnston AA, Rasmussen A, Anaya JM, Aqrawi LA, Bae SC, Baecklund E, Björk A, Brun JG, Bucher SM, Dand N, Eloranta ML, Engelke F, Forsblad-d'Elia H, Fugmann C, Glenn SB, Gong C, Gottenberg JE, Hammenfors D, Imgenberg-Kreuz J, Jensen JL, Johnsen SJA, Jonsson MV, Kelly JA, Khanam S, Kim K, Kvarnström M, Mandl T, Martín J, Morris DL, Nocturne G, Norheim KB, Olsson P, Palm Ø, Pers JO, Rhodus NL, Sjöwall C, Skarstein K, Taylor KE, Tombleson P, Thorlacius GE, Venuturupalli SR, Vital EM, Wallace DJ, Radfar L, Brennan MT, James JA, Scofield RH, Gaffney PM, Criswell LA, Jonsson R, Appel S, Eriksson P, Bowman SJ, Omdal R, Rönnblom L, Warner BM, Rischmueller M, Witte T, Farris AD, Mariette X, Shiboski CH, Wahren-Herlenius M, Alarcón-Riquelme ME, Ng WF, Sivils KL, Guthridge JM, **Adrianto I**, Vyse TJ, Tsao BP, Nordmark G, and Lessard CJ. Variants in the DDX6-CXCR5 autoimmune disease risk locus influence the regulatory network in immune cells and salivary gland. *Ann Rheum Dis* 2025; Epub ahead of print. PMID: 40447495. Full Text

OBJECTIVES: Sjögren's disease (SjD) and systemic lupus erythematosus (SLE) share genetic risk at the DDX6-CXCR5 locus (11q23.3). Identifying and functionally characterising shared SNPs spanning this locus can provide new insights into common genetic mechanisms of autoimmunity. METHODS: Transdisease meta-analyses, fine-mapping, and bioinformatic analyses prioritised shared likely functional single nucleotide polymorphisms (SNPs) for allele-specific and cell type-specific functional interrogation using electromobility shift, luciferase reporter, and quantitative chromatin conformation capture assays and clustered regularly interspaced short palindromic repeat (CRISPR) gene regulation. RESULTS: Five shared SNPs were identified as likely functional in primary human immune cells, salivary gland and kidney tissues: rs57494551, rs4936443, rs4938572, rs7117261, and rs4938573. All 5 SNPs exhibited cell type-specific and allele-specific effects on nuclear protein binding affinity and enhancer/promoter regulatory activity in immune, salivary gland epithelial, and kidney epithelial cell models. Mapping of chromatin-chromatin interactions revealed a chromatin regulatory network that expanded beyond DDX6 and CXCR5 to include PHLDB1, lnc-PHLDB1-1, BCL9L, TRAPPC4, among others. Coalescence of functional assays and multiomic data analyses indicated that these SNPs likely modulate the activity of 3 regulatory regions: intronic rs57494551 regulatory region, intergenic SNP haplotype (rs4938572,

rs4936443, and rs7117261) regulatory region, and rs4938573 regulatory region upstream of the CXCR5 promoter. CONCLUSIONS: Shared genetic susceptibly at the DDX6-CXCR5 locus in SjD and SLE likely alters common mechanisms of autoimmunity, including interferon signalling (DDX6), autophagy (TRAPPC4), and lymphocytic infiltration of disease-target tissues (CXCR5). Further, using multiomic data from patients with SjD, combined with bioinformatic and in vitro functional studies, can provide mechanistic insights into how genetic risk influences the biological pathways that drive complex autoimmunity.

Pulmonary and Critical Care Medicine

Chaddha U, Agrawal A, Ghori U, Kheir F, **Debiane L**, McWilliams A, Cheng G, Balata H, Fong KM, Rzyman W, Mohan A, Triphuridet N, Lam S, Soh J, Yankelevitz D, Lam DC, Beasley MB, Heuvelmans M, Yang D, Huber RM, Gratacos AR, Viola L, Jiang L, and Murgu S. Safety and Sample Adequacy for Comprehensive Biomarker Testing of Bronchoscopic Biopsies: An American Association of Bronchology and Interventional Pulmonology (AABIP) and International Association for the Study of Lung Cancer (IASLC) Clinical Practice Guideline. *J Thorac Oncol* 2025; Epub ahead of print. PMID: 40419141. Full Text

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Linear endobronchial (EBUS) guided sampling of accessible mediastinal lesions is well established as a first-choice modality for lung cancer mediastinal staging. Parenchymal lung lesions, however, are routinely accessed by either a percutaneous (CT-guided) or a bronchoscopic approach. Direct comparisons between the percutaneous approach and bronchoscopy, or EBUS and mediastinoscopy are sparse in regard to diagnostic accuracy and it remains unknown which sampling technique is the safest and offers the most adequate material for comprehensive biomarker testing. This guideline addresses new evidence and aims to answer these questions relevant to contemporary lung cancer clinical practice. A multidisciplinary expert panel from the AABIP and the Early Detection and Screening Committee of the IASLC was convened to address four PICO questions pertaining to the safety and adequacy of comprehensive biomarker testing for commonly used intra-thoracic biopsy techniques. The panel included 24 experts in thoracic procedures, including 18 pulmonologists, 2 radiologists, 1 pathologist and 3 thoracic surgeons from 22 hospitals across 12 countries. All panel members participated in the development of the final recommendations using a modified Delphi technique. Specific recommendations are provided on safety and adequacy of minimally invasive thoracic interventions on patients with confirmed or suspected lung cancer for which comprehensive biomarker testing is needed for standard of care or clinical trials participation.

Pulmonary and Critical Care Medicine
Jabri A, Kumar S, **Shadid AM**, Ramakrishna H, Giustino G, **Fadel RA**, **O'Neill B**, **Alqarqaz M**, **Basir MB**, **Engel-Gonzalez P**, **Frisoli T**, Genereux P, Bagur R, Jimenez-Rodriguez G, Hanson I, Abbas A, Dixon S, **O'Neill W**, and **Villablanca PA**. A Comprehensive Review of Left Atrial Venoarterial Extracorporeal Membrane Oxygenation. *J Cardiothorac Vasc Anesth* 2025; Epub ahead of print. PMID: 40404523. Full Text

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Cardiogenic shock (CS) in patients with structural heart disease (SHD) and severe valvular abnormalities poses unique challenges to traditional mechanical circulatory support (MCS) strategies, such as intra-aortic balloon pumps and ventricular assist devices. These devices may fail to address the complex interplay between ventricular unloading and systemic perfusion. Left atrial venoarterial extracorporeal membrane oxygenation (LAVA-ECMO) incorporating left atrial (LA) drainage into the ECMO circuit to reduce left ventricular (LV) preload, mitigate pulmonary congestion, and maintain systemic perfusion. This review explores the pathophysiologic principles and clinical applications associated with LAVA-ECMO. Studies have demonstrated its efficacy in managing CS due to severe valvular disease, biventricular failure, and complex hemodynamic profiles, such as those complicated by aortic regurgitation or

ventricular septal defect. Although traditional venoarterial ECMO can incorporate LA drainage, LAVA-ECMO offers distinct advantages by actively unloading the left ventricle, thereby preventing such complications as LV distension and pulmonary edema. Clinical evidence suggests its role as a bridge to definitive interventions, including transcatheter and surgical valve replacements. Despite these benefits, challenges remain, including high in-hospital mortality and complications such as bleeding. LAVA-ECMO represents a transformative advancement in MCS, offering superior hemodynamic stabilization and myocardial recovery for patients with refractory CS and severe valvular disease. Its ability to address LV unloading directly positions it as a pivotal tool in critical care and SHD management; however, significant gaps in evidence, particularly in long-term outcomes and optimal patient selection, underscore the need for further research.

Pulmonary and Critical Care Medicine

Peralta AR, and **Shadid AM**. The Role of Bronchoscopy in the Diagnosis of Interstitial Lung Disease: A State-of-the-Art Review. *J Clin Med* 2025; 14(9). PMID: 40364285. Full Text

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The diagnostic evaluation of interstitial lung diseases (ILDs) remains challenging due to their heterogeneous etiologies and overlapping clinical and radiographic patterns. A confident diagnosis often necessitates histopathological sampling, particularly when high-resolution computed tomography and serologic assessments are inconclusive. While surgical lung biopsy (SLB) has long been considered the diagnostic gold standard, its invasiveness, associated morbidity, and limited feasibility in high-risk patients have driven the pursuit of less invasive alternatives. Here, we review the current applications, diagnostic yield, procedural techniques, and complications of several bronchoscopic modalities. Bronchoalveolar lavage (BAL) aids in characterizing inflammatory profiles and differentiating among conditions such as hypersensitivity pneumonitis, sarcoidosis, and eosinophilic pneumonia. Endobronchial biopsies (EBBs) and endobronchial ultrasound transbronchial needle aspiration (EBUS-TBNA) are valuable in diagnosing granulomatous diseases with lymphadenopathy. Transbronchial lung biopsy (TBLB) is effective for peribronchial and centrilobular diseases but is limited by small sample size and tissue distortion. Transbronchial lung cryobiopsy (TBC) enables acquisition of larger, well-preserved parenchymal tissue samples from the peripheral lung. Over recent years, studies have demonstrated that TBC, when interpreted within a multidisciplinary discussion (MDD), achieves diagnostic concordance rates with SLB exceeding 75%, and up to 95% in cases where high diagnostic confidence is reached. When performed in experienced centers using standardized protocols, TBC is considered a viable first-line histopathologic tool in the diagnostic evaluation of ILD. Adequate training and standardization of the TBC procedure are needed to ensure low complication rates and a high yield.

Radiation Oncology

Kim JP, **Cunningham JM**, **Moats E**, **Ghanem AI**, **Movsas B**, **Levin K**, **Feldman AM**, and **Thind K**. Optimizing Dose Reduction to the Left Anterior Descending Artery in Patients With Locally Advanced Lung Cancer Treated With Definitive Radiation Therapy: A Feasibility Study of Coplanar Treatments Using Double-Stacked Multileaf Collimator. *Adv Radiat Oncol* 2025; 10(6):101779. PMID: 40371385. Full Text

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PURPOSE: Recent studies have shown that cardiac substructures and particularly left anterior descending artery (LAD) dose strongly correlates with the incidence of late adverse cardiac events. We evaluated whether greater cardiac and, importantly, LAD dose sparing could be achieved using a newly introduced closed bore (O-ring gantry) linac with a double-stacked multileaf collimator (Varian Ethos) relative to conventional linacs. METHODS AND MATERIALS: Twenty patients with locally advanced non-small cell lung cancer previously treated with definitive chemoradiotherapy were retrospectively evaluated. Volumetric modulated arc therapy plans were retrospectively generated for the Ethos system

using optimization criteria focused on reducing overall heart and LAD doses (Heart_Ethos). Plans were also reoptimized using the same optimization criteria on a conventional C-arm linac (Heart_TB). Investigational plans were compared with the original plans and with each other using standard dose-volume histogram metrics such as percentage (V) volume receiving a specific dose (x) in Gy (Vx) or mean dose (Dmean) in Gy. RESULTS: Statistically significant decreases existed between the Heart_Ethos and original plans for mean heart dose (11.3 vs 14.8 Gy; P < .001) and V5, V30, and V50 (63.6% vs 75.2%; P < .001, 7.1% vs 12.3%; P < .001, 2.1% vs 2.9%; P = .03, respectively) and also for LAD mean dose (4.8 Gy vs 12.0 Gy [P < .001]) and V15 (4.9% vs 21.5%; P < .001). Compared with Heart_TB, Heart_Ethos plans had significantly less mean heart dose (11.6 vs 12.2 Gy; P = .006), and less heart V5 (64.4% vs 67.2%; P = .049) and V30 (7.7% vs 8.8%; P = .03), whereas other parameters were not significant. Optimal target coverage and other organs at risk constraints were maintained for all generated plans. CONCLUSIONS: Heart_Ethos plans showed significant reduction in cardiac and LAD doses in comparison to the original plans while maintaining target and organ at risk goals. Our findings suggest that Ethos technology has the potential for better cardiac toxicity safety because Heart_Ethos plans were still able to reduce cardiac dose compared with Heart_TB plans.

Radiation Oncology
Mudgal M, Balaji S, Gajendiran AP, Subramanya A, Murugan SK, Gondhi V, **Bhatnagar AR**, and Gunasekaran K. Connective Tissue Disorder-Induced Diffuse Alveolar Hemorrhage: A Comprehensive Review with an Emphasis on Airway and Respiratory Management. *Life (Basel)* 2025; 15(5). PMID: 40430219. Full Text

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Diffuse alveolar hemorrhage (DAH), a catastrophic complication of connective tissue disorders (CTDs), manifests as rapid-onset hypoxemia, alveolar infiltrates, and progressive bleeding into the airways. While immune-mediated alveolar-endothelial injury primarily drives its pathophysiology, diagnosis is based on bronchoscopy and chest imaging. The clinical urgency lies in securing the compromised airway and stabilizing respiratory failure, a challenge increased by CTD-specific anatomical alterations such as cervical spine instability, cricoarytenoid arthritis, and subglottic stenosis. High-dose corticosteroids and immunosuppression are essential, while severe cases require extracorporeal membrane oxygenation or plasmapheresis. This comprehensive review introduces two novel approaches to address fundamental gaps in the management of CTD-induced DAH: a structured algorithm for a CTD-specific airway risk stratification tool, integrating anatomical screening and the application of lung ultrasounds (LUSs) for post-intubation CTD-induced DAH ventilation management. The need for a multidisciplinary team approach is also discussed. Despite aggressive care, mortality remains high (25-50%), underscoring the necessity for improved early recognition and intervention strategies for these high-risk patients.

Radiation Oncology
Siddiqui RF, **Al-Antary N**, **Gilbert M**, **Fakhoury L**, Vu M, **Siddiqui F**, and **Adjei Boakye E**. Knowledge of Head and Neck Cancer Risk Factors and Symptoms: A Cross-Sectional Survey Among Arab Americans. *J Immigr Minor Health* 2025; Epub ahead of print. PMID: 40407986. Full Text

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We examined head and neck cancer (HNC) risk factors and symptoms knowledge among Arab Americans in Michigan. A survey of 295 adult Arab Americans (≥ 18 years) was conducted between March and July 2023. Knowledge of HNC risk factors and symptoms were assessed using 10 and 14 questions, respectively. For each question, we asked, "Do you know that the following can be risk factors/symptoms of HNC?" and respondents chose "yes," "no," or "don't know/not sure." Regarding risk factors- tobacco smoking and chewing were the most recognized risk factors, identified by 78.9% and 72.8%, respectively. Less than half identified human papillomavirus (HPV) (40.6%) as risk factor. Regarding symptom knowledge, only 40-50% identified the most common HNC symptoms: nonhealing ulcers (41%), dysphagia or odynophagia (51.4%), and voice changes (48.6%); while 60.6% identified swelling or lump in neck/throat. Approximately, half of the respondents recognized persistent mass or lesion on the tongue (53.3%) and bleeding in the mouth/throat (50.3%) as symptoms of HNC. Education level, household income, and number of sexual partners were associated with knowledge regarding some common symptoms of HNC. While there is higher knowledge about tobacco as a risk factor for HNC, knowledge about HPV as a risk factor is very low. Similarly, knowledge about HNC symptoms is suboptimal in the Arab American community. Findings support the development of interventions for this community to help improve HNC knowledge and related health outcomes.

Radiation Oncology

Witek ME, Ward MC, Bakst R, Chandra RA, **Chang SS**, Choi KY, Galloway T, Hanna GJ, Hu KS, Robbins J, Shukla ME, **Siddiqui F**, Takiar V, Walker GV, Fu Y, and Margalit DN. Paranasal Sinus and Nasal Cavity Cancers: Systematic Review and Executive Summary of the American Radium Society Appropriate Use Criteria. *Head Neck* 2025; Epub ahead of print. PMID: 40344605. Full Text

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Tumors of the paranasal sinus and nasal cavity (PNS/NC) are rare and exhibit diverse histology, anatomic subsite, and malignant potential. Early-stage disease is typically managed with surgery, and locally advanced disease is treated with a combination of surgery, radiotherapy, and chemotherapy. Clinical decision-making is commonly guided by limited retrospective evidence. To address this limitation, we performed a systematic review to inform evidence-based consensus for the management of common clinical scenarios, including the potential roles of radiation and systemic therapy to promote structural preservation, elective neck management, and radiation technique considerations. A librarian-mediated

literature search identified 39 studies of adult patients with PNS/NC tumors treated with curative intent that met the study inclusion criteria. Search results were reported using the preferred reporting items for systematic reviews and meta-analyses (PRISMA) methodology. A modified-Delphi process was used to guide consensus for the appropriate use of various management strategies. Strong consensus existed for the appropriateness of primary surgery for early-stage disease, approaches to locally advanced disease with minimal periorbital fat invasion, and the use of induction chemotherapy with response-directed local therapy. Consensus regarding nodal treatment and the use of proton therapy in the adjuvant setting was less robust. The rarity and diversity of PNS/NC tumors limit randomized phase III trials to guide management. As such, this systematic review and appropriate-use consensus statements provide clinical guidance for the management of this challenging disease spectrum.

Sleep Medicine
Espie CA, Grandner MA, and **Drake CL**. PRO: CBT-I for insomnia treatment can be delivered by a range of healthcare providers. *Sleep* 2025; Epub ahead of print. PMID: 40396901. Full Text

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Sleep Medicine
Jennings MB, **Kalmbach DA**, **Reffi AN**, Miller CB, **Roehrs T**, **Drake CL**, and **Cheng P**. Prevention of Pain Interference in Insomnia Patients via Digital Cognitive-Behavioral Therapy for Insomnia. *Behav Sleep Med* 2025;1-13. Epub ahead of print. PMID: 40324067. Full Text

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OBJECTIVES: Insomnia disorder is co-morbid with and predictive of developing pain conditions and a key factor in pain interference (PI) - the extent to which pain impedes daily living. Emerging literature suggests treating insomnia with cognitive-behavioral therapy for insomnia reduces co-occurring PI. This secondary data analysis tested the extent to which digital CBT-I (dCBT-I) vs. sleep education reduces and prevents significant PI by treating insomnia. METHODS: Insomnia disorder participants were randomized into dCBT-I (n = 697) and sleep education (n = 623) and reported pre- and post-treatment insomnia and PI. Logistic regressions evaluated intervention effects: 1) reduction of insomnia severity changes in PI and 2) prevention of treatment condition on PI. RESULTS: The reduction model showed that dCBT-I participants with moderate-to-severe pre-treatment PI experienced 17% odds increase in reduced PI for each one-point reduction in insomnia severity compared to control, OR = 1.17, 95% CI [1.01, 1.35]. In the prevention model, dCBT-I participants with little-to-no pre-treatment PI exhibited a 32% odds reduction of post-treatment progression to moderate-to-severe PI compared to control, OR = 0.68, 95% CI [0.51, 0.90]. CONCLUSION: dCBT-I demonstrated significant and clinically meaningful reduction and prevention effects against PI in a large sample. dCBT-I may help providers address sleep issues to restore pain-related impairments to daytime function, quality of life, and overall sleep.

Sleep Medicine
Kalmbach DA, Ong JC, **Cheng P**, **Reffi AN**, Swanson LM, **Hirata M**, **Seymour GM**, **Castelan-Cuamatzi AS**, **Jennings MB**, **Pitts DS**, Roth A, **Roth T**, and **Drake CL**. A randomized controlled trial of telemedicine CBTI and PUMAS for prenatal insomnia: Reducing nocturnal cognitive arousal is a treatment mechanism for alleviating insomnia and depression during pregnancy. *Sleep Med* 2025; 133:106570. PMID: 40413907. Full Text

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OBJECTIVE: Insomnia is common in pregnancy and fuels perinatal depression (PND). Cognitive-behavioral therapy for insomnia (CBTI) is effective during pregnancy, but unresolved cognitive arousal limits treatment outcomes. Enhancing reduction of cognitive arousal may improve patient outcomes. This randomized controlled trial (RCT) evaluated the effectiveness of CBTI and Perinatal Understanding of Mindful Awareness for Sleep (PUMAS, which combines mindfulness with behavioral sleep strategies) on insomnia, depression, and nocturnal cognitive arousal relative to sleep hygiene education (SHE). METHODS: A single-site, three-arm RCT of N = 64 pregnant women with clinically significant insomnia symptoms who received CBTI, PUMAS, or SHE. Active treatment was delivered via six weekly telemedicine video sessions. Outcomes included the insomnia severity index (ISI), Edinburgh postnatal depression scale (EPDS), and the pre-sleep arousal scale's cognitive factor (PSASC; nocturnal cognitive arousal). RESULTS: Over 95 % of active therapy patients completed ≥4 sessions, indicating high engagement. CBTI (ΔISI = -11.20 ± 6.93; 65.0 % insomnia remission) and PUMAS (ΔISI = -11.05 ± 3.84; 81.8 % insomnia remission) significantly alleviated insomnia relative to SHE (ΔISI = -4.50 ± 1.71; 13.6 % remission), which was replicated in women with comorbid OSA. PUMAS produced large reductions in PND and nocturnal cognitive arousal relative to SHE, whereas CBTI did not. Mediation analyses supported reducing cognitive arousal as a key mechanism by which PUMAS alleviated insomnia and PND. CONCLUSIONS: CBTI and PUMAS are effective for prenatal insomnia, even in women with comorbid OSA. PUMAS may be especially beneficial for pregnant women presenting with PND and/or high cognitive arousal (including perinatal rumination and worry), whereas CBTI may yield more modest benefits for these non-sleep outcomes.

Sleep Medicine
Khoshakhlagh AH, Yazdanirad S, Gruszecka-Kosowska A, **Drake CL**, and Emerson W. Investigation of relationship between occupational exposure to aerosol and sleep problems: A systematic review and meta-analysis. *PLoS One* 2025; 20(5):e0321515. PMID: 40343941. Full Text

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There are various occupational and industrial activities that are associated with the production of suspended particles. Little is known about sleep disturbance caused by exposure to aerosol exposure. Presented systematic review and meta-analysis study aimed to investigate the impact of various aerosols during occupational exposure on sleep. A systematic search in Scopus, Web of Science, PubMed, Embase, and Medline databases was performed until 20 February 2024. Three sets of keywords and their possible combinations were used in the search algorithm. To evaluate the quality and risk of bias in studies, the Joanna Briggs Institute (JBI) tools and risk of bias in non-randomized studies of exposure

(ROBINS-E) instruments were applied, respectively. The pooled values were also computed by meta-analysis. Based on inclusion/exclusion criteria, 23 articles were entered into the review. 9 out of 11 articles with high quality (81.82 percent), 8 out of 9 articles with moderate quality (88.89 percent), and 2 out of 3 articles with low quality (66.67 percent) indicated that aerosol exposure had a meaningful negative effect on sleep among workers in various occupations. Among articles, 69.6% (N = 16) were given a high risk of bias rating, 13.0% (N = 3) were rated as moderate risk of bias, and 17.4% (N = 4) were rated as low risk of bias. The results of the meta-analysis indicated that the pooled value of the prevalence in the cross-sectional, cohort, and case control studies was 42.35 (95%CI [34.55, 50.16]), 10.82 (95%CI [6.76, 14.87]), and 35.70 (95%CI [13.96, 57.45]), respectively. Also, the results of the meta-analysis showed that the pooled values of the odds ratio in the cross-sectional and cohort studies were 1.82 (95% CI [1.43, 2.21]) and 1.73 (95% CI [1.49, 1.96]), respectively. Totally, most studies indicated that various sources of occupational aerosol exposure significantly affected sleep among employees.

Sleep Medicine
Leary EB, Van Dongen HPA, **Drake C**, Bogan R, Jaeger J, Streicher C, and Tabuteau H. Daily solriamfetol improved performance on a memory and attention task in people with obstructive sleep apnea and excessive daytime sleepiness: a plain language summary. *Postgrad Med* 2025; 137(3-4):209-219. PMID: 40325548. Full Text

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What is this summary about?The SHARP study looked at the effects of a medication called solriamfetol in people with obstructive sleep apnea (sleep apnea for short) who were very sleepy during the day (called excessive daytime sleepiness) and had trouble with things like thinking, concentrating, and remembering (called cognitive impairment). In people with sleep apnea, breathing is regularly interrupted during sleep. This can lead to many problems, including excessive daytime sleepiness and cognitive impairment.In previous studies, people with sleep apnea and excessive daytime sleepiness who took solriamfetol felt more awake during the day compared with people who took an identical tablet with no medication (called a placebo). The SHARP study looked at the effects of solriamfetol on symptoms related to cognitive impairment. To avoid bias from people's personal feelings about their cognition, the cognitive function of people who participated in the study was measured by a cognitive performance test (called objective cognitive function). Subjective ratings were also used; these measured people's personal feelings about their cognitive function (called subjective cognitive function), the severity of their cognitive impairment, and their sleepiness during the day.What are the key takeaways?In the SHARP study, people had more improvement in their objective cognitive function when taking solriamfetol than when they took placebo, and this benefit lasted for 8 hours. People also reported that their subjective cognitive function had improved, their cognitive impairment was less severe, and their daytime sleepiness was better with solriamfetol. The most common side effects were nausea and anxiety.What were the main conclusions reported by the researchers?These findings show that solriamfetol can improve cognitive function in people with cognitive impairment related to sleep apnea and excessive daytime sleepiness.[Box: see text].

Sleep Medicine
Roehrs T, **Koshorek G**, **Sibai M**, **Tabor A**, **Bazan L**, and **Roth T**. A Mechanistic study assessing difficulty discontinuing chronic hypnotic use. *Psychopharmacology (Berl)* 2025; Epub ahead of print. PMID: 40342163. Full Text

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RATIONALE: The abuse liability of chronic hypnotic use remains a clinical concern. OBJECTIVES: This study assessed 1) whether there would be greater difficulty discontinuing chronic hypnotic use for people with insomnia and hyperarousal vs those with insomnia but without hyperarousal and 2) whether those seeking to discontinue chronic hypnotic use of the receptor non-specific hypnotic eszopiclone would have more difficulty than those discontinuing the receptor specific zolpidem XR. METHODS: DSM-V diagnosed insomnia participants, aged 23-61 yrs, (n = 41, 36 females), with no other sleep disorders, unstable medical or psychiatric diseases or drug dependency completed the trial. Following a screening nocturnal polysomnogram (NPSG) participants were randomized to zolpidem XR (12.5 mg), eszopiclone (3 mg), or placebo nightly for 6 months. After 6 months nightly use, over a 2-week discontinuation, they were instructed to discontinue their hypnotic use, but, if necessary, to self-administer before sleep either 1, 2, or 3 capsules, each packaged separately in envelopes labeled 1, 2, and 3, containing their assigned "blinded" medication or placebo. RESULTS: Over the 14 nights 21 participants took zero (51%) capsules and among the 20 taking capsules the median total number chosen was 3. Those people with insomnia and hyperarousal vs those with insomnia but not hyperarousal had more difficulty discontinuing chronic hypnotic use (aim 1) as did those using eszopiclone vs zolpidem or placebo (aim 2). CONCLUSIONS: Most subjects discontinued hypnotic use and among the few continuing to use their use declined from week one to week two of the discontinuation period.

Sleep Medicine
Roth T. Therapeutic Use of γ-Hydroxybutyrate: History and Clinical Utility of Oxybates and Considerations of Once- and Twice-Nightly Dosing in Narcolepsy: Clinical Utility of GHB in Narcolepsy: T. Roth. *CNS Drugs* 2025; 39:37-51. PMID: Not assigned. Full Text

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Sleep Medicine
Roth T, Dauvilliers Y, Bogan RK, Plazzi G, Gow M, and Black J. Effects of oxybate dose and regimen on disrupted nighttime sleep and sleep architecture: A Plain Language Summary. *Future Neurol* 2025; 20(1). PMID: Not assigned. Full Text

Sleep Medicine
Roth T, Thorpy MJ, Kushida CA, and Gudeman J. Efficacy of Once-Nightly Sodium Oxybate in Patients with Narcolepsy: Post Hoc Analyses of Sensitivity, Effect Size, and Numbers Needed to Treat from the Phase 3 REST-ON Trial: Efficacy of Once-Nightly Sodium Oxybate in Narcolepsy: T. Roth et al. *CNS Drugs* 2025; 39:61-70. PMID: Not assigned. Full Text

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Surgery
Aleissa M, **Drelichman E**, and **Bhullar J**. Ischemic Colitis and Small Bowel Ischemia in a Vaccinated Patient with Mild COVID-19 Infection: A Case Report. *Case Rep Gastroenterol* 2025; 19(1):335-339. PMID: 40351853. Full Text

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INTRODUCTION: COVID-19 infection can cause bowel ischemia, with an incidence ranging from 0.22% to 10.5. The COVID-19 vaccine reduces respiratory symptoms and the need for cardiopulmonary support. However, its effects on other manifestations, such as bowel ischemia, have not been extensively studied. Despite having mild respiratory symptoms and receiving three doses of the COVID-19 vaccine, our patient developed ischemic colitis after her first infection and small bowel ischemia following her second infection. CASE PRESENTATION: An 86-year-old woman presented to the emergency department (ED) with abdominal pain after a mild COVID-19 infection. She was admitted with ischemic colitis, but conservative treatment failed. In the operating room, her entire colon was found to be ischemic, necessitating a total colectomy with end ileostomy. Nine months later, she returned to the ED with mild respiratory symptoms and severe right upper quadrant pain. Imaging revealed pneumoperitoneum and a mid-abdominal abscess. An emergency laparotomy revealed small bowel perforation, with final histology confirming ischemia. The patient had received three doses of the COVID-19 vaccine and was on therapeutic anticoagulation for a history of pulmonary embolism. CONCLUSION: COVID-19 may increase the risk of bowel and colon ischemia even after vaccination. Patients presenting to the ED with severe abdominal pain and a recent COVID-19 infection should be carefully evaluated for ischemic events.

Surgery

Choi WJ, **Ivanics T**, Claasen M, Magyar CTJ, Li Z, Tabrizian P, Rocha C, Myers B, O'Kane GM, Reig M, Ferrer Fàbrega J, Holgin V, Parikh ND, Pillai A, Hunold TM, Vogel A, Patel MS, Singal AG, Tadros M, Feld JJ, Hansen B, and Sapisochin G. Direct-acting antivirals lower mortality and recurrence in HCV-related hepatocellular carcinoma post liver resection: A multicenter international study. *Surgery* 2025; 183:109396. PMID: 40334495. Full Text

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BACKGROUND: The impact of treatment on hepatitis C virus with direct-acting antivirals on 90-day postoperative outcomes, overall survival, and recurrence-free survival in patients after liver resection for

hepatocellular carcinoma is unknown. METHODS: We conducted a multicenter retrospective study. Adults who underwent liver resection for hepatitis C virus-related hepatocellular carcinoma between January 2000 and December 2018 were included from 7 international institutions. Groups included direct-acting antiviral treated, non-direct-acting antiviral treated, and untreated hepatitis C virus infection. We used a multivariable model to evaluate the association between receipt of preoperative direct-acting antivirals and 90-day postoperative major complications (Clavien-Dindo class ≥III). RESULTS: We identified 738 patients, including 206 (28%) direct-acting antiviral treated, 241 (33%) non-direct-acting antiviral treated, and 291 (39%) untreated patients. The sustained virologic response rate was 92% in the direct-acting antiviral and 71% in the non-direct-acting antiviral treatment groups. The median follow-up was 7.6 years (95% confidence interval 6.1, 8.6) after surgery for the entire cohort. Patients who received direct-acting antiviral therapy had better 5-year overall and recurrence-free survival than those without antiviral therapy (adjusted hazard ratio [95% confidence interval]: 0.26 [0.19, 0.35] and 0.52 [0.43, 0.64], respectively). Patients who received direct-acting antiviral therapy had better 5-year overall and recurrence-free survival than those who received non-direct-acting antiviral therapy (adjusted hazard ratio [95% confidence interval]: 0.49 [0.36, 0.66] and 0.78 [0.63, 0.96], respectively). There was no significant association between preoperative direct-acting antiviral therapy and 90-day postoperative major complications (adjusted odds ratio 0.34, 95% confidence interval 0.08, 1.01). CONCLUSION: Direct-acting antiviral therapy is associated with improved 5-year overall and recurrence-free survival, without significantly increased risk of 90-day postoperative complications, in patients undergoing liver resection for hepatitis C virus-related hepatocellular carcinoma.

Surgery

Gochi AM, Rafaqat W, Panossian V, Ghneim M, Anandalwar S, Argandykov D, Susai CJ, Alcasid NJ, Anderson GA, Ordoobadi AJ, Teicher EJ, Blake DP, Beaulieu-Jones BR, Sanchez SE, Guidry CA, Teixeira P, Meizoso J, Collie BL, McWilliam S, McGonagill P, Nitschke N, Kortlever T, Galet C, **Nefcy LA**, **Johnson JL**, DeWane MP, Cuschieri J, Himmler A, Rickard J, Gipson J, and Mendoza AE. Surgical Infection Society Multi-Center Observational Study: Empiric Anti-Fungal Coverage after Non-Colonic Gastrointestinal Perforation. *Surg Infect (Larchmt)* 2025; Epub ahead of print. PMID: 40358474. Full Text

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Background: Empiric anti-fungals are frequently administered in patients with non-colonic gastrointestinal (GI) perforations, but there is limited evidence of their benefit. We hypothesized that empiric anti-fungals would offer no clinical benefit compared with a standard course of antimicrobial therapy. Methods: This multi-center prospective cohort study included patients ≥18 years old undergoing operative management for non-colonic GI perforations across 15 centers between August 2021 and January 2024. The primary outcome was organ-space surgical site infection (SSI). We performed propensity score matching to adjust

for confounders and a backward stepwise regression model to identify predictors of an organ-space SSI. A subgroup analysis of spontaneous upper GI perforations was performed as well. Results: A total of 192 patients were included; 138 (71.88%) received empiric anti-fungal therapy, and 17.7% developed an organ-space SSI. Before matching, empiric anti-fungal use was frequent in critically ill patients although not associated with organ-space SSI. After matching, there were no differences in organ-space SSI (17.5% vs. 17.5%, p = 0.99). In multi-variable regression, American Society of Anesthesiologists physical status classification system (ASA) category 3 increased the risk of organ-space SSI (odds ratio [OR] 2.49, p = 0.04), whereas perioperative proton-pump inhibitor (PPI) use was protective (OR 0.15, p = 0.004). In the subgroup analysis (N = 150), empiric anti-fungal therapy did not reduce infection risk. Pre-operative shock increased the risk of organ-space SSI (OR 2.83, p = 0.04), whereas PPI use remained protective (OR 0.15, p = 0.01). Conclusion: Empiric anti-fungal use was not associated with reduced organ-space SSI, even after adjusting for confounders. Given the lack of benefit, we caution against the use of routine empiric anti-fungal therapy in non-colonic GI perforations.

Surgery

Gregg A, **Sly M**, **Lin M**, **Oluborode B**, **McFarlin K**, and **Arnold G**. Small Bowel Obstruction Secondary to Coiling of Gastric Electrical Stimulator Leads: A Rare Complication of Gastroparesis Management. *Radiol Case Rep* 2025; 20(8):4066-4070. PMID: Not assigned. Full Text

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Gastroparesis is a syndrome marked by delayed gastric emptying without mechanical obstruction, and surgical interventions such as gastric electrical stimulation (GES) are typically considered after conservative treatments fail. We present the case of a 53-year-old woman with idiopathic gastroparesis who had undergone GES placement 13 years prior and presented with three days of nausea, vomiting, and abdominal pain. CT imaging revealed a high-grade mechanical small bowel obstruction due to interval coiling and migration of the GES leads, which was confirmed intraoperatively; the patient underwent enterolysis, lead explantation, and placement of a new GES system. This case highlights a rare but serious complication of GES, with only three similar cases previously reported, and underscores the importance of recognizing lead migration as a potential cause of bowel obstruction. Clinicians, especially radiologists and surgeons, should closely assess for changes in lead position on imaging in symptomatic patients with implanted devices, as early diagnosis and intervention are critical to preventing severe outcomes such as bowel ischemia.

Surgery

Halloran PF, Chang J, Mackova M, Madill-Thomsen KS, Akalin E, Alhamad T, Anand S, Arnol M, Baliga R, Banasik M, Blosser CD, Böhmig G, Brennan D, Bromberg J, Budde K, Chamienia A, Chow K, Ciszek M, de Freitas D, Dęborska-Materkowska D, Debska-Ślizień A, Djamali A, Domański L, Durlik M, Einecke G, Eskandary F, Fatica R, **Francis I**, Fryc J, Gill J, Gill J, Glyda M, Gourishankar S, Gryczman M, Gupta G, Hruba P, Hughes P, Jittirat A, Jurekovic Z, Kamal L, Kamel M, Kant S, Kojc N, Konopa J, Lan J, Mannon RB, Matas A, Mazurkiewicz J, Miglinas M, Mueller T, Myślak M, Narins S, Naumnik B, Patel A, Perkowska-Ptasińska A, Picton M, Piecha G, Poggio E, Rajnochová Bloudíčkova S, Schachtner T, Shojai S, Sikosana ML, Slatinská J, Smykal-Jankowiak K, Solanki A, Veceric Haler Ž, Viklicky O, Vucur K, Weir MR, Wiecek A, Włodarczyk Z, Yang H, Zaky Z, Gauthier PT, and Hinze C. A cross-sectional study of the role of epithelial cell injury in kidney transplant outcomes. *JCI Insight* 2025; 10(10). PMID: 40232852. Full Text

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BACKGROUND: Expression of acute kidney injury-associated (AKI-associated) transcripts in kidney transplants may reflect recent injury and accumulation of epithelial cells in "failed repair" states. We hypothesized that the phenomenon of failed repair could be associated with deterioration and failure in kidney transplants. METHODS: We defined injury-induced transcriptome states in 4,502 kidney transplant biopsies injury-induced gene sets and classifiers previously developed in transplants. RESULTS: In principal component analysis (PCA), PC1 correlated with both acute and chronic kidney injury and related inflammation and PC2 with time posttransplant. Positive PC3 was a dimension that correlated with epithelial remodeling pathways and anticorrelated with inflammation. Both PC1 and PC3 correlated with reduced survival, with PC1 effects strongly increasing over time whereas PC3 effects were independent of time. In this model, we studied the expression of 12 "new" gene sets annotated in single-nucleus RNA-sequencing studies of epithelial cells with failed repair in native kidneys. The new gene sets reflecting epithelial-mesenchymal transition correlated with injury PC1 and PC3, lower estimated glomerular filtration rate, higher donor age, and future failure as strongly as any gene sets previously derived in transplants and were independent of nephron segment of origin and graft rejection. CONCLUSION: These results suggest 2 dimensions in the kidney transplant response to injury: PC1, AKI-induced changes, failed repair, and inflammation; and PC3, a response involving epithelial remodeling without inflammation. Increasing kidney age amplifies PC1 and PC3. TRIAL REGISTRATION: INTERCOMEX (ClinicalTrials.gov NCT01299168); Trifecta-Kidney (ClinicalTrials.gov NCT04239703). FUNDING: Genome Canada; Natera, Inc.; and Thermo Fisher Scientific.

Surgery

Madi M, **Araji T**, Hazimeh D, and Adra SW. Battle of the Bots: Assessing the Ability of Four Large Language Models to Tackle Different Surgery Topics. *Am Surg* 2025; Epub ahead of print. PMID: 40420550. Full Text

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Objective: Our study aims to compare the performance of different large language model chatbots on surgical questions of different topics and categories. Materials and Methods: Four different chatbots (ChatGPT 4.0, Medical Chat, Google Bard, and Copilot Ai) were used for our study. 114 multiple-choice surgical questions covering 9 different topics were entered into each chatbot, and their answers were recorded. Results: The performance of ChatGPT was significantly better than Bard ($P < 0.0001$) and Medical Chat ($P = 0.0013$) but not significantly better than Copilot ($P = 0.9663$). We also found a statistically significant difference in ENT ($P = 0.0199$) and GI ($P = 0.0124$) questions between each chatbot when we assessed their performances per surgical specialty. Finally, the mean scores of Bard, Copilot, Medical Chat, and ChatGPT 4.0 on the diagnosis questions were higher than those in the management questions. The difference was only statistically significant, however, for Bard ($P = 0.0281$).Conclusion: Our study offers insight into the performance of different chatbots on surgery-related questions and topics. The strengths and shortcomings of each can provide us with a better understanding of how to use Chatbots in the surgical field, including surgical education.

Surgery
Mohiuddin A, Hussain F, Denha E, **Schad C**, Antaki F, and Rifkin S. An Unexpected Twist: Sigmoid Volvulus Complicated by Peritoneal Metastases. *Cureus* 2025; 17(4):e82570. PMID: 40390728. Full Text

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Sigmoid volvulus is the mechanical torsion of the sigmoid colon, its mesentery, and blood supply around itself, resulting in luminal obstruction and colonic ischemia. Initial management typically involves endoscopic detorsion; however, patients with peritonitis or who fail endoscopic therapy warrant surgical intervention. This case illustrates the rare presentation of recurrent sigmoid volvulus, which was refractory to endoscopic detorsion due to complications of peritoneal metastases, which tethered the sigmoid into a torsed position, ultimately requiring surgical resection. This report emphasizes the need for tailored, collaborative approaches to managing sigmoid volvulus in patients with underlying malignancy.

Surgery
Winder GS, Arab JP, Goswami Banerjee A, **Bryce K**, Fipps DC, Hussain F, Im G, Omary L, Patel AA, **Patel S**, Rubman S, Serper M, Shenoy A, Suzuki J, Zimbrean P, **Brown K**, **Abouljoud M**, and **Mellinger JL**. From embedded interprofessional clinics to expanded alcohol-associated liver disease programs. *Liver Transpl* 2025; Epub ahead of print. PMID: 40359009. Full Text

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Hazardous alcohol use remains a major contributor to acute and chronic liver disease, while alcohol-associated liver disease (ALD) is a leading indication for liver transplantation. In recent years, embedded, interprofessional ALD clinics have improved access to alcohol use disorder care within hepatology and liver transplantation, but more work is needed to meet this challenge. The literature is lacking regarding scaling procedures to provide services for increasingly large ill patient populations. This article begins to fill this gap by describing "expanded ALD care": broad, innovative, longitudinal, interprofessional care delivery strategies surpassing standalone clinics. Drawing from analogous patient populations served by collaborative models in primary care and comprehensive eating disorder treatment, the expanded ALD care framework proposes practical strategies toward specific innovations: equipoise between biomedical and psychosocial care elements, increased clinician number and reach, long-term patient relationships, harm reduction and palliative care, outreach to external agencies and clinicians, and enhanced support for patients and families. The article also defines attributes of innovative healthcare systems that support expanded ALD care.

Urology

Bertini A, **Stephens A**, **Finocchiaro A**, **Silvia V**, **Arjun D**, Elnaz G, **Nicholas C**, Lughezzani G, Buffi N, Di Trapani E, Ficarra V, Briganti A, Salonia A, Montorsi F, Sood A, **Rogers C**, and **Abdollah F**. Association of Area of Deprivation Index With Active Surveillance (AS) Utilization and Adherence to as Guidelines: Results From a Contemporary North American Cohort. *Prostate* 2025; Epub ahead of print. PMID: 40326515. Full Text

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BACKGROUND: Active Surveillance (AS) for Prostate Cancer (PCa) requires regular follow-up, raising concerns that socioeconomic barriers may result in underutilization or decreased adherence to AS guidelines. We examined the relationship between socioeconomic factors, measured by the Area Deprivation Index (ADI), and AS habits in a contemporary North American cohort. METHODS: We included all the patients aged ≤ 75 years and diagnosed with low (ISUP GG = 1, PSA ≤ 10 ng/mL and cT1N0M0) and intermediate risk (ISUP GG = 2, PSA 10-20 ng/mL or cT2N0M0) PCa at Henry Ford Health (HFH) between 1995 and 2023. An ADI score was assigned to each patient based on their residential census block group, ranked as a percentile of deprivation relative to the national level. The higher the ADI, the more the area has a socioeconomic disadvantage. Logistic regression analysis tested the impact of ADI on AS utilization and adherence to AS guidelines. Only patients who underwent at least 1 PSA test per year and at least 1 biopsy every 4 years were considered as "adherent to guidelines". RESULTS: Our final cohort consisted of 4376 patients eligible for AS, 919 of whom actually underwent AS. Older patients (66 vs. 62 years, $p < 0.0001$) and those diagnosed in more recent years (2017 vs. 2010, $p < 0.0001$) had higher probability to undergo AS. Moreover, patients in the AS group more likely to be NHB (36% vs. 25%, $p < 0.0001$), had higher ADI score (61 vs. 55, $p < 0.0001$), more comorbidities according to Charlson Comorbidity Index (CCI) score, (19.5%% vs. 13.8%, $p < 0.0001$) and higher probability to harbor low risk PCa (65.7% vs. 26.6%, $p < 0.0001$), compared to patients who underwent active treatment. Among the 919 patients in AS, only 410 were "adherent to guidelines". Patients

following guidelines were more likely to be NHW (64.1% vs. 52.8%, $p < 0.003$), and had lower ADI percentile (55.5 vs. 66, $p < 0.0003$). Furthermore, AS patients managed according to the prevailing guidelines received more PSAs tests (1.8 vs. 0.8, $p < 0.0001$) and prostate biopsies (0.3 vs. 0.0, $p < 0.0001$) per year, thus reporting both higher upgrading rates during AS (35.6% vs. 23%, $p < 0.0001$) and an increased probability to undergo active treatment (48% vs. 27%, $p < 0.0001$). At MVA, patients with a higher ADI score reported higher probability to undergo AS (OR: 1.06, 95% CI: 1.02-1.10, $p = 0.004$), but at the same time they were less likely to follow AS' guidelines (OR: 0.94, 95% CI: 0.89-0.99, $p = 0.02$). CONCLUSIONS: Patients in the most deprived areas had a higher likelihood of undergoing AS but were more prone to receive guideline-discordant care. This should be taken into consideration by physicians when recommending AS for those men living in the least advantaged neighborhoods. Our study highlights the need for targeted community reforms to enhance proper and informed AS utilization among socioeconomically disadvantaged populations.

Urology

Biasatti A, Bignante G, Ditonno F, Veccia A, Bertolo R, Antonelli A, Lee R, Eun DD, Margulis V, **Abdollah F**, Yoshida T, Derweesh IH, Meagher MF, Simone G, Tuderti G, Bologna E, Mehrazin R, Rais-Bahrami S, Sundaram CP, Yong C, Minervini A, Mari A, Lambertini L, Ferro M, Singla N, Pandolfo SD, Amparore D, Checcucci E, Gonzalgo ML, Porter JR, Ghoreifi A, Contieri R, Perdonà S, Porpiglia F, Djaladat H, Ghodoussipour S, and Autorino R. New Insights into Upper Tract Urothelial Carcinoma: Lessons Learned from the ROBUUST Collaborative Study. *Cancers (Basel)* 2025; 17(10). PMID: 40427165. Full Text

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Upper tract urothelial carcinoma (UTUC) is a rare malignancy, representing only 5-10% of urothelial carcinoma. The mainstay of treatment for high-risk patients is radical nephroureterectomy. Given the aggressive behavior of this disease, additional treatments could be required perioperatively in terms of chemotherapy (CHT), either in a neoadjuvant or adjuvant setting. On the other hand, low-risk and selected cases can be managed with kidney-sparing surgery (KSS). The ROBotic surgery for Upper tract Urothelial cancer STudy (ROBUUST) is an ongoing international, multicenter registry of patients undergoing surgery for UTUC. After conducting a literature search in February 2025 using the MEDLINE (via PubMed) and Embase databases, we identified 14 studies based on the ROBUUST data analyses. There are several key topics concerning UTUC that remain under debate and were therefore addressed in these studies, focusing on preoperative evaluation and planning, surgical techniques and intraoperative procedures, additional perioperative treatments, and outcomes. The ROBUUST registry has served as a valuable source for a growing body of investigations focusing on various aspects of UTUC treatment planning, decision-making, and outcomes, providing innovative tools and enabling large-scale, novel analyses.

Urology

Cannarella R, Çayan S, Giulioni C, Çeker G, Singh K, Khalafalla K, **Rambhatla A**, Galstyan R, Ramgir-Naidu S, Hubbard L, Shamohammadi I, Kesari KK, Rao F, Subarmaniuan A, Kumar V, Putra DE, Moorthv D, Palani A, Dursun M, Pescatori E, Saleh R, Shatylko T, Atmoko W, Zini A, Shah R, and Agarwal A. Impact of Varicocele on Pregnancy and Live Birth Outcomes in Men with Clinical Varicocele Systematic Review of Controlled Studies. *World J Men Health* 2025:11. PMID: Not assigned. Full Text

Purpose: To investigate the impact of varicocele on pregnancy and live birth outcomes in men with clinical varicocele in controlled studies. Materials and Methods: A comprehensive literature search was conducted across the PubMed and Scopus databases using Boolean operators, covering all available records from each database's inception through June 30, 2024. The inclusion criteria focused on controlled studies that compared pregnancy-related outcomes-including pregnancy, miscarriage, and livebirth rates-between men with clinical varicocele and those without. These studies included participants attempting conception either spontaneously or through assisted reproductive techniques. Results: Out of 3,532 articles screened, only two controlled studies met the inclusion criteria. The findings revealed no significant differences between men with and without varicocele in terms of time to achieve pregnancy (5.3 vs. 5.4 months, respectively; p=0.92) or the proportion of men who had previously conceived with their partner (58.9% vs. 63.4%, respectively; p=0.47). However, a significant difference was observed in live birth rates, with men with varicocele showing a lower rate than those without (71.2% vs. 76.4%; p=0.04). Conclusions: The relationship between varicocele and conception remains contentious, primarily due to the limited number of controlled studies available for analysis. Despite an extensive systematic search for controlled studies comparing pregnancy-related outcomes in men with and without clinical varicocele, only two studies met the inclusion criteria. These studies showed no significant differences in time to achieve pregnancy or previous conception rates between the two groups. However, men with varicocele exhibited a slightly lower, statistically significant, live birth rate compared to men without varicocele. This highlights the need for further research on this topic to provide evidence-based guidance on the impact of varicocele on fertility outcomes.

Urology

Finocchiaro A, **Chiarelli G**, **Stephens A**, **Viganó S**, **Bertini A**, **Cusmano N**, Guivatchian E, **Dinesh A**, Ficarra V, Sorce G, Briganti A, Montorsi F, Salonia A, Lughezzani G, Buffi N, Sood A, **Rogers C**, and **Abdollah F**. Active Surveillance for Prostate Cancer in "Real-World" Setting: Exploring Racial Disparities. *J Racial Ethn Health Disparities* 2025; Epub ahead of print. PMID: 40425976. Full Text

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INTRODUCTION AND OBJECTIVES: Active surveillance (AS) is a safe management strategy for low-risk prostate cancer (PCa), but limited "real-world" data exist outside trial cohorts. This study investigates racial disparities in progression to treatment, upgrading, and prostate cancer-specific mortality (PCSM) in a real-world AS population, aiming to improve healthcare quality. METHODS: We retrospectively analyzed data from the Henry Ford Health System (1995-2023) for men diagnosed with PCa (Gleason Grade ≤ 2, ≤ cT2c, N0-M0, PSA ≤ 20 ng/ml, age < 76 years) and enrolled in AS with ≥ 1 post-diagnosis PSA or biopsy and ≥ 1 year follow-up. Non-Hispanic Blacks (NHBs) and Non-Hispanic Whites (NHWs) were included. Surveillance adequacy was defined as ≥ 1 PSA/year and ≥ 1 biopsy every 4 years. Competing-risk cumulative incidence and regression assessed disparities in progression to treatment, upgrading, and PCSM. RESULTS: Among 864 patients (38% NHBs, 62% NHWs), NHBs presented with more advanced disease, including higher rates of GG2 (29% vs. 18%, p < 0.001) and intermediate-risk PCa (39% vs. 32%, p = 0.04). Surveillance adequacy was lower in NHBs (38% vs. 50%, p < 0.001). NHBs progressed to treatment more frequently (45% vs. 36%, p < 0.001), with a 1.46-fold higher risk (95% CI: 1.14-1.87, p = 0.003). NHBs had no higher odds of upgrading but showed higher 10-year PCSM (5.6% vs. 1.4%) and 5.9-fold higher odds of PCSM (95% CI: 1.38-25.37, p = 0.01). CONCLUSIONS: NHBs under AS face more advanced disease, lower follow-up adequacy, higher progression to treatment, and elevated PCSM odds. Targeted strategies are needed to address these disparities and improve equitable PCa care.

Urology
Finocchiaro A, **Tylecki A**, **Viganò S**, **Bertini A**, Ficarra V, Di Trapani E, Salonia A, Briganti A, Montorsi F, Lughezzani G, Buffi N, Sood A, **Rogers C**, and **Abdollah F**. Socioeconomic disparities and bladder cancer stage at diagnosis: a statewide cohort analysis. *JNCI Cancer Spectr* 2025; Epub ahead of print. PMID: 40445186. Full Text

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BACKGROUND AND OBJECTIVE: Bladder cancer (BC) is the ninth most common cancer worldwide. Despite its prevalence, large-scale studies on the relationship between socioeconomic disparities and disease stage at presentation are lacking. This study examines the association between the Area Deprivation Index (ADI), a robust measure of socioeconomic status, and stage at diagnosis among BC patients. MATERIALS AND METHODS: Patients diagnosed with BC (Any T, N, M) from the Michigan Department of Health and Human Services (2004-2019) were retrospectively analyzed. ADI was assigned based on patients' residential census block group and stratified into quartiles, with the 4th quartile (ADI 75-100) representing the most deprived. Multivariable logistic regression tested the impact of ADI on advanced disease stages (≥T2, cN+, cM+). RESULTS: Among 29,010 patients, the majority were Non-Hispanic Whites (92%), males (75%), and residents in metropolitan areas (81%). Patients in

the 3rd and 4th ADI quartiles had higher rates of ≥T2 (22%, 24.5%) compared to the 1st and 2nd quartiles (18%, 19.5%) (p < .001), as well as increased rates of cN + (3.4%, 3.7%) and cM + (2.8%, 3.2%) (p < .001). Multivariable regression showed that each 10-unit rise in ADI increased odds of ≥T2 by 4% (95% CI 1.03-1.06, p < .001), cN+ by 4% (95% CI 1.01-1.07, p = .038), and cM+ by 6% (95% CI 1.02-1.09, p = .003). CONCLUSION: Higher ADI correlates with advanced BC stages at diagnosis. Addressing these disparities is essential to improve outcomes in BC care.

Urology
Hamoda T, Shah R, Mostafa T, Pinggera GM, Atmoko W, **Rambhatla A**, Al Hashimi M, Çayan S, Colpi GM, Alipour H, Ko E, Zini A, Dimitriadis F, Rashed A, Park HJ, Saleh R, Toprak T, Ryzhkov A, Kadioglu A, Kandil H, Kalkanli A, El-Sakka AI, Calik G, Falcone M, Elbardisi H, Arafa M, Ho CCK, Martinez MP, Binsaleh S, Motawi AT, Gherabi N, Tsujimura A, Taniguchi H, Kosgi R, Calogero AE, Shatylko T, Kim D, Thomas C, Tadros NN, Andreadakis S, Musa MU, Konstantinidis C, Preto M, Le TV, Khalafalla KM, Cannarella R, Bowa K, Balagobi B, Katz DJ, Nguyen Q, Tanwar R, Borges E, Jr., and Agarwal A. Global Andrology Forum (GAF) Clinical Guidelines on the Management of Non-obstructive Azoospermia: Bridging the Gap between Controversy and Consensus. *World J Men Health* 2025:16. PMID: Not assigned. Full Text

Purpose: Non-obstructive azoospermia (NOA), defined as the absence of sperm in the ejaculate due to testicular failure, is observed in 5% to 15% of infertile men and accounts for two-thirds of azoospermia cases. The management of NOA is marked by significant controversy and global variation in diagnostic and therapeutic approaches, highlighting the crucial need for well-designed and standardized clinical practice guidelines. We present comprehensive graded clinical practice recommendations and statements for diagnosing and treating NOA, aiming to establish standardized strategies that can glob-ally help guide practitioners in their practice. Materials and Methods: A comprehensive literature review was conducted to gather evidence on the epidemiological, di-agnostic, and therapeutic aspects of NOA. The Global Andrology Forum (GAF) recommendations were developed through the collaboration of a global panel of experts using the Delphi method and surveys to achieve consensus. Statements were graded according to the Oxford Centre for Evidence-Based Medicine "GRADE" classification as either "Strong" or "Weak." Statements receiving at least 80% expert consensus were graded as "Strong," while others were categorized as "Weak." Results: The GAF has formulated a total of 49 recommendations and statements on the diagnosis and treatment of NOA, in-cluding 21 for diagnosis and 28 for treatment. The recommendations and statements were evaluated and graded by a panel of 48 GAF experts from 25 countries worldwide. The majority of experts (60.5%) had more than 10 years of clinical experi-ence in managing NOA. Conclusions: The GAF guidelines address discrepancies in NOA management across diverse clinical settings and provide comprehensive graded recommendations to guide clinicians in its diagnosis and treatment. Developed and graded by a large worldwide panel of experts, the current guidelines present simplified, high-standard strategies that can be seamlessly inte-grated into the daily global practice, offering practitioners a clear framework for managing NOA.

Urology
Lewicki P, Ginsburg K, Meah S, Labardee C, Johnson A, **Abdollah F**, Hafron J, Semerjian A, Lane BR, and Borza T. Opioid prescribing patterns and post-prostatectomy readmission: data from a statewide quality collaborative. *Urology* 2025; Epub ahead of print. PMID: 40456453. Full Text

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OBJECTIVE: To explore whether post-radical prostatectomy (RP) opioid prescription is associated with hospital readmission, given that this may represent a potential means of reducing unplanned health service utilization. METHODS: The Michigan Urological Surgery Improvement Collaborative registry was queried for patients undergoing RP between 5/2018 and 10/2024 who completed a questionnaire on

number of post-RP opioid pills prescribed. Multivariable models were constructed to evaluate the relationship between either 1) the number of pills prescribed or 2) the provider's "default" prescribing practice and hospital readmissions. RESULTS: Of 2,656 patients with opioid prescription data, 77 were readmitted (rate: 2.9%). Unadjusted readmission rate by opioid prescription count was 2.1% for those receiving no pills, 3.0% for 1-6 pills, and 4.2% for >6 pills. Multivariable models demonstrated a significant association of opioid prescription (overall p=0.041; 0 pills [vs. >6 pills]: odds ratio [OR] 0.45, 95% confidence interval [CI] 0.24-0.84, p=0.012) and provider "default" prescribing practice (after switch to "opioid-free" [vs. before]: OR 0.53, 95% CI 0.29-1.00, exact p=0.0495) with readmission. CONCLUSIONS: Omission of post-RP opioid prescription is significantly associated with lower odds of readmission; a change in prescribing habits to "opioid-free" is associated with a decrease in readmission rate. Post-RP opioid prescription is an actionable target in the reduction of unplanned health service utilization.

Urology

Lewicki P, Ginsburg K, Mmonu N, Labardee C, Johnson A, **Peabody J**, Gadzinski A, Semerjian A, Borza T, Lane BR, and Krumm AE. What is lost in an average? Identifying distinct post-radical prostatectomy functional recovery profiles. *BJU Int* 2025; Epub ahead of print. PMID: 40374588. Full Text

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OBJECTIVE: To describe, via latent variable mixture modelling, distinct post-radical prostatectomy (RP) patient-reported outcome (PRO) recovery profiles, which are positioned to complement currently disseminated statistical averages for shared decision-making. PATIENTS AND METHODS: Patients undergoing RP and completing the 26-item Expanded Prostate Cancer Index Composite 12 months after surgery were identified from the Michigan Urological Surgery Improvement Collaborative data registry. Hierarchical cluster analysis and latent variable mixture modelling was applied to urinary incontinence (UI) and sexual function (SF) recovery scores, and final models chosen based on optimal performance. RESULTS: A total of 3956 patients comprised the study cohort. Three distinct UI profiles were identified with prevalence of 49%, 37% and 14% from best to worst recovery, respectively. Four distinct SF profiles were identified with prevalence of 14%, 24%, 42%, and 20%, from best to worst recovery, respectively. The last two SF profiles had similar function scores but differed based on perception of function being bothersome. Limitations include incomplete PRO capture, which may introduce bias. CONCLUSIONS: We identify distinct UI and SF recovery profiles and their prevalence from a large, prospectively maintained registry, potentially improving interpretability of PRO data for decision making.

Administration

Arena CJ, Vanhorn B, **Kenney RM**, **Parke DM**, **Suleyman G**, Davis SL, and **Veve M**. Oral Antimicrobial Therapy Offers in Hospitalized Persons Who Inject Drugs who Elect for Self-directed Discharge. *Open Forum Infect Dis* 2025; 12:S870. Full Text

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Background. Hospitalized Persons Who Inject Drugs (PWID) who elect for selfdirected discharge (SDD) are at an increased risk for poor infection outcomes, but there is limited guidance for infection management in this population. National PWID management guidelines suggest considering oral antimicrobial therapy offers (OATO) as soon as patients are clinically stable to avoid lack of antibiotic therapy at discharge. The study purpose is to evaluate infection management in PWID who elect for SDD and to identify characteristics associated with OATO. Variables Associated with Oral Antimicrobial Offers at Self-directed Discharge Methods. Retrospective cohort of hospitalized adult PWID with an injection drug use (IDU)-related infection who elected for SDD between 1/1/14-1/31/24 at Henry Ford Health in Michigan. Patients were excluded if they were hospitalized for < 24-hours or if antimicrobial treatment was completed prior to SDD. The primary outcome was the proportion of patients with OATO at or prior to SDD. Secondary outcomes at 30-days included retreatment, infection-related readmission, and allcause mortality. Results. 150 patients were included; 55 (37%) were OATO patients, 95 (63%) did not receive an offer. Most patients were white (118, 79%), had prior SDD (90, 60%), and were a median (IQR) age of 34 (30-44) years. Skin infections were most common (81, 54%). Patients that received a source control procedure (27 (49%) vs. 31 (33%), P=0.05) or care from a provider ≤10 years from terminal training (49 [89%] vs. 70 [74%], P=0.04) were more likely to receive an OATO. Patient outcomes were not different between the OATO and no offer groups: infection retreatment 19 (34%) vs. 32 (34%); infection-related readmission 14 (25%) vs. 31 (33%); and all-cause mortality 1 (2%) vs. 3 (3%). Characteristics associated with OATO were prescribing or continuing medications for opioid use disorder during hospitalization, infection source control, and care from providers ≤10 years post-terminal training; infectious diseases consultation had an opposite association (Table 1). Conclusion. Most hospitalized PWID with IDU-related infections with SDD did not receive an OATO. Early career providers more commonly offered oral antimicrobials in PWID with less complicated infection types. Standardizing OATO in PWID at risk for SDD should be considered as a future direction to improve health outcomes. (Table Presented).

Administration

Kenney RM, **Gunaga S**, **Cahill MM**, **Leman L**, **Beaulac-Harris A**, **Eriksson E**, **Geyer A**, **Shallal A**, **Stein TL**, **Mazzetti N**, **Kaiser K**, **Dubay J**, **Arthur A**, **Higginbottom M**, **Jayaprakash N**, **Dass S**, **Haddad A**, **Boxwalla A**, **Kaatz S**, **Tibbetts R**, **Veve M**, and **Suleyman G**. Are we there yet? The ongoing journey for improving management of asymptomatic bacteriuria. *Open Forum Infect Dis* 2025; 12:S1056-S1057. Full Text

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Background. Treating asymptomatic bacteriuria (ASB) with antibiotics contributes to preventable patient harm. This quality improvement study aimed to evaluate the effectiveness of ongoing diagnostic and antibiotic stewardship interventions in reducing unnecessary testing and treatment of ASB. Methods. This retrospective, cross-Sectional quality improvement study spanned from 1/2017-3/2024 at a five-hospital urban and suburban health system in Michigan. Interventions included i). Implementation of urinalysis with reflex to urine culture in 2/2019, with reflex criteria revised in 7/2022 to ≥ 10 WBCs; ii). Adoption of a urine culture hard stop after hospitalization day 3 (3/2021); iii). Introduction of an ASB progress note smart phrase and educational initiative via a 1-page handout and narrated slides in the first quarter of 2023. The primary endpoint was the proportion of patients with ASB who received antibiotic treatment, as defined by Vaughn et al JAMA Intern Med 2023. Secondary endpoints encompassed the number of provider smart phrase documentations; overall urine culture volume per year; proportion of all positive urine cultures representing ASB; and overall ASB antibiotic use, calculated as the ratio of ASB treated

with antibiotics to all positive urine cultures. Results. The annual volume of urine cultures decreased by approximately 25% (Figure 1), from 87,556 in 2017 to 65,955 in 2023. The percentage of positive cultures representing ASB is depicted in Figure 2. The ASB smart phrase was documented in the medical record of 233 patients over one year: 165 (71%) were women, with a median age of 72 [48, 82] years. Emergency medicine providers utilized the smart phrase most frequently (97/233, 42%), followed by consultants (79/233, 34%). Overall ASB antibiotic use ranged from 9.7-22.7% in Q1 2022 and declined to 4.5-7% in Q1 2024. The primary endpoint, the system-wide average treatment of patients with ASB, declined modestly over time, but improvements were inconsistent among hospitals (Figure 3). Conclusion. Ongoing interventions targeting diagnostic and antibiotic stewardship through educational efforts were associated with a reduction in testing and treatment of ASB. However, suboptimal treatment of ASB remain a concern.

Allergy and Immunology

Gaberino CL, Dill-McFarland K, Bacharier LB, Gill M, Stokes J, Liu AH, Cohen R, Kumar R, Lang A, Hershey GKK, Sherenian M, **Zoratti EM**, Teach S, Kattan M, Becker PM, Togias A, Busse WW, Altman MC, and Jackson DJ. Effects of Mepolizumab and Systemic Corticosteroids on Airway Gene Expression Patterns Post-exacerbation in Urban Children With Asthma. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

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Rationale: Systemic corticosteroids are standard-of-care treatment for asthma exacerbations; however, little is known about whether corticosteroid effects on airway inflammatory pathways differ when added to biologic therapies targeting type 2 inflammation. Methods: 290 urban children (6-17 years) with exacerbation-prone eosinophilic asthma were randomized (1:1) to q4 week placebo or mepolizumab injections added to guideline-based care for 52 weeks. Nasal lavage samples were collected at baseline (before treatment), post-exacerbation (5-10 days after starting systemic corticosteroids), and on treatment for RNA-sequencing. Differentially expressed genes (DEGs) were assessed using mixed effects modeling (significance threshold FDR<0.05). Results: 98 participants were evaluated following 170 exacerbation events (placebo:105, mepolizumab:65). In the placebo group, there were no significant differentially expressed genes comparing on treatment to before treatment timepoints. In the placebo group, there were 6363 significant DEGs (2734 increased, 3629 decreased) comparing post-exacerbation to on treatment. In the mepolizumab group, there were 1404 significant DEGs (664 increased, 740 decreased) comparing on treatment to before treatment (Fig1A: x-axis). In the mepolizumab group, there were 1111 significant DEGs (413 increased, 698 decreased) comparing post-exacerbation to on treatment (Figure 1A: y-axis). In the post-exacerbation versus on treatment contrasts, there were 885 overlapping significant DEGs (348 increased, 537 decreased) between the placebo and mepolizumab participants. Mepolizumab reduced expression of eosinophil-associated genes (CCL23, GATA1, CLC, PRSS33, PTGDR2, ADORA3, THBS4) on treatment, with a larger decrease post-corticosteroid (more reduced than placebo) (FDR<0.05) (Fig1B). Mepolizumab did not significantly alter expression of mast cell/T2 cytokine-related genes (HDC, CPA3, GATA2, TPSAB2, IL5, IL13, IL1RL1, ALOX15) on treatment; however, expression of these genes significantly decreased post-corticosteroid (more reduced than placebo) (FDR<0.05) (Fig1B). Mepolizumab increased expression of genes associated with epithelial and airway inflammation (CFTR, ERBB2, BMP3, TRPV4) on treatment; however, expression of these genes returned to baseline levels post-corticosteroid (FDR<0.05) (Fig1B). Conclusions: By comparing differential gene expression across treatment groups and time points, we identified overlapping DEGs related to systemic corticosteroid effects, DEGs related only to mepolizumab treatment, and clusters of functionally related genes with additive effects of mepolizumab plus systemic corticosteroids. Mepolizumab enhances the

actions of oral corticosteroids on eosinophil related pathways in relation to exacerbations. Oral corticosteroids provide the added benefit of down-regulating mast cell and T2 cytokine pathways. Finally, oral corticosteroids reverse the up-regulation of epithelial inflammatory pathways that occurred during mepolizumab treatment.

Allergy and Immunology

Noorduyn S, **Baptist AP**, Germain G, Klimek J, Laliberté F, Schell RC, Forero-Schwanhaeuser S, Moore A, and Paczkowski R. Exacerbation Reduction in Patients With Asthma Following Initiation of Fluticasone Furoate/Umeclidinium/Vilanterol (FF/UMEC/VI) in the United States. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

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Rationale: In the United States (US), up to 50% of patients with asthma remain uncontrolled despite adherence to inhaled corticosteroid/long-acting β2-agonist (ICS/LABA) dual therapy, requiring escalation to triple therapy.Although the efficacy of fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) triple therapy has been demonstrated in clinical trials, real-world evidence on the clinical and economic benefits is sparse.This study evaluated the impact of FF/UMEC/VI on patients with asthma previously on ICS/LABA. Methods: This was a retrospective, longitudinal, pre-post claims study using Medicaid, commercial, and Medicare insurance data from the Komodo Health database. Data were collected from September 9, 2019, to December 31, 2023; the index date was the first pharmacy claim for FF/UMEC/VI. Eligible patients were adults with asthma with ≥12 months of continuous insurance coverage prior to and following the index date (pre- and post-initiation periods) who received ICS/LABA for ≥30 consecutive days during the pre-initiation period. Outcomes assessed included asthma-related exacerbations, oral corticosteroid (OCS) use, short-acting beta-agonist (SABA) use, asthma-related healthcare resource utilization (HRU, emergency department [ED] visits), and asthma-related medical costs. Odds/rate ratios (ORs/RRs; 95% confidence intervals [CIs]) of asthma-related exacerbations were compared pre-initiation versus post-initiation using logistic/Poisson regression models. OCS bursts, SABA canisters, and HRU were analyzed using Poisson regression models (RRs [95% CIs]); asthma-related medical costs were compared pre-initiation versus post-initiation using mean differences from generalized linear models. Results: Of 17,959 eligible patients, mean (standard deviation) age was 50.6 (14.1) and the majority were female (68.2%, n=12,240). Odds of any asthma-related exacerbations were significantly reduced by 52% post- versus pre-initiation (OR [95% CI]: 0.48 [0.46, 0.50], p<0.001); rates were reduced by 38% (RR [95% CI]: 0.62 [0.61, 0.64], p<0.001) (Figure). Rates of OCS bursts were 30% lower (RR [95% CI]: 0.70 [0.69, 0.72], p<0.001), SABA use 18% lower (RR [95% CI]: 0.82 [0.81, 0.83], p<0.001), asthma-related ED visits 39% lower (RR [95% CI]: 0.61 [0.58, 0.64], p<0.001) (Figure), and asthma-related medical costs 46% lower (mean difference [95% CI]: −$1115 [−$1771, −$459], p<0.001) post- versus pre-initiation. Conclusions: Significant reductions in asthma-related exacerbations, as well as lower OCS and SABA use, and reductions in asthma-related ED visits and medical costs were associated with the post-initiation period of FF/UMEC/VI treatment compared with the pre-initiation period. This provides novel, real-world evidence of the benefits of escalation to FF/UMEC/VI from ICS/LABA therapy in patients with asthma in the US, helping to inform treatment decisions in real-world clinical practice.

Anesthesiology

Kapur N, **Birk NK**, **Jayaprakash R**, **Khalil B**, **Singh R**, **Hanna ZW**, **Ramesh M**, and **Alangaden GJ**. Infectious Complications Following Lung Transplant for COVID-19 Related Respiratory Failure. *Open Forum Infect Dis* 2025; 12:S1339-S1340. Full Text

N. Kapur, Henry Ford Hospital, Detroit, MI, United States

Background. Lung transplantation (LT) is a potentially life-Saving treatment option for COVID-19 related irreversible respiratory failure. Early outcomes for 1-year survival and graft failure rates among LT recipients (LTr) for COVID-19 related respiratory failure is similar to LTr for non-COVID etiologies. However, the infectious, real-world analysis of complications following LT among LTr for COVID-19 related respiratory failure in comparison to LTr in COVID-19 unrelated respiratory failure has not been described. Our objective was to compare the post-LT infectious complications among LTr for COVID-19 related and unrelated respiratory failure. Methods. We analyzed all consecutive LT done at Henry Ford Health System from January 2020 to October 2023. All patients received standard antimicrobial prophylaxis. Demographic data was obtained. The primary outcome was the rate of any infectious complication within one year from transplantation. Secondary outcomes were rates of specific infections, time to infection, and all-cause mortality at 30 days, 90 days, and 1- year. Results. A total of 98 lung transplantations were done at our center from January 2020 to October 2023. COVID-19 related LTr accounted for 11% of transplants. Median time of follow up was 365 days (187-365). COVID-19 related LTr were younger (median 53 vs. 64 years [p 0.02]) and predominantly white race ($p < 0.01$). Comorbidities amongst both groups were similar. Rates of post-LTr infectious complications were similar among the two groups, 66% overall. Time to first infection was shorter in the COVID-19 related LTr cohort, however this did not reach significance. Pleuropulmonary infections predominated overall (47%). All-cause post-LT mortality was similar in both groups (Table 1). Conclusion. Patients receiving LT for COVID-19 related respiratory failure have similar, high rates of infectious complications compared to patients with non-COVID-19 related etiologies, but mortality remains low. LT for COVID-19 related respiratory failure is an acceptable modality of treatment.

Behavioral Health Services/Psychiatry/Neuropsychology

Mahr G, **Reffi A**, **Jankowiak L**, **Moore D**, and **Drake C**. Emotional Dream Content of Acute Trauma Patients: Associations with Interpersonal Violence, Nightmares, and PTSD. *Sleep* 2025; 48:A509. Full Text

[Mahr, Greg; Jankowiak, Lily; Moore, David] Henry Ford Hlth, Detroit, MI USA; [Reffi, Anthony; Drake, Christopher] Henry Ford Hlth Syst, Candon, MI USA

Introduction: Dreams are involved in the processing of emotions and can serve as markers of emotional distress. The authors developed a rating scale for affect in dreams and applied it to an acute trauma population. Methods: We recruited 88 patients hospitalized within one week following traumatic injury (Mage = 39.53 ± 14.31 years, 67.0% male, 67.0% Black). Patients who recalled a dream since hospi talization recorded their dream (n = 43). An independent rater scored the dreams using a novel 33-item Affective Neuroscience Dream Rating Scale to indicate the presence of fear, rage, grief, seeking, care, play, and lust. We quantified the emotional valence of dreams by summing positive (seeking + care + play + lust) and negative emotions (fear + rage + grief) and explored their associations with interpersonal violence and clinical outcomes approximately one-month post-trauma. Results: The emotional valence of dreams across all patients was significantly more negative (M = 4.84 ± 2.91) than posi tive (M = 1.26 ± 1.16), p <.001. Experiencing negatively toned dreams was associated with increased odds of being hospitalized for interpersonal violence (OR = 1.45, p =.014, 95% CI = 1.08 – 1.96) and more severe acute stress symptoms (β = 0.36, p =.021), regardless of sex. Reporting more negatively toned dreams dur ing hospitalization prospectively predicted risk for trauma-re lated nightmares one month later (OR = 1.73, p =.045, 95% CI = 1.01 – 2.97), adjusting for time, and was prospectively associated with increased nightmare distress (r =.70, p <.001), night terrors (r =.37, p =.042), and PTSD status (r =.44, p =.033). The dreams of patients who went on to screen positive for PTSD one month after trauma were significantly more negative (M = 5.99) than patients without PTSD (M = 3.70), p =.038, ηp2 = 19, indicating a large effect. Conclusion: Negative affective tone in dreams immediately after trauma predicted subsequent nightmares and future PTSD and can provide a potential tool for assessing PTSD risk in acute trauma patients.

Cardiology/Cardiovascular Research

Anyanwu AC, D'Alessandro D, Patel P, Shudo Y, Daneshmand M, Chan J, Couper G, Esmailian F, Peltz M, Itoh A, Takeda K, Malyala R, Lozonschi L, Klein L, Pal J, Shah A, Ohira S, Meyer D, Kilic A, Pham D, Haft J, Kaczorowski D, Selzman C, Villavicencio M, Funamoto M, Goldstein D, Gruber P, Sun B, Kai M,

Skipper E, Salerno C, Pretorius V, Shaffer A, Sulemanjee N, Durham L, **Williams C**, Ikonomidis J, Stehlik J, Pinney S, Farr M, Milano C, and Schroder J. Organ Care System Heart Perfusion (OHP) Registry Annual Report 2024 - Donation After Circulatory Death (DCD) Donors. *J Heart Lung Transplant* 2025; 44(4):S667. Full Text

Purpose: DCD donation has significantly expanded the donor pool resulting in increased number of heart transplantations. In this study, we examine the outcomes of transplantation from donation after circulatory death (DCD) that used OCS comparing it with non-OCS DCD heart transplantations. Methods: DCD cohort from the OCS heart perfusion (OHP) registry constituted the OCS cohort. Organ Procurement and Transplantation Network (OPTN) database was used to identify DCD transplants from same centers during the same time period that were not supported on OCS, which constituted the non-OCS cohort. Donor and recipient characteristics and survival data was available from the OPTN database for both arms and these data were compared. OCS cohort was further analyzed by cases managed by the National OCS program (NOP) versus direct acquisition by the transplant center. Results: A total of 889 OCS DCD and 354 non-OCS DCD transplants were identified. The recipients in the OCS cohort were more likely to be on ventricular assist device at transplant (38.8% vs 28.2%), had longer distance between donor and recipient (449miles vs 304miles) and be in UNOS status 2 (45.8% vs 31.1%) and less likely to be in status 4 (20.4% vs 32.88%). The cross-clamp time duration on average was higher (379 min vs 226 min) and the ischemic time was shorter (112.7 min vs 226.8 min). Despite the recipient risk differences, 6-month and 1-year survival was similar in both cohorts (92.8% vs 92.5% and 90.4 vs 88.9%; p=0.844) Conclusion: OCS allows DCD hearts to be procured over longer distances, with longer cross-clamp times and also enables utilization for higher risk recipients, without compromise in 1 year post-transplant outcomes. OCS may, therefore, allow increased access to DCD transplantation, particular for the higher risk recipient and where the donor hospital is distant.

Cardiology/Cardiovascular Research

Fang JX. Fish and CHIP: Concurrent Percutaneous Left-Ventricular Thrombus Retrieval and Complex Coronary Intervention With Hemodynamic Support. *J Am Coll Cardiol* 2025; 85(15):S493-S495. Full Text

[Fang, Jonathan X.] Henry Ford Hosp, Northville, MI USA

A 77-year-old female with ACS, LM-triple vessel disease, LVEF 20% and a 1.8cm LVT(Figure 1), with prohibitive surgical risk and cardiac index of 1.5 L/min/m2 on inotropic support, was offered percutaneous coronary intervention (PCI) with concurrent thrombus aspiration with the AngioVAC system (AngioDynamic, USA) per heart team decision. Relevant Test Results Prior to Catheterization. ECG: TWI I, V5-V6, late precordial R transition. Echo: LVEF 20%. Apical aneurysm. 1.8 LV apical thrombus. Moderate mitral regurgitation. Relevant Catheterization Findings. Elevated filling pressures. RA 10mmHg PA 52/12 mmHg mean 32 mmHg, PCWP 28 mmHg Fick Cardiac output/index 2.6 / 1.5 Coronary arteriogram: LM bifurcation medina 1,1,1 disease mLAD subtotal occlusion pLCx 70-80% calcified lesion pRCA CTO, left-to-right collaterals. INTERVENTIONAL MANAGEMENT. Procedural Step. Right femoral vein access with a 26-French sheath with hemostatic valve (DrySeal, Gore Medical USA) preclosed with two proglides (Abbott Cardiovascular, USA) was obtained. Biradial accesses were used for cerebral embolic protection (figure 2, panel A). Transeptal puncture(B) and septostomy(C) followed by balloon-assisted tracking(D) brought a 22 French AngioVAC cannula into the left atrium (E), followed by mitral valve crossing to reach the LV apex via a Confida wire(G-I) (Medtronic, USA), followed by thrombectomy, all under transesophageal echocardiography (TEE) guidance (H-J). Blood was returned through an oxygenator into a 15 French cannula place in 16 French Dryseal sheath via right femoral artery access preclosed with proglides. After thrombectomy, the suction cannula was pulled back into the right atrium with the funnel retracted. At a flow rate of 3.5 liters-per-minute, it served as a venoarterial-extracorporeal membranous oxygenation (VA-ECMO) circuit (figure 3, panel A). Complex high-risk indicated PCI (CHIP) was performed via left femoral artery access to left anterior descending artery (LAD), left circumflex artery (LCx) and LM bifurcation (B-P) with good result on final angiogram (figure 4, panel A). Contrast echocardiography showed no further LV thrombus (B) and unchanged mitral regurgitation (C) after the thrombus was fished out (D). The patient recovered and was discharged. Conclusions. Acute coronary syndrome (ACS) with concurrent left main bifurcation disease, reduced left ventricular ejection fraction (LVEF) and left-ventricular thrombus (LVT) is a challenging situation where the micro axial flow pump for

supporting coronary intervention is contraindicated owing to embolic risk. Off-label AngioVAC use for concurrent left-sided thrombectomy and hemodynamic support for CHIP is possible. Operator proficiency with large bore access and careful cannula positioning to avoid suctioning is required.

Cardiology/Cardiovascular Research
Gulati G, McCallum W, Cantor R, Singletary B, Kirklin J, **Cowger J**, and Kiernan M. Pre-Implant Renal Function and Optimal Outcomes Among Older LVAD Recipients: An STS-INTERMACS Analysis. *J Heart Lung Transplant* 2025; 44(4):S447-S448. Full Text

Purpose: LVAD recipients are increasingly older and often also have renal dysfunction. For older patients, avoiding adverse events may be as or more important than survival, yet the demographics, comorbidity burden, and impact of renal dysfunction on the risk of sub-optimal outcomes in this population are not well understood. Methods: Using the STS-INTERMACS registry, we analyzed adult patients with INTERMACS profiles 3-7 receiving an isolated first HeartMate 3 LVAD between 6/1/2017 and 6/30/2022. Patients were divided into 3 age groups (<65, 65-70, and >70). To quantify the severities of different adverse events (AEs), we quantified the multivariable-adjusted association between important AEs and 3-year mortality. Regression coefficients were used as the score for each AE, with death assigned a score of 14 (greater than the sum of all individual AE scores, Figure). Patients were classified into outcome score groups at 3 years as follows: 0, alive without AEs; 1-3, alive with low AE burden; 3-<14, alive with high AE burden; 14, dead without AEs; >14, dead with any AEs. Patient characteristics were compared across age and outcome score groups. Results: 4880 patients were included (<65: 3113; 65-70: 767; >70: 1000). Patients <70 were more often white and male, had lower eGFR, and a higher prevalence of frailty compared with patients <65. 3-year survival was 78.3%, 68.6%, and 64.6%, respectively (p<0.001). Patients >70 were less likely to survive with low AE burden compared with patients <65 (62% vs 76%). Survival with low AE burden decreased with increasing age and with decreasing eGFR, with patients >70 and with eGFR<30 having the lowest likelihood of survival with low AE burden (33%, Figure). Conclusion: Older LVAD recipients are less likely to have an optimal outcome at 3 years compared with younger patients, especially those patients with impaired renal function. Understanding the interaction between age and renal function on adverse outcomes will be important to optimizing patient selection for LVAD therapy. [Formula presented]

Cardiology/Cardiovascular Research
Walji M, **Affas Z**, **Jacob C**, and **Arnautovic JZ**. Cardiac Critical Care in a Community Setting: Cardiologist-Led vs. Intensivist-Led Outcomes. *JACC Cardiovasc Interv* 2025; 18(4):2. Full Text

[Walji, Mohammed; Affas, Ziad; Arnautovic, Jelena Z.] Henry Ford Macomb Hosp, Clinton Township, MI USA; [Jacob, Chris] Ascens Macomb Oakland Hosp, Macomb, MI USA

Background: The complexity of cardiovascular conditions necessitates specialized cardiac care, yet current staffing models in many community settings lack dedicated critical care cardiologists. Globally, cardiologists specialized in critical care are more common and allow for expertise when managing conditions like acute coronary syndromes (ACS), severe heart failure, advanced cardiac life support, and life-threatening arrhythmias. There is growing recognition of the benefits of critical care cardiologists, especially as the population ages and the prevalence of complex cardiac cases increases. However, the US still lacks specialized programs that promote cardiologists in critical-care medicine. Objective: The study aims to assess two staffing models in cardiac critical care: cardiologist-led versus intensivist-led outcomes in response to the increased need for specialized critical care trained cardiologists. Methods: This is a retrospective review of patients admitted to the critical care unit in a community-hospital from March to November of 2022 who were admitted with a primary cardiac etiology. Non-cardiac and surgical patients were excluded. Cardiologists could choose to either admit the patients to their own service and consult an intensivist as needed such as in the setting of hypoxic respiratory failure where BiPAP/mechanical ventilation was used (collaborative model) or admit patients directly to an intensivist-led service (traditional model). Results: This study included 181 patients: 103 admitted to the intensivist-led model and 78 admitted to the cardiologist-led model. Both groups had similar demographics with no statistical significant difference in cardiac risk factors. The most common admitting diagnoses were ACS, structural heart diseases, and tachyarrhythmias. Overall, there was no statistical difference between

complications or outcomes (length of stay (LOS), mortality, or 30-day readmissions) among cardiologist-led teams and the traditional, intensivist-led model. Conclusion: Cardiologist-led critical care in collaboration with an intensivist is not inferior to the traditional model. The current workforce in community critical care units is not meeting consensus guidelines due to increasing complexities and interplay of medical and cardiovascular conditions requiring specialized care. This creates a unique opportunity for cardiovascular expertise through fellowship and training that can enhance the quality of care in critically-ill patients.

Clinical Quality and Safety

Alvi RBR, **Shanahan C**, **Ruby A**, **Chami E**, **Lanfranco OA**, and **Suleyman G**. Review of Post Cesarian Section Surgical Site Infections in a Tertiary Care Hospital. *Open Forum Infect Dis* 2025; 12:S352-S353. Full Text

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

Background. Surgical site infection (SSI) is one of the most common complications following cesarean section (CSEC), variably ranging from 3% to 18%, and adds a significant burden to the healthcare system. Given its substantial implications, developing strategies to prevent SSIs are essential. We aimed to explore factors associated with an increased risk of these infections. Methods. Retrospective observational study of post-CSEC SSIs from Jan 2021-Dec 2023 at Henry Ford Hospital in Detroit. SSIs were defined according to the National Healthcare Safety Network (NHSN) criteria. Cases were categorized as superficial incisional (SI), deep incisional (DI) and organ space (OS). Demographics, risk factors, clinical features, treatment, and outcomes were Results. 70 (3%) of 2,230 CSECs performed during the study period met criteria for post-CSEC SSI, of which 42 (60%) were SI, 4 (6%) DI, and 24 (34%) OS; 42 (60%) were emergency cases. The majority of patients were Black with mean age of 30.3 years (Table 1). Obesity (BMI >30), anemia (hemoglobin < 11), hypertension, prior abdominal surgery, Group B Strep colonization, and ruptured membranes at presentation were common. Most (86%) received perioperative antibiotics, and 69% were administered within 1 hour of incision; cefazolin was frequently used. Infection was diagnosed after a median of 11.5 days. Wound pain and drainage were the most prevalent symptoms. Manual chart review revealed 21% of cases did not have clinical symptoms or signs of infection. Cultures were obtained in 33% of patients, of which 91% were positive; common skin commensals were frequently isolated (Figure 1). Readmission was common, a quarter of patients required surgical intervention, and most cases were treated with antibiotics (Table 2). Complications included uterine dehiscence (9%) and half of these required hysterectomy.

Clinical Quality and Safety

Arena CJ, Vanhorn B, **Kenney RM**, **Parke DM**, **Suleyman G**, Davis SL, and **Veve M**. Oral Antimicrobial Therapy Offers in Hospitalized Persons Who Inject Drugs who Elect for Self-directed Discharge. *Open Forum Infect Dis* 2025; 12:S870. Full Text

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

Background. Hospitalized Persons Who Inject Drugs (PWID) who elect for selfdirected discharge (SDD) are at an increased risk for poor infection outcomes, but there is limited guidance for infection management in this population. National PWID management guidelines suggest considering oral antimicrobial therapy offers (OATO) as soon as patients are clinically stable to avoid lack of antibiotic therapy at discharge. The study purpose is to evaluate infection management in PWID who elect for SDD and to identify characteristics associated with OATO. Variables Associated with Oral Antimicrobial Offers at Self-directed Discharge Methods. Retrospective cohort of hospitalized adult PWID with an injection drug use (IDU)-related infection who elected for SDD between 1/1/14-1/31/24 at Henry Ford Health in Michigan. Patients were excluded if they were hospitalized for < 24-hours or if antimicrobial treatment was completed prior to SDD. The primary outcome was the proportion of patients with OATO at or prior to SDD. Secondary outcomes at 30-days included retreatment, infection-related readmission, and allcause mortality. Results. 150 patients were included; 55 (37%) were OATO patients, 95 (63%) did not receive an offer. Most patients were white (118, 79%), had prior SDD (90, 60%), and were a median (IQR) age of

34 (30-44) years. Skin infections were most common (81, 54%). Patients that received a source control procedure (27 (49%) vs. 31 (33%), P=0.05) or care from a provider ≤10 years from terminal training (49 [89%] vs. 70 [74%], P=0.04) were more likely to receive an OATO. Patient outcomes were not different between the OATO and no offer groups: infection retreatment 19 (34%) vs. 32 (34%); infection-related readmission 14 (25%) vs. 31 (33%); and all-cause mortality 1 (2%) vs. 3 (3%). Characteristics associated with OATO were prescribing or continuing medications for opioid use disorder during hospitalization, infection source control, and care from providers ≤10 years post-terminal training; infectious diseases consultation had an opposite association (Table 1). Conclusion. Most hospitalized PWID with IDU-related infections with SDD did not receive an OATO. Early career providers more commonly offered oral antimicrobials in PWID with less complicated infection types. Standardizing OATO in PWID at risk for SDD should be considered as a future direction to improve health outcomes. (Table Presented).

Clinical Quality and Safety

Boettcher S, **Kenney RM**, **Arena CJ**, **Beaulac-Harris A**, **Tibbetts R**, **Shallal A**, **Suleyman G**, and **Veve M**. Say it Ain't Steno - Impact of a Microbiology Nudge Comment on Treatment of Respiratory Colonization. *Open Forum Infect Dis* 2025; 12:S1082. Full Text

S. Boettcher, Henry Ford Hospital, Royal Oak, MI, United States

Background. Stenotrophomonas maltophilia (SM) is a known colonizer of the respiratory tract, in which treatment is not required. Microbiological comment nudges have been successful as passive stewardship interventions. The study objective was to describe the effect of a targeted SM respiratory culture nudge on antibiotic use in patients with colonization. Methods. IRB approved quasi-experiment of adult patients with a SM respiratory culture between 01/01/2022-01/27/2023 (pre-nudge) and 03/27/2023-12/31/2023 (postnudge). Patients with criteria for active community/hospital/ventilator-acquired pneumonia or on targeted antibiotics prior to culture were excluded. Nudge comment implemented 2/2023: S. maltophilia is a frequent colonizer of the respiratory tract. Clinical correlation for infection is required. Colonizers do not require antibiotic treatment. The primary outcome was absence of SM therapy; secondary outcomes were SM therapy > 72 hours, hospital and ICU length of stay (LOS), and in-hospital all-cause mortality. Safety outcomes included antibiotic-related adverse events. Results. 94 patients were included: 53 (56.4%) pre- and 41 (43.6%) post-nudge. Most patients were men (53, 56.4%), had underlying lung disease (61, 64.8%), and required invasive ventilatory support (70, 74.5%). 11 (11.7%) patients were admitted from a long-term care facility. The absence of SM therapy was observed in 13 (23.1%) pre- vs 32 (78.0%) post-nudge patients (P< 0.001). There were no differences in SM therapy > 72 hours (36/40 [90%] vs. 8/9 [88.9%], P=1.0), mortality (11 [20.8%] vs. 7 [17.5%], P=0.69), median (IQR) hospital LOS (24 [10-49] vs. 16 [8-29]), P=0.37), and median (IQR) ICU LOS [15 [2-35] vs. 11 [3-25], P=0.40) between pre- and postnudge groups, respectively. Safety outcomes of patients treated > 72 hours (n=41); elevated SCr 12 (29.3%), fluid overload 18 (43.9%), hyponatremia 17 (41.5%), and hyperkalemia 5 (12.2%). After adjustment for confounders, post-nudge was associated with 11-fold increased odds of the absence of SM therapy (Table 1). Conclusion. A targeted SM nudge was associated with a reduction in treatment of SM colonization. Patient outcomes, including length of stay and all-cause mortality, were comparable between the two groups.

Clinical Quality and Safety

Cardenas-Maldonado DDD, **Chevalier T**, **Herc E**, **Lanfranco OA**, and **Suleyman G**. Unveiling Tuberculosis: A Perspective on Active vs. Subclinical Pulmonary Tuberculosis. *Open Forum Infect Dis* 2025; 12:S556. Full Text

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Background. Despite being preventable and curable, tuberculosis (TB) remains one of the world's leading infectious disease killers with 1.5 million people dying each year worldwide. The U.S. has one of the world's lowest rates of TB; however, cases increased 16% from 2022 to 2023. Although risk factors and outcomes associated with TB have been described, reports characterizing TB disease in the U.S. are limited. IQR: interquartile; USA: United States of America; BMI: Body Mass Index; HIV: human immunodeficiency virus; TNF-alpha inhibitors: Tumor necrosis factor-alpha inhibitors; TB: tuberculosis.

Methods. Retrospective case series of patients with TB disease at Henry Ford Health in Southeast Michigan from Jan 2019-Dec 2023. Demographics, risk factors, clinical manifestations, treatment, and outcomes were evaluated. Active and subclinical TB were compared. Active TB was defined as positive imaging and/or microbiologic assay with clinical TB-related symptoms, and subclinical TB as positive imaging and/or microbiologic assay without symptoms. AFB: Acid-Fast-Bacilli; MTB: Mycobacterium tuberculosis; PCR: polymerase chain reaction; IQR: interquartile; TB: tuberculosis; RIPE: Rifampin, Isoniazid, Pyrazinamide, Ethambutol; INH: Isoniazid; RIF: Rifampin. Results. 53 patients were included, of whom 18 (33%) were black and 34 (64%) were male with a median age of 55 years (Table 1). Almost half were born in the U.S., and a quarter lived in Detroit. Prior TB exposure (30%), international travel (21%), persons who inject drugs (23%), and incarceration (17%) were common risk factors. 47 (89%) patients had active TB, and cough (68%) was prevalent. Consolidation and nodular patterns were frequently seen on imaging; cavitation occurred in 42% of cases. All had sputum smear microscopy and culture ordered;MTB PCR was obtained in 72% of cases (Table 2). Both were more likely to be positive in those with active TB. Most patients required inpatient admission; median time to airborne isolation precautions was longer in the subclinical group. Length of stay was prolonged in both groups. All patients with active TB received treatment, whereas 83% were treated in the subclinical group. Most were treated for at least 6 months. Among those completing treatment, 68% achieved cure and 15% expired. Conclusion. In this large cohort of TB patients, almost half were US-born and a third had a known TB exposure. Although less common, subclinical TB contributed to 11% of cases. Despite treatment, clinical cure was suboptimal with a 15% mortality. Early recognition and treatment of latent and active TB are critical disease control and prevention strategies.

Clinical Quality and Safety

Hanna ZW, **Birk NK**, **Alangaden GJ**, **Suleyman G**, **Kaur J**, and **Ramesh M**. Comparison of Clinical Risk Factors, Outcomes and Molecular Epidemiology of ESBL and non-ESBL Enterobacterales Bacteremia in Solid Organ Transplant Recipients. *Open Forum Infect Dis* 2025; 12:S31-S32. Full Text

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

Background. Infections caused by extended-Spectrum beta-lactamase (ESBL)-producing Enterobacterales are associated with adverse outcomes in recipients of solid organ transplants (SOTr). This study aims to elucidate the risk factors, outcomes, and molecular epidemiology associated with ESBL Enterobacterales bacteremia (ESBL EB) in abdominal SOTr. Methods. This observational cohort study was performed on abdominal SOTr with ESBL EB (cases) and non-ESBL EB (controls) at Henry Ford Health between August 2014 and February 2023. We performed whole genome sequencing on all blood isolates; sequencing libraries were created using +QIAGEN QIAseq FX DNA Library Kit according to manufacturer's instructions and sequenced on Illumina NextSeq 2000. Fastq files were used to determine the distribution of traits and resistance genes using the 1928 Platform. Demographic, risk factors, clinical characteristics, outcomes and molecular sequence data were evaluated. Primary outcome was 30-day mortality. Results. 56 patients were included: 31 (55%) cases and 25 (45%) controls. Liver and kidney transplant recipients were 28 (58%) and 18 (32%). Median age was 65 years and 54% were female. Risk factors for ESBL EB included liver transplant recipients ($p < 0.001$), second surgery < 30 days ($p=0.01$), primary graft dysfunction ($p=0.02$), and acute rejection < 3 months prior to BSI ($p=0.001$) (Table 1). Both 30-day ($p=0.001$) and 90-day ($p=0.015$) mortality were higher in the ESBL EB group. ST131 (57%) and ST410 (21%) were the predominant sequence types identified in ESBL E. coli isolates. Among ESBL K. pneumoniae, ST16, ST39, ST45, and ST219 were common. Resistome analysis identified β-lactam mutations in all isolates (figure 1 and figure 2). Additional resistance genes that were not phenotypically expressed in ESBL isolates were identified. Conclusion. Our study demonstrates the high mortality associated with ESBL EB in SOTr and highlights the risk factors and molecular characteristics of these infections. Clinical significance of the additional resistance genes identified needs further investigation. These findings provide insights for targeted management strategies in this high-risk population.

Clinical Quality and Safety

Jagannathan M, **Jordan T**, **Kinsey D**, **Kenney RM**, **Veve M**, **Shallal A**, and **Suleyman G**. A Comparative Analysis of Clindamycin versus Linezolid as Adjunctive Anti-toxin Therapy for Invasive Group A Streptococcal Infections. *Open Forum Infect Dis* 2025; 12:S1028-S1029. Full Text

M. Jagannathan, Henry Ford Hospital, Detroit, MI, United States

Background. Group A Streptococcus (GAS) is an important pathogen that can cause life-threatening disease. Clindamycin (DA) and linezolid (LZD) have been used as adjunctive antitoxin (AT) therapy in high-inoculum GAS infections to inhibit bacterial protein synthesis. However, there is concern about DA efficacy in the era of increasing DA resistance, where LZD may have a role. We evaluated outcomes of patients with invasive GAS infection who received DA or LZD. Methods. Retrospective cohort study comparing patients with positive blood cultures (BC) for GAS from June 2013-Dec 2023 treated with DA or LZD ≥ 48 hours. We identified patients using a data query for positive BC for GAS through Microsoft SQL. Patients aged < 18 years, or those with polymicrobial bacteremia, receipt of both AT therapies, incomplete data, or enrolled in hospice/died within 48-hours of admission were excluded. Collected variables included: demographics, infection characteristics, microbiologic data, adjunct therapy (surgical, immunoglobulin), and clinical outcomes (treatment-associated adverse events, 30-day all-cause mortality and infection-related readmission). Results. 158 patients were included; 117 patients received DA and 41 patients LZD. Baseline characteristics were similar among groups except for chronic kidney disease, which was more common in the LZD group (Table 1). The most common clinical syndrome accompanying bacteremia in both groups was abscess/cellulitis; bone and joint infection was more prevalent in the LZD group. 55 (33.5%) of GAS isolates were DA resistant. There was no significant difference in severity of illness, surgical interventions, or duration of therapy between the two groups (Table 2). Duration of bacteremia was significantly longer in the LZD group. There was no significant difference in readmission (10.3% vs 12.2%, p=0.77) or all-cause mortality within 30 days (17.1% vs 7.3%, p=0.13) in the DA versus LZD groups. Treatment-associated adverse events were low across both groups [Figure 1]. Conclusion. Despite increasing DA resistance at our facility, there was no significant difference in outcomes between patients treated with LZD vs DA plus standard therapy, consistent with prior literature. Further studies are needed to determine optimal therapy for invasive GAS.

Clinical Quality and Safety

Jordan T, **Jagannathan M**, **Kinsey D**, **Kenney RM**, **Veve M**, **Suleyman G**, and **Shallal A**. Analyzing Trends and Outcomes of Clindamycin Resistant Invasive Group A Streptococci Infections. *Open Forum Infect Dis* 2025; 12:S937-S938. Full Text

T. Jordan, Henry Ford Hospital, Detroit, MI, United States

Background. Streptococcus pyogenes (Group A Streptococci; GAS) is a grampositive bacterium that is a leading cause of life-threatening infections. For invasive infections, IDSA recommends high-dose penicillin and clindamycin (DA). However, increasing resistance to DA has been reported. The aim of this study was to determine the prevalence of DA-resistant GAS and evaluate if DA resistance was associated with worse outcomes. Table Comparison of clindamycin susceptible and clindamycin resistant strains of invasive GAS infections Methods. This was a retrospective cohort study from June 2013 to December 2023 across a five-hospital health system in Southeast Michigan of patients with positive blood cultures for GAS who received DA for anti-toxin therapy identified through Microsoft SQL. Children, polymicrobial bacteremia, incomplete data, receiving linezolid empirically, or those who died within 48 hours of admission were excluded. Patients with DA susceptible (DA-S) GAS isolates were compared to patients with DA resistant (DA-R) GAS isolates. Variables included demographics, infection characteristics, microbiologic data, therapy, and clinical outcomes. Figure Cases of GAS bacteremia and percent of clindamycin resistant strains Results. 390 cases were reviewed, and 215 were included in the cohort study [Table]. There was no difference in age, sex, or race among the groups. People who use injection drugs (51.7% vs 48.3%, p=0.07), people experiencing homelessness (PEH; 63.2% vs 36.8%, p=0.001), and chronic hepatitis C infection (HCV; 54.2% vs 45.8%, p=0.007) were more prevalent in the DA-R group; chronic kidney disease was more frequent in the DA-S group (57.1% vs 42.9%, p=0.029). Uncomplicated SSTI was more common in the DA-S group (64.2% vs 35.8%, p=0.022). There was no

significant difference in the severity of illness, duration of bacteremia, surgical management, treatment duration, length of stay, readmission or mortality between the two groups. There was an increased incidence of invasive GAS infections beginning in 2022, and 50% of isolates were DA-R in 2023 [Figure]. Conclusion. Although there is an increase in DA-R in invasive GAS infections, there was no significant difference in outcomes among patients with DA-R and DA-S who received standard of care treatment in addition to DA antitoxin therapy. Further research is needed to determine the clinical significance of these findings to inform optimal therapy for these groups.

Clinical Quality and Safety

Kaur J, **Jagannathan M**, **Jordan T**, **Kinsey D**, **Truppiano M**, **Shallal A**, and **Suleyman G**. Genomic surveillance of invasive Streptococcus pyogenes in Metropolitan Detroit. *Open Forum Infect Dis* 2025; 12:S1094. Full Text

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

Background. Group A streptococcal (GAS) disease is a major problem worldwide and can cause both noninvasive and invasive disease, including necrotizing fasciitis, with significant morbidity and mortality. Overall, the number of invasive GAS infections has been increasing in the United States over the past decade, primarily in adults. We aim to characterize the genomic features of circulating GAS strains causing invasive disease. Table. Patient demographics and genomic characteristics Methods. We performed whole-genome sequencing (WGS) on clinically obtained GAS blood isolates at Henry Ford Health, a comprehensive, integrated, health care organization in Southeast Michigan from Jan 2017-Dec 2023. Sequencing libraries were created using the QIAseq FX DNA Library Kit (Qiagen, USA) according to manufacturer's instructions and sequenced on NextSeq 2000 (Illumina Sandiego, USA). Fastq files were used to determine the distribution of traits, virulence factors, and resistance genes using the 1928 Platform. Results. We sequenced unique isolates from 64 patients, of whom 38 (59%) were males with median age 57 years [Table]. Most isolates were from 2022 (25%) and 2023 (53%). Fifteen M protein (emm) serotypes and 19 sequence type (ST) were obtained from 64 characterized isolates. The most frequent emm lineages were emm1 (n=16) and emm12 (n=12), where most patients had skin and soft tissue infection. The predominant emm1 lineage belonged to ST28. None of the emm1 and emm12 isolates carried aminoglycoside, macrolides/lincosamides/streptogramines (MLS), or tetracycline resistance genes. All the emm11 and emm49 isolates exhibited erm(A) and tetracycline resistance genes. Streptococcal superantigen (SAgs) genes were frequently detected; streptococcal pyrogenic exotoxin (SPE)-G was the most detected SAgs (97%), followed by streptococcal mitogenic exotoxin (SME)-Z (75%). SPE-H and SPE-I were each found in 48% of the isolates. Conclusion. In our cohort of patients with invasive GAS, several SAgs were detected. SPE-A, SPE-G, SME-Z and SPE-J were most frequently found in emm1 lineages. However, there was no correlation between various clinical syndromes and the virulence genes identified. Continued genomic surveillance can help characterize features associated with emerging invasive strains to inform management and infection prevention strategies.

Clinical Quality and Safety

Kenney RM, **Gunaga S**, **Cahill MM**, **Leman L**, **Beaulac-Harris A**, **Eriksson E**, **Geyer A**, **Shallal A**, **Stein TL**, **Mazzetti N**, **Kaiser K**, **Dubay J**, **Arthur A**, **Higginbottom M**, **Jayaprakash N**, **Dass S**, **Haddad A**, **Boxwalla A**, **Kaatz S**, **Tibbetts R**, **Veve M**, and **Suleyman G**. Are we there yet? The ongoing journey for improving management of asymptomatic bacteriuria. *Open Forum Infect Dis* 2025; 12:S1056-S1057. Full Text

R.M. Kenney, Henry Ford Hospital, Detroit, MI, United States

Background. Treating asymptomatic bacteriuria (ASB) with antibiotics contributes to preventable patient harm. This quality improvement study aimed to evaluate the effectiveness of ongoing diagnostic and antibiotic stewardship interventions in reducing unnecessary testing and treatment of ASB. Methods. This retrospective, cross-Sectional quality improvement study spanned from 1/2017-3/2024 at a five-hospital urban and suburban health system in Michigan. Interventions included i). Implementation of urinalysis with reflex to urine culture in 2/2019, with reflex criteria revised in 7/2022 to ≥ 10 WBCs; ii). Adoption of a urine culture hard stop after hospitalization day 3 (3/2021); iii). Introduction of an ASB progress note

smart phrase and educational initiative via a 1-page handout and narrated slides in the first quarter of 2023. The primary endpoint was the proportion of patients with ASB who received antibiotic treatment, as defined by Vaughn et al JAMA Intern Med 2023. Secondary endpoints encompassed the number of provider smart phrase documentations; overall urine culture volume per year; proportion of all positive urine cultures representing ASB; and overall ASB antibiotic use, calculated as the ratio of ASB treated with antibiotics to all positive urine cultures. Results. The annual volume of urine cultures decreased by approximately 25% (Figure 1), from 87,556 in 2017 to 65,955 in 2023. The percentage of positive cultures representing ASB is depicted in Figure 2. The ASB smart phrase was documented in the medical record of 233 patients over one year: 165 (71%) were women, with a median age of 72 [48, 82] years. Emergency medicine providers utilized the smart phrase most frequently (97/233, 42%), followed by consultants (79/233, 34%). Overall ASB antibiotic use ranged from 9.7-22.7% in Q1 2022 and declined to 4.5-7% in Q1 2024. The primary endpoint, the system-wide average treatment of patients with ASB, declined modestly over time, but improvements were inconsistent among hospitals (Figure 3). Conclusion. Ongoing interventions targeting diagnostic and antibiotic stewardship through educational efforts were associated with a reduction in testing and treatment of ASB. However, suboptimal treatment of ASB remain a concern.

Clinical Quality and Safety
Kinsey D, **Jagannathan M**, **Jordan T**, **Kenney RM**, **Veve M**, **Shallal A**, and **Suleyman G**. Invasive Streptococcus pyogenes Infections: Is Anti-toxin Therapy Necessary? *Open Forum Infect Dis* 2025; 12:S582. Full Text

D. Kinsey, Henry Ford Hospital, Detroit, MI, United States

Background. Invasive Streptococcus pyogenes or group A Streptococcus (GAS) carries a high morbidity and mortality rate. In addition to penicillin, adjunct antitoxin therapy (AT) with linezolid or clindamycin is the standard of care. Although the use of AT is supported by in vitro data and observational studies, there are limited conclusive data supporting its efficacy in reducing GAS mortality. Our study aimed to compare clinical outcomes of patients receiving AT versus those who did not. Methods. This was a retrospective cohort study of hospitalized patients with positive blood cultures for GAS at our five-hospital system from June 2013 to August 2023. Patients were identified through Microsoft SQL Server. Patients who received AT therapy for > 48 hours were defined as the AT group; the control group did not receive AT therapy. Patients who received AT for < 48 hours were excluded. Collected variables included demographics, infection & microbiological characteristics, and clinical outcomes. Data was analyzed using SPSS. Results. 265 patients were included in the study of whom 179 (68%) received AT (Table 1). About half were female, and the median age was 58 years. Comorbidities were overall similar between the two groups. Persons who inject drugs or with chronic hepatitis C were more common in the control group. Abscess/cellulitis was the most common clinical syndrome in both groups. Shock requiring vasopressors, need for dialysis and mechanical ventilation, and toxic shock syndrome were prevalent in the AT group. There was no difference in the duration of bacteremia, clindamycin resistance, and management between the two groups except for receipt of intravenous immunoglobulin (IVIG), which was more common in the AT group (Table 2). Outcomes, including length of stay, readmission for infection-related complications, and 30-day mortality, were similar between the two groups. Conclusion. Utilization of AT for invasive GAS infections correlated with severity of illness, but clinical outcomes did not significantly differ between patients receiving AT and those who did not, suggesting a potential opportunity for antimicrobial stewardship. Further research is needed to determine whether AT should be reserved for patients with select infectious syndromes.

Clinical Quality and Safety
Malik A, Brar S, **Shallal A**, and **Suleyman G**. Risk Factors and Clinical Outcomes of Breast Surgery Related Surgical Site Infections in Southeast Michigan. *Open Forum Infect Dis* 2025; 12:S347. Full Text

A. Malik, Henry Ford Hospital, Warren, MI, United States

Background. Surgical site infections (SSI) after breast surgery are important healthcare-associated infections (HAI) that may delay initiation of chemotherapy for underlying malignancy, in addition to

accruing substantial healthcare costs. The reported incidence of breast surgery-related SSI (BSSI) ranges from 0.8%-26% depending on underlying comorbidities. We aimed to describe risk factors and clinical outcomes associated with BSSIs in southeast Michigan. Table 1. Characteristics of patients with breast surgical site infections Methods. Retrospective cross-Sectional study of adult patients with BSSI at a sixhospital healthcare system. Patients who met the definition of BSSI (per National Healthcare Safety Network) from 2021 to 2023 were included. Charts were reviewed for demographics, comorbidities, risk factors, microbiological data, and clinical outcomes. Table 2: Microbiological data of breast surgical site infections Results. A total of 146 patients were identified, of which 78 patients (53%) had clinical infection [Table 1]. Most of the patients were female (95%) and white (62%). Common comorbidities included obesity (36%), active breast cancer (55%), and diabetes mellitus (18%). Prior breast surgery (10%), chemotherapy within last 6 months (12%), and prior chest radiotherapy (9%) were less common. Mastectomy was the most common surgery (51%), often with lymph node dissection (46%), and many had artificial material placed (implant; 32% and tissue expanders; 18%). Only 88% of patients received peri-operative antibiotics, of which 72% received cefazolin. The most common microbes isolated were Staphylococcus aureus (24%), coagulasenegative Staphylococcus spp (23%), Streptococcus spp (19%) and Pseudomonas spp (19%). Most patients required repeat surgical intervention (81%), with hospitalization (59%) and removal of implants (45%). No patients died at 30 and 90 days after initial surgery. Conclusion. In this large study, BSSI was often associated with artificial material implantation, and Staphylococcus aureus was a common pathogen. Most patients required repeat surgical intervention and removal of implants. Significant opportunities were observed with surgical infection prophylaxis.

Clinical Quality and Safety

Malik A, **Shallal A**, **Ruby A**, **Malm J**, **McLenon J**, **Shanahan C**, **Chami E**, **Alangaden GJ**, and **Suleyman G**. Outcome of Candida auris Point Prevalence Survey in a Tertiary Care Hospital in Southeast Michigan. *Open Forum Infect Dis* 2025; 12:S337. Full Text

A. Malik, Henry Ford Hospital, Detroit, MI, United States

Background. C. auris, an emerging multi-drug resistant organism associated with nosocomial outbreaks, is becoming more prevalent in Southeast Michigan due to interfacility healthcare transfer. The CDC recommends contact isolation and screening of epi-linked healthcare contacts of newly identified C. auris patients to prevent spread and assess potential transmission. We describe our institution's experience with C. auris point prevalence surveys (PPS). Methods. PPS was conducted at an 877-bed academic, tertiary care center consisting of private and semi-private rooms in Detroit. In collaboration with Michigan Department of Health and Human Services, we performed PPS by swabbing the axilla and groin of all patients on the implicated unit when a C. auris index case was incidentally identified from June-Dec 2023. In addition, potentially exposed roommates were flagged in the electronic health record for future screening. When additional cases were identified, 2 negative PPS conducted biweekly were required to stop PPS. Results. Six C. auris index cases were identified during the 6-month period. We performed 18 PPS on 9 units and screened 430 patients (Table); 5 refused and 14 were discharged prior to screening. Four (22%) of the PPS resulted in identification of new cases; 2 PPS yielded 1 case each, 1 PPS yielded 3 cases, and the final PPS yielded 2 cases. Of those screened, 7 (1.6%) tested positive on 4 units. Nosocomial transmission was implicated in 4 patients across 2 units after an epidemiologic investigation. Terminal cleaning was performed on units implicated in nosocomial transmission, in addition to ancillary areas visited by the affected patients. Infection Prevention emphasized the importance of adhering to hand hygiene, appropriate PPE use, and cleaning and disinfection of the environment and shared equipment. Conclusion. Controlling the spread of C. auris is a public health priority. However, only 1.6% of cases were detected with intense PPS. Despite considerable effort and healthcare resources being utilized to identify additional cases and mitigate possible nosocomial transmission, C. auris continues to spread in our region. Alternatively, healthcare facilities should consider active surveillance of high-risk patients at the point of hospitalization to mitigate the need for PPS.

Dermatology

Bissonnette R, **Stein Gold LF**, Kircik L, Simpson E, Eichenfield LF, Browning J, Hebert A, A., Alexis AF, Soong W, Piscitelli SC, Tallman AM, Rubenstein DS, Brown PM, and Silverberg JI. Skin clearance, treatment response off-therapy, and safety of tapinarof cream 1% once daily: results from ADORING 3, a

48-week Phase 3 trial in adults and children down to 2 years of age with atopic dermatitis. *J Clin Aesthet Dermatol* 2025; 18(Suppl 1):S44. Full Text

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Introduction: In the ADORING 1 and 2 Phase 3 trials, tapinarof cream 1% (VTAMA®, Dermavant Sciences, Inc.) once daily (QD) demonstrated significant efficacy and was well tolerated in patients down to age 2 years with atopic dermatitis (AD). We present efficacy, safety, and tolerability outcomes from ADORING 3. Methods: Eligible patients from ADORING 1, ADORING 2, from a four-week maximal usage pharmacokinetics trial, and tapinarof-naive patients with mild AD, or moderate or severe AD, that did not meet inclusion criteria for ADORING 1 or 2, received tapinarof cream 1% QD for up to 48 weeks. Efficacy endpoints included achievement of complete disease clearance (Validated Investigator Global Assessment for Atopic Dermatitis™ [vIGA-AD™] score=0 [clear]), and clear or almost clear skin (vIGA-AD™=0 or 1). Safety and tolerability were assessed. Patients entering with vIGAAD™ ≥ 1 were treated with tapinarof until complete clearance (vIGA-AD™=0). Those entering with or achieving complete clearance discontinued tapinarof and were assessed for maintenance of clear or almost clear skin off-treatment (duration of treatment-free interval). Patients whose AD returned to mild (vIGA-AD™ ≥ 2) were re-treated until complete clearance was achieved. Results:
In total, 728 patients enrolled; 83.0 percent were pediatric (2–17 years). Overall, 51.9 percent (378/728) achieved complete disease clearance, and 81.6 percent achieved clear or almost clear skin at least once in the trial. Mean duration of first treatment-free interval was 79.8 consecutive days (standard deviation: 81.4 days). No tachyphylaxis on either continuous or intermittent therapy was observed for up to 48 weeks. Most frequent adverse events were folliculitis (12.1%), nasopharyngitis (6.9%), and upper respiratory tract infection (6.9%). Follicular events and contact dermatitis were mostly mild or moderate

and associated with low discontinuations (1.0% and 0.4%, respectively). Tapinarof was well tolerated locally, even when applied on sensitive skin. Conclusion: Tapinarof cream monotherapy demonstrated a high rate of complete disease clearance in patients down to age 2 years with AD. After discontinuing tapinarof, patients maintained clear or almost clear skin for 79.8 consecutive days. Tapinarof was well tolerated over 48 weeks.

Dermatology
Callender VD, Baldwin H, **Stein Gold LF**, Cook-Bolden FE, and Alexis AF. Efficacy and safety of fixed-dose clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel in hispanic participants with moderate-to-severe acne. *J Clin Aesthet Dermatol* 2025; 18(Suppl 1):S36-S37. Full Text

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Introduction: Acne vulgaris is a common dermatologic condition and a leading dermatologic diagnosis in Black and Hispanic patients. Topical clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% (CAB) gel is the only fixed-dose, triple-combination formulation approved for the treatment of acne. In three published clinical studies of participants with moderate-to-severe acne, CAB gel demonstrated superior efficacy to vehicle and component dyads, with good safety/tolerability. The objective of these analyses was to determine the efficacy, safety, and tolerability of CAB in Hispanic participants of these studies. Methods: In one Phase 2 (NCT03170388) and two Phase 3 (NCT04214652, NCT04214639) randomized, double-blind, 12-week studies, participants aged nine years or older with moderate-to-severe acne were randomized to once-daily CAB or vehicle gel. Endpoints included percentage of participants achieving treatment success (≥2-grade reduction from baseline in Evaluator's Global Severity Score [EGSS] and clear/almost clear skin) and least-squares mean percent change from baseline in

inflammatory/noninflammatory lesion counts at Week 12. Treatment-emergent adverse events (TEAEs) and cutaneous safety and tolerability were also assessed. Pooled data across all three studies were analyzed for participants who self-identified as Hispanic/Latino (herein referred to as Hispanic; n=90 CAB; n=57 vehicle gel). Results: At Week 12, over half of Hispanic participants achieved treatment success with CAB versus less than one-quarter with vehicle gel (56.2% vs. 18.4%; p<0.001). CAB treatment provided more than 75-percent reductions in inflammatory/noninflammatory lesion counts at Week 12 vs 56.4 percent and 45.0 percent, respectively, with vehicle (p<0.001, both). TEAE rates with CAB in the Hispanic population were similar to those in the overall study populations (27% vs. 24.6–36.2%). Most TEAEs were of mild-to-moderate severity, and discontinuations due to AEs were low (<4%). Mean cutaneous safety and tolerability scores (0=none to 3=severe) with CAB at all visits were less than one (mild), similar to the overall study populations. Hyperpigmentation scores decreased from baseline (0.6) to Week 12 (0.3) following CAB treatment. Conclusion: In Hispanic participants with moderate-to-severe acne treated with CAB, over half achieved treatment success and acne lesion reductions were reduced by more than 75 percent by Week 12, without any additional safety signals. These results, combined with those of previous post-hoc analyses in Black study participants, demonstrate that CAB is an efficacious, safe, and tolerable acne treatment for patients of different racial and ethnic groups.

Dermatology
Harper JC, Kircik LH, Gold M, Hebert AA, Sugarman JL, Green L, **Stein Gold L**, Baldwin H, Del Rosso JQ, and Guenin E. Early acne improvements with _ fixed-dose clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel: What to expect in the first 4 weeks of treatment. *J Clin Aesthet Dermatol* 2025; 18(Suppl 1):S36. Full Text

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Introduction: Treatments with fast and substantial acne clearance are highly desirable. While a three-pronged approach can increase treatment efficacy versus monotherapy or dual-combination therapy, it is unknown if triple-combination provides more rapid improvement. CAB gel—clindamycin phosphate (clin) 1.2%/adapalene 0.15%/benzoyl peroxide (BPO) 3.1%—is the first fixed-dose, triple-combination acne topical. Since rapid/substantial acne improvements and fewer side effects can increase adherence, the efficacy and safety of CAB in the first four weeks of treatment was evaluated. Methods: In a Phase 2 (N=741; NCT03170388) and two Phase 3 (N=183; N=180; NCT04214639; NCT04214652), double-blind, 12-week studies, participants aged nine years or older with moderate-to-severe acne were randomized to once-daily CAB or vehicle gel; the Phase 2 study included three additional dyad arms: BPO/adapalene; clin/BPO; and clin/adapalene. Efficacy assessments included least-squares mean percent change from baseline in inflammatory and noninflammatory lesions. Cutaneous safety/tolerability assessments were graded from 0=none to 3=severe. Post-hoc analyses included percentages of participants with one-third and one-half acne lesion reductions. Results: At Week 4, CAB led to approximately 55 percent reductions from baseline in inflammatory acne lesions in the ph2 and pooled ph3 studies, significantly greater than vehicle (~40%) and its three dyads (ph2 range: 44.2-47.6%; $p<0.05$, all). The percentages of participants with one-third and one-half reductions of inflammatory lesions were significantly greater with CAB than vehicle and dyads ($p<0.05$, all). Similar trends were observed for noninflammatory lesions, though reductions were less pronounced. As expected for retinoids, transient increases from baseline to Week 2 in scaling, erythema, itching, burning, and stinging were observed for CAB, BPO/adapalene, and clin/adapalene, with mean scores ≤ 0.6 (1=mild); no trends in dyspigmentation were observed. Mean scores for all cutaneous assessments were highest for BPO/adapalene, indicating that adding a third product in the fixed-dose CAB gel formulation did not worsen tolerability. Conclusion: Acne lesion reductions were significantly greater with clin 1.2%/adapalene 0.15%/BPO 3.1% gel versus its dyads and vehicle gel as early as Week 4. More rapid efficacy with this first fixed-dose triple-combination acne product—coupled with its optimized formulation, once-daily dosing, and tolerability—might positively impact treatment adherence.

Dermatology
Korman NJ, Passeron T, Okubo Y, Bagel J, Warren RB, Spelman L, Winthrop K, Hoyt K, Scharnitz T, Banerjee S, Thaçi D, Shahriari M, and **Stein Gold L**. Deucravacitinib in plaque psoriasis: laboratory parameters through 4 years of treatment in the Phase 3 POETYK PSO-1, PSO-2, and LTE trials. *J Clin Aesthet Dermatol* 2025; 18(Suppl 1):S48-S49. Full Text

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Introduction: Deucravacitinib, an oral, selective, allosteric tyrosine kinase 2 inhibitor, is approved in multiple countries for treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy. Deucravacitinib was efficacious versus placebo and apremilast and was well tolerated in the global, 52-week, Phase 3 POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) parent trials. At Week 52, patients could enroll in the ongoing POETYK long-term extension (LTE) (NCT04036435) trial and receive open-label deucravacitinib. Changes in blood laboratory parameters known to be associated with Janus kinase (JAK) 1,2,3 inhibitors were evaluated through four years of deucravacitinib treatment. Methods: Changes from baseline in lipid (cholesterol, triglycerides), chemistry (alanine aminotransferase [ALT], aspartate aminotransferase [AST], creatinine, creatine phosphokinase [CPK]), and hematology (hemoglobin, lymphocytes, neutrophils, platelets) parameters in the blood known to be affected by JAK1,2,3 inhibitors in clinical trials were evaluated through Week 208 (4 years; data cutoff, November 1, 2023). Treatment discontinuations due to laboratory abnormalities were assessed. Results: A total of 1,519 patients received at least one deucravacitinib dose (total exposure, 4392.8 person-years); 1,203 (79.2%) had at least 52 weeks and 542 (35.7%) had at least 208 weeks of continuous deucravacitinib exposure (median, 185 weeks). No trends or clinically meaningful mean changes from baseline were observed in any of the above laboratory parameters. In total, three patients discontinued treatment due to increased CPK, and one patient each discontinued due to lymphopenia, abnormal hepatic function, increased ALT, and increased AST. Discontinuations due to triglyceride elevations were not observed. Conclusion: In PSO-1/PSO-2/LTE, no trends or clinically meaningful mean changes from baseline were observed in lipid, chemistry, or hematology parameters, in contrast to signature changes (eg, increased cholesterol, creatinine, serum transaminases, CPK, cytopenias) observed with JAK1,2,3 inhibitors. Discontinuations due to laboratory abnormalities noted above were rare (n=7 events) through four years of deucravacitinib treatment. Results suggest deucravacitinib treatment does not warrant routine laboratory testing for all patients, in contrast with the requirements for JAK1,2,3 inhibitors, reflecting its selectivity for TYK2.

Dermatology
Silverberg JI, Ackerman L, Bagel J, **Stein Gold LF**, Blauvelt A, Rosmarin D, Chovatiya R, Zirwas M, Yosipovitch G, Waibel J, Murase JE, Lockshin B, Weisman J, Atwater AR, Harris C, Proper J, Silk M, Pierce E, Buziqui Piruzel ML, montmayeur S, Schuster C, Zhong J, Rueda MJ, Pillai S, and Simpson E. Lebrikizumab improves atopic dermatitis and quality of life in patients with moderate-to-severe atopic dermatitis previously treated with dupilumab: Results from the ADapt trial *J Clin Aesthet Dermatol* 2025; 18(Suppl 1):S40. Full Text

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Introduction: ADapt (NCT05369403), an open-label, Phase 3b, 24-week study, evaluated the efficacy and safety of lebrikizumab (LEB) in patients with moderate-to-severe atopic dermatitis (AD) previously treated with dupilumab (DUPI). Patients must have discontinued DUPI due to inadequate response (non-response, partial response, or loss of response), intolerance or an adverse event (AE), or other reasons. Methods: Four or more weeks after discontinuing DUPI, patients received a 500mg LEB loading dose at baseline and at Week 2 followed by 250mg every two weeks through Week 16 (Q2W). At Week 16, responders (IGA 0 or 1 with ≥ 2-point improvement [IGA0,1] or EASI75 [primary endpoint]) received LEB 250mg once every four weeks (Q4W); other patients continued with 250mg Q2W. Q2W and Q4W data were pooled and analyzed as-observed and with nonresponder/multiple imputation (NRI/MI). Results: Among 86 enrolled patients, 56 percent discontinued DUPI due to inadequate response, 16 percent due to intolerance/AEs to DUPI, and 28 percent for other reasons. For all patients, at Weeks 16 and 24, respectively, proportions of patients achieving: 1) EASI75: 57.4 percent and 60.0 percent, as-observed; 50.7 percent and 52.8 percent NRI/MI; 2) IGA0,1: 38.7 percent and 38.2 percent, as-observed; 35.6 percent and 36.8 percent, NRI/MI; 3) Face-IGA 0: 42 percent and 49 percent, as-observed; 4) Pruritus NRS ≥ 4-point improvement 53.2 percent and 61.5 percent as-observed; 48.8 percent and 47.9 percent NRI/MI; and 5) DLQI ≥ 4-point improvement 83.0 percent and 83.0 percent as-observed. The safety profile was consistent with other LEB Phase 3 trials. Four patients who discontinued DUPI due to conjunctivitis did not report conjunctivitis with LEB. Additionally, 3.5 percent of patients reported treatment-emergent conjunctivitis. Conclusion: In DUPI-experienced patients, treatment of moderate-to-severe AD with LEB resulted in meaningful improvements in skin clearance, itch, and quality of life.

Diagnostic Radiology
Torpoco Rivera DM, Sehgal S, Blake J, Sassalos P, **Marin HL**, and Al-Ahmadi M. Beating the Odds: Successful Same-Day Thrombectomy and Heart Transplant in a Pediatric VAD Patient. *J Heart Lung Transplant* 2025; 44(4):S334. Full Text

Introduction: Thromboembolic strokes (TS) impose a significant challenge in managing pediatric patients on ventricular assist devices, often leading to neurological impairment and jeopardizing heart transplant (HT) candidacy. We present the case of a young male with dilated cardiomyopathy (DCM) supported by an Impella device who underwent successful same-day mechanical thrombectomy and HT. Case Report: A 47 Kg, 13-year-old male with DCM and Klinefelter syndrome presented with worsening heart failure symptoms and severely depressed left ventricular (LV) function. After failing to wean off inotropes, an

Impella 5.5 left ventricular assist device (LVAD) was implanted. He developed de novo HLA antibodies (cPRA of 78%), significantly limiting the donor pool. After 27 days post-LVAD, a donor became available that had no HLA incompatibility. While undergoing donor evaluation, the patient developed acute right facial droop, right-sided weakness, and aphasia, with low-flow Impella alarms. CT angiography confirmed complete occlusion of the left middle cerebral artery (MCA). Stroke team was activated and he underwent mechanical thrombectomy resulting in complete restoration of MCA flow and immediate resolution of neurological symptoms. A multidisciplinary team assessed the risks and benefits of proceeding with HT given the risk of intracranial hemorrhage related to hemorrhagic transformation of the stroke following mechanical thrombectomy versus deactivation from the transplant list. Given the high PRA and potential delay in finding another suitable donor, a decision was made to proceed with HT. The patient underwent successful HT the same day. At 8 months post HT, he has achieved near complete recovery of neurological deficits. Summary: TS in pediatric VAD patients can lead to delays in HT candidacy or ineligibility due to the risk of hemorrhagic conversion and irreversible damage. Timely multidisciplinary decision making for intervention enabled successful neurological recovery and successful HT. [Formula presented]

Diagnostic Radiology

Zahedi S, Khazmi I, **Binette M**, and **Rezik M**. TB or Not TB: Two Unique Cases of Pleural Tuberculosis in Immunocompetent Hosts. *Am J Respir Crit Care Med* 2025; 211:1. Full Text

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A 36-year-old male (JF) who recently immigrated from Venezuela presented to the emergency department with a one-week history of nonproductive cough, fever, and night sweats. His roommate had been diagnosed with tuberculosis (TB). Chest X-ray revealed a large right-sided pleural effusion without parenchymal disease. JF was placed in isolation, but multiple attempts to obtain an induced sputum sample were unsuccessful. A Quantiferon-TB Gold test was positive, and a chest CT confirmed no parenchymal disease. The diagnosis of pleural TB was made based on pleural fluid analysis, which was exudative per Light's criteria and positive for adenosine deaminase (ADA), although acid-fast bacilli (AFB) testing was negative. He was discharged without airborne precautions and started on RIPE therapy. Two weeks later, JF's other roommate, a 35-year-old male (CG), presented with similar symptoms. CG's Quantiferon-TB test was also positive. He produced two sputum samples, which were AFB-negative but positive for Mycobacterium tuberculosis (mTB) PCR. Imaging revealed a large exudative pleural effusion, although ADA testing was not obtained, and pleural fluid AFB cultures were negative. Both patients had shared exposure to the same source and were HIV-negative. Despite their similar symptoms and pleural effusions, JF had isolated pleural TB, while CG had both parenchymal and pleural TB. JF's case is significant due to its rarity; isolated pleural TB constitutes only 5-10% of TB cases and usually arises from hematogenous or lymphatic spread. It is more common in younger patients or those with HIV, none of which applied to JF. Diagnosing pleural TB can be complex and typically requires a positive mTB PCR or ADA in pleural fluid; if both are negative, a pleural biopsy showing caseating granulomas and AFB positivity is necessary. Simultaneous parenchymal and pleural TB, as in CG's case, occurs in only 5-30% of TB cases and is often linked to a high disease burden or immunocompromised status. These atypical presentations emphasize the need for clinical vigilance and a thorough understanding of pleural TB's diagnostic challenges. Early recognition and treatment are essential to improve outcomes and prevent complications such as residual parenchymal fibrosis and increased relapse risk.

Emergency Medicine

Kenney RM, **Gunaga S**, **Cahill MM**, **Leman L**, **Beaulac-Harris A**, **Eriksson E**, **Geyer A**, **Shallal A**, **Stein TL**, **Mazzetti N**, **Kaiser K**, **Dubay J**, **Arthur A**, **Higginbottom M**, **Jayaprakash N**, **Dass S**, **Haddad A**, **Boxwalla A**, **Kaatz S**, **Tibbetts R**, **Veve M**, and **Suleyman G**. Are we there yet? The ongoing journey for improving management of asymptomatic bacteriuria. *Open Forum Infect Dis* 2025; 12:S1056-S1057. Full Text

R.M. Kenney, Henry Ford Hospital, Detroit, MI, United States

Background. Treating asymptomatic bacteriuria (ASB) with antibiotics contributes to preventable patient harm. This quality improvement study aimed to evaluate the effectiveness of ongoing diagnostic and antibiotic stewardship interventions in reducing unnecessary testing and treatment of ASB. Methods. This retrospective, cross-Sectional quality improvement study spanned from 1/2017-3/2024 at a five-hospital urban and suburban health system in Michigan. Interventions included i). Implementation of urinalysis with reflex to urine culture in 2/2019, with reflex criteria revised in 7/2022 to ≥ 10 WBCs; ii). Adoption of a urine culture hard stop after hospitalization day 3 (3/2021); iii). Introduction of an ASB progress note smart phrase and educational initiative via a 1-page handout and narrated slides in the first quarter of 2023. The primary endpoint was the proportion of patients with ASB who received antibiotic treatment, as defined by Vaughn et al JAMA Intern Med 2023. Secondary endpoints encompassed the number of provider smart phrase documentations; overall urine culture volume per year; proportion of all positive urine cultures representing ASB; and overall ASB antibiotic use, calculated as the ratio of ASB treated with antibiotics to all positive urine cultures. Results. The annual volume of urine cultures decreased by approximately 25% (Figure 1), from 87,556 in 2017 to 65,955 in 2023. The percentage of positive cultures representing ASB is depicted in Figure 2. The ASB smart phrase was documented in the medical record of 233 patients over one year: 165 (71%) were women, with a median age of 72 [48, 82] years. Emergency medicine providers utilized the smart phrase most frequently (97/233, 42%), followed by consultants (79/233, 34%). Overall ASB antibiotic use ranged from 9.7-22.7% in Q1 2022 and declined to 4.5-7% in Q1 2024. The primary endpoint, the system-wide average treatment of patients with ASB, declined modestly over time, but improvements were inconsistent among hospitals (Figure 3). Conclusion. Ongoing interventions targeting diagnostic and antibiotic stewardship through educational efforts were associated with a reduction in testing and treatment of ASB. However, suboptimal treatment of ASB remain a concern.

Emergency Medicine

Mann Y, **Hagerman T**, **Malick A**, Rao S, **Harris C**, **Santana-Garcés M**, **Manteuffel J**, **Gudipati S**, and **Brar I**. One Small Step for Man, One Giant Leap for Ending the HIV Epidemic. *Open Forum Infect Dis* 2025; 12:S411-S412. Full Text

Y. Mann, Henry Ford Hospital, Detroit, MI, United States

Background. To achieve the goal to End the HIV Epidemic by 2030, unique interventions are needed to increase testing and subsequently link people with HIV (PWH) to care for rapid start of antiretroviral therapy (ART). Extending testing to include emergency department (ED) based HIV screening initiatives are effective in new case identification, earlier detection, and are encouraged by Centers for Disease Control and Prevention guidelines. Collaborations of infectious diseases (ID) providers with ED providers provides improved linkage to care for HIV and rapid initiation of ART. We describe our combined ED and ID HIV testing and linkage to care program. Methods. This is a retrospective analysis of newly diagnosedPWHat Henry Ford Health (HFH) via reactive HIV fourth generation test by an ED based opt-out HIV screening program from 7/16/2020 - 10/28/2023. A best practice alert (BPA) prompted providers to order an HIV screening test for patients ages 18-65 years old without a previously documented HIV fourth generation test. Patients were informed of the test when ordered and could opt-out of testing if desired. Follow up and linkage to care was provided by a team of ID providers. Results. During the study period, a total of 48,725 fourth generation HIV screening tests were performed, of which 629 tests were reactive (1.24% of tests performed). Of the reactive tests, 86 patients (0.18% of all tests) were found to have a new diagnosis of HIV. Median CD4 cell count was 297 cells/mm3 (IQR: 98-614), 34 patients required hospitalization with 7 (8%) admitted with an opportunistic infection. Excluding the 34 patients hospitalized, the median time from positive result to first attended appointment was 5 days (IQR 2-13) and median time from screening test result to initiation of ART was 6.5 days (IQR: 4-16). At 3- or 6-months following HIV diagnosis, 40 (47%) had an HIV-1 follow-up viral load reported (see Table 1). Conclusion. HIV testing and early linkage to care are two key pillars of the End the HIV Epidemic initiative. As shown by our study, collaboration between ED and ID providers ensures increased testing in the ED, improved linkage to care, and rapid start of ART which will help in achieving the goals of these two pillars.

Family Medicine

Mann Y, Ogbenna UK, **Ishak A**, Kasmikha L, **Numi M**, **Iyer H**, **Rehman S**, Kadouh A, Mangal R, Qasawa A, Dehghani A, Hasso M, Henry J, **Santana-Garcés M**, **Rehman NK**, **Bryce R**, **Zervos M**, and **Joshi S**. Utilization of a Point-of-Care Hepatitis C Test to Treat in People Experiencing Homelessness with Street Medicine Outreach. *Open Forum Infect Dis* 2025; 12:S899. Full Text

Y. Mann, Henry Ford Hospital, Detroit, MI, United States

Background. Persons experiencing homelessness (PEH) have disproportionately higher rates of untreated chronic hepatitis C virus (HCV) than the public. Improved community funding and resources are needed to expand HCV rapid point-of-care (POC), confirmatory testing, treatment and follow-up. Given that PEH face competing priorities (unstable housing, food access, addiction, other infections), it is our role as clinicians to reduce barriers to HCV treatment, understand hesitancies for deferring treatment, and design programs to improve accessibility. This is the pilot project of a Street Medicine (SM) based initiative to use POC testing for HCV amongst PEH with linkage of care to a federally qualified health clinic (FQHC). Hepatitis C Screening and Treatment Protocol HCV- Hepatitis C Virus POC- Point of Care CHASS- Community Health and Social Services HbsAg- Hepatitis B Surface Antigen CBC- Complete Blood Count CMP- Complete Metabolic Panel Methods. SM provides medical care to PEH outside of a hospital setting. Medical students and residents were recruited to form a HCV outreach team at Henry Ford Hospital and trained in HCV testing via OraQuick rapid antibody (Ab) test. During SM outreach, PEH were provided education on HCV and offered POC testing with a $10.00 grocery gift card. If a patient was identified as HCV Ab positive they were provided free transportation to a FQHC for confirmatory testing. If diagnosis was confirmed, they were evaluated for eligibility for simplified HCV treatment, check-ins to assess adherence and sustained virologic response (Figure 1). Results. From February-April 2024, 103 PEH were tested using POC HCV testing on SM runs, with 4 positive results. 3 of 4 patients were confirmed for CHASS clinic appointments. 1 patient presented to clinic follow-up but deferred confirmatory testing bloodwork, demonstrating challenges in arranging for HCV clinic follow-up care. Conclusion. Previous studies have shown that lack of insurance, prior authorization and referral process, active injection drug use or alcohol use, lack of knowledge of HCV treatment, and limited healthcare workforce and infrastructure have all contributed to the low treatment rate in the homeless. Using trusted community organizations with SM, this initiative aims to reduce testing and transportation barriers in order to eliminate HCV in PEH. Larger numbers of positive patients are needed to best assess the feasibility of the program, and if providing all testing and treatment at the point of care is needed to improve compliance.

Gastroenterology

Levy C, Pratt D, Lammert C, **Gordon SC**, Li M, Forman L, Dean R, Yazdanfar M, Patel I, Bordia R, Cosar D, Specht K, Barry F, McLaughlin M, Mukherjee S, Gungabissoon U, and Bowlus CL. Serum levels of IL-31 and autotaxin are independently associated with pruritus severity in patients with primary sclerosing cholangitis. *J Hepatol* 2025; 82:2. Full Text

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Background and aims: Primary Sclerosing Cholangitis (PSC) is a chronic cholestatic liver disease with no approved treatment and few effective off-label therapies to reduce the symptom burden. We previously reported that over 1/3 of patients with PSC experience moderate-to-severe pruritus. However, little is known about biomar_kers of pruritus in patients with PSC. The aim of this analysis was to prospectively identify biomarkers of pruritus in PSC. Method: Patients aged 18 and older, diagnosed with PSC and

without a liver transplant were enrolled at 7 academic medical centers from July 2021 to March 2024. Itch numeric rating scale (NRS), 5-D Itch, PSC-PRO, and SF-36 were completed and serum collected at the time of enrollment. For the NRS, patients reported their average and worst itch (WI) in the past 24 hours, 7 days, and 6 months. Colitis activity was assessed in patients with inflammatory bowel disease (IBD) by the Simple Clinical Colitis Activity Index (P-SCCA). Total serum bile acids (TSBA), liver biochemistries, IL-31, and autotaxin were mea_sured. Spearman rank correlation, general linear models, and area under the receiver operator curve were used to examine the relationships between the WI in the past 7 days (WI-NRS) and serum biomarkers. Results: A total of 200 patients were enrolled (51% male; mean (SD) age of 44.6 (16.1) years; 71% White, 11% Black/African American; 15% cirrhosis). Most patients (77%) had large duct PSC while 4% had small duct PSC and 2% had PSC-AIH. IBD was present in 70% (50% ulcerative colitis/17% Crohn's disease/3% indeterminate). WI-NRS was reported as moderate or severe (WI-NRS 4–7 or 8–10, respectively) by 48 (24%). Alkaline phosphatase (ALP) (r = 0.26), GGT (r = 0.18), ALT (r = 0.15), AST (r = 0.20), total (r = 0.25) and direct bilirubin (r = 0.26), albumin (r = −0.18), total serum bile acids (r = 0.21), autotaxin (r = 0.28), and IL-31 (r = 0.40) all correlated with WI-NRS (all p-values <0.05). Among patients with IBD, P-SCCA also correlated with WI_NRS (r = 0.41, p < 0.0001). General linear modeling demonstrated that log AST (b = −3.2), log direct bilirubin (b = 1.4), log autotaxin (b = 1.9), and IL-31 (b = 0.6) independently associated with WI-NRS (all p_values <0.05). Among patients with IBD, log autotaxin (b = 4.0, p = 0.0006) and P-SCCA (b = 1.5, P = 0.002), but not IL-31 (b = 0.5, p = 0.15) remained independently associated with WI-NRS. The area under the receiver-operator curve (AUROC) for WI-NRS <4 vs ≥ 4 was 0.68 (0.57– 0.78) for autotaxin and 0.67 (0.56–0.79) for IL-31. Combining autotaxin and IL-31 did not improve the AUROC [0.70 (0.60–0.80)]. Conclusion: Both autotaxin and IL-31 independently associated with pruritus severity in patients with PSC. However, only autotaxin remained an independent predictor of pruritus severity after adjusting for colitis activity in patients with concomitant IBD. This study was supported by GSK (214524)

Gastroenterology
Tao M, **Lin CH**, Liu J, Chai W, **Gonzalez HC**, **Lu M**, and **Gordon SC**. Sex- and Race/Ethnicity-Specific Associations Between Food Insecurity and Metabolic Dysfunction-Associated Steatotic Liver Disease in American Adults. *Curr Dev Nutr* 2025; 9. Full Text

Objectives: The study aimed to examine the association between food insecurity and metabolic dysfunction-associated steatotic liver disease (MASLD) across different race/ethnicity or gender using the 2017-March 2020 National Health and Nutrition Examination Survey (NHANES). Methods: The current study included 6618 participants aged ≥19 years. Steatotic liver disease was determined through transient elastography examination. Odds ratios (ORs) and 95% confidence intervals (CIs) for MASLD associated with food insecurity were estimated using logistic regression. Results: Compared to full food security, very low adult food security was associated with increased odds of MASLD (OR=1.35, 95% CI, 1.05-1.73). There were associations of very low adult food security with higher odds of MASLD in women (OR= 1.82, 95% CI, 1.08-3.09) but not in men, with statistically significant interaction between adult food insecurity and gender (p interaction = 0.038). Similarly, the positive association of adult food insecurity with MASLD was mainly found in non-Hispanic Whites and other race, but not in non-Hispanic Black, Hispanic, and non-Hispanic Asian groups. Furthermore, mediation analyses suggested that added sugar intake and intake of whole fruits and vegetables excluding potatoes partially mediated the associations of adult food insecurity with MASLD. Conclusions: The positive association between food insecurity and MASLD might be dependent on race/ethnicity and gender. Increases in whole fruits and vegetables intake and reduction added sugar consumption may partially reduce the impact of food insecurity on MASLD development. Funding Sources: No.

Gastroenterology
Villamil A, Pratt D, Kremer AE, Calvaruso V, Gómez-Domínguez E, Qi X, Proehl S, Barchuk W, Watkins T, and **Gordon SC**. Efficacy and safety of seladelpar in patients previously treated with fibrates or OCA. *J Hepatol* 2025; 82:2. Full Text

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Background and aims: Seladelpar is a first-in-class delpar (selective PPAR-delta agonist) indicated for the treatment of primary biliary cholangitis in combination with ursodeoxycholic acid (UDCA) in patients (pts) with an inadequate response to UDCA or as monotherapy in pts unable to tolerate UDCA. RESPONSE was a Phase 3, randomised, placebo-controlled clinical trial of seladelpar in pts with inadequate response/intolerance to UDCA. Pts completing RESPONSE were eligible to roll over into ASSURE (NCT03301506), an ongoing, open-label, long-term, Phase 3 safety trial. Here we describe data from month 18 (month 6 of ASSURE) in pts with or without prior use of fibrates or obeticholic acid (OCA) who rolled over from RESPONSE into ASSURE. Method: Pts received 10 mg seladelpar orally daily or placebo in RESPONSE; pts received open-label 10 mg seladelpar in ASSURE. Fibrates and OCA were prohibited during the study period and a 6- week washout was required prior to entry in RESPONSE. Data are described for pts in ASSURE with or without prior use of fibrates/OCA and based on whether they received seladelpar (continuous seladel par pts) or placebo (crossover pts) in RESPONSE. Efficacy included the percentage of pts achieving a composite biochemical response (CBR; alkaline phosphatase [ALP] <1.67 × upper limit of normal [ULN], ALP decrease ≥15%, and total bilirubin ≤ULN). Safety assessments included adverse events (AEs) and laboratory parameters. Results: Among pts who continued into ASSURE from RESPONSE (158), 16 continuous seladelpar and 11 crossover pts reported prior use of fibrates/OCA (total, n = 27; 17%); 88 continuous seladelpar and 43 crossover pts reported no prior use of fibrates/OCA (total, n = 131; 83%). At month 18, among continuous seladelpar pts, 9/15 (60%) pts with prior fibrate/OCA use achieved a CBR vs 54/87 (62%) pts without prior fibrate/OCA use. Among crossover pts, 7/11 (64%) pts with prior fibrate/OCA use vs 32/41 (78%) pts without prior fibrate/OCA use achieved a CBR at month 6 of ASSURE. From ASSURE initiation to month 6, incidence of AEs was similar across continuous seladelpar and crossover pts, regardless of prior OCA/fibrate use; no treatment-related serious AEs were reported. Conclusion: In this interim analysis of continuous seladelpar and crossover pts from ASSURE, pts who reported prior use of fibrates/ OCA achieved a similar sustained biochemical response with seladelpar compared with pts who reported no prior use. Seladelpar appeared safe and well tolerated in this subgroup.

Hematology-Oncology

Alrawabdeh J, **Ghosh S**, Raslan S, Di Federico A, Ricciuti B, and **Abu Rous F**. Individual participant data meta-analysis comparing neoadjuvant to perioperative chemoimmunotherapy in early-stage non-small cell lung cancer according to PD-L1 status. *J Clin Oncol* 2025; 43:e20035. Full Text

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Background: Neoadjuvant and perioperative chemo-immunotherapy are two standard-of-care treatment options for patients with early-stage Non-Small Cell Lung Cancer, both of which improve event-free-survival (EFS). A recent reconstructed individual patient data (IPD) meta-analysis found no difference in EFS between these approaches. However, another patient-level analysis of CheckMate trails 816 and 77T reported that perioperative nivolumab significantly improves EFS, particularly in the PD-L1 negative subgroup. Our study aims to compare neoadjuvant and peri-operative chemo-immunotherapy based on PD-L1 status using reconstructed IPD. Methods: Data were collected from Kaplan-Meier curves of eight randomized trials, including five perioperative and three neoadjuvant trials. Only trials with Kaplan-Meier curves stratified by PD-L1 levels were included. Data extraction, IPD reconstruction, and survival analyses were conducted using the IPDfromKM tool. Patients were stratified according to their PD-L1 tumor proportion score (TPS) as negative (#1%), positive (1-49%) and high ($50%). Statistical comparison of EFS between the perioperative and neoadjuvant arms were performed across these

subgroups. Results: A total of 1656 participants were included in our analysis with 1420 patients in the perioperative arm and 236 in the neoadjuvant arm. A total of 447 EFS events were analyzed. The PD-L1 subgroups included 293 patients with negative PD-L1 (#1%), 269 with positive PD-L1, (1-49%), and 192 with high PD-L1 ($50%). No significant differences in EFS were observed between perioperative and neoadjuvant approaches among patients with any PD-L1 TPS (P=0.634) or within any PD-L1 subgroup (negative: P=0.449; positive: P=0.311; high: P=0.334). Conclusions: This reconstructed IPD meta-analysis found no significant difference in EFS between perioperative and neoadjuvant chemo-immunotherapy in ES-NSCLC, regardless of PD-L1 status. Treatment decisions should consider other patient-specific factors beyond PD-L1 status. Larger randomized trials are needed to further identify patients who may benefit from additional immunotherapy after surgery.

Hematology-Oncology

Gambardella V, Navarro A, Jain P, López-Picazo JM, Fernandez Hinojal G, Zugazagoitia J, de Miguel MJ, **Gadgeel SM**, Bhatti SA, Rocha P, Vilalta-Lacarra A, Rodrigo Imedio E, Micallef S, Wessen J, Dozio V, Frederiksen Franzen R, Bellon A, and Paz-Ares LG. Debio 0123, a highly selective WEE1 inhibitor, in combination with carboplatin (C) and etoposide (E), in patients (pts) with recurrent small cell lung cancer (SCLC): Determination of recommended dose (RD) from a phase 1 escalation. *J Clin Oncol* 2025; 43:8098. Full Text

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Background: Debio 0123 is an oral, brain-penetrant, highly selective WEE1 inhibitor. WEE1 inhibition leads to S phase and G2/M cell cycle checkpoint abrogation, allowing mitosis without DNA repair, leading to mitotic catastrophe and subsequent cell death. Debio 0123 is in clinical development in solid tumors, as monotherapy and in combination with different therapeutic agents. Debio 0123 has shown manageable safety profile and initial signals of antitumor activity. SCLC is an aggressive disease that carries a high mutational burden and genomic instability. Debio 0123 has shown to significantly improve the antitumor activity of DNA damaging agents, C + E, in preclinical SCLC models. Methods: This Phase 1 study (NCT05815160) is evaluating Debio 0123 in combination with C + E in pts with recurrent SCLC after first line of platinum-based chemotherapy. Of note, pts with stable brain metastasis were eligible. In the dose escalation, pts who had a chemotherapy-free interval (CFI).45 days since the last dose of platinum chemotherapy, received escalating doses of Debio 0123 (D1–3 and D8–10) in combination with standard C (AUC5) on D1 and E (100 mg/m2) on D1-3 in 21-day cycles. Results: Dose escalation data (cut-off date Oct 24th, 2024) are presented. Overall, 16 pts were treated (44% female, mean age 63.3 years). Using a Bayesian Logistic model-guided dose escalation, tested doses of Debio 0123 ranged from 200-400 mg. The RD was selected at 200 mg. At this dose level, 3/10 pts experienced a dose-limiting toxicity. The treatment was considered well tolerated with a manageable overall safety profile, in line with that expected for the chemotherapy combination. Most frequent Debio 0123 -related toxicities are shown in Table 1. PK data showed Debio 0123 plasma levels increasing proportionally with the dose. Debio 0123 CSF/ plasma ratio was ~40%, suggesting that Debio 0123 crosses the blood brain barrier. At 200 mg, confirmed partial responses (PR) occurred in 4/9 evaluable pts overall, and in 4/7 pts in the subgroup with CFI.90 days, including pt with intracranial response; 4 pts had SD of which 2 had tumor shrinkage of . 20 %. mPFS at the RD (n=10) was 7.2 months. Conclusions: Debio 0123 combined with C + E is well tolerated, with a manageable safety profile, up to 200 mg; this combination led to promising antitumor

activity in pts with recurrent SCLC after prior platinum-based therapy with CFI . 45 days. Further investigation of Debio 0123 at 200 mg in pts with a CFI . 90 days is ongoing. Clinical trial information: NCT05815160.

Hematology-Oncology
Hamilton EP, Han H, Abuhadra N, Kalinsky K, McAndrew NP, Spira A, Chan N, Kelley K, Parajuli R, O'Shaughnessy J, Starks D, Wulf G, **Weise AM**, Chaudhry A, Wang JS, Richardson DL, Meric-Bernstam F, Burger R, Bradshaw C, and Giordano A. 298MO Clinical activity of emiltatug ledadotin (Emi-Le), a B7-H4-directed ADC, in patients with TNBC who received at least one prior topoisomerase-1 inhibitor (Topo-1) ADC. *ESMO Open* 2025; 10(S4). Full Text

Background: Effective treatments for relapsed/refractory TNBC remain an unmet medical need. Standard-of-care single-agent chemotherapy has limited efficacy, with response rates of ~5%, PFS ~7 weeks. Emi-Le (XMT-1660) is a B7-H4-directed Dolasynthen ADC designed with a proprietary auristatin F-HPA microtubule inhibitor payload with controlled bystander effect. Methods: The Phase I trial is investigating Emi-Le monotherapy in adult pts with select advanced/metastatic solid tumors, including TNBC. In dose escalation, eligible pts received Emi-Le at doses of 7.2-115 mg/m2. Tumors were evaluated retrospectively by IHC for B7-H4 expression with a preliminary high cutoff set at tumor proportion score (TPS) ≥70. Results: As of Dec 13, 2024, 130 pts were dosed with 4.5 median prior lines of therapy. 63 pts had TNBC, with a median of 4 prior lines (range 2-9) and 92% having previously received ≥1 topo-1 ADC. Among all 130 pts, the most common TRAEs were transient AST increase (38%, G3 14%), proteinuria (31%, G3 9%), nausea (29%, G3 1%) and fatigue (28%, G3 0%). The only G3 TRAEs in ≥5% of pts were AST increase and proteinuria. No G4 or 5 TRAEs were reported. No observed dose-limiting treatment-related neutropenia, neuropathy, ocular toxicity, interstitial lung disease or thrombocytopenia. In the 13 evaluable pts with TNBC and high B7-H4 expression dosed at 38.1-67.4 mg/m2 per cycle, prior lines of therapy ranged 3-8, and all had previously received at least one topo-1 ADC. The confirmed ORR in this population was 23% (3/13). All 3 confirmed responders had reduction in target lesions of >60%. Of the 13 pts, 7 had received 3-4 prior lines; among these, the ORR was 29% (2/7). As of data cutoff, both responders were ongoing on treatment for >16 weeks. Conclusions: Based on the initial reported data, Emi-Le appears to have encouraging clinical activity and tolerability in a heavily pretreated TNBC population with high B7-H4 expression who had previously received topo-1 ADCs. Further clinical development of Emi-Le is ongoing in the expansion portion of the Ph1 trial at a dose of 67.4 mg/m2 Q4W in pts with advanced/metastatic TNBC who have received 1-4 prior lines of systemic therapy, including at least one topo-1 ADC. Clinical trial identification: NCT05377996.

Hematology-Oncology
Koussa K, **Nassif G**, **Clark J**, **Langley K**, **Kanumuri D**, **Murphy E**, **Cools KS**, **Shah R**, and **Kwon DS**. From disadvantage to advantage: closing the care gap in tertiary health care for vulnerable groups. *HPB (Oxford)* 2025; 27:S127-S128. Full Text

Background: Lower socioeconomic status (SES) has consistently been linked to worse cancer outcomes, including higher mortality rates and lower survival probabilities. The Area Deprivation Index (ADI), a validated measure of neighborhood-level SES, captures these socioeconomic disparities and gives us a better understanding of how social determinants of health impact cancer care and outcomes. Our Multidisciplinary Pancreas Clinic – comprising nurse navigation, medical, surgical, radiation oncologists, psychologists, and nutritionists – aims to provide equitable and efficient care to all patient demographics in our integrated health system. We sought to explore the association between neighborhood disadvantage and time between initial diagnosis and first consultation in patients diagnosed with Pancreatic Ductal Adenocarcinoma (PDAC) as well as clinical tumor staging at diagnosis. Methods: A retrospective analysis of PDAC patients diagnosed between 2016 and 2024 was conducted. To measure neighborhood disadvantage, the cohort was categorized into ADI quartiles: Q1 (1-25), Q2 (26-50), Q3 (51-75) and Q4 (76-100) with 1 and 100 being the least and most disadvantaged groups, respectively. Associations between ADI and time to first consultation (in days) and clinical tumor staging (categorized into localized (Stages I&II) and advanced (Stages III&IV) were studied using Logistic and Linear Regression Models. Results: 551 patients were diagnosed with PDAC between 2016 and 2024. 43 patients had an ADI in Q1 (7.8%), 120 in Q2 (21.8%), 176 in Q3 (31.9%) and 212 in Q4 (38.5%). The

mean age at diagnosis was 67.7 ± 10.2, the median ADI was 65, and the mean time to first consultation was 10.4 ± 6.3 days. 293 patients had localized disease at diagnosis (53.2%), while 258 had advanced disease (46.8%). In our institution, there was no significance in the time from diagnosis to consultation across the four quartiles of ADI. When evaluating ADI and its association with clinical stage at presentation, patients in Q4 (Adjusted OR: 0.51, 95% CI [0.26;0.98], p-value= 0.04) were less likely to present with advanced tumors when compared to those in Q1. Specifically, patients in Q1, Q2, Q3 and Q4 presented with stage IV disease in 34.9%, 28.3%, 25.0% and 22.2% respectively. Conclusion: Our data suggest that a dedicated multidisciplinary pancreas clinic in an integrated health care system can provide equitable access to care for patients newly diagnosed with PDAC. There was no difference in the time to first consultation, with results showing similar times for all ADI ranges and no statistical significance between the quartiles. These results highlight both the dedication of the healthcare team to provide equitable access to patients of all social determinants of health. Interestingly, we identified that patients who came from more disadvantaged neighborhoods (Q4) presented at earlier stages than those in Q1. Further analysis will be performed to assess such associations over time.

Hematology-Oncology

Nadal E, Rittmeyer A, de Marinis F, Lee DH, **Gadgeel S**, Vilariño N, Bria E, Arulananda S, Cronenberg EH, Antic V, Bennett E, Hu Y, Madden-Raja K, Williams P, Prizant H, and Popat S. A phase II trial of tobemstomig (tobe) plus platinum-based chemotherapy (chemo) vs pembrolizumab (pembro) plus chemo in patients (pts) with untreated locally advanced or metastatic non-small cell lung cancer (NSCLC). *J Thorac Oncol* 2025; 20(3):S11-S12. Full Text

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Background: Tobemstomig (tobe) is a novel bispecific antibody targeting programmed death-1 (PD-1) and lymphocyte-activation gene 3 (LAG-3). BO44178 (NCT05775289) is a randomised, double-blind, phase II study evaluating tobe + chemo vs pembro + chemo in pts with NSCLC who are ineligible for surgery or definitive chemoradiotherapy. Methods: Eligible pts with previously untreated, locally advanced unresectable or metastatic NSCLC were randomised 1:1 to receive either induction tobe + chemo (carboplatin + paclitaxel/pemetrexed) or pembro + chemo for four 21-day cycles, followed by maintenance tobe or pembro with/without pemetrexed every 3 weeks until disease progression, toxicity or loss of clinical benefit. Pts were stratified by PD ligand 1 expression, histology and smoking status. Primary endpoints: confirmed objective response rate (ORR); progression-free survival (PFS). Secondary endpoints included overall survival (OS), duration of response (DoR) and safety. Results: At data cutoff (20 June 2024), 181 pts were randomised to receive tobe + chemo (n = 90) or pembro + chemo (n = 91). Median duration of follow-up was 6 months. Baseline characteristics were similar across treatment arms; median age was 66 years. There was no improvement in confirmed ORR with tobe + chemo (41.1%) vs pembro + chemo (46.2%) and no PFS difference was observed between treatment arms (HR 0.99; 95% CI 0.63, 1.56; Table). OS data were immature at this analysis. Efficacy results were consistent across subgroups. The rates of grade 3/4 adverse events (AEs), serious AEs and immune-mediated AEs were higher with tobe + chemo vs pembro + chemo; however, the rate of treatment withdrawal due to AEs was similar between arms. Conclusions: At this interim analysis, no ORR or PFS benefit was observed in pts with untreated locally advanced or metastatic NSCLC receiving tobe + chemo over pembro + chemo. OS data remain immature.

Hematology-Oncology

Siqueira do Amaral P, Szabo A, **Hwang C**, Ghatalia P, Tripathi A, McManus HD, Emamekhoo H, King J, Maughan BL, Zakharia Y, Barata PC, Desai A, Reimers MA, Ged Y, Heath EI, Bilen MA, Brugarolas J, Rini BI, McKay RR, and Kilari D. Efficacy of subsequent treatment after combination therapy in non-clear cell renal cell carcinoma (nccRCC). *J Clin Oncol* 2025; 43(16_suppl):4545. Full Text

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Background: The treatment landscape of front-line nccRCC has evolved with recent trials demonstrating the efficacy of combination systemic therapy. However, the efficacy of treatment after combination therapy is unknown. This study evaluates the efficacy of VEGF-based regimens in nccRCC patients (pts) previously treated with combination regimens. Methods: ORACLE is a real-world, multi-center, retrospective database that includes nccRCC patients that received combination systemic therapies (IO+IO, IO+VEGF and VEGF+ mTOR) in any line. Subsequent treatments were categorized as VEGF only regimens (cabozantinib vs other VEGF), IO+ VEGF and VEGF+ mTOR. The primary endpoint was objective response rate (ORR) assessed by investigator review using RECIST 1.1. Secondary endpoints included disease control rate (DCR), defined as the proportion of patients achieving complete or partial responses or stable
disease, time to treatment progression (TTP), calculated from the date of VEGF-based initiation to progression or last follow-up using the Kaplan-Meier method. Differences between
groups were estimated with the log-rank test, and categorical outcomes were compared with
the chi-square test. Results: 105 pts who received VEGF – based regimens after combination therapy were included in the analysis. Baseline characteristics: median age: 59years, 71 % male, 58% white, 25% black, 87% ECOG 0-2. IMDC-risk categories included:21% favorable, 59% intermediate and 20% poor risk. Histology included papillary (40%), unclassified (32%), chromophobe (16%) and other rare subtypes (12%). Prior combination therapies included IO+IO: 62%, IO+ VEGF: 34% and VEGF+ mTORi:4%. 70% pts received combination therapy in the first line setting while the remainder received combination therapy in a second or later line. Outcomes with subsequent treatments are described in Table1. IMDC risk score correlated with TTP. Conclusions: Modest antitumor activity was observed with VEGF- based approaches in combination therapy refractory nccRCC. Optimal management of nccRCC remains an unmet need.

Hematology-Oncology

Wiesweg M, **Gadgeel S**, Cho B, Lu S, Felip E, Hayashi H, Spira A, Besse B, Thomas M, Owen S, Kim Y, Lee S, Mourao J, Lee Y, Zhao Y, Fang Y, Girard N, Liu Z, Sun P, Cunha Souza Oliveira S, Shen H, Paz-Ares L, Matsumoto S, Tanaka H, Ahmad A, Andabekov T, Sunpaweravong P, Özyilkan Ö, Yang J, Gottfried M, Hernandez O, Kimmich M, Cortinovis D, Kaen D, García Montes L, Popat S, Newsom-Davis T, Spigel D, Xie J, Sun T, Fennema E, Daksh M, Ennis M, Sethi S, Bauml J, and Nguyen D. Amivantamab Plus Lazertinib vs Osimertinib in First-line EGFR-mutant Advanced NSCLC: Longer Follow-up of the MARIPOSA Study. *Pneumologie* 2025; 79:S51-S52. Full Text

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Introduction: Amivantamab (ami) is an EGFR-MET bispecific antibody with immune cell-directing activity. Lazertinib (laz) is a CNS-penetrant 3rd-generation EGFR TKI. In the primary analysis of the phase 3 MARIPOSA study (NCT04487080), at a median follow-up of 22.0 months, ami plus laz significantly improved progression-free survival (PFS) by blinded independent central review vs osimertinib (osi) in patients with treatment-naïve, EGFR-mutated advanced NSCLC (HR, 0.70; 95 % CI, 0.58-0.85; P < 0.001). Early interim overall survival (OS) analysis showed a favorable trend for ami-laz over osi (HR, 0.80; 95 % CI, 0.61-1.05; P = 0.11). Here, we present updated results with longer follow-up from MARIPOSA. Methods: MARIPOSA randomized 1074 patients with treatment-naïve, EGFRmutated (Exon 19 del or Exon 21 L858R substitutions) locally advanced or metastatic NSCLC 2:2:1 to open-label ami-laz (n = 429), blinded osi (n = 429), or blinded laz (n = 216). This analysis, requested by health authorities, compares ami-laz with osi. Results: At a median follow-upof 31.1 months, 44 % (185/421) and 34 % (145/428) of patients were still on treatment in the ami-laz and osi arms, respectively. In total, 155 patients in the ami-laz arm and 233 in the osi arm had investigator-assessed progressive disease and discontinued treatment. Of those, 72 % (111/155) and 74 % (173/233) initiated subsequent therapy, respectively, with carbo-pem being the most common first subsequent therapy across arms (ami-laz, 26 % [29/111]; osi, 28 % [48/173]). PFS after first subsequent therapy (PFS2) favored ami-laz (HR, 0.73; 95 % CI, 0.59-0.91; nominal P = 0.004). Patients receiving ami-laz demonstrated significantly longer median time to treatment discontinuation and time to subsequent therapy vs osi. Intracranial PFS showed a favorable trend for ami-laz vs osi . While not formally tested for significance, median OS was not estimable for ami-laz vs 37.3 months for osi (HR, 0.77; 95 % CI, 0.61-0.96; nominal P = 0.019). At 24 months, 75 % and 70 % of patients were alive in the ami-laz and osi arms, respectively; corresponding values at 36 months were 61 % and 53 %. Conclusions: Ami-laz continues to show a trend towards improved OS while also improving post-progression outcomes vs osi, reaffirming ami-laz as a firstline standard-of-care for EGFR-mutated advanced NSCLC.

Hospital Medicine

Horowitz J, Gupta A, McLaughlin E, Bernstein SJ, Swaminathan L, **Kaatz S**, Posa P, Flanders S, and Prescott HC. Peri-discharge Care Coordination After Sepsis Hospitalization. *Am J Respir Crit Care Med* 2025; 211:1. Full Text

[Horowitz, J.; Gupta, A.; McLaughlin, E.; Bernstein, S. J.; Posa, P.; Flanders, S.] Michigan Med, Ann Arbor, MI USA; [Swaminathan, L.] Trinity Hlth IHA Med Grp, Ann Arbor, MI USA; [Kaatz, S.] Henry Ford, Detroit, MI USA; [Prescott, H. C.] Univ Michigan, Ann Arbor, MI USA

RATIONALE: Patients experience high rates of readmission and mortality after sepsis hospitalization. Since peri-discharge care coordination may improve outcomes, we evaluated hospitals' peri-discharge care coordination practices to support patients after sepsis hospitalization. METHODS: We surveyed 69 hospitals in the Michigan Hospital Medicine Safety Consortium (HMS) Sepsis Initiative, a collaborative quality initiative sponsored by Blue Cross Blue Shield of Michigan. Each hospital's HMS representative completed the survey in fall 2023, with input from relevant hospital staff as needed. The survey included questions on three peri-discharge care coordination practices: mechanisms for patients to contact hospital clinicians for questions related to hospitalization or hospital discharge instructions, post-discharge phone calls, and scheduling of outpatient follow-up. RESULTS: Among 67 hospitals completing the survey (97% response rate), 44 (65.7%) had a mechanism for patients to contact hospital clinicians to discuss post-discharge questions (34 for all patients; 10 for some patients). Of these hospitals, 13

(29.5%) implemented the mechanism in the prior year; another 11 (16.4%) planned to institute a mechanism in the coming year. Hospitals most frequently had centralized care managers (n=20; 29.9%) or service-specific care managers (n=15; 22.4%) answer patient calls, or had hospital operators route patients to on-call physicians (n=25; 37.3%). 53 (79.1%) hospitals made post-discharge telephone calls to patients within 3 days of hospital discharge to follow-up on discharge instructions and/or to assess patient symptoms (10 for all patients; 43 for some patients). Of these hospitals, 7 (13.2%) implemented post-discharge calls in the prior year; 5 additional hospitals (7.5%) planned to implement post-discharge telephone calls in the next year. Calls were most frequently made by transitional care staff (n=31, 46.2%), PCP office staff (n=21, 31.3%) or inpatient staff (n=18, 26.9%). Seven hospitals (10.4%) used automated calls to follow up with patients, connecting to a clinician only if needed based on patient response. Among hospitals doing follow-up calls for some but not all patients, prioritization was most often based on diagnoses, discharge service, or readmission risk score. 31 (46.3%) hospitals had a mechanism in place to ensure patients discharged without follow-up scheduled were scheduled shortly after discharge. CONCLUSIONS: Most hospitals have mechanisms to facilitate, or plan to institute mechanisms in the coming year. However, there is substantial variability in how hospitals implement peri-discharge care coordination and prioritize patients for follow-up calls. Additional research is necessary to identify how these interventions impact patient outcomes.

Hospital Medicine

Kenney RM, **Gunaga S**, **Cahill MM**, **Leman L**, **Beaulac-Harris A**, **Eriksson E**, **Geyer A**, **Shallal A**, **Stein TL**, **Mazzetti N**, **Kaiser K**, **Dubay J**, **Arthur A**, **Higginbottom M**, **Jayaprakash N**, **Dass S**, **Haddad A**, **Boxwalla A**, **Kaatz S**, **Tibbetts R**, **Veve M**, and **Suleyman G**. Are we there yet? The ongoing journey for improving management of asymptomatic bacteriuria. *Open Forum Infect Dis* 2025; 12:S1056-S1057. Full Text

R.M. Kenney, Henry Ford Hospital, Detroit, MI, United States

Background. Treating asymptomatic bacteriuria (ASB) with antibiotics contributes to preventable patient harm. This quality improvement study aimed to evaluate the effectiveness of ongoing diagnostic and antibiotic stewardship interventions in reducing unnecessary testing and treatment of ASB. Methods. This retrospective, cross-Sectional quality improvement study spanned from 1/2017-3/2024 at a five-hospital urban and suburban health system in Michigan. Interventions included i). Implementation of urinalysis with reflex to urine culture in 2/2019, with reflex criteria revised in 7/2022 to ≥ 10 WBCs; ii). Adoption of a urine culture hard stop after hospitalization day 3 (3/2021); iii). Introduction of an ASB progress note smart phrase and educational initiative via a 1-page handout and narrated slides in the first quarter of 2023. The primary endpoint was the proportion of patients with ASB who received antibiotic treatment, as defined by Vaughn et al JAMA Intern Med 2023. Secondary endpoints encompassed the number of provider smart phrase documentations; overall urine culture volume per year; proportion of all positive urine cultures representing ASB; and overall ASB antibiotic use, calculated as the ratio of ASB treated with antibiotics to all positive urine cultures. Results. The annual volume of urine cultures decreased by approximately 25% (Figure 1), from 87,556 in 2017 to 65,955 in 2023. The percentage of positive cultures representing ASB is depicted in Figure 2. The ASB smart phrase was documented in the medical record of 233 patients over one year: 165 (71%) were women, with a median age of 72 [48, 82] years. Emergency medicine providers utilized the smart phrase most frequently (97/233, 42%), followed by consultants (79/233, 34%). Overall ASB antibiotic use ranged from 9.7-22.7% in Q1 2022 and declined to 4.5-7% in Q1 2024. The primary endpoint, the system-wide average treatment of patients with ASB, declined modestly over time, but improvements were inconsistent among hospitals (Figure 3). Conclusion. Ongoing interventions targeting diagnostic and antibiotic stewardship through educational efforts were associated with a reduction in testing and treatment of ASB. However, suboptimal treatment of ASB remain a concern.

Infectious Diseases

Alvi RBR, **Shanahan C**, **Ruby A**, **Chami E**, **Lanfranco OA**, and **Suleyman G**. Review of Post Cesarian Section Surgical Site Infections in a Tertiary Care Hospital. *Open Forum Infect Dis* 2025; 12:S352-S353. Full Text

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Background. Surgical site infection (SSI) is one of the most common complications following cesarean section (CSEC), variably ranging from 3% to 18%, and adds a significant burden to the healthcare system. Given its substantial implications, developing strategies to prevent SSIs are essential. We aimed to explore factors associated with an increased risk of these infections. Methods. Retrospective observational study of post-CSEC SSIs from Jan 2021-Dec 2023 at Henry Ford Hospital in Detroit. SSIs were defined according to the National Healthcare Safety Network (NHSN) criteria. Cases were categorized as superficial incisional (SI), deep incisional (DI) and organ space (OS). Demographics, risk factors, clinical features, treatment, and outcomes were Results. 70 (3%) of 2,230 CSECs performed during the study period met criteria for post-CSEC SSI, of which 42 (60%) were SI, 4 (6%) DI, and 24 (34%) OS; 42 (60%) were emergency cases. The majority of patients were Black with mean age of 30.3 years (Table 1). Obesity (BMI >30), anemia (hemoglobin < 11), hypertension, prior abdominal surgery, Group B Strep colonization, and ruptured membranes at presentation were common. Most (86%) received perioperative antibiotics, and 69% were administered within 1 hour of incision; cefazolin was frequently used. Infection was diagnosed after a median of 11.5 days. Wound pain and drainage were the most prevalent symptoms. Manual chart review revealed 21% of cases did not have clinical symptoms or signs of infection. Cultures were obtained in 33% of patients, of which 91% were positive; common skin commensals were frequently isolated (Figure 1). Readmission was common, a quarter of patients required surgical intervention, and most cases were treated with antibiotics (Table 2). Complications included uterine dehiscence (9%) and half of these required hysterectomy.

Infectious Diseases

Arena CJ, **Mulbah JL**, **Kenney RM**, **Shallal A**, and Davis SL. Vancomycin Resistant Enterococcus faecium Minimum Inhibitory Concentration Trends from 2019-2024: Have We Killed Daptomycin? *Open Forum Infect Dis* 2025; 12:S308-S309. Full Text

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Background. Vancomycin resistant Enterococcus faecium (VRE) has been categorized as a bacterium with serious antibiotic resistance threats in the United States, where daptomycin (DAP) has been a drug of choice. In 2019, the Clinical and Laboratory Standard Institute M100S 29th edition revised DAP breakpoints for VRE to susceptible dose dependent with a minimum inhibitory concentration (MIC) of ≤ 4 mcg/mL. HigherMICs are associated with resistant mechanisms and increased microbiological failure is seen with MICs of 3-4mcg/L. Linezolid (LZD) is an VRE treatment option that has favorable clinical outcomes and microbiological eradication with less emerging resistance, but LZD use can be controversial due to outdated dogma of using a bacteriostatic agent. The purpose of this study was to evaluate MIC trends for DAP and LZD in patients with VRE bloodstream infections (BSI) at a large academic medical center. Bloodstream Infection VRE Comment within the Electronic Health Record: Current and Proposed Methods. IRB-exempt, cross-Sectional study of adult patients with VRE BSI and a healthcare encounter from 2019-2024 at a 5-hospital health-System in southeast Michigan. Patients were identified using Microsoft SQL Server queries based on microbiology results. The primary outcome was the proportion of patients with a DAP MIC > 1 mcg/mL with corresponding LZD MICs. Our health-System currently recommends DAP or LZD for VRE BSI until susceptibilities are available via blood culture comment (Figure 1). Measured MICs of daptomycin and linezolid, 2019-2024 ∗Daptomycin MIC Breakpoints: Susceptible Dose Dependent = ≤ 4 mcg/mL, Resistant = ≥8 mcg/mL. Linezolid MIC Breakpoints: Susceptible = ≤4 mcg/mL, Intermediate = 4 mcg/L, Resistant ≥8 mcg/L Results. 555 LZD and 491 DAP unique MICs from VRE BSI were evaluated. Figure 2 represents the average MICs by month and year for DAP and LZD from 2019-2024. The majority of DAP MICs were measured at 2 (30%), 3 (56%), and 4 (18%) mcg/mL. DAP MIC50 and MIC90 values were calculated at 3 mcg/mL and 4 mcg/mL, respectively. 98.7% of LZD MICs were measured at ≤2 mcg/mL (Table 1). LZD MIC50 and MIC90 values were calculated at 2 mcg/mL. Average daptomycin and linezolid MIC per month and year, 2019-2024 Conclusion. While theVREMICs forDAP are increasing, LZDhas remained stable over the past 5 years. A possible stewardship opportunity is to modify the health-System's current blood culture

comment could suggest LZD as the VRE drug of choice and highdose DAP as an alternative in patients until susceptibilities are available (Figure 1).

Infectious Diseases
Arena CJ, Vanhorn B, **Kenney RM**, **Parke DM**, **Suleyman G**, Davis SL, and **Veve M**. Oral Antimicrobial Therapy Offers in Hospitalized Persons Who Inject Drugs who Elect for Self-directed Discharge. *Open Forum Infect Dis* 2025; 12:S870. Full Text

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

Background. Hospitalized Persons Who Inject Drugs (PWID) who elect for selfdirected discharge (SDD) are at an increased risk for poor infection outcomes, but there is limited guidance for infection management in this population. National PWID management guidelines suggest considering oral antimicrobial therapy offers (OATO) as soon as patients are clinically stable to avoid lack of antibiotic therapy at discharge. The study purpose is to evaluate infection management in PWID who elect for SDD and to identify characteristics associated with OATO. Variables Associated with Oral Antimicrobial Offers at Self-directed Discharge Methods. Retrospective cohort of hospitalized adult PWID with an injection drug use (IDU)-related infection who elected for SDD between 1/1/14-1/31/24 at Henry Ford Health in Michigan. Patients were excluded if they were hospitalized for < 24-hours or if antimicrobial treatment was completed prior to SDD. The primary outcome was the proportion of patients with OATO at or prior to SDD. Secondary outcomes at 30-days included retreatment, infection-related readmission, and allcause mortality. Results. 150 patients were included; 55 (37%) were OATO patients, 95 (63%) did not receive an offer. Most patients were white (118, 79%), had prior SDD (90, 60%), and were a median (IQR) age of 34 (30-44) years. Skin infections were most common (81, 54%). Patients that received a source control procedure (27 (49%) vs. 31 (33%), P=0.05) or care from a provider ≤10 years from terminal training (49 [89%] vs. 70 [74%], P=0.04) were more likely to receive an OATO. Patient outcomes were not different between the OATO and no offer groups: infection retreatment 19 (34%) vs. 32 (34%); infection-related readmission 14 (25%) vs. 31 (33%); and all-cause mortality 1 (2%) vs. 3 (3%). Characteristics associated with OATO were prescribing or continuing medications for opioid use disorder during hospitalization, infection source control, and care from providers ≤10 years post-terminal training; infectious diseases consultation had an opposite association (Table 1). Conclusion. Most hospitalized PWID with IDU-related infections with SDD did not receive an OATO. Early career providers more commonly offered oral antimicrobials in PWID with less complicated infection types. Standardizing OATO in PWID at risk for SDD should be considered as a future direction to improve health outcomes. (Table Presented).

Infectious Diseases
Boettcher S, **Kenney RM**, **Arena CJ**, **Beaulac-Harris A**, **Tibbetts R**, **Shallal A**, **Suleyman G**, and **Veve M**. Say it Ain't Steno - Impact of a Microbiology Nudge Comment on Treatment of Respiratory Colonization. *Open Forum Infect Dis* 2025; 12:S1082. Full Text

S. Boettcher, Henry Ford Hospital, Royal Oak, MI, United States

Background. Stenotrophomonas maltophilia (SM) is a known colonizer of the respiratory tract, in which treatment is not required. Microbiological comment nudges have been successful as passive stewardship interventions. The study objective was to describe the effect of a targeted SM respiratory culture nudge on antibiotic use in patients with colonization. Methods. IRB approved quasi-experiment of adult patients with a SM respiratory culture between 01/01/2022-01/27/2023 (pre-nudge) and 03/27/2023-12/31/2023 (postnudge). Patients with criteria for active community/hospital/ventilator-acquired pneumonia or on targeted antibiotics prior to culture were excluded. Nudge comment implemented 2/2023: S. maltophilia is a frequent colonizer of the respiratory tract. Clinical correlation for infection is required. Colonizers do not require antibiotic treatment. The primary outcome was absence of SM therapy; secondary outcomes were SM therapy > 72 hours, hospital and ICU length of stay (LOS), and in-hospital all-cause mortality. Safety outcomes included antibiotic-related adverse events. Results. 94 patients were included: 53 (56.4%) pre- and 41 (43.6%) post-nudge. Most patients were men (53, 56.4%), had underlying lung disease (61, 64.8%), and required invasive ventilatory support (70, 74.5%). 11 (11.7%) patients were admitted from a

long-term care facility. The absence of SM therapy was observed in 13 (23.1%) pre- vs 32 (78.0%) post-nudge patients (P< 0.001). There were no differences in SM therapy > 72 hours (36/40 [90%] vs. 8/9 [88.9%], P=1.0), mortality (11 [20.8%] vs. 7 [17.5%], P=0.69), median (IQR) hospital LOS (24 [10-49] vs. 16 [8-29]), P=0.37), and median (IQR) ICU LOS [15 [2-35] vs. 11 [3-25], P=0.40) between pre- and postnudge groups, respectively. Safety outcomes of patients treated > 72 hours (n=41); elevated SCr 12 (29.3%), fluid overload 18 (43.9%), hyponatremia 17 (41.5%), and hyperkalemia 5 (12.2%). After adjustment for confounders, post-nudge was associated with 11-fold increased odds of the absence of SM therapy (Table 1). Conclusion. A targeted SM nudge was associated with a reduction in treatment of SM colonization. Patient outcomes, including length of stay and all-cause mortality, were comparable between the two groups.

Infectious Diseases
Cardenas-Maldonado DDD, **Chevalier T**, **Herc E**, **Lanfranco OA**, and **Suleyman G**. Unveiling Tuberculosis: A Perspective on Active vs. Subclinical Pulmonary Tuberculosis. *Open Forum Infect Dis* 2025; 12:S556. Full Text

D.D.D. Cardenas-Maldonado, Henry Ford Hospital, Farmington Hills, MI, United States

Background. Despite being preventable and curable, tuberculosis (TB) remains one of the world's leading infectious disease killers with 1.5 million people dying each year worldwide. The U.S. has one of the world's lowest rates of TB; however, cases increased 16% from 2022 to 2023. Although risk factors and outcomes associated with TB have been described, reports characterizing TB disease in the U.S. are limited. IQR: interquartile; USA: United States of America; BMI: Body Mass Index; HIV: human immunodeficiency virus; TNF-alpha inhibitors: Tumor necrosis factor-alpha inhibitors; TB: tuberculosis. Methods. Retrospective case series of patients with TB disease at Henry Ford Health in Southeast Michigan from Jan 2019-Dec 2023. Demographics, risk factors, clinical manifestations, treatment, and outcomes were evaluated. Active and subclinical TB were compared. Active TB was defined as positive imaging and/or microbiologic assay with clinical TB-related symptoms, and subclinical TB as positive imaging and/or microbiologic assay without symptoms. AFB: Acid-Fast-Bacilli; MTB: Mycobacterium tuberculosis; PCR: polymerase chain reaction; IQR: interquartile; TB: tuberculosis; RIPE: Rifampin, Isoniazid, Pyrazinamide, Ethambutol; INH: Isoniazid; RIF: Rifampin. Results. 53 patients were included, of whom 18 (33%) were black and 34 (64%) were male with a median age of 55 years (Table 1). Almost half were born in the U.S., and a quarter lived in Detroit. Prior TB exposure (30%), international travel (21%), persons who inject drugs (23%), and incarceration (17%) were common risk factors. 47 (89%) patients had active TB, and cough (68%) was prevalent. Consolidation and nodular patterns were frequently seen on imaging; cavitation occurred in 42% of cases. All had sputum smear microscopy and culture ordered;MTB PCR was obtained in 72% of cases (Table 2). Both were more likely to be positive in those with active TB. Most patients required inpatient admission; median time to airborne isolation precautions was longer in the subclinical group. Length of stay was prolonged in both groups. All patients with active TB received treatment, whereas 83% were treated in the subclinical group. Most were treated for at least 6 months. Among those completing treatment, 68% achieved cure and 15% expired. Conclusion. In this large cohort of TB patients, almost half were US-born and a third had a known TB exposure. Although less common, subclinical TB contributed to 11% of cases. Despite treatment, clinical cure was suboptimal with a 15% mortality. Early recognition and treatment of latent and active TB are critical disease control and prevention strategies.

Infectious Diseases
Cardenas-Maldonado DDD, **Gudipati S**, **Santana-Garcés M**, **Maki G**, and **Brar I**. Congenital Syphilis in Southeast Michigan: A Retrospective Case Series. *Open Forum Infect Dis* 2025; 12:S855. Full Text

D.D.D. Cardenas-Maldonado, Henry Ford Hospital, Farmington Hills, MI, United States

Background. Cases of congenital syphilis (CS) have been increasing substantially, but CS is preventable through timely testing and adequate treatment of syphilis during pregnancy. From2012 to 2021, cases of CS in the United States increased by 755%. Our study aims to describe the demographics of pregnant persons infected with syphilis and outcomes in their infants to identify potential predictors of adverse

events. IQR: Interquartile range; HIV: human immunodeficiency virus; Methods. This is a retrospective case series of pregnant persons diagnosed with syphilis who delivered their babies at Henry Ford Health from January 2020 to January 2024. Charts were reviewed for demographic data, syphilis serology, treatment in mothers and infants, and infant outcomes. Descriptive statistics were used to report the study population's demographic and clinical characteristics. Chi-Squared tests were used to determine the association between receipt of penicillin, prenatal care, prior sexually transmitted infection (STI), and CS diagnosis in neonates. Our chosen significance level was 0.05. Results. Forty-three patients were included; 19 (44%) were black; median age 27 years (IQR 24-32.5); 28 (66%) were from Detroit; 18 (53%) reported a history of STI. Eight (18%) did not receive prenatal care. Syphilis was primarily diagnosed during second trimester (34%), and late latent syphilis was reported in 80%. Syphilis treatment was completed 30 days before delivery in 67%. There were 17 early-term deliveries, 1 stillbirth, and 1 elective abortion. Ninety percent of neonates had a normal physical exam. Fifteen lumbar punctures were performed, one positive Venereal Disease Research Laboratory test. Of the 8 placenta studies, 2 had positive immunoperoxidase treponemal stain. Seventeen neonates were treated with 10 days of aqueous Penicillin, 6 neonates had definite/highly probable CS. Using Chi-Square analysis, receipt of penicillin treatment by the mother less than 30 days before delivery was significantly associated with CS in the neonate ($p < 0.001$) Conclusion. In our analysis, we identified a significant association between CS and appropriate timing of treatment of syphilis in the mother. Further studies are needed with a larger cohort to determine if social determinants of health affect appropriate prenatal care in pregnant persons. (Table Presented).

Infectious Diseases

Crew J, **Veve M**, **Fitzmaurice MG**, **Alangaden GJ**, and **Kenney RM**. Short vs. Long Durations of Antibiotic Therapy for Pyelonephritis in Kidney Transplant Recipients. *Open Forum Infect Dis* 2025; 12:S949. Full Text

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Background. Emerging data suggests shorter durations of antibiotic therapy are as effective and safe as longer durations in general populations. The objective of this study is to compare outcomes of short (7-9 days) vs long (10-15 days) durations of antibiotic therapy for acute graft pyelonephritis in kidney transplant recipients (KTRs). Summary of patient, infection and treatment characteristics. Methods. IRB-approved retrospective cohort comparing short (7-9 days) to long courses (10-15 days) of antibiotics. Inclusion: Adult patients, hospitalized from 1/1/14 - 12/31/23, history of kidney transplant, acute pyelonephritis, and receipt of at least 7 days of in vitro active antibiotic therapy. Exclusion: renal or perinephric abscess, prostatitis, ≤ 2 months post-transplant. Primary outcome: clinical success, defined as resolution of infection signs and symptoms and confirmed or presumed microbiologic success at end of therapy (EOT). Secondary outcomes: length of stay from pyelonephritis onset, continued resolution of signs and symptoms at 30 days, C. difficile infection within 30 days of EOT, acute rejection, and adverse effects. Summary of primary and secondary outcomes. Results. 107 patients were included: 19 (17.8%) short-course and 88 (82.2%) long-course. Table 1 describes patient, infection, transplant, and treatment characteristics. There was 1 (5.3%) failure in the short-course group compared to8 (9.1%) failures in the long-course group at EOT (p=0.456). At 30 days, there were 4 (21.1%) failures in the short-course group and 15 (17.0%) in the long-course group (p=0.742). 30-day retreatment was required in 0 short-course and 8 (9.1%) longcourse patients, p=0.346. No significant differences were detected for adverse effects: 0 vs. 3 (3.4%); C. diff: 0 vs. 1 (1.1%); or treated rejection: 1 (5.3%) vs. 0 in the shortcourse vs long-course groups, respectively. Conclusion. We did not detect differences in outcomes for pyelonephritis treatment in KTRs between those who received short compared to longer courses of antibiotic therapy. Further research is needed to solidify the place of short courses of antibiotic therapy in transplant recipients.

Infectious Diseases

Gudipati S, **Warzocha V**, **Brar I**, Baxa D, Homayouni R, and **Markowitz N**. Exploration of Associations Between Social Determinants of Health and Treatment Failure in People with HIV. *Open Forum Infect Dis* 2025; 12:S893-S894. Full Text

S. Gudipati, Henry Ford Health System, Detroit, MI, United States

Background. Addressing Social Determinants of Health (SDOH) and health disparities is at the core of Ending the HIV Epidemic. To address SDOH, there is a funded HIV Care Coordination Program (CCP) at Henry Ford Health (HFH), with support to surmount SDOH in people with HIV (PWH). In this pilot study, we explore associations between SDOH and treatment failure (TF) in this program. Methods. A retrospective study was conducted on PWH in our CCP at HFH from 2022 to 2023. Variables were extracted from data monitoring. CCP enrollment required referral by HIV providers. PWH were surveyed on SDOH related to ART challenges, and these SDOH were assessed throughout the course of one year. HIV genotypes were obtained upon enrollment, and HIV-1 viral load (VL) was collected every 3 months for one year. Significant differences between PWH with or without TF (defined as VL > 200 copies/mL at 1 year) were determined using Chi-Square test for categorical variables and Kruskal-Wallis for continuous variables. Multivariable logistic regression was used to find associations between independent variables and TF. Results. A total of 144 PWH were included in this study and divided into with (n=26) and without (n=118) TF (Table 1). There were no statistically significant differences in age, gender, risk factors and mean years living with HIV between the two groups. TF PWH had significantly lower incidence of insurance issues and need for financial assistance. Using linear regression analysis while adjusting for age, race, gender, genotype and other SDOH factors, there was no significant association between insurance issues or financial assistance. Although drug resistant mutations (DRMs) were not linked to specific demographics or SDOH, TF PWH had a significantly higher number of DRMs at baseline (p< 0.0176, OR 3.45, 95% CI 1.24-9.60) and a trend towards increased low frequency (< 10%) DRMs. Conclusion. TF occurred in 18% of PWH with adverse SDOH at enrollment into CCP. While we were unable to identify an association of specific SDOH with TF, the TF rate was elevated in these PWH. Overcoming SDOH is essential to achieve viral suppression. DRMs at CCP entry were significantly associated with TF, and were present in all those with TF. Our study is ongoing, and with larger numbers, we aim to assess the impact of SDOH in TF PWH in future studies.

Infectious Diseases

Hanna ZW, **Birk NK**, **Alangaden GJ**, **Suleyman G**, **Kaur J**, and **Ramesh M**. Comparison of Clinical Risk Factors, Outcomes and Molecular Epidemiology of ESBL and non-ESBL Enterobacterales Bacteremia in Solid Organ Transplant Recipients. *Open Forum Infect Dis* 2025; 12:S31-S32. Full Text

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Background. Infections caused by extended-Spectrum beta-lactamase (ESBL)-producing Enterobacterales are associated with adverse outcomes in recipients of solid organ transplants (SOTr). This study aims to elucidate the risk factors, outcomes, and molecular epidemiology associated with ESBL Enterobacterales bacteremia (ESBL EB) in abdominal SOTr. Methods. This observational cohort study was performed on abdominal SOTr with ESBL EB (cases) and non-ESBL EB (controls) at Henry Ford Health between August 2014 and February 2023. We performed whole genome sequencing on all blood isolates; sequencing libraries were created using +QIAGEN QIAseq FX DNA Library Kit according to manufacturer's instructions and sequenced on Illumina NextSeq 2000. Fastq files were used to determine the distribution of traits and resistance genes using the 1928 Platform. Demographic, risk factors, clinical characteristics, outcomes and molecular sequence data were evaluated. Primary outcome was 30-day mortality. Results. 56 patients were included: 31 (55%) cases and 25 (45%) controls. Liver and kidney transplant recipients were 28 (58%) and 18 (32%). Median age was 65 years and 54% were female. Risk factors for ESBL EB included liver transplant recipients (p < 0.001), second surgery < 30 days (p=0.01), primary graft dysfunction (p=0.02), and acute rejection < 3 months prior to BSI (p=0.001) (Table 1). Both 30-day (p=0.001) and 90-day (p=0.015) mortality were higher in the ESBL EB group. ST131 (57%) and ST410 (21%) were the predominant sequence types identified in ESBL E. coli isolates. Among ESBL K. pneumoniae, ST16, ST39, ST45, and ST219 were common. Resistome analysis identified β-lactam mutations in all isolates (figure 1 and figure 2). Additional resistance genes that were not phenotypically expressed in ESBL isolates were identified. Conclusion. Our study demonstrates the high mortality associated with ESBL EB in SOTr and highlights the risk factors and molecular characteristics of these infections. Clinical significance of the additional resistance genes identified needs further investigation. These findings provide insights for targeted management strategies in this high-risk population.

Infectious Diseases

Jabbour JF, Li Y, Boutzoukas AE, Wang M, Li L, Yu Y, Liu Z, Hanson BM, Gao H, Zong Z, Doi Y, Cober E, **Herc E**, Komarow L, Arias CA, Paterson D, Satlin MJ, Fowler VG, Bonomo RA, and Van Duin D. Effects of Comorbidities and Charlson Comorbidity Index Application on Patient Outcomes in Blood and Respiratory Carbapenem-Resistant Gram-Negative Bacterial Infections. *Open Forum Infect Dis* 2025; 12:S297-S298. Full Text

J.-F. Jabbour, Duke University Medical Center, Durham, NC, United States

Background. Infections with carbapenem-resistant (CR) organisms are more likely in patients with comorbidities and are associated with worse prognosis. The effect of specific and multiple comorbidities on the outcomes of patients with CR infections is not known. Age-adjusted Charlson Comorbidity Index calculation. The Charlson Comorbidity Index (CCI) scores for patients were calculated according to weights for respective comorbid conditions, as defined by the original CCI scoring system. Age adjustment was consecutively done to obtain the final age-adjusted CCI score. Methods. A secondary analysis was conducted on patients enrolled into MDRO Network studies (CRACKLE-2, SNAP, POP), between December 2018 and November 2019, who had blood and respiratory infections with CR Enterobacterales (CRE), Acinetobacter baumannii (CRAb), or Pseudomonas aeruginosa (CRPa). Respiratory cultures were physician-adjudicated. Patients were stratified into 4 groups according to their age-adjusted Charlson Comorbidity Index (CCI) score: 0-2, 3-4, 5-6, and 7+ (Figure 1). Primary outcome was 30-day all-cause mortality; absolute mortality differences comparing presence and absence of comorbidities and 95% score confidence intervals were calculated. Age-adjusted Charlson Comorbidity Index and 30-day mortality. 30-day mortality for patients with carbapenem-resistant Gram-negative bloodstream and respiratory infections increases progressively with increasing age-adjusted Charlson Comorbidity Index score groups. Results. 2468 patients were included, of which 66% had CRE, 17% had CRAb, and 17% had CRPa. We found a progressive increase in 30-day mortality rates with rising age-adjusted CCI scores ($p < 0.001$, Mantel Haenszel Chi-Square); 18% (CCI 0-2) to 25% (3-4), further to 28% (5-6), and peak at 35% (7+) (Figure 2). Patients with lower CCI acquired infections later during hospitalization [Median (IQR) days (CCI 0-2: 11 (2, 24.5); 3-4: 10 (2, 26); 5-6: 8 (1, 24); 7+: 9 (1, 25) (Kruskal Wallis p=0.025)], and tended to have a longer length of stay [Median (IQR) days (CCI 0-2: 32 (16, 60); 3-4: 29 (15, 48); 5-6: 25 (13, 50); 7+: 24 (13, 47) (Kruskal Wallis $p < 0.001$)]. Diabetes was associated with higher 30-day mortality: 23% in non-diabetics, 27% in diabetics without end-organ damage, and 38% in diabetics with end-organ damage ($p < 0.001$). Diseases with the highest mortality difference when present were cirrhosis with portal hypertension (14.9% [3.2%, 27.8%] 95% CI, p=0.01), diabetes with end-organ damage (14.7% [8.2%, 21.6%], $p< 0.001$), and lymphoma (12.1% [0%, 25.9%], p=0.05) (Table 1). 30-day mortality differences of Charlson Score components among blood and respiratory infections. 30-day mortality for individual comorbid conditions in the Charlson Comorbidity Index (CCI) is observed using unadjusted risk difference. Each component was compared to patients without each respective comorbidity. The highest risk differences are observed in diabetes with end-organ damage, chronic kidney disease, lymphoma, and cirrhosis with portal hypertension. Conclusion. Increasing comorbidities as measured by age-adjusted CCI are associated with worse outcomes in the setting of CR Gram-negative bacterial blood and respiratory infections. Diabetes contributes to this association to a great extent. This may help identify patients at-risk for poor outcomes. (Figure Presented).

Infectious Diseases

Jagannathan M, **Jordan T**, **Kinsey D**, **Kenney RM**, **Veve M**, **Shallal A**, and **Suleyman G**. A Comparative Analysis of Clindamycin versus Linezolid as Adjunctive Anti-toxin Therapy for Invasive Group A Streptococcal Infections. *Open Forum Infect Dis* 2025; 12:S1028-S1029. Full Text

M. Jagannathan, Henry Ford Hospital, Detroit, MI, United States

Background. Group A Streptococcus (GAS) is an important pathogen that can cause life-threatening disease. Clindamycin (DA) and linezolid (LZD) have been used as adjunctive antitoxin (AT) therapy in high-inoculum GAS infections to inhibit bacterial protein synthesis. However, there is concern about DA

efficacy in the era of increasing DA resistance, where LZD may have a role. We evaluated outcomes of patients with invasive GAS infection who received DA or LZD. Methods. Retrospective cohort study comparing patients with positive blood cultures (BC) for GAS from June 2013-Dec 2023 treated with DA or LZD ≥ 48 hours. We identified patients using a data query for positive BC for GAS through Microsoft SQL. Patients aged < 18 years, or those with polymicrobial bacteremia, receipt of both AT therapies, incomplete data, or enrolled in hospice/died within 48-hours of admission were excluded. Collected variables included: demographics, infection characteristics, microbiologic data, adjunct therapy (surgical, immunoglobulin), and clinical outcomes (treatment-associated adverse events, 30-day all-cause mortality and infection-related readmission). Results. 158 patients were included; 117 patients received DA and 41 patients LZD. Baseline characteristics were similar among groups except for chronic kidney disease, which was more common in the LZD group (Table 1). The most common clinical syndrome accompanying bacteremia in both groups was abscess/cellulitis; bone and joint infection was more prevalent in the LZD group. 55 (33.5%) of GAS isolates were DA resistant. There was no significant difference in severity of illness, surgical interventions, or duration of therapy between the two groups (Table 2). Duration of bacteremia was significantly longer in the LZD group. There was no significant difference in readmission (10.3% vs 12.2%, p=0.77) or all-cause mortality within 30 days (17.1% vs 7.3%, p=0.13) in the DA versus LZD groups. Treatment-associated adverse events were low across both groups [Figure 1]. Conclusion. Despite increasing DA resistance at our facility, there was no significant difference in outcomes between patients treated with LZD vs DA plus standard therapy, consistent with prior literature. Further studies are needed to determine optimal therapy for invasive GAS.

Infectious Diseases

Jordan T, **Jagannathan M**, **Kinsey D**, **Kenney RM**, **Veve M**, **Suleyman G**, and **Shallal A**. Analyzing Trends and Outcomes of Clindamycin Resistant Invasive Group A Streptococci Infections. *Open Forum Infect Dis* 2025; 12:S937-S938. Full Text

T. Jordan, Henry Ford Hospital, Detroit, MI, United States

Background. Streptococcus pyogenes (Group A Streptococci; GAS) is a grampositive bacterium that is a leading cause of life-threatening infections. For invasive infections, IDSA recommends high-dose penicillin and clindamycin (DA). However, increasing resistance to DA has been reported. The aim of this study was to determine the prevalence of DA-resistant GAS and evaluate if DA resistance was associated with worse outcomes. Table Comparison of clindamycin susceptible and clindamycin resistant strains of invasive GAS infections Methods. This was a retrospective cohort study from June 2013 to December 2023 across a five-hospital health system in Southeast Michigan of patients with positive blood cultures for GAS who received DA for anti-toxin therapy identified through Microsoft SQL. Children, polymicrobial bacteremia, incomplete data, receiving linezolid empirically, or those who died within 48 hours of admission were excluded. Patients with DA susceptible (DA-S) GAS isolates were compared to patients with DA resistant (DA-R) GAS isolates. Variables included demographics, infection characteristics, microbiologic data, therapy, and clinical outcomes. Figure Cases of GAS bacteremia and percent of clindamycin resistant strains Results. 390 cases were reviewed, and 215 were included in the cohort study [Table]. There was no difference in age, sex, or race among the groups. People who use injection drugs (51.7% vs 48.3%, p=0.07), people experiencing homelessness (PEH; 63.2% vs 36.8%, p=0.001), and chronic hepatitis C infection (HCV; 54.2% vs 45.8%, p=0.007) were more prevalent in the DA-R group; chronic kidney disease was more frequent in the DA-S group (57.1% vs 42.9%, p=0.029). Uncomplicated SSTI was more common in the DA-S group (64.2% vs 35.8%, p=0.022). There was no significant difference in the severity of illness, duration of bacteremia, surgical management, treatment duration, length of stay, readmission or mortality between the two groups. There was an increased incidence of invasive GAS infections beginning in 2022, and 50% of isolates were DA-R in 2023 [Figure]. Conclusion. Although there is an increase in DA-R in invasive GAS infections, there was no significant difference in outcomes among patients with DA-R and DA-S who received standard of care treatment in addition to DA antitoxin therapy. Further research is needed to determine the clinical significance of these findings to inform optimal therapy for these groups.

Infectious Diseases

Kapur N, **Birk NK**, **Jayaprakash R**, **Khalil B**, **Singh R**, **Hanna ZW**, **Ramesh M**, and **Alangaden GJ**. Infectious Complications Following Lung Transplant for COVID-19 Related Respiratory Failure. *Open Forum Infect Dis* 2025; 12:S1339-S1340. Full Text

N. Kapur, Henry Ford Hospital, Detroit, MI, United States

Background. Lung transplantation (LT) is a potentially life-Saving treatment option for COVID-19 related irreversible respiratory failure. Early outcomes for 1-year survival and graft failure rates among LT recipients (LTr) for COVID-19 related respiratory failure is similar to LTr for non-COVID etiologies. However, the infectious, real-world analysis of complications following LT among LTr for COVID-19 related respiratory failure in comparison to LTr in COVID-19 unrelated respiratory failure has not been described. Our objective was to compare the post-LT infectious complications among LTr for COVID-19 related and unrelated respiratory failure. Methods. We analyzed all consecutive LT done at Henry Ford Health System from January 2020 to October 2023. All patients received standard antimicrobial prophylaxis. Demographic data was obtained. The primary outcome was the rate of any infectious complication within one year from transplantation. Secondary outcomes were rates of specific infections, time to infection, and all-cause mortality at 30 days, 90 days, and 1- year. Results. A total of 98 lung transplantations were done at our center from January 2020 to October 2023. COVID-19 related LTr accounted for 11% of transplants. Median time of follow up was 365 days (187-365). COVID-19 related LTr were younger (median 53 vs. 64 years [p 0.02]) and predominantly white race ($p < 0.01$). Comorbidities amongst both groups were similar. Rates of post-LTr infectious complications were similar among the two groups, 66% overall. Time to first infection was shorter in the COVID-19 related LTr cohort, however this did not reach significance. Pleuropulmonary infections predominated overall (47%). All-cause post-LT mortality was similar in both groups (Table 1). Conclusion. Patients receiving LT for COVID-19 related respiratory failure have similar, high rates of infectious complications compared to patients with non-COVID-19 related etiologies, but mortality remains low. LT for COVID-19 related respiratory failure is an acceptable modality of treatment.

Infectious Diseases

Kaur J, **Jagannathan M**, **Jordan T**, **Kinsey D**, **Truppiano M**, **Shallal A**, and **Suleyman G**. Genomic surveillance of invasive Streptococcus pyogenes in Metropolitan Detroit. *Open Forum Infect Dis* 2025; 12:S1094. Full Text

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

Background. Group A streptococcal (GAS) disease is a major problem worldwide and can cause both noninvasive and invasive disease, including necrotizing fasciitis, with significant morbidity and mortality. Overall, the number of invasive GAS infections has been increasing in the United States over the past decade, primarily in adults. We aim to characterize the genomic features of circulating GAS strains causing invasive disease. Table. Patient demographics and genomic characteristics Methods. We performed whole-genome sequencing (WGS) on clinically obtained GAS blood isolates at Henry Ford Health, a comprehensive, integrated, health care organization in Southeast Michigan from Jan 2017-Dec 2023. Sequencing libraries were created using the QIAseq FX DNA Library Kit (Qiagen, USA) according to manufacturer's instructions and sequenced on NextSeq 2000 (Illumina Sandiego, USA). Fastq files were used to determine the distribution of traits, virulence factors, and resistance genes using the 1928 Platform. Results. We sequenced unique isolates from 64 patients, of whom 38 (59%) were males with median age 57 years [Table]. Most isolates were from 2022 (25%) and 2023 (53%). Fifteen M protein (emm) serotypes and 19 sequence type (ST) were obtained from 64 characterized isolates. The most frequent emm lineages were emm1 (n=16) and emm12 (n=12), where most patients had skin and soft tissue infection. The predominant emm1 lineage belonged to ST28. None of the emm1 and emm12 isolates carried aminoglycoside, macrolides/lincosamides/streptogramines (MLS), or tetracycline resistance genes. All the emm11 and emm49 isolates exhibited erm(A) and tetracycline resistance genes. Streptococcal superantigen (SAgs) genes were frequently detected; streptococcal pyrogenic exotoxin (SPE)-G was the most detected SAgs (97%), followed by streptococcal mitogenic exotoxin (SME)-Z (75%). SPE-H and SPE-I were each found in 48% of the isolates. Conclusion. In our cohort of patients

with invasive GAS, several SAgs were detected. SPE-A, SPE-G, SME-Z and SPE-J were most frequently found in emm1 lineages. However, there was no correlation between various clinical syndromes and the virulence genes identified. Continued genomic surveillance can help characterize features associated with emerging invasive strains to inform management and infection prevention strategies.

Infectious Diseases
Kenney RM, **Gunaga S**, **Cahill MM**, **Leman L**, **Beaulac-Harris A**, **Eriksson E**, **Geyer A**, **Shallal A**, **Stein TL**, **Mazzetti N**, **Kaiser K**, **Dubay J**, **Arthur A**, **Higginbottom M**, **Jayaprakash N**, **Dass S**, **Haddad A**, **Boxwalla A**, **Kaatz S**, **Tibbetts R**, **Veve M**, and **Suleyman G**. Are we there yet? The ongoing journey for improving management of asymptomatic bacteriuria. *Open Forum Infect Dis* 2025; 12:S1056-S1057. Full Text

R.M. Kenney, Henry Ford Hospital, Detroit, MI, United States

Background. Treating asymptomatic bacteriuria (ASB) with antibiotics contributes to preventable patient harm. This quality improvement study aimed to evaluate the effectiveness of ongoing diagnostic and antibiotic stewardship interventions in reducing unnecessary testing and treatment of ASB. Methods. This retrospective, cross-Sectional quality improvement study spanned from 1/2017-3/2024 at a five-hospital urban and suburban health system in Michigan. Interventions included i). Implementation of urinalysis with reflex to urine culture in 2/2019, with reflex criteria revised in 7/2022 to ≥ 10 WBCs; ii). Adoption of a urine culture hard stop after hospitalization day 3 (3/2021); iii). Introduction of an ASB progress note smart phrase and educational initiative via a 1-page handout and narrated slides in the first quarter of 2023. The primary endpoint was the proportion of patients with ASB who received antibiotic treatment, as defined by Vaughn et al JAMA Intern Med 2023. Secondary endpoints encompassed the number of provider smart phrase documentations; overall urine culture volume per year; proportion of all positive urine cultures representing ASB; and overall ASB antibiotic use, calculated as the ratio of ASB treated with antibiotics to all positive urine cultures. Results. The annual volume of urine cultures decreased by approximately 25% (Figure 1), from 87,556 in 2017 to 65,955 in 2023. The percentage of positive cultures representing ASB is depicted in Figure 2. The ASB smart phrase was documented in the medical record of 233 patients over one year: 165 (71%) were women, with a median age of 72 [48, 82] years. Emergency medicine providers utilized the smart phrase most frequently (97/233, 42%), followed by consultants (79/233, 34%). Overall ASB antibiotic use ranged from 9.7-22.7% in Q1 2022 and declined to 4.5-7% in Q1 2024. The primary endpoint, the system-wide average treatment of patients with ASB, declined modestly over time, but improvements were inconsistent among hospitals (Figure 3). Conclusion. Ongoing interventions targeting diagnostic and antibiotic stewardship through educational efforts were associated with a reduction in testing and treatment of ASB. However, suboptimal treatment of ASB remain a concern.

Infectious Diseases
Kenney RM, **Veve M**, **Shallal A**, **Tibbetts R**, and **Mulbah JL**. HECK-Yes This is The Remix!! Ceftriaxone vs Cefepime or Carbapenems for Definitive Treatment of Low-Risk AmpC-Harboring Enterobacterales Bloodstream Infections. *Open Forum Infect Dis* 2025; 12:S593. Full Text

R.M. Kenney, Henry Ford Hospital, Detroit, MI, United States

Background. Recent literature suggests ceftriaxone as a viable treatment of lowrisk AmpC-producing organisms, allowing for the preservation of AmpC-Stable therapies for moderate to high-risk organisms. This study aimed to determine whether ceftriaxone is effective in patients with bloodstream infections (BSI) caused by lowrisk AmpC harboring Enterobacterales compared to AmpC-Stable therapies. Methods. This was an IRB-approved, retrospective cohort of hospitalized patients ≥18 years old with a BSI due to Serratia marcescens, Morganella morganii, or Providencia spp. from 1/1/2017-2/28/2024. Patients were compared according to definitive therapy with ceftriaxone vs AmpC stable therapy (cefepime or carbapenem). The primary endpoint was 30-day all-cause mortality; secondary endpoints were clinical failure, development of ceftriaxone resistance, and hospital length of stay (LOS) after index culture. Clinical failure was defined as persistent signs and symptoms of infection, repeat positive blood cultures on days 3-5 of therapy, antibiotic escalation, or death. Results. 163 patients were included: 54

(33.1%) received ceftriaxone vs 109 (66.9%) AmpC stable therapies. Baseline, infection, and treatment characteristics are found in Table 1. 30-day all-cause mortality was observed in 5 (9.3%) ceftriaxone vs 11 (10.1%) AmpC stable patients (P=0.87). There were no differences in clinical success (49 [90.7%] vs 86 [78.9%], P=0.059), relapsing infection (3 [5.6%] vs 10 [9.3%], P=0.55), or rehospitalization (11 [20.4%] vs 38 [34.9%], P=0.06) between ceftriaxone and AmpC stable patients, respectively. Ceftriaxone resistance was only observed in AmpC stable patients (0 vs. 4 [3.7%], P=0.302), and median (IQR) LOS was similar between groups (5 [4-8] vs 6 [3-13] days, P=0.39). After adjustment for vasopressor use (adjOR 4.2; 95%CI, 1.3-13.1), ceftriaxone definitive therapy (adjOR, 0.79; 95%CI, 0.23-2.3) was not independently associated with 30-day all-cause mortality Conclusion. Patients treated with definitive ceftriaxone for low-risk AmpC Enterobacterales BSI achieved comparable outcomes to those treated with AmpC stable therapies. These findings support ceftriaxone as a treatment option for low-risk AmpC producers.

Infectious Diseases
Kinsey D, **Jagannathan M**, **Jordan T**, **Kenney RM**, **Veve M**, **Shallal A**, and **Suleyman G**. Invasive Streptococcus pyogenes Infections: Is Anti-toxin Therapy Necessary? *Open Forum Infect Dis* 2025; 12:S582. Full Text

D. Kinsey, Henry Ford Hospital, Detroit, MI, United States

Background. Invasive Streptococcus pyogenes or group A Streptococcus (GAS) carries a high morbidity and mortality rate. In addition to penicillin, adjunct antitoxin therapy (AT) with linezolid or clindamycin is the standard of care. Although the use of AT is supported by in vitro data and observational studies, there are limited conclusive data supporting its efficacy in reducing GAS mortality. Our study aimed to compare clinical outcomes of patients receiving AT versus those who did not. Methods. This was a retrospective cohort study of hospitalized patients with positive blood cultures for GAS at our five-hospital system from June 2013 to August 2023. Patients were identified through Microsoft SQL Server. Patients who received AT therapy for > 48 hours were defined as the AT group; the control group did not receive AT therapy. Patients who received AT for < 48 hours were excluded. Collected variables included demographics, infection & microbiological characteristics, and clinical outcomes. Data was analyzed using SPSS. Results. 265 patients were included in the study of whom 179 (68%) received AT (Table 1). About half were female, and the median age was 58 years. Comorbidities were overall similar between the two groups. Persons who inject drugs or with chronic hepatitis C were more common in the control group. Abscess/cellulitis was the most common clinical syndrome in both groups. Shock requiring vasopressors, need for dialysis and mechanical ventilation, and toxic shock syndrome were prevalent in the AT group. There was no difference in the duration of bacteremia, clindamycin resistance, and management between the two groups except for receipt of intravenous immunoglobulin (IVIG), which was more common in the AT group (Table 2). Outcomes, including length of stay, readmission for infection-related complications, and 30-day mortality, were similar between the two groups. Conclusion. Utilization of AT for invasive GAS infections correlated with severity of illness, but clinical outcomes did not significantly differ between patients receiving AT and those who did not, suggesting a potential opportunity for antimicrobial stewardship. Further research is needed to determine whether AT should be reserved for patients with select infectious syndromes.

Infectious Diseases
Mackow NA, Shao W, Ge L, Komarow L, Boutzoukas AE, Jiang J, Chen L, **Herc E**, Doi Y, Arias CA, Albin O, Saade E, Miller LG, Jacob JT, Satlin MJ, Krsak M, Huskins WC, Dhar S, Shelburne SA, Hill C, Greenwood-Quaintance K, Schmidt-Malan S, Patel R, Fowler VG, Tamma P, Kreiswirth BN, and Van Duin D. CTX-M-15-producing H30 ST131 Escherichia coli contributes to carbapenem use for E. coli bloodstream infections in the United States. *Open Forum Infect Dis* 2025; 12:S602-S603. Full Text

N.A. Mackow, University of North Carolina Chapel Hill, Chapel Hill, NC, United States

Background. Drug-resistant E. coli is a leading cause of antimicrobial resistance-associated deaths globally. Specifically, resistance to ceftriaxone (CRO-R) is increasing in E. coli. High-risk clonal group ST131 and its pandemic H30 subclone are of high concern yet studies characterizing these infections are

limited. We evaluated baseline characteristics and clinical outcomes associated with H30 ST131, non-H30 ST131 and non-ST131 E. coli bloodstream infections (BSI). Methods. Patients with monomicrobial carbapenem-Susceptible E. coli BSI that were matched 1:1 by study site (CRO-R and CRO-Susceptible community-acquired and hospital onset cases) were prospectively enrolled from 14 United States hospitals between November 12, 2020 to April 28, 2021 in the multicenter Study of Highly Resistant E. coli (SHREC). Isolates underwent whole genome sequencing. The primary outcome was a 30-day Desirability of Outcome Ranking (DOOR) after index culture including clinical response to treatment and all-cause mortality Results. There were 92 (33%) H30 ST131, 29 (10%) non-H30 ST131, and 161 (57%) non-ST131 isolates in 282 E. coli BSI (Table 1). Most ceftriaxone resistance was conferred by CTX-M-15 produced by H30 ST131 isolates (Figure 1, Table 1). H30 ST131 BSI patients were older (median age [IQR] 70.5 [63,76] vs. 67 [56,77] vs 65 [51,74] years, p = 0.017), had higher Charlson comorbidity indices (3 [2,5] vs. 2 [1,4] vs. 2 [1,4], p=0.009), and were more often admitted from long-term care facilities (18/92 [20%] vs. 3/29 [10%] vs. 7/161 [4%], p = 0.003) compared to non-H30 ST131 and non-ST131 BSI patients. Among H30 ST131 isolates, high rates of antibiotic resistance were observed to cephalosporins and fluoroquinolones, resulting in significantly more carbapenem use compared with non-H30 ST131 and non-ST131 isolates (75/92 [82%] vs. 14/29 [48%] vs. 50/161 [31%], p < 0.001) (Figure 2). 30-day DOOR and hospital length of stay did not differ between groups (Table 2). Conclusion. Compared with non-H30 ST131 and non-ST131 E. coli BSI, H30 ST131 E. coli BSI have a unique epidemiology with more healthcare exposures, comorbidities and antibiotic resistance and are more likely to be treated with carbapenems, though no significant difference in clinical outcomes was observed.

Infectious Diseases

Malik A, Brar S, **Shallal A**, and **Suleyman G**. Risk Factors and Clinical Outcomes of Breast Surgery Related Surgical Site Infections in Southeast Michigan. *Open Forum Infect Dis* 2025; 12:S347. Full Text

A. Malik, Henry Ford Hospital, Warren, MI, United States

Background. Surgical site infections (SSI) after breast surgery are important healthcare-associated infections (HAI) that may delay initiation of chemotherapy for underlying malignancy, in addition to accruing substantial healthcare costs. The reported incidence of breast surgery-related SSI (BSSI) ranges from 0.8%-26% depending on underlying comorbidities. We aimed to describe risk factors and clinical outcomes associated with BSSIs in southeast Michigan. Table 1. Characteristics of patients with breast surgical site infections Methods. Retrospective cross-Sectional study of adult patients with BSSI at a sixhospital healthcare system. Patients who met the definition of BSSI (per National Healthcare Safety Network) from 2021 to 2023 were included. Charts were reviewed for demographics, comorbidities, risk factors, microbiological data, and clinical outcomes. Table 2: Microbiological data of breast surgical site infections Results. A total of 146 patients were identified, of which 78 patients (53%) had clinical infection [Table 1]. Most of the patients were female (95%) and white (62%). Common comorbidities included obesity (36%), active breast cancer (55%), and diabetes mellitus (18%). Prior breast surgery (10%), chemotherapy within last 6 months (12%), and prior chest radiotherapy (9%) were less common. Mastectomy was the most common surgery (51%), often with lymph node dissection (46%), and many had artificial material placed (implant; 32% and tissue expanders; 18%). Only 88% of patients received peri-operative antibiotics, of which 72% received cefazolin. The most common microbes isolated were Staphylococcus aureus (24%), coagulasenegative Staphylococcus spp (23%), Streptococcus spp (19%) and Pseudomonas spp (19%). Most patients required repeat surgical intervention (81%), with hospitalization (59%) and removal of implants (45%). No patients died at 30 and 90 days after initial surgery. Conclusion. In this large study, BSSI was often associated with artificial material implantation, and Staphylococcus aureus was a common pathogen. Most patients required repeat surgical intervention and removal of implants. Significant opportunities were observed with surgical infection prophylaxis.

Infectious Diseases

Malik A, **Shallal A**, **Ruby A**, **Malm J**, **McLenon J**, **Shanahan C**, **Chami E**, **Alangaden GJ**, and **Suleyman G**. Outcome of Candida auris Point Prevalence Survey in a Tertiary Care Hospital in Southeast Michigan. *Open Forum Infect Dis* 2025; 12:S337. Full Text

A. Malik, Henry Ford Hospital, Detroit, MI, United States

Background. C. auris, an emerging multi-drug resistant organism associated with nosocomial outbreaks, is becoming more prevalent in Southeast Michigan due to interfacility healthcare transfer. The CDC recommends contact isolation and screening of epi-linked healthcare contacts of newly identified C. auris patients to prevent spread and assess potential transmission. We describe our institution's experience with C. auris point prevalence surveys (PPS). Methods. PPS was conducted at an 877-bed academic, tertiary care center consisting of private and semi-private rooms in Detroit. In collaboration with Michigan Department of Health and Human Services, we performed PPS by swabbing the axilla and groin of all patients on the implicated unit when a C. auris index case was incidentally identified from June-Dec 2023. In addition, potentially exposed roommates were flagged in the electronic health record for future screening. When additional cases were identified, 2 negative PPS conducted biweekly were required to stop PPS. Results. Six C. auris index cases were identified during the 6-month period. We performed 18 PPS on 9 units and screened 430 patients (Table); 5 refused and 14 were discharged prior to screening. Four (22%) of the PPS resulted in identification of new cases; 2 PPS yielded 1 case each, 1 PPS yielded 3 cases, and the final PPS yielded 2 cases. Of those screened, 7 (1.6%) tested positive on 4 units. Nosocomial transmission was implicated in 4 patients across 2 units after an epidemiologic investigation. Terminal cleaning was performed on units implicated in nosocomial transmission, in addition to ancillary areas visited by the affected patients. Infection Prevention emphasized the importance of adhering to hand hygiene, appropriate PPE use, and cleaning and disinfection of the environment and shared equipment. Conclusion. Controlling the spread of C. auris is a public health priority. However, only 1.6% of cases were detected with intense PPS. Despite considerable effort and healthcare resources being utilized to identify additional cases and mitigate possible nosocomial transmission, C. auris continues to spread in our region. Alternatively, healthcare facilities should consider active surveillance of high-risk patients at the point of hospitalization to mitigate the need for PPS.

Infectious Diseases

Mann Y, **Hagerman T**, **Malick A**, Rao S, **Harris C**, **Santana-Garcés M**, **Manteuffel J**, **Gudipati S**, and **Brar I**. One Small Step for Man, One Giant Leap for Ending the HIV Epidemic. *Open Forum Infect Dis* 2025; 12:S411-S412. Full Text

Y. Mann, Henry Ford Hospital, Detroit, MI, United States

Background. To achieve the goal to End the HIV Epidemic by 2030, unique interventions are needed to increase testing and subsequently link people with HIV (PWH) to care for rapid start of antiretroviral therapy (ART). Extending testing to include emergency department (ED) based HIV screening initiatives are effective in new case identification, earlier detection, and are encouraged by Centers for Disease Control and Prevention guidelines. Collaborations of infectious diseases (ID) providers with ED providers provides improved linkage to care for HIV and rapid initiation of ART. We describe our combined ED and ID HIV testing and linkage to care program. Methods. This is a retrospective analysis of newly diagnosedPWHat Henry Ford Health (HFH) via reactive HIV fourth generation test by an ED based opt-out HIV screening program from 7/16/2020 - 10/28/2023. A best practice alert (BPA) prompted providers to order an HIV screening test for patients ages 18-65 years old without a previously documented HIV fourth generation test. Patients were informed of the test when ordered and could opt-out of testing if desired. Follow up and linkage to care was provided by a team of ID providers. Results. During the study period, a total of 48,725 fourth generation HIV screening tests were performed, of which 629 tests were reactive (1.24% of tests performed). Of the reactive tests, 86 patients (0.18% of all tests) were found to have a new diagnosis of HIV. Median CD4 cell count was 297 cells/mm3 (IQR: 98-614), 34 patients required hospitalization with 7 (8%) admitted with an opportunistic infection. Excluding the 34 patients hospitalized, the median time from positive result to first attended appointment was 5 days (IQR 2-13) and median time from screening test result to initiation of ART was 6.5 days (IQR: 4-16). At 3- or 6-months following HIV diagnosis, 40 (47%) had an HIV-1 follow-up viral load reported (see Table 1). Conclusion. HIV testing and early linkage to care are two key pillars of the End the HIV Epidemic initiative. As shown by our study, collaboration between ED and ID providers ensures increased testing in the ED, improved linkage to care, and rapid start of ART which will help in achieving the goals of these two pillars.

Infectious Diseases

Mann Y, **Ishak A**, Ogbenna UK, Kasmikha L, **Cherabuddi MR**, **Joyce K**, **Harris C**, **Numi M**, **Santana-Garcés M**, **Rehman NK**, **Bryce R**, **Joshi S**, and **Zervos M**. Influenza Vaccine Amongst Persons Experiencing Homelessness: Evaluating Attitudes, Barriers, and Trust. *Open Forum Infect Dis* 2025; 12:S898-S899. Full Text

Y. Mann, Henry Ford Hospital, Detroit, MI, United States

Background. In Detroit, persons experiencing homelessness (PEH) have been a vulnerable part of society due to their comorbidities and unique barriers in access to care. Despite PEH experiencing higher rates of vaccine-preventable diseases, there is a lack of information on strategies to improve vaccine rates. The objective of this project is to obtain an understanding of enablers and barriers in influenza vaccine uptake amongst PEH, to inform future work to increase vaccine uptake. Methods. This is a cross-Sectional study of survey data from adult PEH encountered during Street Medicine (SM) outreach in Detroit to assess enablers and barriers in influenza vaccination. Respondents were provided a complimentary bus pass for participation. Descriptive statistics were conducted on sociodemographic variables with analysis of variables related to level of homelessness, vaccine concerns, vaccination status, and underlying health problems. Results. 43 participants' surveys were analyzed. Participant vaccine status and level of homelessness varied with majority (35%) reporting spending at least 1 night in a tent or other dwelling. Regarding participant demographics, 86% (n=37) were male and 81% (n=35) were Black or African American (AA) (Table 1). Amongst survey respondents, the highest sources of trust for information regarding influenza vaccine was found amongst: 'Social Services Agencies or Other Services' 95.2% (n=20) and 'Experts and Scientists' 93.8% (n=15) (Figures 1 and 2). Variables regarding sources of information trusted were analyzed via chi-Square analysis to evaluate for statistical significance (p-value < 0.05) amongst demographic variables (Figure 3). Conclusion. Previous literature regarding attitudes towards vaccines amongst PEH has demonstrated distrust in healthcare. Results of this study are unique in identifying healthcare members as resources trusted by most participants in providing information on vaccines. This emphasizes the importance of SM outreach in Detroit in building trusting relationships with PEH in addition to decreasing barriers in access to care, to help target future vaccination initiatives.

Infectious Diseases

Mann Y, **Numi M**, Edwards RA, Lai J, **Joshi S**, Patel P, Blankenship HM, Soehnlen MK, **Zervos M**, Mossing M, and **Rehman NK**. B.1.617.2 Outbreak Mitigation on an International Steel Cargo Ship Utilizing a Multidisciplinary Approach. *Open Forum Infect Dis* 2025; 12:S1164. Full Text

Y. Mann, Henry Ford Hospital, Detroit, MI, United States

Background. The SARS-CoV-2 B.1.617.2 (Delta) variant emerged in India and became widespread in the United States in 2021. Evidence suggested it was more transmissible than other variants. Figure 1: SARS-CoV-2 Cases on the Steel Cargo Ship Timeline Methods. From 01 May to 22 May 2021, 14 cases of COVID-19 were linked to an international steel cargo ship docked on the Detroit River, after 5 new members joined the crew from India. Cases were reported to the Detroit Health Department (DHD) on 08 May 2021. A strict weekly testing schedule was maintained by DHD. Control measures included a multidisciplinary partnership between DHD, local universities and hospitals. The multidisciplinary team (MDT) considered environmental health, infection control and behavioral health interventions. Measures for control included testing, and quarantine, vaccine, antibody therapy, and access to hospital care. Results. 14 out of 21 total crew members were confirmed positive (attack rate 67%). Once no new cases were found, a 14-day working quarantine was applied per the Centers for Disease Control (CDC) guidance. On 13 May 2021, the DHD vaccine outreach team administered Janssen COVID-19 vaccine, without incident, to all medically eligible crew (n = 19). Janssen was selected considering the ship's upcoming departure from Detroit and the limitation for follow-up doses. Conclusion. Response measures taken for this ship involved quarantine, isolation, disinfection and ventilation protocols, installation of filter units, behavioral health recommendations for anxiety-reducing strategies, antibody therapy, hospital care, vaccine administration and education. A MDT approach and multicomponent control strategy was critical to mitigate further spread. DHD's communicable diseases investigations, vaccination, and testing

capabilities were essential, including continued guidance from the Michigan Department of Health and Human Services (MDHHS) and CDC. Full transparency from the ship crew prevented potential spread of the variant in Detroit.

Infectious Diseases
Mann Y, Ogbenna UK, **Ishak A**, Kasmikha L, **Numi M**, **Iyer H**, **Rehman S**, Kadouh A, Mangal R, Qasawa A, Dehghani A, Hasso M, Henry J, **Santana-Garcés M**, **Rehman NK**, **Bryce R**, **Zervos M**, and **Joshi S**. Utilization of a Point-of-Care Hepatitis C Test to Treat in People Experiencing Homelessness with Street Medicine Outreach. *Open Forum Infect Dis* 2025; 12:S899. Full Text

Y. Mann, Henry Ford Hospital, Detroit, MI, United States

Background. Persons experiencing homelessness (PEH) have disproportionately higher rates of untreated chronic hepatitis C virus (HCV) than the public. Improved community funding and resources are needed to expand HCV rapid point-of-care (POC), confirmatory testing, treatment and follow-up. Given that PEH face competing priorities (unstable housing, food access, addiction, other infections), it is our role as clinicians to reduce barriers to HCV treatment, understand hesitancies for deferring treatment, and design programs to improve accessibility. This is the pilot project of a Street Medicine (SM) based initiative to use POC testing for HCV amongst PEH with linkage of care to a federally qualified health clinic (FQHC). Hepatitis C Screening and Treatment Protocol HCV- Hepatitis C Virus POC- Point of Care CHASS- Community Health and Social Services HbsAg- Hepatitis B Surface Antigen CBC- Complete Blood Count CMP- Complete Metabolic Panel Methods. SM provides medical care to PEH outside of a hospital setting. Medical students and residents were recruited to form a HCV outreach team at Henry Ford Hospital and trained in HCV testing via OraQuick rapid antibody (Ab) test. During SM outreach, PEH were provided education on HCV and offered POC testing with a $10.00 grocery gift card. If a patient was identified as HCV Ab positive they were provided free transportation to a FQHC for confirmatory testing. If diagnosis was confirmed, they were evaluated for eligibility for simplified HCV treatment, check-ins to assess adherence and sustained virologic response (Figure 1). Results. From February-April 2024, 103 PEH were tested using POC HCV testing on SM runs, with 4 positive results. 3 of 4 patients were confirmed for CHASS clinic appointments. 1 patient presented to clinic follow-up but deferred confirmatory testing bloodwork, demonstrating challenges in arranging for HCV clinic follow-up care. Conclusion. Previous studies have shown that lack of insurance, prior authorization and referral process, active injection drug use or alcohol use, lack of knowledge of HCV treatment, and limited healthcare workforce and infrastructure have all contributed to the low treatment rate in the homeless. Using trusted community organizations with SM, this initiative aims to reduce testing and transportation barriers in order to eliminate HCV in PEH. Larger numbers of positive patients are needed to best assess the feasibility of the program, and if providing all testing and treatment at the point of care is needed to improve compliance.

Infectious Diseases
Moss CT, Hsu JL, **Ramesh M**, Gauvreau GM, Turner J, Duong M, Sheshadri A, McCulloch D, Ignacio RB, Boeckh M, Nettles R, Chien J, Negrou E, Boateng F, Talantov D, and Cheng G. The Burden of Community-acquired Respiratory Viral Infections in High-risk Immunocompromised Patients After the COVID-19 Pandemic. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

[Moss, C. T.; Hsu, J. L.] Stanford Univ, Sch Med, Dept Med, Div Pulm Allergy & Crit Care Med, Stanford, CA USA; [Ramesh, M.] Henry Ford Hosp, Dept Med, Div Infect Dis, Detroit, MI USA; [Gauvreau, G. M.; Turner, J.; Duong, M.] McMaster Univ, Dept Med, Div Respirol, Hamilton, ON, Canada; [Sheshadri, A.] Univ Texas MD Anderson Canc Ctr, Dept Pulm Med, Div Internal Med, Houston, TX USA; [McCulloch, D.; Ignacio, R. Bender; Boeckh, M.] Univ Washington, Fred Hutchinson Canc Ctr, Dept Med, Vaccine & Infect Dis Div,Sch Med, Seattle, WA USA; [Nettles, R.; Chien, J.; Negrou, E.; Boateng, F.; Talantov, D.] Johnson & Johnson, San Diego, CA USA; [Cheng, G.] Univ Washington, Fred Hutchinson Canc Ctr, Dept Med, Div Pulm Crit Care & Sleep Med,Sch Med, Seattle, WA USA

Rationale The COVID-19 pandemic and subsequent public health measures significantly altered the landscape of community-acquired respiratory viral infections (CARVs). Those experiencing

immunosuppression from treatment of hematologic malignancies, including hematopoietic cell transplantation (HCT), are particularly susceptible to poor outcomes. Our study sought to better understand the incidence and clinical impact of CARVs in these immunocompromised individuals in the year immediately following the COVID-19 pandemic. Methods This prospective, multicenter, observational study was conducted at four large academic centers from January 2023 to March 2024. Eligibility criteria included adults (>18 years of age) with active hematological malignancies and after HCT. Participants were followed every 2 weeks for respiratory symptoms using a cloud-based symptom tracker for up to 12 months. Following a positive acute respiratory infection (ARI) symptom screen, in person evaluations were conducted which included physical examination, laboratory tests, and a nasal swab for polymerase chain reaction (PCR) testing for 18 viral and 4 bacterial pathogens with a commercially available assay (BioFire). Results A total of 140 participants were enrolled and 80% completed the study. The most common reasons for study discontinuation was death (20%, 12/28), and subject withdrawl (6.4%, 9/28). The median age of participants was 60 years and 75 (53.6%) were female. Participants were non-Hispanic, caucasian (72.1%), Asian (14%) and black (10.3%). The majority had received an HCT (83.6%, n=117); median time between transplantation and enrollment was 1 year. At least once before or during the study, 99 (71%) participants received a COVID-19 vaccine, and 32 (22.9%) participants received an Influenza vaccine. The symptom tracker triggered 100 ARI visits in 64 participants, of which 60 (43%, 60/140) had clinically confirmed infection with 87% of confirmed cases having a positive respiratory viral PCR panel. The incidence rate of clinically confirmed ARIs was 5.01 per 100 participant months (95% CI: 3.86-6.41). The most common CARV was rhinovirus/enterovirus (n=14, 23.3%) followed by COVID-19 (n=13, 21.7%) and seasonal coronavirus (n=5, 8.3%) (Figure 1). There were no confirmed bacterial infections. Hospitalization occurred in 8 participants (13.3%), with 4 requiring intensive care unit admission. In total, 12 deaths occurred; 3 followed a clinically confirmed ARI including one attributed to respiratory failure. Conclusions This study underscores the significant burden of CARVs in immunocompromised individuals, particularly those post-HCT. The findings highlight the need for robust public health strategies, improved vaccination efforts, and research into effective diagnostic and therapeutic interventions to mitigate the risks faced by this vulnerable population.

Infectious Diseases

Sheth R, Bhaskara A, Brown HM, Varley CD, Streifel AC, Maier M, Sikka MK, and Evans C. Infections in Gender-Affirming Surgery: A Single-center Experience with Gender-affirming Vaginoplasty. *Open Forum Infect Dis* 2025; 12:S354-S355. Full Text

R. Sheth, Henry Ford Health, Ann Arbor, MI, United States

Background. There are an estimated 1.3 million transgender adults in the US and about 25% undergo some form of gender-affirming surgery (GAS). Data on infectious complications following GAS is limited. We describe the epidemiology and incidence of infections following gender-affirming vaginoplasty (GAV). We also describe HIV screening and pre-exposure prophylaxis (PrEP) use in this population as transwomen are disproportionately affected by HIV and have the highest prevalence compared to any other group of US adults. Methods. In this single-center retrospective cohort study, we identified 398 patients aged ≥18 years who underwent GAV at Oregon Health and Science University from 2016 to 2023. We reviewed medical records up to 6 months from the initial surgery and used standardized criteria to diagnose surgical site infections (SSI), urinary tract infections (UTI), and sexually transmitted infections (STI). Data around HIV screening and PrEP use was also obtained. Results. 381 patients underwent primary vaginoplasty and 17 underwent revision of the primary surgery. 332 had standard penile inversion, 64 had robotic vaginoplasty, and 2 patients had intestinal vaginoplasty. UTI was the most common postoperative complication (incidence 13.8 per 100 individuals; n=55), followed by SSI (incidence 5.5 per 100 individuals; n=22). We identified 4 episodes of bacteremia related to surgery- all due to E coli- and one case of pelvic abscess. Only 2 STIs were identified and neither involved the neogenitalia- 1 was primary syphilis and the other was gonococcal urethritis. 16 patients had positive HIV serostatus. All 16 were prescribed ART and 11/16 had an undetectable viral load at the time of surgery. Only 22.5% of HIV seronegative patients had screening within a year before surgery and only 6% were on PrEP at the time of surgery. Conclusion. In our study, UTIs and SSIs were the most common infections post-GAV. Serious infections were rare. We also identified a significant gap in HIV screening

and PrEP uptake in this especially vulnerable group. Transgender surgery programs should incorporate HIV screening and counseling around PrEP.

Infectious Diseases

Stapleton RD, Rubenfeld GD, Dasgupta S, Needham DM, Hite R, Peltan ID, Burnham EL, Exline MC, Fisher C, Files D, Rice TW, **Ramesh M**, Goodwin AJ, Guillamet CV, Gong MN, Duggal A, Hyzy RC, Gunn S, Parker A, Kimball L, Ardren S, Gundacker H, Zhou Z, Chen Y, Huang Y, Leisenring W, Boeckh M, and Limaye AP. Ganciclovir to Prevent Reactivation of Cytomegalovirus in Patients With Sepsis-associated Acute Respiratory Failure: A Phase 3 Randomized Placebo-controlled Trial. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

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Introduction and Rationale: Cytomegalovirus (CMV) reactivation in critically ill adults is associated with worse respiratory and clinical outcomes, but a causal role remains uncertain. We sought to determine whether ganciclovir prophylaxis, by decreasing CMV reactivation, increases respiratory support-free days (RSFDs) in critically ill CMV-seropositive adults with sepsis-associated acute respiratory failure. Methods: This double-blind, placebo-controlled, 16-center randomized trial enrolled immunocompetent CMV-seropositive adults with sepsis-associated acute respiratory failure from June 2021-October 2024. Participants were randomized (1:1) to receive either intravenous ganciclovir (5 mg/kg twice daily for 5 days, then once daily) or placebo until the earlier of hospital discharge or 28 days. Participants were followed for 180 days. The primary outcome was RSFDs by day 28. Key secondary outcomes were also analyzed, including mortality through day 28 and day 180, hematologic and renal toxicities, CMV reactivation in plasma, and other reportable adverse events. Results: Among 213 randomized participants (mean age 59 years, 53% women, 76% on invasive mechanical ventilation at enrollment), 205 (96%) received ≥1 dose of study medication (N=106 ganciclovir, N=99 placebo). By day 180, 62 died, 17 were unable to be contacted but 8 of these were known to be alive, 8 withdrew/refused further contact, 24 continue in follow-up, and 94 have completed the study. The trial was terminated early, based on DSMB recommendation, with N=213 participants enrolled representing 43% of the N=500 target sample size. Study termination was recommended due to concerns of futility and increased mortality in the ganciclovir arm. Among participants receiving ≥1 dose of study drug, RSFDs were similar between study arms, and mortality was higher among ganciclovir recipients at both day 28 and day 180 (Table). There were no significant differences in neutropenia, thrombocytopenia, or renal dysfunction by day 28 between the arms. By day 28, CMV reactivation in plasma was significantly lower in the ganciclovir group (Table). Full follow-up data and additional secondary and exploratory endpoint data will be available at the ATS International Conference presentation. Conclusions: Among critically ill, CMV-seropositive adults with sepsis-associated respiratory failure, ganciclovir prophylaxis did not increase RSFDs and was associated with higher mortality, but without increased known ganciclovir-associated toxicities. The mechanism(s) underlying increased mortality with ganciclovir warrant further investigation. Ganciclovir should not be routinely used for prophylaxis of CMV reactivation in critically-ill adults without an underlying immunosuppressive condition.

Infectious Diseases

Stratton P, **Kenney RM**, **Veve M**, **Fitzmaurice MG**, **Alangaden GJ**, and **Franco-Palacios D**. Impact of a Short Course Post-Operative Antibiotic Prophylaxis Duration on Nephrotoxicity in Lung Transplant Recipients. *Open Forum Infect Dis* 2025; 12:S1356. Full Text

P. Stratton, Henry Ford Hospital, Royal Oak, MI, United States

Background. Vancomycin plus an antipseudomonal β-lactam is used as lung transplant surgical prophylaxis, but an optimal post-operative duration is not defined. The study objective was to assess the impact of a shortened antibacterial surgical infection prophylaxis (SIP) duration on post-operative nephrotoxicity in lung transplant recipients. Table 1 Variables associated with AKI Methods. IRB approved quasi experiment of lung transplant recipients who received SIP from 1/1/2016-9/30/2020 (pre-group) to 10/1/2020-7/31/24 (post-group). Intervention: implementation of shortened SIP duration to 72-hours of cefepime and vancomycin post-operatively. Inclusion: eGFR >30 mL/min/1.73m2 between transplant day ±2. Exclusion: renal replacement ≤ 3-months, simultaneous organ transplants, donor bronchi with Gram-positive bacterial growth, or new COVID-19 infection between transplant day ±7. The primary endpoint was the incidence of acute kidney injury (AKI), defined by the KDIGO criteria, while receiving post-operative vancomycin up to 14 days. Secondary endpoints were vancomycin consensus guideline (VCG) AKI definition at 14-days and time to AKI. Results. 77 patients were included: 45 (58%) pre-, 32 (42%) post-intervention. 73% vs. 47% male (p=0.018). 49% vs. 34% (p=0.205) KDIGO AKI while on vancomycin. Post-group associated with approximately 40% decreased odds of developing KDIGO AKI (Table 1). Secondary endpoints: 33% vs. 19% VCG AKI (p=0.157). Median time to AKI was three days, with no differences detected between groups and AKI definitions. Similar rates of C. diff infection, positive bacterial respiratory cultures, new multidrug resistant organisms, surgical site infections. 57.8% vs. 84.4% patients received treatment for new pneumonias after SIP completion (p=0.013), with one new MRSA pneumonia in the pre-group and one in the post-group. Conclusion. Implementation of a shortened antibacterial prophylaxis protocol for lung transplant resulted in numerically fewer AKIs. Maturation, regression to the mean, and reliance on manual chart review are all limitations of this retrospective study. Ongoing analysis of this intervention, such as with multicenter prospective studies, can help to characterize the decreased nephrotoxicity risk with shorter course prophylaxis post-transplant.

Infectious Diseases

Terrazas WC, **Kenney RM**, **Argyris A**, **Shallal A**, and **Veve M**. Judicious Use of Benzathine Penicillin G in Response to a Medication Shortage Alert. *Open Forum Infect Dis* 2025; 12:S898. Full Text

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Background. The national shortage of benzathine penicillin G (BPG) poses challenges in the treatment of syphilis. In response to this critical BPG shortage, our health system implemented a medication shortage alert within the electronic health record (EHR). The alert provides recommendations to optimize BPG utilization. This study investigates the impact of the BPG drug shortage on clinical practice. Methods. This was an IRB-approved, retrospective cohort study focusing on patients >3 months who received BPG between 5/9/23-2/28/24. The study included inpatient and outpatient visits after implementing the medication shortage alert. Exclusions were applied for severe penicillin allergy, neurosyphilis, or congenital syphilis. Two cohorts were analyzed: the judicious BPG group (patients with primary, secondary, or latent syphilis receiving BPG), and the non-judicious group (patients receiving BPG for alternative diagnoses). The study assessed social determinants of health (SDOH) as primary outcomes and compared a separate cohort of syphilis patients receiving BPG or alternative therapy (e.g., doxycycline). Results. 453 patients were included. Majority of patients were non-Hispanic Black (273, 60%) men (272, 60%), with a median age of 32 years (IQR: 22-44). Of these patients, 318 (70%) received judicious BPG, while 135 (30%) received non-judicious BPG. The most common non-judicious diagnosis was streptococcal pharyngitis (128, 95%). In multivariable logistic regression (Table 1), variables associated with judicious use included: age >32 years (adjOR: 2.273; 95% CI: 1.488-3.472), male sex at birth (adjOR: 1.835; 95% CI: 1.206-2.792), and black race (adjOR: 1.847; 95% CI: 1.212-2.815). Among a cohort of 128 syphilis patients who received either BPG (64, 50%) or doxycycline (64, 50%) treatment, those who received doxycycline were more likely to lack health insurance (35 [54.7%] vs.

43 [67.2%], p=0.15) and receive outpatient treatment (3 [4.7%] vs. 12 [18.7%], p=0.13) (Table 2). SDOH data were reported in < 50% of patient charts. Conclusion. Despite implementing an EHR drug shortage alert, 30% of BPG use was suboptimal and mostly for pharyngitis. Optimizing SDOH documentation represents an opportunity to assess health inequities and the impacts on patient outcomes for syphilis management.

Infectious Diseases
Toiv A, Doshi N, **Ishak A**, and **Lanfranco OA**. Highly Resistant Myroides Species Infections: Insights from a Comprehensive Case Series and Antibiogram Analysis. *Open Forum Infect Dis* 2025; 12:S540. Full Text

A. Toiv, Henry Ford Hospital, Detroit, MI, United States

Background. Myroides species (spp.) are rare opportunistic gram-negative bacteria that are highly resistant to commonly used empiric antibiotics. Able to survive in natural and hospital environments, these microbes pose a growing risk of resistant nosocomial infections. Here we present a case series and antibiogram of Myroides infections at an academic medical center, highlighting this potential pathogen's antibiotic sensitivity to aid clinicians in choosing effective antimicrobial therapies. Antibiogram Methods. Retrospective chart review of all patients diagnosed with Myroides spp. infection at Henry Ford Health between January 1, 2019 and December 31, 2023. Patient characteristics, treatments, and outcomes were analyzed. An antibiogram of Myroides spp. susceptibility to 10 antibiotics was generated. Results. A total of 43 patients (median age 62 yr; range 30-94) presented with 46 Myroides spp. infections. Positive cultures were evenly distributed between hospitalizations (50%) and outpatient (50%) settings. Of the 46 infections, 35 (76%) were in a lower extremity wound. Of the 43 patients, 17 (40%) had sepsis at presentation, including 8 (13%) with Myroides bacteremia. Most Myroides spp. cultures (83%) grew additional organisms, including E. faecalis (34%), S. aureus (21%), Proteus mirabilis (21%), and Pseudomonas spp. (16%). Empiric antibiotics were prescribed in 35/46 cases (76%), mostly vancomycin (17/35) and cefepime (9/35); however, Myroides spp. were sensitive to the empiric agents in only 4 cases (11%). Antibiogram analysis showed 100% susceptibility to meropenem and 0%-50% susceptibility to 9 other agents (Table). A total of 5 (12%) patients died, and 6 patients (14%) required readmission within 1 month of treatment. Conclusion. Myroides spp. exhibited significant resistance to most empiric antibiotics. Our antibiogram analysis revealed meropenem as the sole effective empiric antibiotic for this opportunistic pathogen. We recommend the prompt empirical use of meropenem when Myroides spp. are identified on antimicrobial culture.

Infectious Diseases
Yared NF, **Gudipati S**, **Payne S**, and **Brar I**. Assessment of Failures of Long-Acting Cabotegravir and Rilpivirine in a Real-World Treatment Setting. *Open Forum Infect Dis* 2025; 12:S449-S450. Full Text

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

Background. Cabotegravir (CAB) + rilpivirine (RPV) is the first complete longacting all injectable (LAI) antiretroviral therapy (ART). While well-tolerated with low risk of virologic failure (VF), understanding reasons for CAB + RPV (CAR) discontinuation in a real-world setting was the objective of our study, so as to better define appropriate patients for LAI. Methods. We performed a retrospective cohort study to assess CAR failures. CAR failure was defined as regimen discontinuation after receipt of at least one CAR dose due to either virologic failure (VF) or side effects. VF was defined as viral load (VL) ≥ 30 copies/mL on 2 occasions at least 4 weeks apart. Genotypes incorporated detection of drug resistance mutations (DRMs) at frequency < 10%. We included PWH at Henry Ford Health who were virologically suppressed on their current ART and switched to CAR on or before March 2023. Demographics, clinical characteristics, and outcomes were extracted from the electronic medical record (Table 1). Results. Of the 58 PWH initiating CAR, 46 had HIV VL testing available at 12 months after initiation of CAR and 45/46 PWH (97.8%) were undetectable (< 30 copies/ mL). FivePWHfailed CAR: 2/5 secondary to injection site reactions and 3/5 due to VF with new resistance (Table 2). Among those with VF, they had been living with HIV for a mean of 20 years and all had BMI > 30 kg/m2. One had a pre-existing G140R DRM (1.2% frequency) and developed the E138K NNRTI and Q148R INSTI DRMs (> 10% frequency). A second

patient developed the Y188L and E138E/K NNRTI and Q148K INSTI DRMs (> 10% frequency). The third patient with history of oral NNRTI use developed the M230I and E138E/K NNRTI DRMs (>10% frequency). Conclusion. In our clinic more patients (8.6%) discontinued CAR than had been reported in randomized clinical trials. While the clinical significance of < 10% DRMs is unclear, one patient with pre-existing G140R < 10% DRM developed VF despite on-time injections leading to loss of NNRTI and INSTI class efficacy. Previous studies have shown that the detection of drug-resistant < 10% DRMs in NNRTI significantly increases the risk of treatment failure. Larger studies are needed to determine the impact of HIV-1 < 10% DRMs for other classes of ARTs, such as INSTIs, as this may have a big impact while evaluating appropriateness of a patient for CAR (Table Presented).

Internal Medicine

Aziz N, Nabi W, Khan M, Makhkamov S, Cheema A, Akbar N, Usama A, Basharat A, LaBelle E, **Tareen H**, Bhat A, Majeed MW, Mudassar M, Ahmad RU, Javed MJ, Anwar J, Ilyas U, Faisal MS, and Shahzad M. Comparative survival outcomes among histological subtypes of pulmonary adenocarcinoma: A nationwide study. *J Clin Oncol* 2025; 43:e20066. Full Text

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Background: Adenocarcinoma of the lung is a heterogeneous malignancy with multiple histological subtypes. In the US, population survival outcomes across these subtypes remain underexplored. Methods: A retrospective analysis of patients with various Lung Adenocarcinomas (Acinar, Lepidic, Papillary, Solid & solid type, Invasive mucinous, Mixed mucinous/non-mucinous, Colloid, Fetal, and Enteric type), diagnosed between 2010 and 2017, was conducted using the National Cancer Database in accordance with STROBE guidelines. Unadjusted median overall survival (mOS) was estimated using Kaplan-Meier survival analysis. Multivariate regression analysis was performed using accelerated failure time model to estimate covariate-adjusted hazard ratios (HR). Covariates included age, sex, race, tumor grade, TNM stage, Charlson Comorbidity Index, insurance status, year of diagnosis, facility type, and treatment modality. Lepidic carcinoma served as the reference arm for HR calculations. Results: A total of 46,218 patients were included in this large cohort study. 39,865 patients (86.3%) were white, 27,094 (58.6%) were female, 31,827 (69%) were aged $65 years, 29,843 (64.57%) had Medicare insurance, and 18,788 (40.65%) were treated in academic or research institutions. For unadjusted mOS, Acinar adenocarcinoma (n=15,877; 34.35%) demonstrated the best outcomes (mOS: 97.84 months, p,0.05). After covariate adjustment, Solid adenocarcinoma (n=1,736; 3.76%) had the most favorable prognosis (HR = 0.85, p,0.01). In contrast, Enteric type adenocarcinoma (n=33; 0.07%) exhibited the poorest survival, with an mOS of only 27.24 months (HR = 1.63, p,0.05). Lepidic adenocarcinoma (n=8,923; 19.31%), the reference group, demonstrated an mOS of 73.03 months with HR of 1. Other subtypes, such as Mixed/non mucinous adenocarcinoma (n=195; 0.42%; mOS: 85.22 months, HR = 0.91, p = 0.377) and Papillary adenocarcinoma (n=6,094; 13.19%; mOS: 64.79 months, HR = 0.97, p = 0.236), showed intermediate survival, with no statistically significant differences. On the other hand, significant differences were observed for Fetal adenocarcinoma (n=46; 0.10%; mOS: 39.82 months, HR = 1.17, p = 0.467), Invasive mucinous adenocarcinoma (n=1,254; 2.71%; mOS: 51.81 months, HR = 1.17, p,0.01), and Colloid adenocarcinoma (n=12,060; 26.09%; mOS: 44.09 months, HR = 1.29, p,0.01). Conclusions:

This study highlights marked differences in survival across lung adenocarcinoma subtypes. These results stress the importance of further research to develop therapies tailored to specific histological variants.

Internal Medicine
Belevender C, **Ozeir S**, **Bugazia S**, **Badhwar A**, **Shakaroun D**, **Carlin A**, **Roehrs T**, and **Skiba V**. The Role of Age, Gender, and Daytime Sleepiness in Predicting CPAP Adherence Following Bariatric Surgery. *Sleep* 2025; 48:A585. Full Text

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Introduction: Obstructive sleep apnea (OSA) is a common comorbidity in bariatric surgery patients, with continuous pos itive airway pressure (CPAP) serving as a primary treatment. While bariatric surgery often results in significant weight loss and improvement in apnea severity, the roles of age, gender, and baseline daytime sleepiness—measured by the Epworth Sleepiness Scale (ESS)—in predicting CPAP adherence remain unclear. Methods: This retrospective chart study reviewed 140 patients evaluated at the Henry Ford Bariatric Clinic and referred to the Henry Ford Sleep Disorders and Research Center for preoperative sleep testing between April and August 2023. CPAP adherence, defined as any reported usage, was analyzed in rela tion to ESS scores, age, and gender. Results: Preliminary analyses revealed positive correlation between ESS scores and CPAP adherence, suggesting patients with higher daytime sleepiness are more likely to adhere to CPAP therapy. Older patients demonstrated higher adherence rates. Significant differences in adherence were also observed between genders, with male patients showing consistently higher adherence across all follow-up points. Conclusion: Age, gender, and baseline ESS appear to play significant roles in predicting CPAP adherence following bariatric surgery. These findings highlight the importance of tailoring postoperative CPAP management to demographic factors, with particular attention to younger and female patients who may benefit from additional adherence support.

Internal Medicine
Bhargava A, Szpunar SM, **Sharma M**, and Saravolatz L. Risk Factors Associated with Longer Hospital Stay in Elderly Patients with Respiratory Syncytial Virus Infections. *Open Forum Infect Dis* 2025; 12:S504. Full Text

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Background. Annually, 3-7% of healthy older patients and 4-10% of high-risk adults develop respiratory syncytial virus (RSV) infections. Elderly patients above 65 years of age, with congestive heart failure, chronic lung disease, or weakened immune systems are at high risk for severe RSV infections. Little is known about the factors that are associated with the length of hospital stay (LOS) among these elderly individuals. Methods. A multicenter historical cohort study was conducted on elderly patients (>65 years of age) hospitalized for laboratory-confirmed RSV-related diseases in Ascension hospitals in Southeast Michigan between January 2017 and December 2022. Hospitalized patients were identified using ICD 10 codes for RSV-related diseases. Electronic medical records were reviewed after IRB approval. LOS was categorized as below the mean LOS or at the mean and above. Data were analyzed using Student's t-test, the chi-Squared test, the Mann-Whitney U test and logistic regression using SPSS v. 29.0. Results. Of 239 patients, the mean (sd) age of the cohort was 78.3 + 8.4 years, 157 (65.7%) were female and 176 (73.6%) were white. The mean body mass index (BMI) was 29.5 + 8.8 kg/m2. The mean Charlson Weighted Index of Comorbidity (CWIC) score was 2.4 + 2.0. The mean hospital LOS was 7.5 + 5.1 days. Prolonged LOS was noted in 89 (37.2%) patients. Factors associated with longer LOS (>7.5) in univariable analysis were chronic lung disease, solid tumors, CWIC score, smoking status, home oxygen, oxygen requirement during hospitalization, qSOFA, abnormal admission chest x-ray (CXR), lower respiratory tract infection, and respiratory failure requiring intubation. The multivariable logistic regression revealed that predictors for prolonged LOS among elderly patients were smoking status (OR, 2.2; 95% CI 1.2-4.0), abnormal admission CXR (OR, 2.1; 95% CI 1.2-3.7), and respiratory failure requiring intubation (OR, 9.4; 95% CI 2.6-34.4). Conclusion. Our study finds that patient's smoking status, abnormal

admission CXR and respiratory failure requiring intubation were significantly associated with prolonged LOS among elderly patients with RSV infections. Knowing these risk factors may help identify patients who would benefit from early interventions to mitigate the duration of hospitalization.

Internal Medicine
Jagannathan M, **Jordan T**, **Kinsey D**, **Kenney RM**, **Veve M**, **Shallal A**, and **Suleyman G**. A Comparative Analysis of Clindamycin versus Linezolid as Adjunctive Anti-toxin Therapy for Invasive Group A Streptococcal Infections. *Open Forum Infect Dis* 2025; 12:S1028-S1029. Full Text

M. Jagannathan, Henry Ford Hospital, Detroit, MI, United States

Background. Group A Streptococcus (GAS) is an important pathogen that can cause life-threatening disease. Clindamycin (DA) and linezolid (LZD) have been used as adjunctive antitoxin (AT) therapy in high-inoculum GAS infections to inhibit bacterial protein synthesis. However, there is concern about DA efficacy in the era of increasing DA resistance, where LZD may have a role. We evaluated outcomes of patients with invasive GAS infection who received DA or LZD. Methods. Retrospective cohort study comparing patients with positive blood cultures (BC) for GAS from June 2013-Dec 2023 treated with DA or LZD ≥ 48 hours. We identified patients using a data query for positive BC for GAS through Microsoft SQL. Patients aged < 18 years, or those with polymicrobial bacteremia, receipt of both AT therapies, incomplete data, or enrolled in hospice/died within 48-hours of admission were excluded. Collected variables included: demographics, infection characteristics, microbiologic data, adjunct therapy (surgical, immunoglobulin), and clinical outcomes (treatment-associated adverse events, 30-day all-cause mortality and infection-related readmission). Results. 158 patients were included; 117 patients received DA and 41 patients LZD. Baseline characteristics were similar among groups except for chronic kidney disease, which was more common in the LZD group (Table 1). The most common clinical syndrome accompanying bacteremia in both groups was abscess/cellulitis; bone and joint infection was more prevalent in the LZD group. 55 (33.5%) of GAS isolates were DA resistant. There was no significant difference in severity of illness, surgical interventions, or duration of therapy between the two groups (Table 2). Duration of bacteremia was significantly longer in the LZD group. There was no significant difference in readmission (10.3% vs 12.2%, p=0.77) or all-cause mortality within 30 days (17.1% vs 7.3%, p=0.13) in the DA versus LZD groups. Treatment-associated adverse events were low across both groups [Figure 1]. Conclusion. Despite increasing DA resistance at our facility, there was no significant difference in outcomes between patients treated with LZD vs DA plus standard therapy, consistent with prior literature. Further studies are needed to determine optimal therapy for invasive GAS.

Internal Medicine
Kale-Pradhan P, Channey S, **Sharma M**, Lebovic D, Giuliano C, Johnson LB, and Bhargava A. Epidemiology, Clinical Features and Outcomes of COVID 19 Patients Post Evusheld Therapy Among Immunosuppressed Patients. *Open Forum Infect Dis* 2025; 12:S1210-S1211. Full Text

P. Kale-Pradhan, Wayne State University Eugene Applebaum, College of Pharmacy and Health Sciences, Detroit, MI, United States

Background. Evusheld® is a combination of two monoclonal antibodies, Tixagevimab and Cilgavimab. It was developed for the pre-exposure prophylaxis (PrEP) and treatment of COVID-19 illness for those who are immunocompromised. There is paucity of long-term real-world data on the use of Evusheld among the immunosuppressed patients against the SARS-CoV-2 Omicron variants. Methods. A retrospective cohort chart review of patients 18 years and older who received the two dose Evusheld regimen from December 1, 2021 to January 31, 2023 at a community teaching institution was performed to evaluate the effectiveness of Evusheld as PrEP of COVID-19 patients. Evusheld as PrEP was indicated for patients with active solid tumor and hematologic malignancies or those receiving immunosuppressive treatment including CART therapy, biologic agents and high-dose corticosteroids (i.e., ≥ 20 mg prednisone or equivalent per day when administered for ≥ 2 weeks). The following data was collected: patient demographic, development of COVID19 after receiving Evusheld®, intensive care unit (ICU) length of stay (LOS), hospital LOS, ventilation requirement, duration of ventilation, and mortality among these patients within six months of receiving Evusheld therapy. Results. Of the 663 patients screened, 459 were

excluded primarily for duplicate patients. The mean age of the 204 included patients was 68.3 years and 97 (47.5%) were female. Eighteen (8.8%) patients had a positive COVID-19 test within 180 days of receiving Evusheld. None of the COVID positive patients were admitted to the hospital or required mechanical ventilation. All COVID positive patients survived. Conclusion. Our study shows that Evusheld was effective in preventing COVID-19 among the immunocompromised patients during the six-month followup period. This study also showed that patients who developed COVID-19 after Evusheld did not develop severe disease or require hospitalization.

Internal Medicine
Kaur J, **Jagannathan M**, **Jordan T**, **Kinsey D**, **Truppiano M**, **Shallal A**, and **Suleyman G**. Genomic surveillance of invasive Streptococcus pyogenes in Metropolitan Detroit. *Open Forum Infect Dis* 2025; 12:S1094. Full Text

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

Background. Group A streptococcal (GAS) disease is a major problem worldwide and can cause both noninvasive and invasive disease, including necrotizing fasciitis, with significant morbidity and mortality. Overall, the number of invasive GAS infections has been increasing in the United States over the past decade, primarily in adults. We aim to characterize the genomic features of circulating GAS strains causing invasive disease. Table. Patient demographics and genomic characteristics Methods. We performed whole-genome sequencing (WGS) on clinically obtained GAS blood isolates at Henry Ford Health, a comprehensive, integrated, health care organization in Southeast Michigan from Jan 2017-Dec 2023. Sequencing libraries were created using the QIAseq FX DNA Library Kit (Qiagen, USA) according to manufacturer's instructions and sequenced on NextSeq 2000 (Illumina Sandiego, USA). Fastq files were used to determine the distribution of traits, virulence factors, and resistance genes using the 1928 Platform. Results. We sequenced unique isolates from 64 patients, of whom 38 (59%) were males with median age 57 years [Table]. Most isolates were from 2022 (25%) and 2023 (53%). Fifteen M protein (emm) serotypes and 19 sequence type (ST) were obtained from 64 characterized isolates. The most frequent emm lineages were emm1 (n=16) and emm12 (n=12), where most patients had skin and soft tissue infection. The predominant emm1 lineage belonged to ST28. None of the emm1 and emm12 isolates carried aminoglycoside, macrolides/lincosamides/streptogramines (MLS), or tetracycline resistance genes. All the emm11 and emm49 isolates exhibited erm(A) and tetracycline resistance genes. Streptococcal superantigen (SAgs) genes were frequently detected; streptococcal pyrogenic exotoxin (SPE)-G was the most detected SAgs (97%), followed by streptococcal mitogenic exotoxin (SME)-Z (75%). SPE-H and SPE-I were each found in 48% of the isolates. Conclusion. In our cohort of patients with invasive GAS, several SAgs were detected. SPE-A, SPE-G, SME-Z and SPE-J were most frequently found in emm1 lineages. However, there was no correlation between various clinical syndromes and the virulence genes identified. Continued genomic surveillance can help characterize features associated with emerging invasive strains to inform management and infection prevention strategies.

Internal Medicine
Kinsey D, **Jagannathan M**, **Jordan T**, **Kenney RM**, **Veve M**, **Shallal A**, and **Suleyman G**. Invasive Streptococcus pyogenes Infections: Is Anti-toxin Therapy Necessary? *Open Forum Infect Dis* 2025; 12:S582. Full Text

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Background. Invasive Streptococcus pyogenes or group A Streptococcus (GAS) carries a high morbidity and mortality rate. In addition to penicillin, adjunct antitoxin therapy (AT) with linezolid or clindamycin is the standard of care. Although the use of AT is supported by in vitro data and observational studies, there are limited conclusive data supporting its efficacy in reducing GAS mortality. Our study aimed to compare clinical outcomes of patients receiving AT versus those who did not. Methods. This was a retrospective cohort study of hospitalized patients with positive blood cultures for GAS at our five-hospital system from June 2013 to August 2023. Patients were identified through Microsoft SQL Server. Patients who received AT therapy for > 48 hours were defined as the AT group; the control group did not receive AT therapy. Patients who received AT for < 48 hours were excluded. Collected variables included demographics,

infection & microbiological characteristics, and clinical outcomes. Data was analyzed using SPSS. Results. 265 patients were included in the study of whom 179 (68%) received AT (Table 1). About half were female, and the median age was 58 years. Comorbidities were overall similar between the two groups. Persons who inject drugs or with chronic hepatitis C were more common in the control group. Abscess/cellulitis was the most common clinical syndrome in both groups. Shock requiring vasopressors, need for dialysis and mechanical ventilation, and toxic shock syndrome were prevalent in the AT group. There was no difference in the duration of bacteremia, clindamycin resistance, and management between the two groups except for receipt of intravenous immunoglobulin (IVIG), which was more common in the AT group (Table 2). Outcomes, including length of stay, readmission for infection-related complications, and 30-day mortality, were similar between the two groups. Conclusion. Utilization of AT for invasive GAS infections correlated with severity of illness, but clinical outcomes did not significantly differ between patients receiving AT and those who did not, suggesting a potential opportunity for antimicrobial stewardship. Further research is needed to determine whether AT should be reserved for patients with select infectious syndromes.

Internal Medicine

Konja J, **Major J**, **Thavarajah K**, **Sayf AA**, **Calo S**, **Martirosov A**, and **Hameed AMA**. Anti-Ro52 Associated Interstitial Lung Disease: A Retrospective Analysis. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

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Rationale: Interstitial Lung Disease (ILD) is a common manifestation of myositis and is associated with worse morbidity and higher mortality. Antibodies to SSA antigen (Ro52/Ro60) consist of two distinct auto-antibody systems with different clinical associations. Ro52 antigen has been identified as a 52 kDa protein, belonging to the tripartite motif (TRIM) protein family and it is the most common myositis-associated autoantibody (MAA) found in patients with myositis. The co-existence of anti-Ro52 antibody with other myositis-specific autoantibodies (MSA) is thought to be predictive of an aggressive ILD course. This study aims to describe the characteristics of patients with ILD and a positive anti-Ro52 antibody. Methods: A retrospective cohort study of patients evaluated by a provider of the Henry Ford Health (HFH) ILD program and a positive anti-Ro52 antibody was performed. We collected demographic data including gender, age at diagnosis, ethnicity, insurance, and zip code as well as diagnostic makers such as serology results, pulmonary function tests (PFT), and imaging. We further reviewed evaluations by sub-specialties including rheumatology, dermatology, and neurology to assess confirmation of diagnosis of myositis. Descriptive statistics were performed. Categorical variables are reported as (n) total counts with percentages and continuous variables are reported with mean and standard deviation (SD). Univariate differences were assessed between anti-Ro52 positive patients with and without an MSA using Pearson's chi-squared test and t-tests. Results: Our study included 78 patients with a positive anti-Ro52 antibody evaluated by the HFH ILD provider team. Of these, 43 (55.1%) were female and 21 (26.9%) also had a positive MSA including 3 Jo1, 3 PL7, 2 PL12, 1 OJ, 4 MDA5, 4 TIFF, 3 NXP, 2 MI2, and 1 SRP autoantibodies. Evaluations included 41 (52.6%) by rheumatology, 26 (33.3%) by dermatology, and 31 (39.7%) by neurology and 17 (21.8%) had a confirmed diagnosis of myositis. Pulmonary Function Tests (PFT) of these patients showed mean forced vital capacity (FVC) percent of 62.4% (S.D 21.1%) and mean diffuse capacity of carbon monoxide (DLCO) percent of 38.6% (S.D 16.3%). High resolution CT imaging showed 64 of the patients (82.1%) with ground glass opacities, 11 (14.1%) with consolidations, 38 (48.7%) with reticulations, 43 (55.1%) with bronchiectasis, 19 (24.4%) with honeycombing, and 2 (2.6%) with air trapping. Conclusions: Our patient population represented primarily female gender with the majority not having confirmed myositis. When comparing patients with positive anti-Ro52 antibody with and without MSA, there were no statistically significant characteristics found.

Internal Medicine

Major J, **Konja J**, **Thavarajah K**, **Calo S**, **Abu Sayf A**, **Martirosov A**, and **Hameed AMA**. Myositis Specific Antibodies and Interstitial Lung Disease: A Single Center Retrospective Study. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

[Major, J.; Konja, J.; Thavarajah, K.; Martirosov, A.; Hameed, A. M. Abdul] Henry Ford Hosp, Detroit, MI USA; [Calo, S.] Cleveland Clin, Cleveland, OH USA; [Abu Sayf, A.] Pulm & Crit Care, Detroit, MI USA
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Rationale: Myositis-specific antibodies (MSA) are commonly present in patients with myositis. Interstitial lung disease (ILD) is a common extra-skeletal manifestation of myositis that often precedes muscular or skin involvement. Many individuals with MSA and ILD never progress to develop typical features of myositis. This study aims to describe the characteristics of patients with ILD and a positive MSA. Methods: A retrospective cohort study of patients evaluated by a provider of the Henry Ford Health (HFH) ILD program and an MSA antibody was performed. MSA included Jo-1, PL7, PL12, EJ, OJ, MDA5, TIFF, NXP, Mi2 and SRP autoantibodies. Demographic data including gender, age at diagnosis, and diagnostic makers such as serology results, pulmonary function tests (PFT), and High-resolution computed tomography (CT) findings at the time of initial evaluation were collected. Evaluations by sub-specialties including rheumatology, dermatology, and neurology were reviewed for a formal myositis diagnosis. Descriptive statistics were performed. CT findings and PFTs at the time of diagnosis were analyzed for statistical differences between patients with a confirmed diagnosis of myositis-associated ILD (M-ILD) and idiopathic ILD with a positive MSA (I-ILD w/MSA) Results: This study included 127 patients of whom 62% were female. 69.3% were evaluated by rheumatology, 42.4% by dermatology, 47.2% by neurology, and 40.9% were confirmed to have a diagnosed with myositis. MSA included 47 Jo-1, 8 PL7, 14 PL12, 1 EJ, 2 OJ, 15 MDA5, 11 TIFF, 18 NXP, 9 MI2, and 7 SRP. The mean percentage of predicted Forced Vital Capacity (FVC) was 68.4% with a standard deviation of 19.6. Mean Diffusion Capacity for Carbon Monoxide (DLCO) was 46.9% with a standard deviation of 19.3. Imaging demonstrated 70.9% with ground glass opacities, 15.7% consolidation, 42.5% reticulation, 55.1% bronchiectasis, and 16.5% honeycombing. Statistical significance was found for M-ILD to present with consolidation on imaging, whereas I-ILD w/MSA was more likely to present with honeycombing. Conclusions: This cohort represents a female predominance in those with ILD and positive MSA. Furthermore, those with I-ILD w/MSA more frequently presented with honeycombing on imaging suggesting advanced disease at the time of presentation compared to M-ILD. Ultimately, given only 40.9% of this population possessed a formal diagnosis of myositis, further investigation regarding the relationship of MSA and ILD is warranted. Future studies should elicit disease course and response to treatment between these two groups. Figure 1: Characteristics of our patient population. Standard deviation for PFT's within brackets. Significant P values are bolded.

Internal Medicine

Mann Y, Ogbenna UK, **Ishak A**, Kasmikha L, **Numi M**, **Iyer H**, **Rehman S**, Kadouh A, Mangal R, Qasawa A, Dehghani A, Hasso M, Henry J, **Santana-Garcés M**, **Rehman NK**, **Bryce R**, **Zervos M**, and **Joshi S**. Utilization of a Point-of-Care Hepatitis C Test to Treat in People Experiencing Homelessness with Street Medicine Outreach. *Open Forum Infect Dis* 2025; 12:S899. Full Text

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Background. Persons experiencing homelessness (PEH) have disproportionately higher rates of untreated chronic hepatitis C virus (HCV) than the public. Improved community funding and resources are needed to expand HCV rapid point-of-care (POC), confirmatory testing, treatment and follow-up. Given that PEH face competing priorities (unstable housing, food access, addiction, other infections), it is our role as clinicians to reduce barriers to HCV treatment, understand hesitancies for deferring treatment, and design programs to improve accessibility. This is the pilot project of a Street Medicine (SM) based initiative to use POC testing for HCV amongst PEH with linkage of care to a federally qualified health clinic (FQHC). Hepatitis C Screening and Treatment Protocol HCV- Hepatitis C Virus POC- Point of Care CHASS- Community Health and Social Services HbsAg- Hepatitis B Surface Antigen CBC- Complete Blood Count CMP- Complete Metabolic Panel Methods. SM provides medical care to PEH outside of a hospital setting. Medical students and residents were recruited to form a HCV outreach team at Henry Ford Hospital and trained in HCV testing via OraQuick rapid antibody (Ab) test. During SM outreach, PEH were provided education on HCV and offered POC testing with a $10.00 grocery gift card. If a patient was identified as HCV Ab positive they were provided free transportation to a FQHC for confirmatory testing. If

diagnosis was confirmed, they were evaluated for eligibility for simplified HCV treatment, check-ins to assess adherence and sustained virologic response (Figure 1). Results. From February-April 2024, 103 PEH were tested using POC HCV testing on SM runs, with 4 positive results. 3 of 4 patients were confirmed for CHASS clinic appointments. 1 patient presented to clinic follow-up but deferred confirmatory testing bloodwork, demonstrating challenges in arranging for HCV clinic follow-up care. Conclusion. Previous studies have shown that lack of insurance, prior authorization and referral process, active injection drug use or alcohol use, lack of knowledge of HCV treatment, and limited healthcare workforce and infrastructure have all contributed to the low treatment rate in the homeless. Using trusted community organizations with SM, this initiative aims to reduce testing and transportation barriers in order to eliminate HCV in PEH. Larger numbers of positive patients are needed to best assess the feasibility of the program, and if providing all testing and treatment at the point of care is needed to improve compliance.

Internal Medicine

Miller C, Bradley D, Wood I, **Willens D**, **Nair A**, **Brennan B**, **Bole S**, **Poisson L**, Hall S, Thomson G, **Hirata M**, **Kalmbach D**, and **Drake C**. Digital CBT for Insomnia Is Linked to Reductions in Healthcare Use in Real-world Settings at Henry Ford Health. *Sleep* 2025; 48:A236. Full Text

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Introduction: Digital CBT-I offers a scalable solution for insomnia treatment, but evidence of its real-world adoption and impact in U.S. clinical settings is limited. This study evaluates the implementation and effects of digital CBT-I within a U.S. healthcare system, utilizing Normalization Process Theory to integrate it into clinical workflows. We compare healthcare utilization between patients who engaged with digital CBT-I and those who were offered but did not use it. Methods: Patients with insomnia were offered digital CBT-I via electronic and clinical workflows at the Internal Medicine and Sleep clinics within Henry Ford Health, Detroit, Michigan. Normalization Process Theory guided implementation. Electronic order rates and patient sign-ups assessed implemen tation success and workflow acceptability. Clinician training sessions and educational materials supported uptake. A propen sity-matched case-control design compared healthcare utilization rates between 340 digital CBT-I users and 340 matched controls, who were offered digital CBT-I but did not use it. We analyzed patient chart data and standardized time across patients. We evaluated the odds of medication fills and visits before and after. Results: A total of 340 patients utilizing digital CBT-I from treat ing practitioners were matched with 340 controls who did not. Digital CBT-I patients exhibited a 64% reduction in medication fills (for any condition) during the post-treatment period rela tive to before ($p< 0.001$), and were 53% less likely to fill insom nia-specific prescriptions compared to pre-treatment ($p=0.013$). Controls showed no significant changes. Time-varied logistic regression indicated that digital CBT-I patients had 37% higher odds of using outpatient services within the initial 30-60 days ($p=0.048$), but subsequently showed 28% lower odds at 120-150 days ($p=0.041$), and 41% lower odds at 150-180 days ($p=0.039$). Conclusion: Normalization Process Theory effectively facilitated the integration of digital CBT-I into clinical workflows, providing immediate access with minimal workflow disruptions. Training ses sions and ongoing clinician reminders promoted patient uptake of standard care for insomnia management. Findings indicate that dig ital CBT-I is associated with reduced medication fills and decreased odds of outpatient visits over time, suggesting its potential as an effective, scalable treatment for insomnia in clinical settings

Internal Medicine

Morgan S, **Rocha I**, **Parsons A**, and **Karmally R**. Management of Rapidly Reaccumulating Pleural Effusion Secondary to Pancreaticopleural Fistula in a Nonsurgical Candidate. *Am J Respir Crit Care Med* 2025; 211:1. Full Text

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INTRODUCTION: Pancreaticopleural fistula (PPF) is a rare complication of chronic pancreatitis. Current treatment options include medical management with thoracentesis and octreotide, endoscopic retrograde cholangiopancreatography (ERCP) with stenting to close off the fistula tract, and pancreatic salvage surgery for fistula repair. We present a complicated case of PPF with rapidly re-accumulating pleural effusion and failed pancreatic stenting in non-surgical candidate. CASE: A 33-year-old man with past medical history of chronic alcoholic pancreatitis and severe malnutrition (body mass index 15.86) presented with dyspnea on exertion and pleuritic chest pain. Computed tomography (CT) showed large left-sided pleural effusion, complete collapse of the lung, and chronic pancreatitis. Thoracentesis revealed exudative fluid. Chest x-ray showed a small pneumothorax ex-vacuo and re-accumulation of pleural effusion. Magnetic resonance cholangiopancreatography (MRCP) showed a defect in the left diaphragmatic crura and a fistula from the pancreatic tail to the retro-crural region. Pleural effusion was initially managed with interval thoracentesis until chest tube placement. This was complicated by enlargement of the pneumothorax with lung collapse. ERCP demonstrated large ductal stones that precluded deep cannulation of the dorsal pancreatic duct, so the ventral pancreatic duct was accessed for stent placement. The large pneumothorax self-resolved, but the chest tube continued to have high output. Octreotide was started at 50 mcg every 8 hours for 1 day, then increased to 100 mcg every 8 hours, which resulted in decreased chest tube output over several days. He was discharged with the chest tube. Octreotide was discontinued on discharge, and he required several additional collection devices. Extracorporeal shockwave lithotripsy and ERCP with dorsal pancreatic duct stenting were planned outpatient for definitive management of the PPF. DISCUSSION: This case highlights multiple complexities of PPF treatment. Rapid re-accumulation of large-volume pleural effusions indicated a large fistula tract that required diversional stenting. Despite multiple ERCP attempts, large ductal stones in the pancreatic head prevented deep cannulation. Surgical intervention was considered, however severe malnutrition made him not a surgical candidate. Additionally, large volume drainage of exudative pleural effusion was complicated by a large pneumothorax ex-vacuo due to trapped lung pathology. Thoracic intervention was considered, however, the pneumothorax self-resolved. Due to high volume output from chest tube, octreotide was initiated for splanchnic vasoconstriction and resulted in reduced output. In patients who are not surgical candidates and fail endoscopic management, octreotide can be helpful in managing recurrent pleural effusion secondary to PPF, and further evaluation of efficacy is warranted.

Internal Medicine

Nakdali R, and **Bradley P**. Waxing and Waning Nodules: A Rare Diagnosis of Pulmonary Malt Lymphoma. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

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Introduction: Mucosa-associated lymphoid tissue (MALT) lymphoma is a rare type of non-Hodgkin's lymphoma that can involve extranodal sites, including the lungs. Primary pulmonary MALT lymphoma is an uncommon diagnosis, presenting incidentally or with nonspecific symptoms. We present a patient with long-standing pulmonary nodules and several inconclusive biopsies, ultimately diagnosed with pulmonary MALT lymphoma. Case: A 60-year-old man, with a 70-pack year smoking history, was incidentally found to have bilateral noncalcified pulmonary nodules, measuring up to 2.4cm, on routine lung cancer screening seven years prior to presentation to our clinic. The nodules were followed by annual computed tomography (CT) scans with waxing and waning size of the nodules. At the onset, he underwent two lung biopsies, however pathology was inconclusive with reactive changes, fibrous stroma and scattered chronic inflammatory cells. He deferred surgical biopsy due to concern for risks of surgery, which led to ongoing CT surveillance without definitive diagnosis. Imaging in 2024 demonstrated progression of the pulmonary nodules, with the largest nodule in the right upper lobe now measuring 5.5 x 3.7 cm, along with new nodules in both lungs. The patient remained asymptomatic, denying cough, hemoptysis, fever, chills, shortness of breath, and chest pain. A positron emission tomography (PET) scan revealed a hypermetabolic right upper lobe mass measuring 5.5 x 3.7 cm, with multiple foci of mild hypermetabolic satellites variable in size along with a hypermetabolic 1.7cm x 2.4cm pleural based pulmonary nodule in the left lower lobe, suggestive of malignancy. There was no evidence of metastatic disease. The patient underwent a bronchoscopic biopsy of the right upper lobe nodule. Pathology revealed a diagnosis of low-grade B-cell lymphoma, specifically extranodal marginal zone lymphoma of MALT type. Discussion: This

case highlights the evasive nature of pulmonary MALT lymphoma on imaging. In this case, our patient had bilateral pulmonary nodules that fluctuated in size over seven years and biopsies yielded two inconclusive results. A high index of suspicion led to the patient being reevaluated and eventual diagnosis. MALT lymphoma is the most common type of primary pulmonary lymphoma, which constitutes only 1% of all pulmonary malignancies. It is often indolent and can be asymptomatic, with a variety of findings on CT as described by numerous papers. Treatment options include surveillance, surgical intervention, chemotherapy, or immunotherapy, depending on the extent and progression of disease.

Internal Medicine
Nakdali R, **Ladzinski A**, Hashmi M, and **Kapadia D**. Asthma or Airway Obstruction? A Case of Substernal Goiter Presenting in Pregnancy. *Am J Respir Crit Care Med* 2025; 211:3. Full Text

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Introduction: A thyroid goiter, particularly a substernal goiter, can cause significant airway obstruction, which requires prompt management. In this case, we present a patient who initially presented as an asthma exacerbation with wheezing and was found to have a large thyroid goiter extending into the mediastinum and causing external compression of the trachea. Case Report: A 38-year-old female with a medical history of chronic hypertension with superimposed preeclampsia requiring C-section and asthma presented to the hospital at 36 weeks pregnant due to a 2-month history of shortness of breath with multiple emergency room visits, attributed to asthma exacerbations. During this presentation, she developed respiratory distress, requiring intubation in the emergency room. She was initially treated for an asthma exacerbation along with pre-eclampsia however due to concern for pulmonary embolism, she underwent a computed tomography (CT) scan which showed a large middle mediastinal mass causing mass effect on the esophagus and severe mass effect at the level of the carina. The mass measured 3.8 cm in the axial direction and 9 cm in the craniocaudal direction and extended out of the field of view of the CT scan. She underwent a rigid bronchoscopy with biopsy of the mediastinal mass followed by a C-section. Biopsy revealed thyroid follicular cells. Repeat bronchoscopy showed extrinsic compression of the trachea down to the main carina, with narrowing in the proximal (30%), mid (80%), and distal trachea (90%). She underwent placement of a metal self-expanding stent in the distal trachea as a silicone Y-stent could not be placed due to significant posterior extrinsic compression of the trachea preventing safe advancement of the rigid bronchoscope. Nuclear thyroid scan confirmed uptake throughout mediastinal mass contiguous with thyroid gland suggestive of substernal goiter. Thyroid labs were normal. The patient underwent hemi-thyroidectomy with pathological evaluation of resected mass showing a multinodular thyroid goiter. With relief of her tracheal obstruction, the patient subsequently underwent removal of her tracheal stent without complication a few weeks later. Conclusion: Several studies have suggested that pregnancy can increase the size of a thyroid goiter or pre-existing thyroid nodules. Substernal thyroid goiters can cause significant airway obstruction due to size which can be life threatening. Our patient presented several times for shortness of breath, which was attributed to asthma however recurrent "exacerbations" despite optimal medical therapy in patients should always prompt further investigations for other causes.

Internal Medicine
Ogedegbe OJ, Ntukidem OL, Saparov D, Olafimihan AG, Nwachukwu CE, Gold-Olufadi S, Becerra H, Shrestha N, Cheema AY, Atencah SN, **Bai S**, and Malik D. Comparative effectiveness of CAR-T cell therapy and BiTE therapy in relapsed/refractory diffuse large B-cell lymphoma: A propensity score matching analysis using real-world data from the US collaborative network database. *J Clin Oncol* 2025; 43:e19020. Full Text

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Background: Diffuse Large B-cell lymphoma is the most common form of non-Hodgkin lymphoma. Relapsed/refractory Diffuse Large B-cell Lymphoma (DLBCL) presents significant treatment challenges. CAR-T cell therapy and BiTE therapies have emerged as promising options. This study aims to compare their effectiveness using propensity score matching, leveraging real-world data from the TriNetX network to assess clinical outcomes and guide treatment decisions for DLBCL. Methods: This retrospective cohort study utilized the TriNetX database, a global health research network, to identify adult patients with relapsed/refractory Diffuse Large B-cell Lymphoma (DLBCL) who received CAR-T cell therapy or BiTE therapy. The CAR-T cell therapy included axicabtagene, lisocabtagene, tisagenlecleucel) or BiTE therapy included Epcoritamab and Glofitamab. A propensity score matching (PSM) approach was used to balance baseline characteristics between the two treatment groups, minimizing confounding biases. Key covariates such as age, sex, comorbidities, model. 1:1 matching was performed using nearest-neighbour matching without replacement, ensuring comparability between the CAR-T and BiTE groups. Results: Before PSM, there were 1,533 patients in the CAR-T cohort and 142 patients in the BITE therapy cohort; however, after PSM, there were 133 patients in both cohorts. Mean age (59.4 vs 57.9 years), male (60.53% vs 57.04%), white (76.69% vs 72.18%). Compared to BITE therapy, CAR-T therapy demonstrated improved overall survival (OS) (hazard ratio [HR] 0.45 (95% CI 0.32-0.61, p , 0.95). BITE therapy also had a higher risk for pancytopenia (odds ratio [OR] 4.663 [2.35-9.26], p , 0.01). The risk of diarrhoea and fatigue was, however, not statistically significant. Conclusions: This study provides valuable realworld insights into the comparative effectiveness of CAR-T cell therapy and BiTE therapy for relapsed/refractory DLBCL. The results, derived from propensity score-matched cohorts, offer far-reaching help to guide the holistic management of this patient population.

Internal Medicine
Olafimihan AG, Jackson I, Ntukidem OL, Ogedegbe OJ, George LJ, **Ethakota J**, **Bai S**, and Farooqui MW. Inpatient characteristics and outcomes of diffuse large B-cell lymphoma in adolescents and young adults. *J Clin Oncol* 2025; 43(16_suppl):e19042. Full Text

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Background: Diffuse large B-cell lymphoma (DLBCL) is the most commonly aggressive nonHodgkin's lymphoma known to also affect adolescents and young adults (AYA). This population faces unique challenges such as financial toxicity, physical and emotional concerns. We examined the inpatient characteristics and outcomes of AYA patients with a diagnosis of DLBCL. Methods: A retrospective cohort analysis using the Nationwide Inpatient Sample database from 2008 to 2021, DLBCL patients with non-elective hospitalizations were identified using ICD-9 and ICD-10 codes. Descriptive analyses were conducted using STATA version 17.0 to compare sociodemographic and clinical characteristics between AYA and older populations. Multivariable logistic and linear regression models were used to examine the association between the age groups and inpatient mortality, prolonged (.5 days) length of stay (LOS), and total hospital charges. Results: There were 346,185 non-elective hospitalizations with DLBCL within the 14-year study period. Of these, 23,163 (6.7%) were in the AYA cohort.The mean age was 30 years in the AYA group and 68.4 years in the older group (P=0.001). There was a higher proportion of males in the AYA group compared to the older group (59.2% vs 56.4%, P = 0.001) but a lower distribution of non-

Hispanic Whites (48.6% vs 71.7%, P , 0.001). Regarding clinical characteristics, AYA-DLBCL patients had a higher frequency of febrile neutropenia (19.5 vs 13.6%, P,0.001), bone marrow transplant (4.7 vs 3.8%, P,0.004), HIV (14.5 vs 2.6%, P,0.001), superior vena cava syndrome (3.8 vs 0.9%, P,0.001) and cardiac tamponade (1 vs 0.2%, P,0.001). AYA-DLBCL patients had a lower frequency of severe sepsis (6.3 vs 8.1%, P,0.001), AKI (12.8 vs 23.6%, P,0.001), and acute respiratory failure (6.4 vs 10.5%, P,0.001). On multivariable logistic regression, the AYA group had 50% lower odds of mortality relative to the older adult group (adjusted odds ratio [aOR]: 0.51, 95% confidence interval [CI]: 0.43-0.60, P , 0.001).There was a lower odd of prolonged hospital stay in the AYA group (aOR: 0.88, 95% CI: 0.82-0.93, P , .001).TheAYA cohort had higher odds of increased hospital expenditure (b-Coefficient: 11,260, 95% CI: 3,794–18,728, P = 0.003). Conclusions: This represents the largest epidemiological study to date on DLBCL hospitalizations in AYA. The AYA cohort had lower inpatient mortality, increased hospital costs, and higher rates of febrile neutropenia and HIV. Higher hospital charges may be due to more febrile neutropenia rates, bone marrow transplants and other aggressive interventions performed in younger patients. Additional studies are needed to understand and improve long-term treatment-related toxicities in this population.

Internal Medicine

Patrus M, **Pradeep A**, **Altahan O**, and **Parsons A**. A Case of Leptospirosis Induced Acute Respiratory Distress Syndrome. *Am J Respir Crit Care Med* 2025; 211:1. Full Text

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INTRODUCTION: Leptospirosis is an infection that is often overlooked due to its low incidence in the United States, especially in cooler climates. It is also underdiagnosed due to its mild clinical course in many patients. We present a case of severe leptospirosis in a patient presenting with sepsis and multiorgan involvement. CASE: A 66-year-old female with a past medical history of hyperlipidemia presented with a five-day history of fatigue, chills, nausea, and vomiting. She was found to be tachycardic, tachypneic, febrile, and hypoxic initially requiring 2 liters via nasal cannula. Her preliminary workup was significant for hyponatremia, acute kidney injury, transaminitis, hyperbilirubinemia, and thrombocytopenia. Urinalysis and creatinine kinase were consistent with rhabdomyolysis. Her chest x-ray was unremarkable, with computed tomography (CT) abdomen and pelvis showing tree-in-bud nodules in the lung bases. She was started on antibiotics, however continued to worsen and was admitted to the medical intensive care unit. Her oxygen requirements continued to escalate, up to 30 liters via heated high-flow nasal cannula. CT chest showed interval worsening of diffuse lung disease with bilateral ground glass opacities and septal thickening concerning for acute respiratory distress syndrome (ARDS). Her PaO2/FiO2 ratio was 146, suggestive of moderate severity ARDS. An extensive workup by multiple specialties did not reveal the cause of her overall clinical picture, with respiratory viral panel, legionella, autoimmune liver panel, and multiple myeloma testing all negative. On hospital day four, it was noted that the patient was a gardener and had recently cleaned out rat traps around her garden. Antibiotics were changed to ceftriaxone and azithromycin due to concern for leptospirosis, with a positive IgM confirming the high clinical suspicion of our infectious disease team. She completed antibiotic therapy with continued improvement in her oxygen requirements, creatinine, thrombocytopenia, and bilirubin. A repeat chest x-ray done one week after discharge showed no abnormality. DISCUSSION: This patient presented with a constellation of symptoms classic for icteric leptospirosis, including jaundice, renal failure, thrombocytopenia, and ARDS. In addition, she was found to have known risk factors of rodent and contaminated soil exposure while gardening. Of note, this patient was originally on ampicillin-sulbactam and changed to ceftriaxone once there was suspicion for leptospirosis. Placing leptospirosis on the differential as well as taking a detailed social history in similar cases may allow for earlier diagnosis and more targeted antibiotic therapy.

Internal Medicine

Payal F, **Bai S**, Yagnik K, Aakash F, Adwani R, and Du D. From Pancreas to Pleura: Insights Into Pancreatic Fistula as a Result of Recurrent Pancreatic Inflammation. *Am J Respir Crit Care Med* 2025; 211:1. Full Text

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Introduction:Pleuro-pancreatic fistula (PPF) is a rare complication of chronic pancreatitis, involving anabnormal connection between the pancreatic duct and pleural space due to pancreaticinflammation. It typically presents with recurrent pleural effusions and pulmonary symptoms,often without overt pancreatic signs. Key indicators include a history of pancreatitis, significantweight loss, and pleural effusions or ascites unresponsive to diuretics.Case presentation:A 33-year-old male with a history of alcohol use disorder, chronic pancreatitis, pseudocystformation, and a pleuropancreatic fistula presented with worsening shortness of breath and chestpain. He had a recent large pleural effusion, with thoracentesis revealing pleural fluid pancreaticamylase at 300 U/L. Imaging showed a large left pleural effusion and new pancreatic cysticlesions. After thoracentesis and chest tube placement, a trapped lung was revealed. An attemptedERCP was complicated by pancreatic duct obstruction, but a stent was eventually placed. Hiscondition worsened due to ongoing fistula leakage, and a pancreaticoduodenal arterypseudoaneurysm was identified, requiring IR-guided embolization. He was transferred to atertiary hospital, where a mini atrium collecting system was placed for fluid drainage. He wasdischarged with a left chest tube and scheduled for outpatient follow-up.Discussion:Pleuro-pancreatic fistula (PPF) is a rare complication, occurring in less than 1% of acutepancreatitis cases and 4.5% of pancreatic pseudocyst cases, primarily linked to alcohol-relatedchronic pancreatitis. Diagnosis involves chest X-ray, CT scans, and thoracentesis, with pleuralfluid analysis showing high pancreatic amylase levels, often above 10,000 U/L. MRCP is thepreferred imaging modality for confirming the fistula. Treatment options include medicalmanagement with octreotide and TPN (31%-65% success), ERCP stenting, or surgery. Surgery ismost effective (94% success), particularly in cases where medical and ERCP treatments fail. The choice of treatment depends on imaging findings, with surgery indicated for complete duct-obstruction or disruption in the pancreatic tail.Conclusion:In conclusion, PF diagnosis relies on clinical suspicion, high pleural fluid amylase, and the imaging.,with treatment—medical, endoscopic, or surgical— determined by case specifics and a multidisciplinary approach.

Internal Medicine

Sharma M, Szpunar SM, Bhargava A, and Saravolatz L. Risk Factors Associated with Lower Respiratory Tract Infections in Adult Patients with Respiratory Syncytial Virus Infections. *Open Forum Infect Dis* 2025; 12:S520. Full Text

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Background. Respiratory Syncytial Virus (RSV) is known to cause severe disease in elderly individuals and patients with underlying cardiopulmonary or immunocompromised conditions. Little is known about the factors associated with the lower respiratory tract infections (LRTI). Methods. A multicenter historical cohort study was conducted on adult patients hospitalized for laboratory-confirmed RSV-related diseases in Ascension hospitals in Southeast Michigan between January 2017 and December 2021. Hospitalized patients were identified using ICD 10 codes for RSV-related diseases. Medical records were reviewed after IRB approval. LRTI was defined as an acute respiratory disorder meeting at least three out of four criteria: respiratory signs/symptoms (cough/ dyspnea/ tachypnea), fever, oxygen saturation below 94%, and abnormal chest x-ray at the time of hospital admission. Data were analyzed using Student's t-test, the chi-Squared test, the Mann-Whitney U test and logistic regression using SPSS v. 29.0. Results. Of 360 patients, 143 (39.7%) had LRTI. The mean (sd) age of patients with LRTI was 69.1 + 15.3 years, and 76 (53.1%) were female. The mean Charlson Weighted Index of Comorbidity score was 2.5 + 2.1. Factors associated with LRTI in univariable analysis were age, sex, asthma, time period (TP) (pre-COVID (2017-2019) and COVID (2020-2021), maximum temperature within 24 hours of admission (Tmax), lowest diastolic blood pressure, oxygen requirement and neutrophil count at admission, infectious disease (ID) consultation, and antibiotics given for >1 day. Predictors for LRTI in multivariable logistic regression were COVID TP (odds ratios [OR], 2.0; 95% CI 1.2-3.4), Tmax ([OR], 1.2; 95% CI 1.0-1.5), oxygen requirement at presentation (OR, 2.1; 95% CI 1.2-3.4), ID consultation ([OR], 2.7; 95% CI 1.6-4.4), antibiotics given for

>1 day (OR, 3.7; 95% CI 2.2-6.2) while female sex was inversely related to LRTI episodes ([OR], 0.4; 95% CI 0.3-0.7) . Conclusion. Our study finds that COVID time period, maximum temperature within 24 hours of admission, oxygen requirement at admission, ID consultation, and antibiotics given >1 day were significantly associated with LRTI among adult patients with RSV infection. Female sex was less likely to have LRTI. Further studies needed to confirm these findings.

Internal Medicine
Toiv A, Doshi N, **Ishak A**, and **Lanfranco OA**. Highly Resistant Myroides Species Infections: Insights from a Comprehensive Case Series and Antibiogram Analysis. *Open Forum Infect Dis* 2025; 12:S540. Full Text

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Background. Myroides species (spp.) are rare opportunistic gram-negative bacteria that are highly resistant to commonly used empiric antibiotics. Able to survive in natural and hospital environments, these microbes pose a growing risk of resistant nosocomial infections. Here we present a case series and antibiogram of Myroides infections at an academic medical center, highlighting this potential pathogen's antibiotic sensitivity to aid clinicians in choosing effective antimicrobial therapies. Antibiogram Methods. Retrospective chart review of all patients diagnosed with Myroides spp. infection at Henry Ford Health between January 1, 2019 and December 31, 2023. Patient characteristics, treatments, and outcomes were analyzed. An antibiogram of Myroides spp. susceptibility to 10 antibiotics was generated. Results. A total of 43 patients (median age 62 yr; range 30-94) presented with 46 Myroides spp. infections. Positive cultures were evenly distributed between hospitalizations (50%) and outpatient (50%) settings. Of the 46 infections, 35 (76%) were in a lower extremity wound. Of the 43 patients, 17 (40%) had sepsis at presentation, including 8 (13%) with Myroides bacteremia. Most Myroides spp. cultures (83%) grew additional organisms, including E. faecalis (34%), S. aureus (21%), Proteus mirabilis (21%), and Pseudomonas spp. (16%). Empiric antibiotics were prescribed in 35/46 cases (76%), mostly vancomycin (17/35) and cefepime (9/35); however, Myroides spp. were sensitive to the empiric agents in only 4 cases (11%). Antibiogram analysis showed 100% susceptibility to meropenem and 0%-50% susceptibility to 9 other agents (Table). A total of 5 (12%) patients died, and 6 patients (14%) required readmission within 1 month of treatment. Conclusion. Myroides spp. exhibited significant resistance to most empiric antibiotics. Our antibiogram analysis revealed meropenem as the sole effective empiric antibiotic for this opportunistic pathogen. We recommend the prompt empirical use of meropenem when Myroides spp. are identified on antimicrobial culture.

Internal Medicine
Venkatesh HK, **Salib N**, and **Osobamiro O**. A CASE OF FIBRILLARY GLOMERULONEPHRITIS ASSOCIATED WITH PEMBROLIZUMAB USE DURING BREAST CANCER TREATMENT. *Am J Kidney Dis* 2025; 85(4):2. Full Text

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Prior studies have enumerated various immune-mediated effects of which 1-2% involve the kidneys, starting from 10 days of initiation up to 3 months after discontinuation. AIN is the most common picture, although other pathologies like ATN, MCD, IgA nephropathy, FSGS, crescenteric GN, anti-GBM GN, C3 GN and ANCA-associated vasculitis have also been demonstrated. 4 cases of fibrillary glomerulonephritis (FGN) were ascribed to nivolumab, ipilimumab and atezolizumab, however, this report possibly describes the first occurrence related to pembrolizumab. A 73-year-old Caucasian female, with no history of CKD or proteinuria, was treated for invasive ductal carcinoma with pembrolizumab, doxorubicin and cyclophosphamide. Within 3-4 days of completing the 3rd cycle, she developed new-onset hypertension, with a corresponding creatinine rise from 0.94 to 2.05 mg/dL in 1 month and urine Alb/Cr ratio of 8253.8 mg/g. Renal biopsy revealed fibrillary glomerulopathy with moderate interstitial fibrosis and tubular atrophy. The only remarkable immunologic workup was a positive ANA. Creatinine appeared to improve initially with a prednisone taper over 5 months but eventually progressed to 2 mg/dL in 2 years. At 1 year, empagliflozin was added to stabilize proteinuria successfully. FGN is an infrequent renal disease with

characteristic disorderly fibrils on microscopy. Although the exact mechanism remains unascertained, it has been linked to multiple malignancies including 5 cases of breast cancer. Higher age, creatinine and proteinuria worsen the prognosis with nearly 50% progressing to ESRD within 4 years, despite steroids and cytotoxic agents. In this case, FGN could reasonably correlate with both breast cancer and pembrolizumab use. However, the timing of disease onset in the setting of cancer remission favors the latter. In summary, considering the novelty of immune checkpoint inhibitors, an AKI attributable to their use demands early recognition to avoid potentially inappropriate treatment and grave consequences. Multicenter controlled trials can further uncover therapeutic options to prevent FGN progression.

Nephrology

Rajanayagam J, **Huang TS**, **Elshayeb M**, and **Reddy S**. ELTROMBOPAG: A RARE CAUSE OF ACUTE INTERSTITAL NEPHRITIS. *Am J Kidney Dis* 2025; 85(4):2. Full Text

[Rajanayagam, Jocelynn; Huang, Tseng Sen; Elshayeb, Mohamed; Reddy, Snigdha] Henry Ford Hlth, Detroit, MI USA

Acute interstitial nephritis (AIN) commonly causes acute kidney injury (AKI) and accounts for 15–27% of renal biopsies performed. AIN occurs when there is inflammatory damage to the renal parenchyma caused by T-cell stimulation, medication-induced tubular damage and/or antibody mediated cellular injury. The known causes of AIN include antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), immune checkpoint inhibitors, and infections. However, this case will highlight Eltrombopag, a thrombopoietin receptor agonist, as a potential inciting factor of AIN. 70 year-old female with recent biopsy-proven aplastic anemia on cyclosporine, hypertension and pancytopenia presented with acute kidney injury (AKI) with a serum creatinine (SCr) 2.89mg/dL increased from baseline SCr 0.4-0.7mg/dL. Urinalysis showed 1+ blood and no albuminuria. Kidney ultrasound showed no hydronephrosis. AKI was unresponsive to volume repletion and progressively worsened. Serologic tests including C3/C4, CPK, LDH, haptoglobin, Anti-GBM, ANA, Anti double-stranded DNA, MPO/PR-3, anti-histone Ab, Anti-SCL–70, cryoglobulins were negative. Upon further review, Eltrombopag was initiated for refractory thrombocytopenia after which she developed a morbilliform rash of the trunk and extremities. Although she received other medications including cyclosporine, ciprofloxacin, anti-thymocyte globulin, and oxcarbazepine, the type and temporal relationship to rash onset is not commonly associated with these medications. Since kidney biopsy was not safe due to thrombocytopenia, it was reasonably assumed function returned to baseline within 8 days and the rash also resolved. Majority of AIN cases are commonly attributed to NSAIDs, antibiotics, and checkpoint inhibitors. This case is unique since Eltrombopag is not often associated with AIN. The temporal relationship between the AKI and rash along with the morbilliform drug eruption made Eltrombopag the probable cause of AIN. The prompt improvement in both the rash and renal function with discontinuation of Eltrom additionally supports Eltrombopag as the inciting agent for AIN.

Neurology

Korpole P, **Jaffery SH**, **Arcila-Londono X**, and **Bazan LF**. Description of Positive Airway Pressure Settings in Bulbar Onset Amyotrophic Lateral Sclerosis Patients Requiring Non-invasive Ventilation. *Am J Respir Crit Care Med* 2025; 211:1. Full Text

[Korpole, P.; Jaffery, S. H.; Arcila-Londono, X.; Bazan, L. F.] Henry Ford Hosp, Detroit, MI USA

Introduction : Amyotrophic Lateral Sclerosis (ALS) in general and bulbar onset ALS patients in particular are at high risk of developing respiratory failure secondary to neuromuscular weakness. Optimal Non-Invasive Positive Pressure Ventilation (NIPPV) settings are not clearly defined in this subgroup. Methods : A retrospective chart review study was designed to describe NIPPV settings in bulbar onset ALS patients who met initial compliance with NIPPV. Bulbar onset ALS patients were identified from a database including patients diagnosed with Motor Neuron Disease at Henry Ford Hospital from January 1, 2019 to December 31, 2023. Results : A total of 45 patients with bulbar onset ALS were identified and 37 patients were initiated on NIPPV therapy with 26 patients (70%) meeting compliance requirements. Amongst the compliant patients, 14 patients were initiated on Bilevel Positive Airway Pressure - Spontaneous Timed (BPAP-ST) mode and 12 patients on Volume Assured Pressure Support (VAPS) mode. At compliance, mean Positive Airway Pressure (PAP) therapy usage for more than or equal to 4 hours per 24 hours and

mean duration of PAP therapy use per 24 hours in the BPAP-ST and VAPS groups was 88% and 5.6 hours versus 81.5% and 5.7 hours respectively. In the BPAP-ST group, mean values of PAP settings and data were as follows: Inspiratory PAP (IPAP) 10.6 cm water, Expiratory PAP (EPAP) 5.7 cm water, backup rate 8.8 breaths per minute, tidal volume 447.3 ml, respiratory rate 17 breaths per minute, minute ventilation 7.5 liters per minute and Apnea Hypopnea Index (AHI) 5.4 per hour. In the VAPS group, mean values of PAP settings and data were as follows: target alveolar ventilation 4.2 liters per minute, back up rate 14 breaths per minute, minimum Pressure Support (PS) 4.6 cm water, maximum PS 13.9 cm water, EPAP 4.3 cm water, median IPAP 11.6 cm water, median EPAP 4.4 cm water, tidal volume 423.9 ml, respiratory rate 16.2 breaths per minute, minute ventilation 7.2 liters per minute and AHI 4.53 per hour. Conclusion : Both BPAP-ST and VAPS modes appear to be well tolerated in bulbar onset ALS patients requiring NIPPV. Further studies are required to analyze settings associated with NIPPV compliance in greater detail in bulbar onset ALS patients.

Obstetrics, Gynecology and Women's Health Services

Afaneh H, **Hirata M**, **Kalmbach D**, **Cheng P**, and **Pitts D**. Financial Toxicity, Racial Disparities, and Healthcare Access in Pregnant Women with Insomnia. *Sleep* 2025; 48:A260. Full Text

[Afaneh, Heba; Cheng, Philip; Pitts, D'Angela] Henry Ford Hlth, Detroit, MI USA; [Hirata, Mika; Kalmbach, David] Henry Ford Sleep Res, Detroit, MI USA; [Cheng, Philip] Michigan State Univ Hlth Sci, E Lansing, MI USA

Introduction: Insomnia affects half of women during pregnancy, which reduces quality of life and harms maternal health. As awareness of prenatal insomnia increases, more pregnant women are seeking help for their sleep. However, little is known about real-world barriers pregnant women face when seeking insomnia treatment. The present study explored associations of race and financial toxicity with clinical morbidity and care access among pregnant women seeking insomnia care. Methods: Three-hundred-and-ninety-three pregnant women (Age: 30.7 ± 4.9yrs; Gestation: 25.7 ± 3.4wks) seeking treatment for insomnia in a large health system completed an online survey. Outcomes included sociodemographics, the Comprehensive Score of financial Toxicity survey, Edinburgh Postnatal Depression Scale, and Perinatal Rumination Scale-Night. We employed chi-square analyses and multivariate linear and logistic regression. Results: Half of treatment-seeking patients identified racially as white (52.7%), whereas 21.7% identified as Black (most well-represented groups). Nearly half of the sample reported no/mild financial toxicity, whereas 39.2% endorsed moderate financial toxicity and 13.9% endorsed severe financial toxicity. Regarding health insurance, 29.9% of patients had public insurance. Relative to white patients, non-white patients reported higher levels of moderate-to-severe financial toxicity (62.4% vs 45.0%) and greater utilization of public insurance (40.9% vs 20.1%). Multivariate regression showed that financial toxicity was independently associated with depression (b=-.252, p<.001), perinatal rumination (b=-.491, p<.001), and suicidal ideation (SI; OR=1.07, p<.001), whereas race was not. Indeed, more severe financial toxicity was associated with greater disease burden as indicated by higher rates of comorbid depression (Severe toxicity: 80.0%; Moderate: 61.9%; No/Mild: 29.7%), perinatal rumination (Severe: 80.0%; Moderate: 56.8%; No/Mild: 28.1%), and SI (Severe: 23.6%; Moderate: 16.8%; No/Mild: 5.4%). Unfortunately, patients with greater financial toxicity were less likely to be able to afford copays for psychotherapy services (Severe toxicity: 69.1% cannot afford copays; Moderate: 57.1%, No/Mild: 27.2%). Conclusion: Pregnant women seeking insomnia treatment present with high rates of depression, perinatal rumination, and SI. Non-white women are over-represented among those with moderate-to-severe financial toxicity, and greater financial toxicity is associated with greater clinical morbidity. Despite this greater disease burden, patients with greater financial toxicity are disproportionately unable to afford care, thereby severely limiting treatment access for those with highest need.

Obstetrics, Gynecology and Women's Health Services

Chavez AG, **Xu TFY**, **Hirata M**, **Kalmbach D**, **Cheng PL**, **Drake C**, and **Pitts D**. Implementability of a Perinatal Sleep Clinic. *Sleep* 2025; 48:A565. Full Text

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Christopher] Henry Ford Hlth Syst, Detroit, MI USA; [Pitts, D'Angela] Henry Ford Hlth, Dept Obstet & Gynecol, Detroit, MI USA

Introduction: Sleep problems have been historically viewed as a normal feature of pregnancy, but a burgeoning literature high lights the high prevalence and morbidity of prenatal insomnia Half of pregnant women report speaking to their prenatal care provider about their sleep problems. However, care access is severely limited as most health systems do not have clearly iden tified clinics in which prenatal insomnia is managed. In 2023, Henry Ford Health (HFH) implemented the Perinatal Sleep Clinic (PSC), a telemedicine clinic co-directed by a clinical psychologist and obstetrician. As pregnant women with sleep disorders are not routinely treated in the HFH sleep clinic or behavioral health clinic, the PSC was intended to address an unmet patient need. The present study evaluated the implement ability of the PSC in a large health system. Methods: ~10,000 live births occur annually at HFH. The PSC launched to treat pregnant women with insomnia. We reviewed electronic medical records to describe patient throughput from January 2023 through November 2024. We surveyed 53 stake holders within and outside of HFH who had roles in health system leadership and/or clinical care in the areas of obstet rics-gynecology, maternal-fetal medicine, perinatal mental health, and/or sleep medicine. Surveys included the Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM). Scale scores range from 1-5 with higher scores indicating more favorable implementation ratings. Results: In 2 years, the PSC treated 110 pregnant women with insomnia. Among our surveyed stakeholders, 74.5% were employed by HFH. Stakeholders rated the PSC as highly accept able (AIM: 4.52±.67), highly appropriate (IAM: 4.61±.57), and highly feasible at HFH (FIM: 4.23±.68). Additionally, stake holders rated the clinic favorably for providing an unmet clini cal need (4.65±.52) and providing an important clinical service (4.65±.59). Most stakeholders (82.4%) indicated that the clinic should be hybrid, offering both telemedicine and in-person care options. Conclusion: As women increasingly seek help for their sleep dur ing pregnancy, clinic resources must be made available for these patients. Leadership and provider stakeholders supported the acceptability, appropriateness, and feasibility of the PSC (ide ally, as a hybrid clinic), thereby supporting its implementation in a large health system.

Obstetrics, Gynecology and Women's Health Services

Kheil M, **Miller M**, **Battiston S**, and **Vilkins A**. The Best Way Out: Outcomes of Vaginal vs Abdominal Morcellation in Hysterectomies. *Obstet Gynecol* 2025; 145(5S):2. Full Text

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INTRODUCTION: Laparoscopic hysterectomies often require man-ual morcellation of the uterus to allow for extraction abdominally orvaginally. While surgeon preference often drives this intraoperative decision, limited studies have compared perioperative and patient-centered outcomes across the two modes of morcellation. OBJECTIVE: To investigate the association between morcellation inlaparoscopic hysterectomy (LH) and patient-reported and objectivesurgical outcomes. METHODS: 73 patients undergoing LH for benign indications from 4/2023 to 2/2024 were recruited. Surveys assessing patient-reportedoutcomes including satisfaction with cosmesis (Likert scale 1–5; 1 - not satisfied, 5 - satisfied), incisional and deep pelvic pain (scale 0–10; 0 - no pain, 10 - excruciating pain), and return to baselineactivity level (yes/no) were administered 2 and 6 weeks postoperatively. Chart review was conducted to capture operative outcomes of interest. Appropriate statistical analyses were used to compare outcomes between patients who underwent morcellation vs those whodid not and a subanalysis was performed by type of morcellation (vaginal vs abdominal). RESULTS: Of the 73 patients, 45 (61.6%) did not undergo uterine morcellation and 28 (38.3%) did. Of the 28 patients, 9 (32.1%) underwent abdominal morcellation and 19 (67.8%) vaginal. Baseline group characteristics (e.g. average age, race, BMI, prior surgeries, medical co-morbidities, and lysis of adhesions) did not differ significantly. Comparison of surgical outcomes between the morcellation and no morcellation groups revealed longer procedure average time with morcellation compared to those without (247.2 min vs 194.6 min, p< 0.001) but no significant differences in estimated blood loss (p-0.356), length of stay (p-0.417), or postoperative complications (p> 0.999). No significant differences in EBL, length of procedure,length of stay, or post-op complications were noted when comparing vaginal vs abdominal morcellation (p>0.05). Patient-centered outcomes did not significantly vary between morcellation and no morcellation groups at 2 and 6 weeks:

cosmetic satisfaction (p-0.283 and 0.563, respectively), surgical site pain (p-0.429 and 0.09), deep pelvic pain (p-0.724 and 0.727), and return to daily activities (p-0.326 and 0.384). No significant differences were observed when comparing the same outcomes by morcellation site at 2 and 6 weeks: cosmetic satisfaction (p-0.669 and 0.353, respectively), surgical site pain (p-0.538 and >0.999), deep pelvic pain (p-0.790 and >0.999), and return to daily activities (p-0.407 and >0.999). CONCLUSIONS: Morcellation increases operative time; however, no differences in other objective or patient-centered outcomes were observed. This encourages surgeons to continue using this extraction method via their preferred route.

Pathology and Laboratory Medicine

Binte Tahir N, Venkataraman G, Rojek A, Symes E, Kaur A, Tjota M, Fitzpatrick C, Arber D, Wang P, Lager A, Perry A, Bell R, Chang H, Zhou Q, Menon M, Patel J, Patel A, Tariq H, Zhang J, Sojitra P, Nawas M, Patel A, DuVall A, Patil E, Badar T, Velmurugan S, Hasan F, and **Ghosh S**. 1295 Prognostic Impact of Chromosome 7 Losses in High-Grade TP53 Mutated Myeloid Neoplasms. *Lab Investig* 2025; 105(3). Full Text

Background: TP53 mutation (TP53MUT) and chromosome 7 loss (-7/7q) are both independently considered as adverse prognostic factors in high-grade (HG) myeloid neoplasms (MN). Whether the co-occurrence of -7/7q further worsens the poor prognosis of TP53MUT is unclear. To answer this, we evaluated the differential impact of -7/7q in HG TP53MUT MN. Design: We identified 322 patients with TP53MUT MN carrying ≥1 TP53MUT at a VAF ≥3% diagnosed between 2014-2024 across 10 centers with blasts ≥10% at diagnosis. Baseline clinical, pathological, cytogenetic and somatic information was extracted while stratifying patients by -7/7q status. The primary endpoint was to compare 24-month overall survival (OS24). Additional end-points included complete response to first-line (CR1) therapy per ELN 2022 guidelines (Table 1 footnote). Descriptive and outcome analyses were conducted in Stata 18 using flexible parametric (FP) and non-parametric survival methods. Results: The median age at diagnosis was 68.4 years. There was no difference in baseline characteristics stratified by -7/7q status (see Table 1). Patients with -7/7q were marginally more likely to harbor complex karyotype (P = .09) with significantly greater proportion harboring -17/17p (46.2% vs. 33.8%; P = .031) and TP53 VAF>25% (85.6% vs. 76.4%; P = .042) compared to those without -7/7q. The median duration of follow up (from diagnosis of TP53MUT MN to study exit) was 6.2 months (range: 0.0–72.8 months) with 77.0% receiving frontline non-intensive therapies, mostly HMA-based. First-line response was evaluable in 251 patients with 28.7% achieving CR, 24.7% had partial response, and 46.6% had non-response/stable-progressive disease. -7/7q was not associated with inferior frontline response (P = .35) in the entire cohort as well as in the intensively-treated subgroup (P = .92). Significantly greater proportions of those lacking -7/7q went on to receive alloSCT (20.7% vs. 11.1%; P = .023). In the entire cohort OS24 analysis, -7/7q was associated with inferior overall survival (HR = 1.5 [1.2–2.0]; Pfpm = .002; N = 298). In separate analysis by blast count and therapies, the adverse impact was restricted only to those subgroups with either high blast count or intensive therapy (See figure 1). [Formula presented] [Formula presented] Conclusions: Presence of -7/7q adversely impacts the prognosis of TP53MUT MN, an effect which is accentuated in patients receiving intensive chemotherapy and ≥ 20% blast count at diagnosis, supporting its prognostic utility in this context.

Pathology and Laboratory Medicine

Boettcher S, **Kenney RM**, **Arena CJ**, **Beaulac-Harris A**, **Tibbetts R**, **Shallal A**, **Suleyman G**, and **Veve M**. Say it Ain't Steno - Impact of a Microbiology Nudge Comment on Treatment of Respiratory Colonization. *Open Forum Infect Dis* 2025; 12:S1082. Full Text

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Background. Stenotrophomonas maltophilia (SM) is a known colonizer of the respiratory tract, in which treatment is not required. Microbiological comment nudges have been successful as passive stewardship interventions. The study objective was to describe the effect of a targeted SM respiratory culture nudge on antibiotic use in patients with colonization. Methods. IRB approved quasi-experiment of adult patients with a SM respiratory culture between 01/01/2022-01/27/2023 (pre-nudge) and 03/27/2023-12/31/2023 (postnudge). Patients with criteria for active community/hospital/ventilator-acquired pneumonia or on targeted antibiotics prior to culture were excluded. Nudge comment implemented 2/2023: S. maltophilia is

a frequent colonizer of the respiratory tract. Clinical correlation for infection is required. Colonizers do not require antibiotic treatment. The primary outcome was absence of SM therapy; secondary outcomes were SM therapy > 72 hours, hospital and ICU length of stay (LOS), and in-hospital all-cause mortality. Safety outcomes included antibiotic-related adverse events. Results. 94 patients were included: 53 (56.4%) pre- and 41 (43.6%) post-nudge. Most patients were men (53, 56.4%), had underlying lung disease (61, 64.8%), and required invasive ventilatory support (70, 74.5%). 11 (11.7%) patients were admitted from a long-term care facility. The absence of SM therapy was observed in 13 (23.1%) pre- vs 32 (78.0%) post-nudge patients (P< 0.001). There were no differences in SM therapy > 72 hours (36/40 [90%] vs. 8/9 [88.9%], P=1.0), mortality (11 [20.8%] vs. 7 [17.5%], P=0.69), median (IQR) hospital LOS (24 [10-49] vs. 16 [8-29]), P=0.37), and median (IQR) ICU LOS [15 [2-35] vs. 11 [3-25], P=0.40) between pre- and postnudge groups, respectively. Safety outcomes of patients treated > 72 hours (n=41); elevated SCr 12 (29.3%), fluid overload 18 (43.9%), hyponatremia 17 (41.5%), and hyperkalemia 5 (12.2%). After adjustment for confounders, post-nudge was associated with 11-fold increased odds of the absence of SM therapy (Table 1). Conclusion. A targeted SM nudge was associated with a reduction in treatment of SM colonization. Patient outcomes, including length of stay and all-cause mortality, were comparable between the two groups.

Pathology and Laboratory Medicine

Kenney RM, **Gunaga S**, **Cahill MM**, **Leman L**, **Beaulac-Harris A**, **Eriksson E**, **Geyer A**, **Shallal A**, **Stein TL**, **Mazzetti N**, **Kaiser K**, **Dubay J**, **Arthur A**, **Higginbottom M**, **Jayaprakash N**, **Dass S**, **Haddad A**, **Boxwalla A**, **Kaatz S**, **Tibbetts R**, **Veve M**, and **Suleyman G**. Are we there yet? The ongoing journey for improving management of asymptomatic bacteriuria. *Open Forum Infect Dis* 2025; 12:S1056-S1057. Full Text

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Background. Treating asymptomatic bacteriuria (ASB) with antibiotics contributes to preventable patient harm. This quality improvement study aimed to evaluate the effectiveness of ongoing diagnostic and antibiotic stewardship interventions in reducing unnecessary testing and treatment of ASB. Methods. This retrospective, cross-Sectional quality improvement study spanned from 1/2017-3/2024 at a five-hospital urban and suburban health system in Michigan. Interventions included i). Implementation of urinalysis with reflex to urine culture in 2/2019, with reflex criteria revised in 7/2022 to ≥ 10 WBCs; ii). Adoption of a urine culture hard stop after hospitalization day 3 (3/2021); iii). Introduction of an ASB progress note smart phrase and educational initiative via a 1-page handout and narrated slides in the first quarter of 2023. The primary endpoint was the proportion of patients with ASB who received antibiotic treatment, as defined by Vaughn et al JAMA Intern Med 2023. Secondary endpoints encompassed the number of provider smart phrase documentations; overall urine culture volume per year; proportion of all positive urine cultures representing ASB; and overall ASB antibiotic use, calculated as the ratio of ASB treated with antibiotics to all positive urine cultures. Results. The annual volume of urine cultures decreased by approximately 25% (Figure 1), from 87,556 in 2017 to 65,955 in 2023. The percentage of positive cultures representing ASB is depicted in Figure 2. The ASB smart phrase was documented in the medical record of 233 patients over one year: 165 (71%) were women, with a median age of 72 [48, 82] years. Emergency medicine providers utilized the smart phrase most frequently (97/233, 42%), followed by consultants (79/233, 34%). Overall ASB antibiotic use ranged from 9.7-22.7% in Q1 2022 and declined to 4.5-7% in Q1 2024. The primary endpoint, the system-wide average treatment of patients with ASB, declined modestly over time, but improvements were inconsistent among hospitals (Figure 3). Conclusion. Ongoing interventions targeting diagnostic and antibiotic stewardship through educational efforts were associated with a reduction in testing and treatment of ASB. However, suboptimal treatment of ASB remain a concern.

Pathology and Laboratory Medicine

Kenney RM, **Veve M**, **Shallal A**, **Tibbetts R**, and **Mulbah JL**. HECK-Yes This is The Remix!! Ceftriaxone vs Cefepime or Carbapenems for Definitive Treatment of Low-Risk AmpC-Harboring Enterobacterales Bloodstream Infections. *Open Forum Infect Dis* 2025; 12:S593. Full Text

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Background. Recent literature suggests ceftriaxone as a viable treatment of lowrisk AmpC-producing organisms, allowing for the preservation of AmpC-Stable therapies for moderate to high-risk organisms. This study aimed to determine whether ceftriaxone is effective in patients with bloodstream infections (BSI) caused by lowrisk AmpC harboring Enterobacterales compared to AmpC-Stable therapies. Methods. This was an IRB-approved, retrospective cohort of hospitalized patients ≥18 years old with a BSI due to Serratia marcescens, Morganella morganii, or Providencia spp. from 1/1/2017-2/28/2024. Patients were compared according to definitive therapy with ceftriaxone vs AmpC stable therapy (cefepime or carbapenem). The primary endpoint was 30-day all-cause mortality; secondary endpoints were clinical failure, development of ceftriaxone resistance, and hospital length of stay (LOS) after index culture. Clinical failure was defined as persistent signs and symptoms of infection, repeat positive blood cultures on days 3-5 of therapy, antibiotic escalation, or death. Results. 163 patients were included: 54 (33.1%) received ceftriaxone vs 109 (66.9%) AmpC stable therapies. Baseline, infection, and treatment characteristics are found in Table 1. 30-day all-cause mortality was observed in 5 (9.3%) ceftriaxone vs 11 (10.1%) AmpC stable patients (P=0.87). There were no differences in clinical success (49 [90.7%] vs 86 [78.9%], P=0.059), relapsing infection (3 [5.6%] vs 10 [9.3%], P=0.55), or rehospitalization (11 [20.4%] vs 38 [34.9%], P=0.06) between ceftriaxone and AmpC stable patients, respectively. Ceftriaxone resistance was only observed in AmpC stable patients (0 vs. 4 [3.7%], P=0.302), and median (IQR) LOS was similar between groups (5 [4-8] vs 6 [3-13] days, P=0.39). After adjustment for vasopressor use (adjOR 4.2; 95%CI, 1.3-13.1), ceftriaxone definitive therapy (adjOR, 0.79; 95%CI, 0.23-2.3) was not independently associated with 30-day all-cause mortality Conclusion. Patients treated with definitive ceftriaxone for low-risk AmpC Enterobacterales BSI achieved comparable outcomes to those treated with AmpC stable therapies. These findings support ceftriaxone as a treatment option for low-risk AmpC producers.

Pathology and Laboratory Medicine

Umar A, Faquih A, Babalola T, **Ozcan K**, **Montecalvo J**, and **Ahsan B**. Unmasking Diffuse Idiopathic Pulmonary Neuroendocrine Cell Hyperplasia: Clinicopathologic Features of a Rare Pulmonary Disorder. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

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Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) is a rare and poorly understood lung disorder that predominantly affects women. It often presents with nonspecific pulmonary symptoms, leading to delayed diagnosis. Given the limited literature, we aimed to investigate its clinical, radiologic, and pathologic characteristics.We conducted a retrospective study analyzing 33 patients histologically diagnosed with DIPNECH. Clinical and radiologic data were collected from electronic medical records. Hematoxylin and eosin (H&E) slides and relevant immunohistochemistry slides were reviewed. Clinical follow-up data were obtained.Patients were categorized as symptomatic (n = 13) or asymptomatic (n = 20). In the symptomatic group, the median age was 70 years, with 92.3% being female. Ethnic distribution was 69.2% Caucasian, 23.1% African American, and 7.7% Italian. In the asymptomatic group, the median age was 75 years, with 85% being female. Ethnic distribution was 75% Caucasian and 25% African American. Among symptomatic patients, 76.9% experienced shortness of breath, followed by cough, wheezing, and hemoptysis. Radiologically, all patients had lung nodules, with the largest measuring 3.2 cm. In the symptomatic group, 39% were non-smokers, while 61% had a smoking history. Among asymptomatic patients, 70% were smokers and 30% were non-smokers.All patients underwent surgical resection of radiologically identified nodules, with favorable post-surgical outcomes.Histologic examination revealed neuroendocrine hyperplasia, multiple carcinoid tumorlets, and carcinoid tumors in all cases. Constrictive bronchiolitis was observed in six cases. Notably, two patients had a concurrent diagnosis of adenocarcinoma, one of whom was also found to have brain metastasis secondary to adenocarcinoma at the time of diagnosis. Additionally, two patients had complex oncologic histories: one with prior squamous cell carcinoma followed by adenocarcinoma (both treated), and the other initially diagnosed with adenocarcinoma, later progressing to small cell carcinoma (treated accordingly). Both

patients ultimately developed DIPNECH in subsequent years. Of the cohort, 31 patients are alive, while two were lost to follow-up. None required additional treatment for DIPNECH beyond surgical resection. This study represents the largest single- institution series of DIPNECH patients reported to date. The condition primarily affects older women and generally has a favorable prognosis. However, unlike previous reports, shortness of breath was the most prevalent symptom. Notably, none required octreotide treatment. Our findings emphasize the importance of vigilant imaging and follow-up, particularly in smokers, to prevent disease progression and improve long-term outcomes.

Pharmacy

Al Musawa M, Caniff KE, Judd C, **Veve M**, and Rybak MJ. Short-Duration vs. Long-Duration of Therapy for Hospital-Acquired or Ventilator-Associated Pneumonia due to Multi-Drug Resistant Pseudomonas aeruginosa. *Open Forum Infect Dis* 2025; 12:S301. Full Text

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Background. The duration of therapy for hospital-acquired pneumonia (HAP) or ventilator-associated pneumonia (VAP) due to non-lactose fermenter Gram-negatives bacilli including Pseudomonas aeruginosa (PsA) remains a topic of debate. Our study aimed to compare the efficacy of short-duration (≤8 days) to longduration (>8 days) therapy for HAP/VAP due to multi-drug resistant (MDR) or difficult-to-treat (DTR) PsA infection. Methods. A two-center, retrospective cohort study was conducted from 5/2010 to 12/2022. We included all patients ≥18 years old with HAP or VAP due to MDRor DTR-PsA in respiratory cultures who were treated for ≥72 hours. The primary outcome was a 30-day recurrence from the index culture, and the secondary outcomes were a 60-day recurrence, 30-day, and 60-day mortality from the index culture. Results. Overall, 203 patients (short duration, n=91 and long duration, n=112) were included. Sixty-nine percent were male, and 58.6% were of African American descent. The mean (SD) for age and APACHE II score were 58.5 (15.8) and 23.9 (7.9), respectively. The common comorbidities were diabetes (39.9%), cerebrovascular disease (28.6%), and chronic obstructive pulmonary disease (24.1%). The primary admission source was a nursing home (44.8%). VAP was diagnosed in 53.0% of patients, with DTR-PsA accounting for 58.1% of all infections. Polymicrobial infection was present in 20.1% of the cases with Enterobactarales species present in all cases. Ceftazidime-avibactam and ceftolozane-tazobactam were used for treatment in 33.0% and 47.8%, respectively; combination therapy was used for 11.8% of cases. The 30-day recurrence was significantly lower in the long-duration therapy compared with the short-duration (5.4% vs. 15.9%, p = 0.017). Similarly, there was a lower 60-day recurrence rate in the long-duration group vs. short-duration group (8.9% vs. 24.4%, p=0.026). There were no significant differences in 30-day and 60-day mortality rates observed. Conclusion. Prolonged duration (>8 days) has resulted in lower recurrence rates of HAP/VAP caused by MDR/DTR PsA infection at 30 and 60 days. Although our study is insightful, a larger-Scale study is necessary, and logistic regression should be conducted to determine the predictors of the significant differences in the primary outcome.

Pharmacy

Arena CJ, **Mulbah JL**, **Kenney RM**, **Shallal A**, and Davis SL. Vancomycin Resistant Enterococcus faecium Minimum Inhibitory Concentration Trends from 2019-2024: Have We Killed Daptomycin? *Open Forum Infect Dis* 2025; 12:S308-S309. Full Text

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

Background. Vancomycin resistant Enterococcus faecium (VRE) has been categorized as a bacterium with serious antibiotic resistance threats in the United States, where daptomycin (DAP) has been a drug of choice. In 2019, the Clinical and Laboratory Standard Institute M100S 29th edition revised DAP breakpoints for VRE to susceptible dose dependent with a minimum inhibitory concentration (MIC) of ≤ 4 mcg/mL. HigherMICs are associated with resistant mechanisms and increased microbiological failure is seen with MICs of 3-4mcg/L. Linezolid (LZD) is an VRE treatment option that has favorable clinical outcomes and microbiological eradication with less emerging resistance, but LZD use can be controversial due to outdated dogma of using a bacteriostatic agent. The purpose of this study was to

evaluate MIC trends for DAP and LZD in patients with VRE bloodstream infections (BSI) at a large academic medical center. Bloodstream Infection VRE Comment within the Electronic Health Record: Current and Proposed Methods. IRB-exempt, cross-Sectional study of adult patients with VRE BSI and a healthcare encounter from 2019-2024 at a 5-hospital health-System in southeast Michigan. Patients were identified using Microsoft SQL Server queries based on microbiology results. The primary outcome was the proportion of patients with a DAP MIC > 1 mcg/mL with corresponding LZD MICs. Our health-System currently recommends DAP or LZD for VRE BSI until susceptibilities are available via blood culture comment (Figure 1). Measured MICs of daptomycin and linezolid, 2019-2024 ∗Daptomycin MIC Breakpoints: Susceptible Dose Dependent = ≤ 4 mcg/mL, Resistant = ≥8 mcg/mL. Linezolid MIC Breakpoints: Susceptible = ≤4 mcg/mL, Intermediate = 4 mcg/L, Resistant ≥8 mcg/L Results. 555 LZD and 491 DAP unique MICs from VRE BSI were evaluated. Figure 2 represents the average MICs by month and year for DAP and LZD from 2019-2024. The majority of DAP MICs were measured at 2 (30%), 3 (56%), and 4 (18%) mcg/mL. DAP MIC50 and MIC90 values were calculated at 3 mcg/mL and 4 mcg/mL, respectively. 98.7% of LZD MICs were measured at ≤2 mcg/mL (Table 1). LZD MIC50 and MIC90 values were calculated at 2 mcg/mL. Average daptomycin and linezolid MIC per month and year, 2019-2024 Conclusion. While theVREMICs forDAP are increasing, LZDhas remained stable over the past 5 years. A possible stewardship opportunity is to modify the health-System's current blood culture comment could suggest LZD as the VRE drug of choice and highdose DAP as an alternative in patients until susceptibilities are available (Figure 1).

Pharmacy

Arena CJ, Vanhorn B, **Kenney RM**, **Parke DM**, **Suleyman G**, Davis SL, and **Veve M**. Oral Antimicrobial Therapy Offers in Hospitalized Persons Who Inject Drugs who Elect for Self-directed Discharge. *Open Forum Infect Dis* 2025; 12:S870. Full Text

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Background. Hospitalized Persons Who Inject Drugs (PWID) who elect for selfdirected discharge (SDD) are at an increased risk for poor infection outcomes, but there is limited guidance for infection management in this population. National PWID management guidelines suggest considering oral antimicrobial therapy offers (OATO) as soon as patients are clinically stable to avoid lack of antibiotic therapy at discharge. The study purpose is to evaluate infection management in PWID who elect for SDD and to identify characteristics associated with OATO. Variables Associated with Oral Antimicrobial Offers at Self-directed Discharge Methods. Retrospective cohort of hospitalized adult PWID with an injection drug use (IDU)-related infection who elected for SDD between 1/1/14-1/31/24 at Henry Ford Health in Michigan. Patients were excluded if they were hospitalized for < 24-hours or if antimicrobial treatment was completed prior to SDD. The primary outcome was the proportion of patients with OATO at or prior to SDD. Secondary outcomes at 30-days included retreatment, infection-related readmission, and allcause mortality. Results. 150 patients were included; 55 (37%) were OATO patients, 95 (63%) did not receive an offer. Most patients were white (118, 79%), had prior SDD (90, 60%), and were a median (IQR) age of 34 (30-44) years. Skin infections were most common (81, 54%). Patients that received a source control procedure (27 (49%) vs. 31 (33%), P=0.05) or care from a provider ≤10 years from terminal training (49 [89%] vs. 70 [74%], P=0.04) were more likely to receive an OATO. Patient outcomes were not different between the OATO and no offer groups: infection retreatment 19 (34%) vs. 32 (34%); infection-related readmission 14 (25%) vs. 31 (33%); and all-cause mortality 1 (2%) vs. 3 (3%). Characteristics associated with OATO were prescribing or continuing medications for opioid use disorder during hospitalization, infection source control, and care from providers ≤10 years post-terminal training; infectious diseases consultation had an opposite association (Table 1). Conclusion. Most hospitalized PWID with IDU-related infections with SDD did not receive an OATO. Early career providers more commonly offered oral antimicrobials in PWID with less complicated infection types. Standardizing OATO in PWID at risk for SDD should be considered as a future direction to improve health outcomes. (Table Presented).

Pharmacy

Boettcher S, **Kenney RM**, **Arena CJ**, **Beaulac-Harris A**, **Tibbetts R**, **Shallal A**, **Suleyman G**, and **Veve M**. Say it Ain't Steno - Impact of a Microbiology Nudge Comment on Treatment of Respiratory Colonization. *Open Forum Infect Dis* 2025; 12:S1082. Full Text

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Background. Stenotrophomonas maltophilia (SM) is a known colonizer of the respiratory tract, in which treatment is not required. Microbiological comment nudges have been successful as passive stewardship interventions. The study objective was to describe the effect of a targeted SM respiratory culture nudge on antibiotic use in patients with colonization. Methods. IRB approved quasi-experiment of adult patients with a SM respiratory culture between 01/01/2022-01/27/2023 (pre-nudge) and 03/27/2023-12/31/2023 (postnudge). Patients with criteria for active community/hospital/ventilator-acquired pneumonia or on targeted antibiotics prior to culture were excluded. Nudge comment implemented 2/2023: S. maltophilia is a frequent colonizer of the respiratory tract. Clinical correlation for infection is required. Colonizers do not require antibiotic treatment. The primary outcome was absence of SM therapy; secondary outcomes were SM therapy > 72 hours, hospital and ICU length of stay (LOS), and in-hospital all-cause mortality. Safety outcomes included antibiotic-related adverse events. Results. 94 patients were included: 53 (56.4%) pre- and 41 (43.6%) post-nudge. Most patients were men (53, 56.4%), had underlying lung disease (61, 64.8%), and required invasive ventilatory support (70, 74.5%). 11 (11.7%) patients were admitted from a long-term care facility. The absence of SM therapy was observed in 13 (23.1%) pre- vs 32 (78.0%) post-nudge patients (P< 0.001). There were no differences in SM therapy > 72 hours (36/40 [90%] vs. 8/9 [88.9%], P=1.0), mortality (11 [20.8%] vs. 7 [17.5%], P=0.69), median (IQR) hospital LOS (24 [10-49] vs. 16 [8-29]), P=0.37), and median (IQR) ICU LOS [15 [2-35] vs. 11 [3-25], P=0.40) between pre- and postnudge groups, respectively. Safety outcomes of patients treated > 72 hours (n=41); elevated SCr 12 (29.3%), fluid overload 18 (43.9%), hyponatremia 17 (41.5%), and hyperkalemia 5 (12.2%). After adjustment for confounders, post-nudge was associated with 11-fold increased odds of the absence of SM therapy (Table 1). Conclusion. A targeted SM nudge was associated with a reduction in treatment of SM colonization. Patient outcomes, including length of stay and all-cause mortality, were comparable between the two groups.

Pharmacy

Caniff KE, Judd C, Eubank TA, Garey KW, Krekel T, Kufel WD, Andrade JA, Cerenzio J, **Veve M**, and Rybak MJ. Patient Characteristics and Clinical Outcomes Associated with Meropenem/Vaborbactam Treatment in Carbapenem-Resistant Enterobacterales Pneumonia. *Open Forum Infect Dis* 2025; 12:S917-S918. Full Text

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Background. Carbapenem-resistant Enterobacterales (CRE) are a major public health threat due to increasing prevalence and limited effective treatment options. Meropenem/vaborbactam (M/V) is a beta-lactam/beta-lactamase inhibitor agent designed to treat CRE. There is a paucity of data related to patient characteristics and associated outcomes with the utilization of M/V in pneumonia due to CRE. The objective of this study was to describe real-world experience with M/V in this setting. Methods. This is a retrospective, observational, multicenter, cross-Sectional study of patients ≥ 18 years old who received M/V for ≥ 72 hours for clinically-diagnosed hospital-acquired (HAP) or ventilator-associated pneumonia (VAP) due to CRE between 6/2020-2/2024. The primary outcome was clinical success, defined as resolution or improvement in signs/symptoms of infection and without the need for additional therapy. The secondary outcomes included 30-day mortality, 30-day microbiologic recurrence, 30-day symptomatic recurrence and adverse drug reaction(s). Results. Sixty-two patients were included from six U.S. medical centers. The mean age (standard deviation [SD]) was 58.2 (15.4) years; patients were predominantly male (71.0%) and Caucasian (58.1%). At time of culture collection, the mean (SD) APACHE II score was 22.1 (7.8) and most patients (78.0%) were admitted to the intensive care unit. Klebsiella pneumoniae was the predominant species isolated in culture (43.5%). Notably, 65.6% were diagnosed with VAP, 32.3% had a COVID-19-related hospitalization and 29.0% developed secondary bacteremia. Patients received a

median (interquartile range [IQR]) of 7.2 (6.1-12.0) days of M/ V, with 21.0% receiving systemic combination therapy. Clinical success was achieved in 69.4% of patients and 30-day mortality occurred in 33.9%. Microbiologic and symptomatic recurrence occurred in 11.2% and 8.1% of cases, respectively. One patient experienced Clostridioides difficile infection attributed to the use of M/V. Conclusion. Our study demonstrates promising clinical success with the use of M/V for treatment of pneumonia. Larger, comparative studies are needed in this population to identify patient factors associated with clinical success and assess M/V's efficacy compared to other available therapies.

Pharmacy
Collins CD, Hartsfield E, Cleary RK, **Veve M**, and Brockhaus KK. Timing Variations for Surgical Prophylaxis Within One Hour Pre-Incision: Impact on Surgical Site Infections in Elective Colorectal Surgery Procedures. *Open Forum Infect Dis* 2025; 12:S347. Full Text

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Background. The optimal timing of surgical infection prophylaxis (SIP) is generally recommended to be given 60 minutes, or in some cases 120 minutes, prior to incision. Conflicting results have hampered further optimization of prophylaxis timing within this timing window. This study aimed to assess the impact of alternative prophylaxis timing on surgical outcomes, particularly surgical site infections (SSIs). Methods. A large, validated database of elective colorectal surgeries in Michigan was used to perform a multi-center, retrospective cohort study. Cohorts included patients who received SIP within 0-15 minutes and 16-60 minutes prior to incision. Adult patients who received colorectal surgeries spanning from July 2012 to June 2021 were included. Emergent or urgent surgeries, missing follow-up and antibiotic information, and patients who did not receive all prophylaxis prior to incision were excluded. The primary outcome was incidence of SSIs. A multivariable logistic regression model analyzed the impact of timing and other confounding variables on SSIs. Results. A total of 21,061 procedures were included. Of these, 6,405 patients (30.4%) received prophylaxis 0-15 minutes pre-incision and 14,656 (69.6%) received prophylaxis within 16-60 minutes. Cohorts were generally similar with differences in patients receiving β-lactam prophylaxis (97.1% vs 96%; P = <0.001), mechanical and oral bowel preparation (64.5% vs. 67; P= 0.023), and adherence to recommended dosing (82% vs. 83.7%; P=0.002). There was no difference between cohorts in totalSSIs (6.8%vs.7.1%, P=0.419) orCDI (1.1% vs. 1%; P =0.324); however, deep SSIs were increased in the 16-60-minute cohort (0.8% vs. 1.1%; P=0.032).Multivariable logistic regression showed no association between prophylaxis timing and SSIs (adjusted odds ratio (aOR) 0.98; 95% CI 0.86-1.13; P = 0.817). Conclusion. Timing differences (0-15 minutes vs. 16-60 minutes pre-incision) did not significantly impacts overall SSIs incidence in elective colorectal surgeries.

Pharmacy
Crew J, **Veve M**, **Fitzmaurice MG**, **Alangaden GJ**, and **Kenney RM**. Short vs. Long Durations of Antibiotic Therapy for Pyelonephritis in Kidney Transplant Recipients. *Open Forum Infect Dis* 2025; 12:S949. Full Text

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Background. Emerging data suggests shorter durations of antibiotic therapy are as effective and safe as longer durations in general populations. The objective of this study is to compare outcomes of short (7-9 days) vs long (10-15 days) durations of antibiotic therapy for acute graft pyelonephritis in kidney transplant recipients (KTRs). Summary of patient, infection and treatment characteristics. Methods. IRB-approved retrospective cohort comparing short (7-9 days) to long courses (10-15 days) of antibiotics. Inclusion: Adult patients, hospitalized from 1/1/14 - 12/31/23, history of kidney transplant, acute pyelonephritis, and receipt of at least 7 days of in vitro active antibiotic therapy. Exclusion: renal or perinephric abscess, prostatitis, ≤ 2 months post-transplant. Primary outcome: clinical success, defined as resolution of infection signs and symptoms and confirmed or presumed microbiologic success at end of therapy (EOT). Secondary outcomes: length of stay from pyelonephritis onset, continued resolution of signs and symptoms at 30 days, C. difficile infection within 30 days of EOT, acute rejection, and adverse effects. Summary of primary and secondary outcomes. Results. 107 patients were included: 19 (17.8%) short-course and 88 (82.2%) long-course. Table 1 describes patient, infection, transplant, and treatment

characteristics. There was 1 (5.3%) failure in the short-course group compared to8 (9.1%) failures in the long-course group at EOT (p=0.456). At 30 days, there were 4 (21.1%) failures in the short-course group and 15 (17.0%) in the long-course group (p=0.742). 30-day retreatment was required in 0 short-course and 8 (9.1%) longcourse patients, p=0.346. No significant differences were detected for adverse effects: 0 vs. 3 (3.4%); C. diff: 0 vs. 1 (1.1%); or treated rejection: 1 (5.3%) vs. 0 in the shortcourse vs long-course groups, respectively. Conclusion. We did not detect differences in outcomes for pyelonephritis treatment in KTRs between those who received short compared to longer courses of antibiotic therapy. Further research is needed to solidify the place of short courses of antibiotic therapy in transplant recipients.

Pharmacy

Jagannathan M, **Jordan T**, **Kinsey D**, **Kenney RM**, **Veve M**, **Shallal A**, and **Suleyman G**. A Comparative Analysis of Clindamycin versus Linezolid as Adjunctive Anti-toxin Therapy for Invasive Group A Streptococcal Infections. *Open Forum Infect Dis* 2025; 12:S1028-S1029. Full Text

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Background. Group A Streptococcus (GAS) is an important pathogen that can cause life-threatening disease. Clindamycin (DA) and linezolid (LZD) have been used as adjunctive antitoxin (AT) therapy in high-inoculum GAS infections to inhibit bacterial protein synthesis. However, there is concern about DA efficacy in the era of increasing DA resistance, where LZD may have a role. We evaluated outcomes of patients with invasive GAS infection who received DA or LZD. Methods. Retrospective cohort study comparing patients with positive blood cultures (BC) for GAS from June 2013-Dec 2023 treated with DA or LZD ≥ 48 hours. We identified patients using a data query for positive BC for GAS through Microsoft SQL. Patients aged < 18 years, or those with polymicrobial bacteremia, receipt of both AT therapies, incomplete data, or enrolled in hospice/died within 48-hours of admission were excluded. Collected variables included: demographics, infection characteristics, microbiologic data, adjunct therapy (surgical, immunoglobulin), and clinical outcomes (treatment-associated adverse events, 30-day all-cause mortality and infection-related readmission). Results. 158 patients were included; 117 patients received DA and 41 patients LZD. Baseline characteristics were similar among groups except for chronic kidney disease, which was more common in the LZD group (Table 1). The most common clinical syndrome accompanying bacteremia in both groups was abscess/cellulitis; bone and joint infection was more prevalent in the LZD group. 55 (33.5%) of GAS isolates were DA resistant. There was no significant difference in severity of illness, surgical interventions, or duration of therapy between the two groups (Table 2). Duration of bacteremia was significantly longer in the LZD group. There was no significant difference in readmission (10.3% vs 12.2%, p=0.77) or all-cause mortality within 30 days (17.1% vs 7.3%, p=0.13) in the DA versus LZD groups. Treatment-associated adverse events were low across both groups [Figure 1]. Conclusion. Despite increasing DA resistance at our facility, there was no significant difference in outcomes between patients treated with LZD vs DA plus standard therapy, consistent with prior literature. Further studies are needed to determine optimal therapy for invasive GAS.

Pharmacy

Jordan T, **Jagannathan M**, **Kinsey D**, **Kenney RM**, **Veve M**, **Suleyman G**, and **Shallal A**. Analyzing Trends and Outcomes of Clindamycin Resistant Invasive Group A Streptococci Infections. *Open Forum Infect Dis* 2025; 12:S937-S938. Full Text

T. Jordan, Henry Ford Hospital, Detroit, MI, United States

Background. Streptococcus pyogenes (Group A Streptococci; GAS) is a grampositive bacterium that is a leading cause of life-threatening infections. For invasive infections, IDSA recommends high-dose penicillin and clindamycin (DA). However, increasing resistance to DA has been reported. The aim of this study was to determine the prevalence of DA-resistant GAS and evaluate if DA resistance was associated with worse outcomes. Table Comparison of clindamycin susceptible and clindamycin resistant strains of invasive GAS infections Methods. This was a retrospective cohort study from June 2013 to December 2023 across a five-hospital health system in Southeast Michigan of patients with positive blood cultures for GAS who received DA for anti-toxin therapy identified through Microsoft SQL. Children, polymicrobial bacteremia, incomplete data, receiving linezolid empirically, or those who died within 48

hours of admission were excluded. Patients with DA susceptible (DA-S) GAS isolates were compared to patients with DA resistant (DA-R) GAS isolates. Variables included demographics, infection characteristics, microbiologic data, therapy, and clinical outcomes. Figure Cases of GAS bacteremia and percent of clindamycin resistant strains Results. 390 cases were reviewed, and 215 were included in the cohort study [Table]. There was no difference in age, sex, or race among the groups. People who use injection drugs (51.7% vs 48.3%, p=0.07), people experiencing homelessness (PEH; 63.2% vs 36.8%, p=0.001), and chronic hepatitis C infection (HCV; 54.2% vs 45.8%, p=0.007) were more prevalent in the DA-R group; chronic kidney disease was more frequent in the DA-S group (57.1% vs 42.9%, p=0.029). Uncomplicated SSTI was more common in the DA-S group (64.2% vs 35.8%, p=0.022). There was no significant difference in the severity of illness, duration of bacteremia, surgical management, treatment duration, length of stay, readmission or mortality between the two groups. There was an increased incidence of invasive GAS infections beginning in 2022, and 50% of isolates were DA-R in 2023 [Figure]. Conclusion. Although there is an increase in DA-R in invasive GAS infections, there was no significant difference in outcomes among patients with DA-R and DA-S who received standard of care treatment in addition to DA antitoxin therapy. Further research is needed to determine the clinical significance of these findings to inform optimal therapy for these groups.

Pharmacy

Kabalka E, **Smith Z**, **Tatem G**, and **August B**. INCIDENCE OF DEXMEDETOMIDINEINDUCED CARDIOVASCULAR ADVERSE DRUG EVENTS IN PATIENTS WITH CIRRHOSIS. *Crit Care Med* 2025; 53. Full Text

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INTRODUCTION: Dexmedetomidine (DEX) is a first line sedative option that is an alpha-2 receptor agonist. This contributes to cardiovascular adverse drug reactions (CVADRs), such as hypotension and bradycardia. Metabolism of DEX is proportional to hepatic blood flow, potentially causing accumulation in cirrhosis patients. The purpose of this study was to assess the impact of liver disease severity on the incidence of clinically significant (CS) CV-ADRs in patients with cirrhosis receiving DEX. METHODS: This was an IRB-approved, retrospective, observational, propensity-adjusted, case-control study. Patients were included if they had cirrhosis defined by ICD- 9 and 10 codes and were admitted to the ICU from July 1, 2018, through June 30, 2023. Those with mechanical circulatory support and electrical pacing were excluded. Cases were defined by experiencing a CV-ADR with documentation of a MAP< 60 mmHg, HR< 55 BPM and/ or SBP< 90 mmHg plus a clinical intervention 60 minutes from the CV-ADR. Clinical interventions included fluid bolus administration, vasopressor initiation, DEX tapered faster than protocol, switching sedatives, vasopressor dose increase, or discontinuation of AV nodal blocking drugs. An inverse probability of treatment weighing was completed using the criteria of BMI, age and baseline hemodynamics. The primary outcome was the odds of developing a CS CV-ADR based on liver disease severity according to the ALBI (albuminbilirubin) grade. The secondary outcome was identification of independent risk factors associated with CS CV-ADRs. The primary outcome was compared using a chi squared test and the secondary outcome was analyzed with a multivariable regression. RESULTS: 190 patients were included. The median SOFA score was 8 in each group, and 54 (28%) patients required vasopressors. Among cases, the median time to CS CVADR was 2.4 hours. Patients with severe liver disease (ALBI grade 3) had a significantly higher rate of CS CV-ADR when compared to those with less severe liver disease (ALBI Grade 1 and 2) at 70.5% vs. 50.5%, p = 0.005) ALBI grade 3 was independently associated with development of a CS CV-ADR (Adjusted OR 2.19; 95% CI [1.44-3.33]). CONCLUSIONS: Patients with more severe liver disease according to ALBI grade had an increased risk of experiencing a CS CV-ADR when sedated with DEX. .

Pharmacy

Kenney RM, **Gunaga S**, **Cahill MM**, **Leman L**, **Beaulac-Harris A**, **Eriksson E**, **Geyer A**, **Shallal A**, **Stein TL**, **Mazzetti N**, **Kaiser K**, **Dubay J**, **Arthur A**, **Higginbottom M**, **Jayaprakash N**, **Dass S**, **Haddad A**, **Boxwalla A**, **Kaatz S**, **Tibbetts R**, **Veve M**, and **Suleyman G**. Are we there yet? The ongoing journey for improving management of asymptomatic bacteriuria. *Open Forum Infect Dis* 2025; 12:S1056-S1057. Full Text

R.M. Kenney, Henry Ford Hospital, Detroit, MI, United States

Background. Treating asymptomatic bacteriuria (ASB) with antibiotics contributes to preventable patient harm. This quality improvement study aimed to evaluate the effectiveness of ongoing diagnostic and antibiotic stewardship interventions in reducing unnecessary testing and treatment of ASB. Methods. This retrospective, cross-Sectional quality improvement study spanned from 1/2017-3/2024 at a five-hospital urban and suburban health system in Michigan. Interventions included i). Implementation of urinalysis with reflex to urine culture in 2/2019, with reflex criteria revised in 7/2022 to ≥ 10 WBCs; ii). Adoption of a urine culture hard stop after hospitalization day 3 (3/2021); iii). Introduction of an ASB progress note smart phrase and educational initiative via a 1-page handout and narrated slides in the first quarter of 2023. The primary endpoint was the proportion of patients with ASB who received antibiotic treatment, as defined by Vaughn et al JAMA Intern Med 2023. Secondary endpoints encompassed the number of provider smart phrase documentations; overall urine culture volume per year; proportion of all positive urine cultures representing ASB; and overall ASB antibiotic use, calculated as the ratio of ASB treated with antibiotics to all positive urine cultures. Results. The annual volume of urine cultures decreased by approximately 25% (Figure 1), from 87,556 in 2017 to 65,955 in 2023. The percentage of positive cultures representing ASB is depicted in Figure 2. The ASB smart phrase was documented in the medical record of 233 patients over one year: 165 (71%) were women, with a median age of 72 [48, 82] years. Emergency medicine providers utilized the smart phrase most frequently (97/233, 42%), followed by consultants (79/233, 34%). Overall ASB antibiotic use ranged from 9.7-22.7% in Q1 2022 and declined to 4.5-7% in Q1 2024. The primary endpoint, the system-wide average treatment of patients with ASB, declined modestly over time, but improvements were inconsistent among hospitals (Figure 3). Conclusion. Ongoing interventions targeting diagnostic and antibiotic stewardship through educational efforts were associated with a reduction in testing and treatment of ASB. However, suboptimal treatment of ASB remain a concern.

Pharmacy

Kenney RM, **Veve M**, **Shallal A**, **Tibbetts R**, and **Mulbah JL**. HECK-Yes This is The Remix!! Ceftriaxone vs Cefepime or Carbapenems for Definitive Treatment of Low-Risk AmpC-Harboring Enterobacterales Bloodstream Infections. *Open Forum Infect Dis* 2025; 12:S593. Full Text

R.M. Kenney, Henry Ford Hospital, Detroit, MI, United States

Background. Recent literature suggests ceftriaxone as a viable treatment of lowrisk AmpC-producing organisms, allowing for the preservation of AmpC-Stable therapies for moderate to high-risk organisms. This study aimed to determine whether ceftriaxone is effective in patients with bloodstream infections (BSI) caused by lowrisk AmpC harboring Enterobacterales compared to AmpC-Stable therapies. Methods. This was an IRB-approved, retrospective cohort of hospitalized patients ≥18 years old with a BSI due to Serratia marcescens, Morganella morganii, or Providencia spp. from 1/1/2017-2/28/2024. Patients were compared according to definitive therapy with ceftriaxone vs AmpC stable therapy (cefepime or carbapenem). The primary endpoint was 30-day all-cause mortality; secondary endpoints were clinical failure, development of ceftriaxone resistance, and hospital length of stay (LOS) after index culture. Clinical failure was defined as persistent signs and symptoms of infection, repeat positive blood cultures on days 3-5 of therapy, antibiotic escalation, or death. Results. 163 patients were included: 54 (33.1%) received ceftriaxone vs 109 (66.9%) AmpC stable therapies. Baseline, infection, and treatment characteristics are found in Table 1. 30-day all-cause mortality was observed in 5 (9.3%) ceftriaxone vs 11 (10.1%) AmpC stable patients (P=0.87). There were no differences in clinical success (49 [90.7%] vs 86 [78.9%], P=0.059), relapsing infection (3 [5.6%] vs 10 [9.3%], P=0.55), or rehospitalization (11 [20.4%] vs 38 [34.9%], P=0.06) between ceftriaxone and AmpC stable patients, respectively. Ceftriaxone resistance was only observed in AmpC stable patients (0 vs. 4 [3.7%], P=0.302), and median (IQR) LOS was similar between groups (5 [4-8] vs 6 [3-13] days, P=0.39). After adjustment for vasopressor use (adjOR 4.2; 95%CI, 1.3-13.1), ceftriaxone definitive therapy (adjOR, 0.79; 95%CI, 0.23-2.3) was not independently associated with 30-day all-cause mortality Conclusion. Patients treated with definitive ceftriaxone for low-risk AmpC Enterobacterales BSI achieved comparable outcomes to those treated with AmpC stable therapies. These findings support ceftriaxone as a treatment option for low-risk AmpC producers.

Pharmacy

Kinsey D, **Jagannathan M**, **Jordan T**, **Kenney RM**, **Veve M**, **Shallal A**, and **Suleyman G**. Invasive Streptococcus pyogenes Infections: Is Anti-toxin Therapy Necessary? *Open Forum Infect Dis* 2025; 12:S582. Full Text

D. Kinsey, Henry Ford Hospital, Detroit, MI, United States

Background. Invasive Streptococcus pyogenes or group A Streptococcus (GAS) carries a high morbidity and mortality rate. In addition to penicillin, adjunct antitoxin therapy (AT) with linezolid or clindamycin is the standard of care. Although the use of AT is supported by in vitro data and observational studies, there are limited conclusive data supporting its efficacy in reducing GAS mortality. Our study aimed to compare clinical outcomes of patients receiving AT versus those who did not. Methods. This was a retrospective cohort study of hospitalized patients with positive blood cultures for GAS at our five-hospital system from June 2013 to August 2023. Patients were identified through Microsoft SQL Server. Patients who received AT therapy for > 48 hours were defined as the AT group; the control group did not receive AT therapy. Patients who received AT for < 48 hours were excluded. Collected variables included demographics, infection & microbiological characteristics, and clinical outcomes. Data was analyzed using SPSS. Results. 265 patients were included in the study of whom 179 (68%) received AT (Table 1). About half were female, and the median age was 58 years. Comorbidities were overall similar between the two groups. Persons who inject drugs or with chronic hepatitis C were more common in the control group. Abscess/cellulitis was the most common clinical syndrome in both groups. Shock requiring vasopressors, need for dialysis and mechanical ventilation, and toxic shock syndrome were prevalent in the AT group. There was no difference in the duration of bacteremia, clindamycin resistance, and management between the two groups except for receipt of intravenous immunoglobulin (IVIG), which was more common in the AT group (Table 2). Outcomes, including length of stay, readmission for infection-related complications, and 30-day mortality, were similar between the two groups. Conclusion. Utilization of AT for invasive GAS infections correlated with severity of illness, but clinical outcomes did not significantly differ between patients receiving AT and those who did not, suggesting a potential opportunity for antimicrobial stewardship. Further research is needed to determine whether AT should be reserved for patients with select infectious syndromes.

Pharmacy

Konja J, **Major J**, **Thavarajah K**, **Sayf AA**, **Calo S**, **Martirosov A**, and **Hameed AMA**. Anti-Ro52 Associated Interstitial Lung Disease: A Retrospective Analysis. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

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Rationale: Interstitial Lung Disease (ILD) is a common manifestation of myositis and is associated with worse morbidity and higher mortality. Antibodies to SSA antigen (Ro52/Ro60) consist of two distinct auto-antibody systems with different clinical associations. Ro52 antigen has been identified as a 52 kDa protein, belonging to the tripartite motif (TRIM) protein family and it is the most common myositis-associated autoantibody (MAA) found in patients with myositis. The co-existence of anti-Ro52 antibody with other myositis-specific autoantibodies (MSA) is thought to be predictive of an aggressive ILD course. This study aims to describe the characteristics of patients with ILD and a positive anti-Ro52 antibody. Methods: A retrospective cohort study of patients evaluated by a provider of the Henry Ford Health (HFH) ILD program and a positive anti-Ro52 antibody was performed. We collected demographic data including gender, age at diagnosis, ethnicity, insurance, and zip code as well as diagnostic makers such as serology results, pulmonary function tests (PFT), and imaging. We further reviewed evaluations by sub-specialties including rheumatology, dermatology, and neurology to assess confirmation of diagnosis of myositis. Descriptive statistics were performed. Categorical variables are reported as (n) total counts with percentages and continuous variables are reported with mean and standard deviation (SD). Univariate differences were assessed between anti-Ro52 positive patients with and without an MSA using Pearson's

chi-squared test and t-tests. Results: Our study included 78 patients with a positive anti-Ro52 antibody evaluated by the HFH ILD provider team. Of these, 43 (55.1%) were female and 21 (26.9%) also had a positive MSA including 3 Jo1, 3 PL7, 2 PL12, 1 OJ, 4 MDA5, 4 TIFF, 3 NXP, 2 MI2, and 1 SRP autoantibodies. Evaluations included 41 (52.6%) by rheumatology, 26 (33.3%) by dermatology, and 31 (39.7%) by neurology and 17 (21.8%) had a confirmed diagnosis of myositis. Pulmonary Function Tests (PFT) of these patients showed mean forced vital capacity (FVC) percent of 62.4% (S.D 21.1%) and mean diffuse capacity of carbon monoxide (DLCO) percent of 38.6% (S.D 16.3%). High resolution CT imaging showed 64 of the patients (82.1%) with ground glass opacities, 11 (14.1%) with consolidations, 38 (48.7%) with reticulations, 43 (55.1%) with bronchiectasis, 19 (24.4%) with honeycombing, and 2 (2.6%) with air trapping. Conclusions: Our patient population represented primarily female gender with the majority not having confirmed myositis. When comparing patients with positive anti-Ro52 antibody with and without MSA, there were no statistically significant characteristics found.

Pharmacy

Major J, **Konja J**, **Thavarajah K**, **Calo S**, **Abu Sayf A**, **Martirosov A**, and **Hameed AMA**. Myositis Specific Antibodies and Interstitial Lung Disease: A Single Center Retrospective Study. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

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Rationale: Myositis-specific antibodies (MSA) are commonly present in patients with myositis. Interstitial lung disease (ILD) is a common extra-skeletal manifestation of myositis that often precedes muscular or skin involvement. Many individuals with MSA and ILD never progress to develop typical features of myositis. This study aims to describe the characteristics of patients with ILD and a positive MSA. Methods: A retrospective cohort study of patients evaluated by a provider of the Henry Ford Health (HFH) ILD program and an MSA antibody was performed. MSA included Jo-1, PL7, PL12, EJ, OJ, MDA5, TIFF, NXP, Mi2 and SRP autoantibodies. Demographic data including gender, age at diagnosis, and diagnostic makers such as serology results, pulmonary function tests (PFT), and High-resolution computed tomography (CT) findings at the time of initial evaluation were collected. Evaluations by sub-specialties including rheumatology, dermatology, and neurology were reviewed for a formal myositis diagnosis. Descriptive statistics were performed. CT findings and PFTs at the time of diagnosis were analyzed for statistical differences between patients with a confirmed diagnosis of myositis-associated ILD (M-ILD) and idiopathic ILD with a positive MSA (I-ILD w/MSA) Results: This study included 127 patients of whom 62% were female. 69.3% were evaluated by rheumatology, 42.4% by dermatology, 47.2% by neurology, and 40.9% were confirmed to have a diagnosed with myositis. MSA included 47 Jo-1, 8 PL7, 14 PL12, 1 EJ, 2 OJ, 15 MDA5, 11 TIFF, 18 NXP, 9 MI2, and 7 SRP. The mean percentage of predicted Forced Vital Capacity (FVC) was 68.4% with a standard deviation of 19.6. Mean Diffusion Capacity for Carbon Monoxide (DLCO) was 46.9% with a standard deviation of 19.3. Imaging demonstrated 70.9% with ground glass opacities, 15.7% consolidation, 42.5% reticulation, 55.1% bronchiectasis, and 16.5% honeycombing. Statistical significance was found for M-ILD to present with consolidation on imaging, whereas I-ILD w/MSA was more likely to present with honeycombing. Conclusions: This cohort represents a female predominance in those with ILD and positive MSA. Furthermore, those with I-ILD w/MSA more frequently presented with honeycombing on imaging suggesting advanced disease at the time of presentation compared to M-ILD. Ultimately, given only 40.9% of this population possessed a formal diagnosis of myositis, further investigation regarding the relationship of MSA and ILD is warranted. Future studies should elicit disease course and response to treatment between these two groups. Figure 1: Characteristics of our patient population. Standard deviation for PFT's within brackets. Significant P values are bolded.

Pharmacy

Stratton P, **Kenney RM**, **Veve M**, **Fitzmaurice MG**, **Alangaden GJ**, and **Franco-Palacios D**. Impact of a Short Course Post-Operative Antibiotic Prophylaxis Duration on Nephrotoxicity in Lung Transplant Recipients. *Open Forum Infect Dis* 2025; 12:S1356. Full Text

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Background. Vancomycin plus an antipseudomonal β-lactam is used as lung transplant surgical prophylaxis, but an optimal post-operative duration is not defined. The study objective was to assess the impact of a shortened antibacterial surgical infection prophylaxis (SIP) duration on post-operative nephrotoxicity in lung transplant recipients. Table 1 Variables associated with AKI Methods. IRB approved quasi experiment of lung transplant recipients who received SIP from 1/1/2016-9/30/2020 (pre-group) to 10/1/2020-7/31/24 (post-group). Intervention: implementation of shortened SIP duration to 72-hours of cefepime and vancomycin post-operatively. Inclusion: eGFR >30 mL/min/1.73m2 between transplant day ±2. Exclusion: renal replacement ≤ 3-months, simultaneous organ transplants, donor bronchi with Gram-positive bacterial growth, or new COVID-19 infection between transplant day ±7. The primary endpoint was the incidence of acute kidney injury (AKI), defined by the KDIGO criteria, while receiving post-operative vancomycin up to 14 days. Secondary endpoints were vancomycin consensus guideline (VCG) AKI definition at 14-days and time to AKI. Results. 77 patients were included: 45 (58%) pre-, 32 (42%) post-intervention. 73% vs. 47% male (p=0.018). 49% vs. 34% (p=0.205) KDIGO AKI while on vancomycin. Post-group associated with approximately 40% decreased odds of developing KDIGO AKI (Table 1). Secondary endpoints: 33% vs. 19% VCG AKI (p=0.157). Median time to AKI was three days, with no differences detected between groups and AKI definitions. Similar rates of C. diff infection, positive bacterial respiratory cultures, new multidrug resistant organisms, surgical site infections. 57.8% vs. 84.4% patients received treatment for new pneumonias after SIP completion (p=0.013), with one new MRSA pneumonia in the pre-group and one in the post-group. Conclusion. Implementation of a shortened antibacterial prophylaxis protocol for lung transplant resulted in numerically fewer AKIs. Maturation, regression to the mean, and reliance on manual chart review are all limitations of this retrospective study. Ongoing analysis of this intervention, such as with multicenter prospective studies, can help to characterize the decreased nephrotoxicity risk with shorter course prophylaxis post-transplant.

Pharmacy

Terrazas WC, **Kenney RM**, **Argyris A**, **Shallal A**, and **Veve M**. Judicious Use of Benzathine Penicillin G in Response to a Medication Shortage Alert. *Open Forum Infect Dis* 2025; 12:S898. Full Text

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Background. The national shortage of benzathine penicillin G (BPG) poses challenges in the treatment of syphilis. In response to this critical BPG shortage, our health system implemented a medication shortage alert within the electronic health record (EHR). The alert provides recommendations to optimize BPG utilization. This study investigates the impact of the BPG drug shortage on clinical practice. Methods. This was an IRB-approved, retrospective cohort study focusing on patients >3 months who received BPG between 5/9/23-2/28/24. The study included inpatient and outpatient visits after implementing the medication shortage alert. Exclusions were applied for severe penicillin allergy, neurosyphilis, or congenital syphilis. Two cohorts were analyzed: the judicious BPG group (patients with primary, secondary, or latent syphilis receiving BPG), and the non-judicious group (patients receiving BPG for alternative diagnoses). The study assessed social determinants of health (SDOH) as primary outcomes and compared a separate cohort of syphilis patients receiving BPG or alternative therapy (e.g., doxycycline). Results. 453 patients were included. Majority of patients were non-Hispanic Black (273, 60%) men (272, 60%), with a median age of 32 years (IQR: 22-44). Of these patients, 318 (70%) received judicious BPG, while 135 (30%) received non-judicious BPG. The most common non-judicious diagnosis was streptococcal pharyngitis (128, 95%). In multivariable logistic regression (Table 1), variables associated with judicious use included: age >32 years (adjOR: 2.273; 95% CI: 1.488-3.472), male sex at birth (adjOR: 1.835; 95% CI: 1.206-2.792), and black race (adjOR: 1.847; 95% CI: 1.212-2.815). Among a cohort of 128 syphilis patients who received either BPG (64, 50%) or doxycycline (64, 50%) treatment, those who received doxycycline were more likely to lack health insurance (35 [54.7%] vs. 43 [67.2%], p=0.15) and receive outpatient treatment (3 [4.7%] vs. 12 [18.7%], p=0.13) (Table 2). SDOH data were reported in < 50% of patient charts. Conclusion. Despite implementing an EHR drug shortage alert, 30% of BPG use was suboptimal and mostly for pharyngitis. Optimizing SDOH documentation represents an opportunity to assess health inequities and the impacts on patient outcomes for syphilis management.

Public Health Sciences

Alrawabdeh J, **Ghosh S**, Raslan S, Di Federico A, Ricciuti B, and **Abu Rous F**. Individual participant data meta-analysis comparing neoadjuvant to perioperative chemoimmunotherapy in early-stage non-small cell lung cancer according to PD-L1 status. *J Clin Oncol* 2025; 43:e20035. Full Text

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Background: Neoadjuvant and perioperative chemo-immunotherapy are two standard-of-care treatment options for patients with early-stage Non-Small Cell Lung Cancer, both of which improve event-free-survival (EFS). A recent reconstructed individual patient data (IPD) meta-analysis found no difference in EFS between these approaches. However, another patient-level analysis of CheckMate trails 816 and 77T reported that perioperative nivolumab significantly improves EFS, particularly in the PD-L1 negative subgroup. Our study aims to compare neoadjuvant and peri-operative chemo-immunotherapy based on PD-L1 status using reconstructed IPD. Methods: Data were collected from Kaplan-Meier curves of eight randomized trials, including five perioperative and three neoadjuvant trials. Only trials with Kaplan-Meier curves stratified by PD-L1 levels were included. Data extraction, IPD reconstruction, and survival analyses were conducted using the IPDfromKM tool. Patients were stratified according to their PD-L1 tumor proportion score (TPS) as negative (#1%), positive (1-49%) and high ($50%). Statistical comparison of EFS between the perioperative and neoadjuvant arms were performed across these subgroups. Results: A total of 1656 participants were included in our analysis with 1420 patients in the perioperative arm and 236 in the neoadjuvant arm. A total of 447 EFS events were analyzed. The PD-L1 subgroups included 293 patients with negative PD-L1 (#1%), 269 with positive PD-L1, (1-49%), and 192 with high PD-L1 ($50%). No significant differences in EFS were observed between perioperative and neoadjuvant approaches among patients with any PD-L1 TPS (P=0.634) or within any PD-L1 subgroup (negative: P=0.449; positive: P=0.311; high: P=0.334). Conclusions: This reconstructed IPD meta-analysis found no significant difference in EFS between perioperative and neoadjuvant chemo-immunotherapy in ES-NSCLC, regardless of PD-L1 status. Treatment decisions should consider other patient-specific factors beyond PD-L1 status. Larger randomized trials are needed to further identify patients who may benefit from additional immunotherapy after surgery.

Public Health Sciences

Babatunde OA, Osazuwa-Peters N, and **Adjei Boakye E**. Family mental illness and physical abuse for predicting cannabis use among cancer survivors. *J Clin Oncol* 2025; 43:e22616. Full Text

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Background: Adults with a history of Adverse Childhood Experiences (ACEs) are more likely to engage in health-risk behaviors. While the link between ACEs and such behaviors has been well-studied in the general population, limited research focuses specifically on cancer survivors. This study explores the relationship between three specific ACEs—family mental illness, physical abuse, and sexual abuse—and cannabis use among cancer survivors. Methods: Using cross-sectional data from the 2020 Behavioral Risk Factor Surveillance System, we analyzed a sample of 7,896 cancer survivors aged 18 and older. The exposure variables included three ACEs: having a family member with a mental illness, experiencing physical abuse, and experiencing sexual abuse before the age of 18 dichotomized as yes/no. The outcome measure was cannabis use dichotomized as yes/no. Weighted multivariable logistic regression models were used to evaluate the association between ACEs and cannabis use adjusting for sociodemographic factors. Results: In this sample of cancer survivors, 15.5%, 23.6%, and 6.3% reported experiencing the three ACEs: mental illness in family members, physical abuse, and sexual abuse, respectively. Regarding cannabis use, 6.1% used cannabis. Adjusted models revealed that cancer

survivors with a history of mental illness in family members had significantly higher odds of using cannabis (aOR: 2.38, 95% CI: 1.58–3.58). Survivors who reported physical abuse had higher odds of using cannabis (aOR: 1.74, 95% CI: 1.21–2.51). However, the adjusted models showed no statistically significant association between sexual abuse and cannabis use among cancer survivors. Conclusions: This study underscores the complex relationship between adverse childhood experiences and health behaviors in cancer survivors. Identifying ACEs such as family mental illness and physical abuse as significant factors influencing cannabis use highlights the importance of integrating trauma-informed care into survivorship programs. Addressing these underlying factors may improve health outcomes in this vulnerable population. Individuals with a history of ACEs may constitute a critical target group for preventive interventions designed to mitigate this risk and promote healthier behaviors.

Public Health Sciences

Cardenas-Maldonado DDD, **Gudipati S**, **Santana-Garcés M**, **Maki G**, and **Brar I**. Congenital Syphilis in Southeast Michigan: A Retrospective Case Series. *Open Forum Infect Dis* 2025; 12:S855. Full Text

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Background. Cases of congenital syphilis (CS) have been increasing substantially, but CS is preventable through timely testing and adequate treatment of syphilis during pregnancy. From2012 to 2021, cases of CS in the United States increased by 755%. Our study aims to describe the demographics of pregnant persons infected with syphilis and outcomes in their infants to identify potential predictors of adverse events. IQR: Interquartile range; HIV: human immunodeficiency virus; Methods. This is a retrospective case series of pregnant persons diagnosed with syphilis who delivered their babies at Henry Ford Health from January 2020 to January 2024. Charts were reviewed for demographic data, syphilis serology, treatment in mothers and infants, and infant outcomes. Descriptive statistics were used to report the study population's demographic and clinical characteristics. Chi-Squared tests were used to determine the association between receipt of penicillin, prenatal care, prior sexually transmitted infection (STI), and CS diagnosis in neonates. Our chosen significance level was 0.05. Results. Forty-three patients were included; 19 (44%) were black; median age 27 years (IQR 24-32.5); 28 (66%) were from Detroit; 18 (53%) reported a history of STI. Eight (18%) did not receive prenatal care. Syphilis was primarily diagnosed during second trimester (34%), and late latent syphilis was reported in 80%. Syphilis treatment was completed 30 days before delivery in 67%. There were 17 early-term deliveries, 1 stillbirth, and 1 elective abortion. Ninety percent of neonates had a normal physical exam. Fifteen lumbar punctures were performed, one positive Venereal Disease Research Laboratory test. Of the 8 placenta studies, 2 had positive immunoperoxidase treponemal stain. Seventeen neonates were treated with 10 days of aqueous Penicillin, 6 neonates had definite/highly probable CS. Using Chi-Square analysis, receipt of penicillin treatment by the mother less than 30 days before delivery was significantly associated with CS in the neonate ($p < 0.001$) Conclusion. In our analysis, we identified a significant association between CS and appropriate timing of treatment of syphilis in the mother. Further studies are needed with a larger cohort to determine if social determinants of health affect appropriate prenatal care in pregnant persons.

Public Health Sciences

De Cuir J, Zhu Y, Johnson C, Lauring AS, Martin ET, Gaglani M, Columbus C, Peltan I, Ginde AA, Mohr N, Gibbs K, Hager D, Prekker M, Mohamed A, Johnson N, Steingrub JS, Khan A, Busse L, Lau L, Chang S, Mallow C, Kwon JH, Shapiro N, **Vaughn I**, Safdar B, Mosier J, Ellington S, Dawood FS, Self WH, and Surie D. Updated 2023-2024 (Monovalent XBB.1.5) COVID-19 Vaccine Effectiveness Against COVID-19-associated Hospitalization Among Adults - IVY Network, 20 U.S. States. *Open Forum Infect Dis* 2025; 12:S1228-S1229. Full Text

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Background. On September 12, 2023, the Advisory Committee on Immunization Practices recommended updated 2023-2024 (Monovalent XBB.1.5) COVID-19 vaccination for all persons aged ≥6 months to prevent COVID-19. Few data are available on the effectiveness of updated 2023-2024 COVID-19 vaccine against COVID-19-associated hospitalization among adults, particularly in high-risk groups, including older adults, persons with comorbidities, and immunocompromised persons. Methods. Data from the

Investigating Respiratory Viruses in the Acutely Ill (IVY) Network were used to conduct a case-control analysis estimating updated 2023-2024 COVID-19 vaccine effectiveness (VE) against COVID-19-associated hospitalization. During September 21, 2023-March 31, 2024, adults aged ≥18 years with COVID-19-like illness were enrolled at 26 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. VE was estimated using multivariable logistic regression comparing the odds of receipt of an updated 2023-2024 COVID-19 vaccine dose versus no updated dose among case and control patients. VE models were adjusted for age, sex, race and ethnicity, admission date, and geographic region. Results were stratified by age, Charlson Comorbidity Index (CCI) score, and immunocompromised status. Results. A total of 7843 adults were enrolled, including 2090 COVID-19 case patients and 5753 control patients. Among immunocompetent adults, VE against COVID-19-associated hospitalization was 41% (95% CI=28%-51%, median time since updated dose = 73 days) among persons aged ≥18 years, 48% (95% CI=19%- 66%) among persons aged 18-64 years, 42% (95% CI=27%-53%) among persons aged ≥65 years, 42% (95% CI=22%-57%) among persons with CCI < 5, and 41% (95% CI=23%-54%) among persons with CCI ≥5 (Figure). Among immunocompromised adults, VE against COVID-19-associated hospitalization was 25% (95% CI=0%-44%, median time since updated dose = 74 days). Conclusion. Updated 2023-2024 COVID-19 vaccination provided protection against COVID-19-associated hospitalization among immunocompetent adults. VE was similar across age groups and CCI scores, but may be lower among immunocompromised adults.

Public Health Sciences

Mann Y, **Hagerman T**, **Malick A**, Rao S, **Harris C**, **Santana-Garcés M**, **Manteuffel J**, **Gudipati S**, and **Brar I**. One Small Step for Man, One Giant Leap for Ending the HIV Epidemic. *Open Forum Infect Dis* 2025; 12:S411-S412. Full Text

Y. Mann, Henry Ford Hospital, Detroit, MI, United States

Background. To achieve the goal to End the HIV Epidemic by 2030, unique interventions are needed to increase testing and subsequently link people with HIV (PWH) to care for rapid start of antiretroviral therapy (ART). Extending testing to include emergency department (ED) based HIV screening initiatives are effective in new case identification, earlier detection, and are encouraged by Centers for Disease Control and Prevention guidelines. Collaborations of infectious diseases (ID) providers with ED providers provides improved linkage to care for HIV and rapid initiation of ART. We describe our combined ED and ID HIV testing and linkage to care program. Methods. This is a retrospective analysis of newly diagnosedPWHat Henry Ford Health (HFH) via reactive HIV fourth generation test by an ED based opt-out HIV screening program from 7/16/2020 - 10/28/2023. A best practice alert (BPA) prompted providers to order an HIV screening test for patients ages 18-65 years old without a previously documented HIV fourth generation test. Patients were informed of the test when ordered and could opt-out of testing if desired. Follow up and linkage to care was provided by a team of ID providers. Results. During the study period, a total of 48,725 fourth generation HIV screening tests were performed, of which 629 tests were reactive (1.24% of tests performed). Of the reactive tests, 86 patients (0.18% of all tests) were found to have a new diagnosis of HIV. Median CD4 cell count was 297 cells/mm3 (IQR: 98-614), 34 patients required hospitalization with 7 (8%) admitted with an opportunistic infection. Excluding the 34 patients hospitalized, the median time from positive result to first attended appointment was 5 days (IQR 2-13) and median time from screening test result to initiation of ART was 6.5 days (IQR: 4-16). At 3- or 6-months following HIV diagnosis, 40 (47%) had an HIV-1 follow-up viral load reported (see Table 1). Conclusion. HIV testing and early linkage to care are two key pillars of the End the HIV Epidemic initiative. As shown by our study, collaboration between ED and ID providers ensures increased testing in the ED, improved linkage to care, and rapid start of ART which will help in achieving the goals of these two pillars.

Public Health Sciences

Mann Y, **Ishak A**, Ogbenna UK, Kasmikha L, **Cherabuddi MR**, **Joyce K**, **Harris C**, **Numi M**, **Santana-Garcés M**, **Rehman NK**, **Bryce R**, **Joshi S**, and **Zervos M**. Influenza Vaccine Amongst Persons Experiencing Homelessness: Evaluating Attitudes, Barriers, and Trust. *Open Forum Infect Dis* 2025; 12:S898-S899. Full Text

Y. Mann, Henry Ford Hospital, Detroit, MI, United States

Background. In Detroit, persons experiencing homelessness (PEH) have been a vulnerable part of society due to their comorbidities and unique barriers in access to care. Despite PEH experiencing higher rates of vaccine-preventable diseases, there is a lack of information on strategies to improve vaccine rates. The objective of this project is to obtain an understanding of enablers and barriers in influenza vaccine uptake amongst PEH, to inform future work to increase vaccine uptake. Methods. This is a cross-Sectional study of survey data from adult PEH encountered during Street Medicine (SM) outreach in Detroit to assess enablers and barriers in influenza vaccination. Respondents were provided a complimentary bus pass for participation. Descriptive statistics were conducted on sociodemographic variables with analysis of variables related to level of homelessness, vaccine concerns, vaccination status, and underlying health problems. Results. 43 participants' surveys were analyzed. Participant vaccine status and level of homelessness varied with majority (35%) reporting spending at least 1 night in a tent or other dwelling. Regarding participant demographics, 86% (n=37) were male and 81% (n=35) were Black or African American (AA) (Table 1). Amongst survey respondents, the highest sources of trust for information regarding influenza vaccine was found amongst: 'Social Services Agencies or Other Services' 95.2% (n=20) and 'Experts and Scientists' 93.8% (n=15) (Figures 1 and 2). Variables regarding sources of information trusted were analyzed via chi-Square analysis to evaluate for statistical significance (p-value < 0.05) amongst demographic variables (Figure 3). Conclusion. Previous literature regarding attitudes towards vaccines amongst PEH has demonstrated distrust in healthcare. Results of this study are unique in identifying healthcare members as resources trusted by most participants in providing information on vaccines. This emphasizes the importance of SM outreach in Detroit in building trusting relationships with PEH in addition to decreasing barriers in access to care, to help target future vaccination initiatives.

Public Health Sciences

Mann Y, Ogbenna UK, **Ishak A**, Kasmikha L, **Numi M**, **Iyer H**, **Rehman S**, Kadouh A, Mangal R, Qasawa A, Dehghani A, Hasso M, Henry J, **Santana-Garcés M**, **Rehman NK**, **Bryce R**, **Zervos M**, and **Joshi S**. Utilization of a Point-of-Care Hepatitis C Test to Treat in People Experiencing Homelessness with Street Medicine Outreach. *Open Forum Infect Dis* 2025; 12:S899. Full Text

Y. Mann, Henry Ford Hospital, Detroit, MI, United States

Background. Persons experiencing homelessness (PEH) have disproportionately higher rates of untreated chronic hepatitis C virus (HCV) than the public. Improved community funding and resources are needed to expand HCV rapid point-of-care (POC), confirmatory testing, treatment and follow-up. Given that PEH face competing priorities (unstable housing, food access, addiction, other infections), it is our role as clinicians to reduce barriers to HCV treatment, understand hesitancies for deferring treatment, and design programs to improve accessibility. This is the pilot project of a Street Medicine (SM) based initiative to use POC testing for HCV amongst PEH with linkage of care to a federally qualified health clinic (FQHC). Hepatitis C Screening and Treatment Protocol HCV- Hepatitis C Virus POC- Point of Care CHASS- Community Health and Social Services HbsAg- Hepatitis B Surface Antigen CBC- Complete Blood Count CMP- Complete Metabolic Panel Methods. SM provides medical care to PEH outside of a hospital setting. Medical students and residents were recruited to form a HCV outreach team at Henry Ford Hospital and trained in HCV testing via OraQuick rapid antibody (Ab) test. During SM outreach, PEH were provided education on HCV and offered POC testing with a $10.00 grocery gift card. If a patient was identified as HCV Ab positive they were provided free transportation to a FQHC for confirmatory testing. If diagnosis was confirmed, they were evaluated for eligibility for simplified HCV treatment, check-ins to assess adherence and sustained virologic response (Figure 1). Results. From February-April 2024, 103 PEH were tested using POC HCV testing on SM runs, with 4 positive results. 3 of 4 patients were confirmed for CHASS clinic appointments. 1 patient presented to clinic follow-up but deferred confirmatory testing bloodwork, demonstrating challenges in arranging for HCV clinic follow-up care. Conclusion. Previous studies have shown that lack of insurance, prior authorization and referral process, active injection drug use or alcohol use, lack of knowledge of HCV treatment, and limited healthcare workforce and infrastructure have all contributed to the low treatment rate in the homeless. Using trusted

community organizations with SM, this initiative aims to reduce testing and transportation barriers in order to eliminate HCV in PEH. Larger numbers of positive patients are needed to best assess the feasibility of the program, and if providing all testing and treatment at the point of care is needed to improve compliance.

Public Health Sciences

Miller C, Bradley D, Wood I, **Willens D**, **Nair A**, **Brennan B**, **Bole S**, **Poisson L**, Hall S, Thomson G, **Hirata M**, **Kalmbach D**, and **Drake C**. Digital CBT for Insomnia Is Linked to Reductions in Healthcare Use in Real-world Settings at Henry Ford Health. *Sleep* 2025; 48:A236. Full Text

[Miller, Christopher; Bradley, Danielle; Wood, Ian; Hall, Shana; Thomson, Greig] Big Hlth, London, England; [Willens, David; Nair, Anupama; Brennan, Benjamin; Bole, Shane; Poisson, Laila] Henry Ford Hlth, Detroit, MI USA; [Hirata, Mika; Kalmbach, David] Henry Ford Sleep Res, Detroit, MI USA; [Drake, Christopher] Henry Ford Hlth Syst, Candon, MI USA

Introduction: Digital CBT-I offers a scalable solution for insomnia treatment, but evidence of its real-world adoption and impact in U.S. clinical settings is limited. This study evaluates the implementation and effects of digital CBT-I within a U.S. healthcare system, utilizing Normalization Process Theory to integrate it into clinical workflows. We compare healthcare utilization between patients who engaged with digital CBT-I and those who were offered but did not use it. Methods: Patients with insomnia were offered digital CBT-I via electronic and clinical workflows at the Internal Medicine and Sleep clinics within Henry Ford Health, Detroit, Michigan. Normalization Process Theory guided implementation. Electronic order rates and patient sign-ups assessed implemen tation success and workflow acceptability. Clinician training sessions and educational materials supported uptake. A propen sity-matched case-control design compared healthcare utilization rates between 340 digital CBT-I users and 340 matched controls, who were offered digital CBT-I but did not use it. We analyzed patient chart data and standardized time across patients. We evaluated the odds of medication fills and visits before and after. Results: A total of 340 patients utilizing digital CBT-I from treat ing practitioners were matched with 340 controls who did not. Digital CBT-I patients exhibited a 64% reduction in medication fills (for any condition) during the post-treatment period rela tive to before ($p< 0.001$), and were 53% less likely to fill insom nia-specific prescriptions compared to pre-treatment ($p=0.013$). Controls showed no significant changes. Time-varied logistic regression indicated that digital CBT-I patients had 37% higher odds of using outpatient services within the initial 30-60 days ($p=0.048$), but subsequently showed 28% lower odds at 120-150 days ($p=0.041$), and 41% lower odds at 150-180 days ($p=0.039$). Conclusion: Normalization Process Theory effectively facilitated the integration of digital CBT-I into clinical workflows, providing immediate access with minimal workflow disruptions. Training ses sions and ongoing clinician reminders promoted patient uptake of standard care for insomnia management. Findings indicate that dig ital CBT-I is associated with reduced medication fills and decreased odds of outpatient visits over time, suggesting its potential as an effective, scalable treatment for insomnia in clinical settings

Public Health Sciences

Montenegro J, Pinto de Oliveira CL, Armet AM, Berg A, Sharma AM, Mereu L, Cominetti C, **Ghosh S**, Richard C, Walter J, and Prado CM. A Powdered Meal Replacement Improves Lipid Profiles, Body Composition, and Resting Energy Expenditure in People With Excess Body Weight. *Curr Dev Nutr* 2025; 9. Full Text

Objectives: Excess body weight is associated with metabolic abnormalities, including insulin resistance, dyslipidemia, and chronic low-grade inflammation. Meal replacements are commonly used for weight loss, which improves metabolic and inflammation markers. This study aimed to assess the impact of a soy protein-yogurt-honey powdered meal replacement (PMR) on metabolic and inflammatory markers in individuals with excess body weight in absence of weight loss. Methods: The Premium Study was a 12-week parallel-arm RCT. N=88 adults (18–50 years) with excess body weight (BMI 25–37 kg/m2) were randomized into two groups: control (CON, usual diet) or PMR (adding 50 g of PMR twice daily). Both groups were asked to maintain a stable body weight. Participants attended three study visits at baseline, week 6, and week 12. Outcomes included: inflammation markers (e.g., interleukin-6 [IL-6]; primary outcome), glucose, insulin, lipid profiles, body composition (via dual-energy X-ray absorptiometry), and

resting energy expenditure (REE, via whole-room indirect calorimetry). Adherence, dietary intake, and physical activity were monitored. Results: N=63 participants completed the study (CON n=34; PMR n=29). Participants in PMR group had adherence of 98% (interquartile interval: 96.4–100%), consumed more protein (p< 0.001) and less lipids (p< 0.001) than the CON group. By design, there were no significant changes in body weight. There was a group effect on lean soft tissue (p=0.042), which increased in PMR on week 6 (0.38±0.88 kg, p=0.025) and remained higher than CON until week 12 (p=0.031). Likewise, there was a group effect on REE (p=0.045), which increased in PMR on week 12 (58.3±121.4 kcal/day, p=0.021). Group-time interactions were observed for total cholesterol (p=0.022) and LDL-C (p=0.008) concentrations, both of which reduced in PMR on week 6 (-0.25±0.55 mmol/L, p=0.027; -0.20±0.40 mmol/L, p=0.013, respectively). There were no significant changes in IL-6 and remaining outcomes. Conclusions: The addition of PMR to the diet improved lipid profiles and increased lean soft tissue and REE in individuals with excess body weight, in absence of weight loss. It is possible that weight loss is needed to improve other health parameters, such as improving glucose regulation and inflammatory markers. Funding Sources: Almased Wellness GmbH (Bienenbüttel, Germany).

Public Health Sciences

Munhoz J, Newell M, Goruk S, Sena MR, Mazurak V, Joy AA, Bigras G, **Ghosh S**, Courneya KS, and Field CJ. Oxylipins in the Regulation of Immune Responses: Secondary Analysis From the Docosahexaenoic Acid (DHA) for Women With Breast Cancer in the Neoadjuvant Setting (DHA WIN) Trial. *Curr Dev Nutr* 2025; 9. Full Text

Objectives: Oxylipins are immune cell signalling molecules derived from n-3 and n-6 polyunsaturated fatty acids (PUFAs) oxidation. While PUFAs are recognized for their immunomodulatory effects, the role of oxylipins in mediating immune function remains poorly understood. We previously demonstrated that supplementation with 4.4 g/day of docosahexaenoic acid (DHA) for 18 weeks during breast cancer neoadjuvant chemotherapy (NAC) preserved peripheral blood mononuclear cells (PBMCs) lipopolysaccharides (LPS)-stimulated production of TNF-α and IFN-γ. To explore mechanisms, this study investigated whether DHA supplementation alters the oxylipin profile of PBMCs. We hypothesized that DHA supplementation may enhance the immune response during NAC by stimulating cytokine production through the release of n-6 and n-3 derived oxylipins. Methods: This is a secondary analysis of the DHA WIN controlled trial. PBMCs were isolated from whole blood (n = 10 in each group) at baseline and 15 weeks of therapy. PBMCs were stimulated ex vivo with LPS (10 μg/mL) for 48 hours to evaluate immune response, and supernatants were collected after centrifugation. Oxylipins were prepared using solid-phase extraction and quantified by liquid chromatography-mass spectrometry. Statistical significance was assessed using independent t-tests and Spearman's correlation analysis. Results: The total concentration of n-6 derived oxylipins significantly differed between groups, decreasing in the placebo group (20% reduction) and increasing in the DHA group (~2-fold) at 15 weeks, compared to baseline (P< 0.001). This difference was observed in most n-6 oxylipins from linoleic and arachidonic acid. As expected, n-3 derived oxylipins increased in the DHA group (~2-fold, P = 0.029) but remained unchanged in the placebo group. Within the placebo group, the concentration of total n-6 derived oxylipins at 15 weeks was positively correlated with LPS-stimulated production of TNF-α (r = 0.636, P = 0.048) and IFN-γ (r = 0.766, P = 0.010). Conclusions: These findings suggest that the maintenance of cytokine production by PBMCs from breast cancer patients supplemented with DHA may be partially due to the production of n-6 and n-3 oxylipins. Funding Sources: CIHR and CCI Researcher Initiated Grant. JM: scholarships from Dr. Elizabeth A. Donald, Hazel McIntyre, CRINA, and Anthony Fellowship in Human Nutrition.

Public Health Sciences

Ravindran S, **Treger M**, **Russell J**, **Coyne P**, **McCray C**, **Drake C**, Walch O, and **Cheng P**. User Experience of a Mobile Application to Reduce Circadian Misalignment in Night Shift Workers. *Sleep* 2025; 48:A385. Full Text

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Introduction: Around 80% of night shift workers experience cir cadian misalignment, leading to excessive sleepiness and decline of safety and work satisfaction. To address this, our team devel oped a mobile application, Arcashift, which tracks users' circa dian rhythms and makes personalized activity recommendations (i.e. when to avoid light, when to exercise, etc.) based on user goals (i.e. wake up earlier). While the app was built with patient input and has been tested in randomized controlled trial settings, the real-world user experience is not yet well-established. Methods: Night shift workers who habitually slept for less than 6 hours and presented with excessive sleepiness used Arcashift with pre mium access for 30 weeks (n = 28) in a hybrid type I effectiveness-im plementation trial. Upon completion of the implementation period, participants completed a user feedback survey in which participants rated overall experience and ease of use on a 5-point scale ranging from negative to positive and completed 6 short answer questions. Results: Among the users, 64% rated their overall experience as positive ("positive" or "somewhat positive") and 36% rated their experience as neutral. No users reported a negative ("negative" or "somewhat negative") experience. Eighty-two percent of users reported Arcashift was easy to use, whereas only 11% and 7% reported neutral and negative ease of use, respectively. Most liked features were the personalized recommendations (39%), the ease of inputting their work shifts and other obligations to the calendar (21%). The most common complaints were the app being unintui tive to use (11%) and the desire for more information about sleep in the app (14%). Other barriers included app glitches when enter ing shifts and other events into the calendar (7%). Conclusion: Participants generally appreciate the individualized approach of Arcashift. The app was well received but modifi cations may be needed to further improve the user experience. Future directions include the information about improving sleep in Arcashift being made more accessible to the users of the app, as well as continuing to improve and providing great support to night shift workers in adapting to their schedules and decreasing their circadian misalignment.

Public Health Sciences

Tao M, **Lin CH**, Liu J, Chai W, **Gonzalez HC**, **Lu M**, and **Gordon SC**. Sex- and Race/Ethnicity-Specific Associations Between Food Insecurity and Metabolic Dysfunction-Associated Steatotic Liver Disease in American Adults. *Curr Dev Nutr* 2025; 9. Full Text

Objectives: The study aimed to examine the association between food insecurity and metabolic dysfunction-associated steatotic liver disease (MASLD) across different race/ethnicity or gender using the 2017-March 2020 National Health and Nutrition Examination Survey (NHANES). Methods: The current study included 6618 participants aged ≥19 years. Steatotic liver disease was determined through transient elastography examination. Odds ratios (ORs) and 95% confidence intervals (CIs) for MASLD associated with food insecurity were estimated using logistic regression. Results: Compared to full food security, very low adult food security was associated with increased odds of MASLD (OR=1.35, 95% CI, 1.05-1.73). There were associations of very low adult food security with higher odds of MASLD in women (OR= 1.82, 95% CI, 1.08-3.09) but not in men, with statistically significant interaction between adult food insecurity and gender (p interaction = 0.038). Similarly, the positive association of adult food insecurity with MASLD was mainly found in non-Hispanic Whites and other race, but not in non-Hispanic Black, Hispanic, and non-Hispanic Asian groups. Furthermore, mediation analyses suggested that added sugar intake and intake of whole fruits and vegetables excluding potatoes partially mediated the associations of adult food insecurity with MASLD. Conclusions: The positive association between food insecurity and MASLD might be dependent on race/ethnicity and gender. Increases in whole fruits and vegetables intake and reduction added sugar consumption may partially reduce the impact of food insecurity on MASLD development. Funding Sources: No.

Pulmonary and Critical Care Medicine

Bin Hameed U, Amal T, **Nazneen W**, and Moazzam M. Dynamic Evolution of Pleural Effusion: Hepatic Chylothorax Transforming Into Hydrothorax With Trapped Lung in Advanced Cirrhosis. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

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Chylothorax is a rare complication in cirrhosis, seen in only 1% of cases, typically due to thoracic duct disruptions caused by elevated venous and lymphatic pressures from cirrhosis-induced portal hypertension. In contrast, hepatic hydrothorax affects 5-10% of cirrhotic patients and involves the translocation of ascitic fluid into the pleural space through diaphragmatic defects. The shift from chylothorax to hepatic hydrothorax in cirrhosis is a rare clinical occurrence, requiring a deeper understanding of the evolving fluid dynamics and complex pathophysiology involved. A 69-year-old male with NASH cirrhosis, HFrEF, and recurrent ascites who presented with worsening dyspnea and abdominal distension. He had experienced a 50-pound unintentional weight loss over six months due to poor appetite and required paracentesis every 1-2 weeks for refractory ascites.Upon admission, imaging revealed a large right-sided pleural effusion. Diagnostic thoracentesis drained 2 liters of yellow, milky fluid, which showed elevated triglycerides (153 mg/dL) and low cholesterol (15 mg/dL), consistent with chylothorax. Lymphangiography identified a small thoracic duct leak near the diaphragm. Despite thoracic duct embolization, the effusion persisted, with chest tube drainage of 3-4 liters daily, and intermittent clamping was required to manage hypotensive episodes.Over time, repeat pleural fluid analysis revealed decreasing triglycerides (59 mg/dL), increasing protein (2.0 g/dL), and elevated LDH (134 U/L), suggesting a shift towards a transudative hepatic hydrothorax. Repeated invasive interventions led to secondary infections with Staphylococcus lugdunensis and Staphylococcus auricularis, causing fibrinous pleuritis and limiting therapeutic options like long-term PleurX catheter placement.The patient underwent VATS with partial decortication and pleurodesis. Multiple loculated collections and a trapped right lung limited pleurodesis success. Tailored antibiotic therapy was administered based on culture results, initially using vancomycin and later transitioning to Bactrim. This case highlights the evolving nature of pleural effusions in cirrhotic patients, transitioning from chylothorax to hepatic hydrothorax. Chylothorax was diagnosed by elevated triglycerides and milky pleural fluid, confirmed by a lymphangiogram showing a thoracic duct leak likely due to portal hypertension. Despite thoracic duct embolization, persistent effusions indicated ongoing fluid accumulation driven by high portal pressures. As fluid analysis showed declining triglycerides and increased protein, the effusion shifted towards hepatic hydrothorax. Repeated interventions led to infections with Staphylococcus species, causing fibrinous pleuritis and a trapped lung. The patient underwent VATS with partial decortication, but ongoing infection and lung entrapment precluded long-term catheter placement. This case underscores the need for careful monitoring and adaptive management in complex cirrhotic patients.

Pulmonary and Critical Care Medicine

Cherabuddi MR, and **Bradley P**. An Unexpected Myriad of Pulmonary Complications Following Vaping and Anabolic Steroid Use. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

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Introduction Vaping use is known to cause multiple radiologic pulmonary abnormalities including bilateral ground-glass opacities, consolidation, interlobular septal thickening, reversed halo sign and can present as organizing pneumonia, diffuse alveolar hemorrhage and occasionally eosinophilic pneumonia. Anabolic steroid use can cause lung injury, which may present as acute respiratory distress syndrome, pulmonary edema or thromboembolic events, although not well studied. We present a case of a young male with vaping and anabolic steroid use resulting in multiple pulmonary complications and prolonged ventilator dependence. Case Description A young previously healthy male with recent vaping and anabolic steroid use for one year, presented with cough and shortness of breath after being exposed to sick contacts and required intubation for hypoxia. Initial workup was notable for positive influenza A, and respiratory culture with Streptococcus pneumoniae. Chest computed tomography demonstrated bilateral multifocal ground-glass opacities, numerous pneumatoceles predominant in both lower lobes and the lingula, largest in left lower lobe 5.9 x 5.5 x 8.8 cm, with no prior imaging for comparison. He was treated with oseltamivir and ceftriaxone. Due to difficult ventilator liberation and concern for infection, repeat chest imaging was done showing right apical pneumothorax, pneumomediastinum, new air fluid levels in pneumatoceles concerning for infection as well as pericardial effusion without evidence of tamponade. He was treated with ampicillin-sulbactam, required chest tube placement and pressors in the setting of obstructive shock. He was not to be a candidate for extracorporeal membrane oxygenation given the

timing of his initial insult and not a transplant candidate due to active infection with ongoing complications. He remained ventilator-dependent for 25 days, eventually underwent tracheostomy and gastrostomy tube placement, was discharged to a inpatient rehabilitation facility, is now recovering well since discharge home. Discussion Vaping and anabolic steroid use are known to cause lung injury, though are not typically associated with the development of pneumatoceles. Influenza complicated by streptococcal pneumonia generally does not lead to pneumatoceles either. In this case, the presence of pneumatoceles likely resulted in complications such as pneumothorax, lung abscesses, and prolonged ventilator dependence. The rising prevalence of vaping and anabolic steroid use may result in unexpected lung injuries, making it crucial to recognize atypical clinical presentations. Early transfer to ECMO-capable centers should be prioritized to enhance patient outcomes in severe cases. Monitoring patients with a history of vaping or steroid use for complications is essential, as their clinical presentations may differ from conventional cases.

Pulmonary and Critical Care Medicine

Kabalka E, **Smith Z**, **Tatem G**, and **August B**. INCIDENCE OF DEXMEDETOMIDINEINDUCED CARDIOVASCULAR ADVERSE DRUG EVENTS IN PATIENTS WITH CIRRHOSIS. *Crit Care Med* 2025; 53. Full Text

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INTRODUCTION: Dexmedetomidine (DEX) is a first line sedative option that is an alpha-2 receptor agonist. This contributes to cardiovascular adverse drug reactions (CVADRs), such as hypotension and bradycardia. Metabolism of DEX is proportional to hepatic blood flow, potentially causing accumulation in cirrhosis patients. The purpose of this study was to assess the impact of liver disease severity on the incidence of clinically significant (CS) CV-ADRs in patients with cirrhosis receiving DEX. METHODS: This was an IRB-approved, retrospective, observational, propensity-adjusted, case-control study. Patients were included if they had cirrhosis defined by ICD- 9 and 10 codes and were admitted to the ICU from July 1, 2018, through June 30, 2023. Those with mechanical circulatory support and electrical pacing were excluded. Cases were defined by experiencing a CV-ADR with documentation of a MAP< 60 mmHg, HR< 55 BPM and/ or SBP< 90 mmHg plus a clinical intervention 60 minutes from the CV-ADR. Clinical interventions included fluid bolus administration, vasopressor initiation, DEX tapered faster than protocol, switching sedatives, vasopressor dose increase, or discontinuation of AV nodal blocking drugs. An inverse probability of treatment weighing was completed using the criteria of BMI, age and baseline hemodynamics. The primary outcome was the odds of developing a CS CV-ADR based on liver disease severity according to the ALBI (albuminbilirubin) grade. The secondary outcome was identification of independent risk factors associated with CS CV-ADRs. The primary outcome was compared using a chi squared test and the secondary outcome was analyzed with a multivariable regression. RESULTS: 190 patients were included. The median SOFA score was 8 in each group, and 54 (28%) patients required vasopressors. Among cases, the median time to CS CVADR was 2.4 hours. Patients with severe liver disease (ALBI grade 3) had a significantly higher rate of CS CV-ADR when compared to those with less severe liver disease (ALBI Grade 1 and 2) at 70.5% vs. 50.5%, p = 0.005) ALBI grade 3 was independently associated with development of a CS CV-ADR (Adjusted OR 2.19; 95% CI [1.44-3.33]). CONCLUSIONS: Patients with more severe liver disease according to ALBI grade had an increased risk of experiencing a CS CV-ADR when sedated with DEX. .

Pulmonary and Critical Care Medicine

Konja J, **Major J**, **Thavarajah K**, **Sayf AA**, **Calo S**, **Martirosov A**, and **Hameed AMA**. Anti-Ro52 Associated Interstitial Lung Disease: A Retrospective Analysis. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

[Konja, J.; Major, J.; Thavarajah, K.; Sayf, A. Abu; Calo, S.; Martirosov, A.; Hameed, A. M. Abdul] Henry Ford Hosp, Detroit, MI USA
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Rationale: Interstitial Lung Disease (ILD) is a common manifestation of myositis and is associated with worse morbidity and higher mortality. Antibodies to SSA antigen (Ro52/Ro60) consist of two distinct auto-

antibody systems with different clinical associations. Ro52 antigen has been identified as a 52 kDa protein, belonging to the tripartite motif (TRIM) protein family and it is the most common myositis-associated autoantibody (MAA) found in patients with myositis. The co-existence of anti-Ro52 antibody with other myositis-specific autoantibodies (MSA) is thought to be predictive of an aggressive ILD course. This study aims to describe the characteristics of patients with ILD and a positive anti-Ro52 antibody. Methods: A retrospective cohort study of patients evaluated by a provider of the Henry Ford Health (HFH) ILD program and a positive anti-Ro52 antibody was performed. We collected demographic data including gender, age at diagnosis, ethnicity, insurance, and zip code as well as diagnostic makers such as serology results, pulmonary function tests (PFT), and imaging. We further reviewed evaluations by sub-specialties including rheumatology, dermatology, and neurology to assess confirmation of diagnosis of myositis. Descriptive statistics were performed. Categorical variables are reported as (n) total counts with percentages and continuous variables are reported with mean and standard deviation (SD). Univariate differences were assessed between anti-Ro52 positive patients with and without an MSA using Pearson's chi-squared test and t-tests. Results: Our study included 78 patients with a positive anti-Ro52 antibody evaluated by the HFH ILD provider team. Of these, 43 (55.1%) were female and 21 (26.9%) also had a positive MSA including 3 Jo1, 3 PL7, 2 PL12, 1 OJ, 4 MDA5, 4 TIFF, 3 NXP, 2 MI2, and 1 SRP autoantibodies. Evaluations included 41 (52.6%) by rheumatology, 26 (33.3%) by dermatology, and 31 (39.7%) by neurology and 17 (21.8%) had a confirmed diagnosis of myositis. Pulmonary Function Tests (PFT) of these patients showed mean forced vital capacity (FVC) percent of 62.4% (S.D 21.1%) and mean diffuse capacity of carbon monoxide (DLCO) percent of 38.6% (S.D 16.3%). High resolution CT imaging showed 64 of the patients (82.1%) with ground glass opacities, 11 (14.1%) with consolidations, 38 (48.7%) with reticulations, 43 (55.1%) with bronchiectasis, 19 (24.4%) with honeycombing, and 2 (2.6%) with air trapping. Conclusions: Our patient population represented primarily female gender with the majority not having confirmed myositis. When comparing patients with positive anti-Ro52 antibody with and without MSA, there were no statistically significant characteristics found.

Pulmonary and Critical Care Medicine

Korpole P, **Jaffery SH**, **Arcila-Londono X**, and **Bazan LF**. Description of Positive Airway Pressure Settings in Bulbar Onset Amyotrophic Lateral Sclerosis Patients Requiring Non-invasive Ventilation. *Am J Respir Crit Care Med* 2025; 211:1. Full Text

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Introduction : Amyotrophic Lateral Sclerosis (ALS) in general and bulbar onset ALS patients in particular are at high risk of developing respiratory failure secondary to neuromuscular weakness. Optimal Non-Invasive Positive Pressure Ventilation (NIPPV) settings are not clearly defined in this subgroup. Methods : A retrospective chart review study was designed to describe NIPPV settings in bulbar onset ALS patients who met initial compliance with NIPPV. Bulbar onset ALS patients were identified from a database including patients diagnosed with Motor Neuron Disease at Henry Ford Hospital from January 1, 2019 to December 31, 2023. Results : A total of 45 patients with bulbar onset ALS were identified and 37 patients were initiated on NIPPV therapy with 26 patients (70%) meeting compliance requirements. Amongst the compliant patients, 14 patients were initiated on Bilevel Positive Airway Pressure - Spontaneous Timed (BPAP-ST) mode and 12 patients on Volume Assured Pressure Support (VAPS) mode. At compliance, mean Positive Airway Pressure (PAP) therapy usage for more than or equal to 4 hours per 24 hours and mean duration of PAP therapy use per 24 hours in the BPAP-ST and VAPS groups was 88% and 5.6 hours versus 81.5% and 5.7 hours respectively. In the BPAP-ST group, mean values of PAP settings and data were as follows: Inspiratory PAP (IPAP) 10.6 cm water, Expiratory PAP (EPAP) 5.7 cm water, backup rate 8.8 breaths per minute, tidal volume 447.3 ml, respiratory rate 17 breaths per minute, minute ventilation 7.5 liters per minute and Apnea Hypopnea Index (AHI) 5.4 per hour. In the VAPS group, mean values of PAP settings and data were as follows: target alveolar ventilation 4.2 liters per minute, back up rate 14 breaths per minute, minimum Pressure Support (PS) 4.6 cm water, maximum PS 13.9 cm water, EPAP 4.3 cm water, median IPAP 11.6 cm water, median EPAP 4.4 cm water, tidal volume 423.9 ml, respiratory rate 16.2 breaths per minute, minute ventilation 7.2 liters per minute and AHI 4.53 per hour. Conclusion : Both BPAP-ST and VAPS modes appear to be well tolerated in bulbar onset ALS patients requiring NIPPV. Further studies are required to analyze settings associated with NIPPV compliance in greater detail in bulbar onset ALS patients.

Pulmonary and Critical Care Medicine

Major J, **Konja J**, **Thavarajah K**, **Calo S**, **Abu Sayf A**, **Martirosov A**, and **Hameed AMA**. Myositis Specific Antibodies and Interstitial Lung Disease: A Single Center Retrospective Study. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

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Rationale: Myositis-specific antibodies (MSA) are commonly present in patients with myositis. Interstitial lung disease (ILD) is a common extra-skeletal manifestation of myositis that often precedes muscular or skin involvement. Many individuals with MSA and ILD never progress to develop typical features of myositis. This study aims to describe the characteristics of patients with ILD and a positive MSA. Methods: A retrospective cohort study of patients evaluated by a provider of the Henry Ford Health (HFH) ILD program and an MSA antibody was performed. MSA included Jo-1, PL7, PL12, EJ, OJ, MDA5, TIFF, NXP, Mi2 and SRP autoantibodies. Demographic data including gender, age at diagnosis, and diagnostic makers such as serology results, pulmonary function tests (PFT), and High-resolution computed tomography (CT) findings at the time of initial evaluation were collected. Evaluations by sub-specialties including rheumatology, dermatology, and neurology were reviewed for a formal myositis diagnosis. Descriptive statistics were performed. CT findings and PFTs at the time of diagnosis were analyzed for statistical differences between patients with a confirmed diagnosis of myositis-associated ILD (M-ILD) and idiopathic ILD with a positive MSA (I-ILD w/MSA) Results: This study included 127 patients of whom 62% were female. 69.3% were evaluated by rheumatology, 42.4% by dermatology, 47.2% by neurology, and 40.9% were confirmed to have a diagnosed with myositis. MSA included 47 Jo-1, 8 PL7, 14 PL12, 1 EJ, 2 OJ, 15 MDA5, 11 TIFF, 18 NXP, 9 MI2, and 7 SRP. The mean percentage of predicted Forced Vital Capacity (FVC) was 68.4% with a standard deviation of 19.6. Mean Diffusion Capacity for Carbon Monoxide (DLCO) was 46.9% with a standard deviation of 19.3. Imaging demonstrated 70.9% with ground glass opacities, 15.7% consolidation, 42.5% reticulation, 55.1% bronchiectasis, and 16.5% honeycombing. Statistical significance was found for M-ILD to present with consolidation on imaging, whereas I-ILD w/MSA was more likely to present with honeycombing. Conclusions: This cohort represents a female predominance in those with ILD and positive MSA. Furthermore, those with I-ILD w/MSA more frequently presented with honeycombing on imaging suggesting advanced disease at the time of presentation compared to M-ILD. Ultimately, given only 40.9% of this population possessed a formal diagnosis of myositis, further investigation regarding the relationship of MSA and ILD is warranted. Future studies should elicit disease course and response to treatment between these two groups. Figure 1: Characteristics of our patient population. Standard deviation for PFT's within brackets. Significant P values are bolded.

Pulmonary and Critical Care Medicine

Mann Y, **Ishak A**, Ogbenna UK, Kasmikha L, **Cherabuddi MR**, **Joyce K**, **Harris C**, **Numi M**, **Santana-Garcés M**, **Rehman NK**, **Bryce R**, **Joshi S**, and **Zervos M**. Influenza Vaccine Amongst Persons Experiencing Homelessness: Evaluating Attitudes, Barriers, and Trust. *Open Forum Infect Dis* 2025; 12:S898-S899. Full Text

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Background. In Detroit, persons experiencing homelessness (PEH) have been a vulnerable part of society due to their comorbidities and unique barriers in access to care. Despite PEH experiencing higher rates of vaccine-preventable diseases, there is a lack of information on strategies to improve vaccine rates. The objective of this project is to obtain an understanding of enablers and barriers in influenza vaccine uptake amongst PEH, to inform future work to increase vaccine uptake. Methods. This is a cross-Sectional study of survey data from adult PEH encountered during Street Medicine (SM) outreach in Detroit to assess enablers and barriers in influenza vaccination. Respondents were provided a complimentary bus pass for participation. Descriptive statistics were conducted on sociodemographic variables with analysis of variables related to level of homelessness, vaccine concerns, vaccination

status, and underlying health problems. Results. 43 participants' surveys were analyzed. Participant vaccine status and level of homelessness varied with majority (35%) reporting spending at least 1 night in a tent or other dwelling. Regarding participant demographics, 86% (n=37) were male and 81% (n=35) were Black or African American (AA) (Table 1). Amongst survey respondents, the highest sources of trust for information regarding influenza vaccine was found amongst: 'Social Services Agencies or Other Services' 95.2% (n=20) and 'Experts and Scientists' 93.8% (n=15) (Figures 1 and 2). Variables regarding sources of information trusted were analyzed via chi-Square analysis to evaluate for statistical significance (p-value < 0.05) amongst demographic variables (Figure 3). Conclusion. Previous literature regarding attitudes towards vaccines amongst PEH has demonstrated distrust in healthcare. Results of this study are unique in identifying healthcare members as resources trusted by most participants in providing information on vaccines. This emphasizes the importance of SM outreach in Detroit in building trusting relationships with PEH in addition to decreasing barriers in access to care, to help target future vaccination initiatives.

Pulmonary and Critical Care Medicine
McIntosh J, and **Jennings JH**. Impact of Clinical Guidelines on Inhaler Prescriptions for COPD Exacerbation Admissions. *Am J Respir Crit Care Med* 2025; 211:1. Full Text

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Introduction Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disease that is associated with significant morbidity and mortality. Long-acting muscarinic agonists (LAMAs) and long-acting beta agonists (LABAs) are two types of long-acting bronchodilators (LABDs) that have been shown to improve both symptoms of breathlessness and rates of exacerbations and hospitalizations. Recent GOLD guidelines recommend that patients who have had at least one COPD exacerbation leading to hospital admission should be discharged with a combination of LABA and LAMA. Here, we assess the effect of these guidelines on inhaler prescribing practices for patients admitted for COPD exacerbation. Methods We conducted a retrospective cohort study of patients with a clinical diagnosis of COPD who were admitted to Henry Ford Hospital between December 2017 and July 2024 with a diagnosis of COPD exacerbation. Patients aged 18 years or older were included in this study. The Institutional Review Board of Henry Ford Health approved the study, and the requirement for informed consent was waived. Results A total of 17,116 consecutive patients admitted with COPD listed as a problem were screened. Among these, 2,537 patients had a primary diagnosis of COPD exacerbation, with 2,139 admitted before the updated guidelines (pre-guidelines) and 224 admitted after the publication of the new guidelines (post-guidelines). Before the guidelines, 813 patients (38.01%) were discharged on double LABD, and this number significantly increased to 224 patients (56.28%) post-guidelines ($p < 0.001$). Double LABD prescriptions increased after the guidelines in patients admitted with no LABD (14.7% to 32.9%, $p < 0.001$), single LABD (24.7% to 39.2%, $p < 0.001$) and double LABD (85.32% to 94.33%, $p < 0.001$). Significant predictors of appropriate discharge of double LABD included post-guideline period (OR 2.57, 95% CI 1.96-3.36, $p < 0.001$), admission to the pulmonary service (OR 1.51 [95% CI 1.25-2.03], $p<0.001$), admission on a single inhaler (OR 1.73 [95% CI 1.37-2.19], $p<0.001$), and admission on double inhalers (OR 32.91 [95% CI 25.08-43.18], $p<0.001$). Conclusions Our study demonstrated that the guidelines were associated with an increased rate of discharge on double LABD after admission for COPD exacerbation. Additionally, the involvement of the pulmonary service positively affected discharge on guideline-directed therapy.

Pulmonary and Critical Care Medicine
McIntosh J, **Jennings JH**, and **Bradley P**. A Case of Sarcoidosis Associated With Anti-interleukin-17A Therapy. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

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Introduction: Sarcoidosis is a multisystemic inflammatory disorder characterized by the pathological finding of non-caseating granulomas. All organ systems can be affected although common presentations include mediastinal adenopathy, Lung parenchymal disease and cutaneous disease. There have been a

number of reports of sarcoidosis and sarcoidosis like granulomatous disease manifesting after treatment with biologic agents such as TNF alpha inhibitors and immune checkpoint inhibitors and is suspected to be due to immune dysregulation. Here, we present a rare case of sarcoidosis with generalized adenopathy and pulmonary nodules presenting after treatment anti-interleukin-17A therapy (anti-IL-17A) for Hidradenitis suppurativa (HS). Case Description 45-year-old female never smoker with history of HS treated with Secukinumab presented to pulmonary clinic for evaluation of Abnormal CT scan. She had a gradual onset and progression of shortness of breath for 2 months. Other symptoms include chest pain, intermittent abdominal pain and intentional weight loss of 30-40 pounds over 6 months. Physical examination was unremarkable. Investigations done by her primary care physician resulted in CT scan with Pulmonary Embolism protocol completed with multiple bilateral pulmonary nodules measuring up to 8 mm, multiple enlarged bilateral subpectoral and axillary lymph nodes. Pulmonary function testing showed normal spirometry and diffusion capacity. Differential diagnosis included malignancy, inflammatory process, and infection. Navigational bronchoscopy was deferred due to size and peripheral location of nodules. PET scan showed Innumerable prominent and hypermetabolic lymph nodes throughout the neck, chest, abdomen, and pelvis. She subsequently underwent ultrasound guided biopsy of left external Iliac chain lymph node which demonstrated necrotizing and non-necrotizing granulomatous inflammation. Investigations for autoimmune conditions and endemic mycosis were negative, and the patient was diagnosed with sarcoidosis associated with anti-interleukin-17A therapy. After discussion of treatment options, patient preferred to monitor with surveillance and on 3 month follow up there was no noted significant symptomatic or radiologic progression in disease with resolution of some pulmonary nodules. DiscussionSecukinumab is a human IgG1 monoclonal antibody that selectively binds and neutralizes protein interleukin-17A. In the literature there have been few cases of sarcoidosis reported manifesting as hilar lymphadenopathy and cutaneous sarcoidosis in patients treated for Psoriatic arthritis. As sarcoidosis is a diagnosis of exclusion it is important to first evaluate and rule out other differential diagnosis such as malignancy, inflammatory, autoimmune or infectious causes. Management options include discontinuation of offending agent, steroids therapy and antimetabolite therapy such as methotrexate. Our case highlights a rare adverse reaction to an interleukin-17A inhibitor.

Pulmonary and Critical Care Medicine

Nakdali R, and **Bradley P**. Waxing and Waning Nodules: A Rare Diagnosis of Pulmonary Malt Lymphoma. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

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Introduction: Mucosa-associated lymphoid tissue (MALT) lymphoma is a rare type of non-Hodgkin's lymphoma that can involve extranodal sites, including the lungs. Primary pulmonary MALT lymphoma is an uncommon diagnosis, presenting incidentally or with nonspecific symptoms. We present a patient with long-standing pulmonary nodules and several inconclusive biopsies, ultimately diagnosed with pulmonary MALT lymphoma. Case: A 60-year-old man, with a 70-pack year smoking history, was incidentally found to have bilateral noncalcified pulmonary nodules, measuring up to 2.4cm, on routine lung cancer screening seven years prior to presentation to our clinic. The nodules were followed by annual computed tomography (CT) scans with waxing and waning size of the nodules. At the onset, he underwent two lung biopsies, however pathology was inconclusive with reactive changes, fibrous stroma and scattered chronic inflammatory cells. He deferred surgical biopsy due to concern for risks of surgery, which led to ongoing CT surveillance without definitive diagnosis. Imaging in 2024 demonstrated progression of the pulmonary nodules, with the largest nodule in the right upper lobe now measuring 5.5 x 3.7 cm, along with new nodules in both lungs. The patient remained asymptomatic, denying cough, hemoptysis, fever, chills, shortness of breath, and chest pain. A positron emission tomography (PET) scan revealed a hypermetabolic right upper lobe mass measuring 5.5 x 3.7 cm, with multiple foci of mild hypermetabolic satellites variable in size along with a hypermetabolic 1.7cm x 2.4cm pleural based pulmonary nodule in the left lower lobe, suggestive of malignancy. There was no evidence of metastatic disease. The patient underwent a bronchoscopic biopsy of the right upper lobe nodule. Pathology revealed a diagnosis of low-grade B-cell lymphoma, specifically extranodal marginal zone lymphoma of MALT type. Discussion: This case highlights the evasive nature of pulmonary MALT lymphoma on imaging. In this case, our patient had bilateral pulmonary nodules that fluctuated in size over seven years and biopsies yielded two

inconclusive results. A high index of suspicion led to the patient being reevaluated and eventual diagnosis. MALT lymphoma is the most common type of primary pulmonary lymphoma, which constitutes only 1% of all pulmonary malignancies. It is often indolent and can be asymptomatic, with a variety of findings on CT as described by numerous papers. Treatment options include surveillance, surgical intervention, chemotherapy, or immunotherapy, depending on the extent and progression of disease.

Pulmonary and Critical Care Medicine
Nakdali R, **Ladzinski A**, Hashmi M, and **Kapadia D**. Asthma or Airway Obstruction? A Case of Substernal Goiter Presenting in Pregnancy. *Am J Respir Crit Care Med* 2025; 211:3. Full Text

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Introduction: A thyroid goiter, particularly a substernal goiter, can cause significant airway obstruction, which requires prompt management. In this case, we present a patient who initially presented as an asthma exacerbation with wheezing and was found to have a large thyroid goiter extending into the mediastinum and causing external compression of the trachea. Case Report: A 38-year-old female with a medical history of chronic hypertension with superimposed preeclampsia requiring C-section and asthma presented to the hospital at 36 weeks pregnant due to a 2-month history of shortness of breath with multiple emergency room visits, attributed to asthma exacerbations. During this presentation, she developed respiratory distress, requiring intubation in the emergency room. She was initially treated for an asthma exacerbation along with pre-eclampsia however due to concern for pulmonary embolism, she underwent a computed tomography (CT) scan which showed a large middle mediastinal mass causing mass effect on the esophagus and severe mass effect at the level of the carina. The mass measured 3.8 cm in the axial direction and 9 cm in the craniocaudal direction and extended out of the field of view of the CT scan. She underwent a rigid bronchoscopy with biopsy of the mediastinal mass followed by a C-section. Biopsy revealed thyroid follicular cells. Repeat bronchoscopy showed extrinsic compression of the trachea down to the main carina, with narrowing in the proximal (30%), mid (80%), and distal trachea (90%). She underwent placement of a metal self-expanding stent in the distal trachea as a silicone Y-stent could not be placed due to significant posterior extrinsic compression of the trachea preventing safe advancement of the rigid bronchoscope. Nuclear thyroid scan confirmed uptake throughout mediastinal mass contiguous with thyroid gland suggestive of substernal goiter. Thyroid labs were normal. The patient underwent hemi-thyroidectomy with pathological evaluation of resected mass showing a multinodular thyroid goiter. With relief of her tracheal obstruction, the patient subsequently underwent removal of her tracheal stent without complication a few weeks later. Conclusion: Several studies have suggested that pregnancy can increase the size of a thyroid goiter or pre-existing thyroid nodules. Substernal thyroid goiters can cause significant airway obstruction due to size which can be life threatening. Our patient presented several times for shortness of breath, which was attributed to asthma however recurrent "exacerbations" despite optimal medical therapy in patients should always prompt further investigations for other causes.

Pulmonary and Critical Care Medicine
Pritchett M, Garwood S, Jiwani AZ, Abedi A, Bawaadam HS, Icard BL, **Peralta AR**, Revelo AE, Reisenauer J, Oh SS, and Postigo M. Diagnosis of Sub-centimeter Nodules Through Shape-sensing Robotic Assisted Bronchoscopy: Real-world Outcomes From the Ion Registry. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

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RATIONALE: As technology for biopsy of peripheral pulmonary nodules advances, the size of suspicious nodules referred for biopsy has decreased. This can be partly attributed to tools such as shape-sensing robotic-assisted bronchoscopy (ssRAB), which can increase the likelihood of a diagnostic result. Literature describing the biopsy of sub-centimeter nodules is primarily single center with a reported diagnostic yield for robotic bronchoscopy of 67%1, and 71%2 for CT-guided percutaneous biopsy; robust prospective multi-center data is needed to further understand the feasibility and clinical value of <1cm nodule biopsies. Herein, we report data from the prospective Ion Registry describing outcomes for patients with sub-centimeter nodules biopsied using ssRAB. METHODS: Patients with at least one (1) nodule <1cm that underwent ssRAB biopsy were identified from those enrolled in the Ion Registry. Subjects with multiple lesions were included if all nodules were <1cm in largest diameter. Nodule and procedure characteristics are reported with descriptive statistics; diagnostic yield was assessed using the ATS/ACCP recommended guidelines of index biopsy results only. Safety was assessed as the rate of pneumothorax requiring intervention and Nashville Grade ≥3 bleeding. RESULTS: Fifty-four (54) subjects and 57 sub-centimeter nodules were identified across 9 centers and 15 investigators; procedures were completed October 2023 through September 2024. The majority of nodules (47.4%) were incidental findings. Median nodule diameter was 8 mm (IQR: 7,9; range: 4.0-9.7 mm) with 66.7% of nodules located in the outer-third of the lung, and predominantly (57.9%) in the upper lobes. CT bronchus sign was present in 24.6% of nodules, and most (89.5%) nodule were solid. Median procedure time was 34.5 mins (IQR: 26,47; range: 9-89 mins); fixed or mobile CBCT was utilized for 80.7% (46/57) of nodules. The flexision biopsy needle and cryoprobe were used in 91% and 49% of biopsies, respectively. Diagnostic yield was 83% (45/54) using index biopsy results, 59% of which were malignant. No (0%) pneumothorax requiring intervention, Nashville Grade ≥3 bleeding events. CONCLUSION: Preliminary results from this prospective, multi-center registry cohort demonstrate peripheral nodules <1cm can be safely and effectively diagnosed through ssRAB biopsy and highlight the impact of ssRAB in enhancing lung nodule diagnosis, particularly when combined with CBCT. These findings suggest ssRAB may be considered a viable option for the biopsy of suspicious sub-centimeter nodules, further optimizing the management of patients with suspected lung cancer.

Pulmonary and Critical Care Medicine

Stratton P, **Kenney RM**, **Veve M**, **Fitzmaurice MG**, **Alangaden GJ**, and **Franco-Palacios D**. Impact of a Short Course Post-Operative Antibiotic Prophylaxis Duration on Nephrotoxicity in Lung Transplant Recipients. *Open Forum Infect Dis* 2025; 12:S1356. Full Text

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Background. Vancomycin plus an antipseudomonal β-lactam is used as lung transplant surgical prophylaxis, but an optimal post-operative duration is not defined. The study objective was to assess the impact of a shortened antibacterial surgical infection prophylaxis (SIP) duration on post-operative nephrotoxicity in lung transplant recipients. Table 1 Variables associated with AKI Methods. IRB approved quasi experiment of lung transplant recipients who received SIP from 1/1/2016-9/30/2020 (pre-group) to 10/1/2020-7/31/24 (post-group). Intervention: implementation of shortened SIP duration to 72-hours of cefepime and vancomycin post-operatively. Inclusion: eGFR >30 mL/min/1.73m2 between transplant day ±2. Exclusion: renal replacement ≤ 3-months, simultaneous organ transplants, donor bronchi with Gram-positive bacterial growth, or new COVID-19 infection between transplant day ±7. The primary endpoint was the incidence of acute kidney injury (AKI), defined by the KDIGO criteria, while receiving post-operative vancomycin up to 14 days. Secondary endpoints were vancomycin consensus guideline (VCG) AKI definition at 14-days and time to AKI. Results. 77 patients were included: 45 (58%) pre-, 32 (42%) post-intervention. 73% vs. 47% male (p=0.018). 49% vs. 34% (p=0.205) KDIGO AKI while on vancomycin. Post-group associated with approximately 40% decreased odds of developing KDIGO AKI (Table 1). Secondary endpoints: 33% vs. 19% VCG AKI (p=0.157). Median time to AKI was three days, with no differences detected between groups and AKI definitions. Similar rates of C. diff infection, positive bacterial respiratory cultures, new multidrug resistant organisms, surgical site infections. 57.8% vs. 84.4% patients received treatment for new pneumonias after SIP completion (p=0.013), with one new MRSA pneumonia in the pre-group and one in the post-group. Conclusion. Implementation of a shortened antibacterial prophylaxis protocol for lung transplant resulted in numerically fewer AKIs. Maturation, regression to the mean, and reliance on manual chart review are all limitations of this retrospective study.

Ongoing analysis of this intervention, such as with multicenter prospective studies, can help to characterize the decreased nephrotoxicity risk with shorter course prophylaxis post-transplant.

Pulmonary and Critical Care Medicine
Versha F, Lohana A, Chander S, Patel V, and **Iribarren JB**. Finding the Best Fit: A Head-To-Head Comparison of Triple Therapy Regimens in COPD. *Am J Respir Crit Care Med* 2025; 211:2. Full Text

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Introduction: Chronic obstructive pulmonary disease (COPD) represents a significant global health challenge, particularly in its moderate to severe cases, where effective management is crucial to improving patient outcomes. The integration of inhaled corticosteroids with long-acting β2-adrenoceptor agonists and long-acting muscarinic antagonists in fixed-dose combinations has emerged as a cornerstone of therapy. This study evaluates the efficacy of two triple therapy regimens — Glycopyrrolate, Budesonide, and Formoterol Fumarate (GLY/BUD/FOR) and Fluticasone Furoate, Vilanterol, and Umeclidinium (FF/VI/UMEC) —in adults aged 45 and older with diagnosed COPD with FEV1/FVC < 70% to assess the impact of these regimens on the preventing COPD exacerbations and acute hypoxemic respiratory failure. Methods: A retrospective cohort analysis was conducted using the TriNetX database. Patients with moderate to severe COPD and FEV1/FVC < 70% were identified based on ICD codes, and two cohorts were formed based on the prescribed inhaler therapy: GLY/BUD/FOR and FF/VI/UMEC. Patients with comorbid asthma, heart failure, or pneumonia were excluded. A 1:1 propensity-score matching (PSM) analysis was performed to balance covariates such as age, gender, smoking status, and baseline lung function to minimize confounding and bias. Post-matching, both had 16,052 patients. Ultimately, 23,331 patients (FF/VI/UMEC: 11,234, GLY/BUD/FOR: 12,097) with a mean age of 67.4 ± 10.1 years and 55.3% males were included. Results:Among groups, 10.4% of patients on FF/VI/UMEC experienced COPD exacerbations compared to 6.7% on GLY/BUD/FOR (Risk Ratio: 1.55, 95% CI: 1.42-1.69, $p < 0.001$). Kaplan-Meier analysis showed a lower survival probability in the FF/VI/UMEC group (77.7% vs. 83.9%, $p < 0.001$). For acute respiratory failure, 3.5% of patients on FF/VI/UMEC experienced this outcome compared to 2.8% on GLY/BUD/FOR (Risk Ratio: 1.28, 95% CI: 1.12-1.45, $p = 0.003$). Conclusion: Our study suggests that FF/VI/UMEC demonstrated an increased risk of COPD exacerbations and acute hypoxic respiratory failure compared to the group receiving GLY/BUD/FOR. This indicates that GLY/BUD/FOR may provide enhanced protective benefits in patients with moderate to severe COPD, improving disease management and minimizing healthcare resource utilization. Further studies are warranted to explore the long-term benefits and potential mechanisms underlying the observed differences.

Pulmonary and Critical Care Medicine
Zahedi S, Khazmi I, **Binette M**, and **Rezik M**. TB or Not TB: Two Unique Cases of Pleural Tuberculosis in Immunocompetent Hosts. *Am J Respir Crit Care Med* 2025; 211:1. Full Text

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A 36-year-old male (JF) who recently immigrated from Venezuela presented to the emergency department with a one-week history of nonproductive cough, fever, and night sweats. His roommate had been diagnosed with tuberculosis (TB). Chest X-ray revealed a large right-sided pleural effusion without parenchymal disease. JF was placed in isolation, but multiple attempts to obtain an induced sputum sample were unsuccessful. A Quantiferon-TB Gold test was positive, and a chest CT confirmed no parenchymal disease. The diagnosis of pleural TB was made based on pleural fluid analysis, which was exudative per Light's criteria and positive for adenosine deaminase (ADA), although acid-fast bacilli (AFB) testing was negative. He was discharged without airborne precautions and started on RIPE therapy. Two weeks later, JF's other roommate, a 35-year-old male (CG), presented with similar symptoms. CG's

Quantiferon-TB test was also positive. He produced two sputum samples, which were AFB-negative but positive for Mycobacterium tuberculosis (mTB) PCR. Imaging revealed a large exudative pleural effusion, although ADA testing was not obtained, and pleural fluid AFB cultures were negative. Both patients had shared exposure to the same source and were HIV-negative. Despite their similar symptoms and pleural effusions, JF had isolated pleural TB, while CG had both parenchymal and pleural TB. JF's case is significant due to its rarity; isolated pleural TB constitutes only 5-10% of TB cases and usually arises from hematogenous or lymphatic spread. It is more common in younger patients or those with HIV, none of which applied to JF. Diagnosing pleural TB can be complex and typically requires a positive mTB PCR or ADA in pleural fluid; if both are negative, a pleural biopsy showing caseating granulomas and AFB positivity is necessary. Simultaneous parenchymal and pleural TB, as in CG's case, occurs in only 5-30% of TB cases and is often linked to a high disease burden or immunocompromised status. These atypical presentations emphasize the need for clinical vigilance and a thorough understanding of pleural TB's diagnostic challenges. Early recognition and treatment are essential to improve outcomes and prevent complications such as residual parenchymal fibrosis and increased relapse risk.

Sleep Medicine

Afaneh H, **Hirata M**, **Kalmbach D**, **Cheng P**, and **Pitts D**. Financial Toxicity, Racial Disparities, and Healthcare Access in Pregnant Women with Insomnia. *Sleep* 2025; 48:A260. Full Text

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Introduction: Insomnia affects half of women during pregnancy, which reduces quality of life and harms maternal health. As awareness of prenatal insomnia increases, more pregnant women are seeking help for their sleep. However, little is known about real-world barriers pregnant women face when seeking insomnia treatment. The present study explored associations of race and financial toxicity with clinical morbidity and care access among pregnant women seeking insomnia care. Methods: Three-hundred-and-ninety-three pregnant women (Age: 30.7 ± 4.9yrs; Gestation: 25.7 ± 3.4wks) seeking treatment for insomnia in a large health system completed an online survey. Outcomes included sociodemographics, the Comprehensive Score of financial Toxicity survey, Edinburgh Postnatal Depression Scale, and Perinatal Rumination Scale-Night. We employed chi-square analyses and multivariate linear and logistic regression. Results: Half of treatment-seeking patients identified racially as white (52.7%), whereas 21.7% identified as Black (most well-represented groups). Nearly half of the sample reported no/mild financial toxicity, whereas 39.2% endorsed moderate financial toxicity and 13.9% endorsed severe financial toxicity. Regarding health insurance, 29.9% of patients had public insurance. Relative to white patients, non-white patients reported higher levels of moderate-to-severe financial toxicity (62.4% vs 45.0%) and greater utilization of public insurance (40.9% vs 20.1%). Multivariate regression showed that financial toxicity was independently associated with depression (b=-.252, p<.001), perinatal rumination (b=-.491, p<.001), and suicidal ideation (SI; OR=1.07, p<.001), whereas race was not. Indeed, more severe financial toxicity was associated with greater disease burden as indicated by higher rates of comorbid depression (Severe toxicity: 80.0%; Moderate: 61.9%; No/Mild: 29.7%), perinatal rumination (Severe: 80.0%; Moderate: 56.8%; No/Mild: 28.1%), and SI (Severe: 23.6%; Moderate: 16.8%; No/Mild: 5.4%). Unfortunately, patients with greater financial toxicity were less likely to be able to afford copays for psychotherapy services (Severe toxicity: 69.1% cannot afford copays; Moderate: 57.1%, No/Mild: 27.2%). Conclusion: Pregnant women seeking insomnia treatment present with high rates of depression, perinatal rumination, and SI. Non-white women are over-represented among those with moderate-to-severe financial toxicity, and greater financial toxicity is associated with greater clinical morbidity. Despite this greater disease burden, patients with greater financial toxicity are disproportionately unable to afford care, thereby severely limiting treatment access for those with highest need.

Sleep Medicine

Belevender C, **Ozeir S**, **Bugazia S**, **Badhwar A**, **Shakaroun D**, **Carlin A**, **Roehrs T**, and **Skiba V**. The Role of Age, Gender, and Daytime Sleepiness in Predicting CPAP Adherence Following Bariatric Surgery. *Sleep* 2025; 48:A585. Full Text

[Belevender, Claire; Ozeir, Serene; Bugazia, Seif; Badhwar, Ankita; Shakaroun, Dania; Carlin, Arthur; Roehrs, Timothy; Skiba, Virginia] Henry Ford Hosp, Detroit, MI USA

Introduction: Obstructive sleep apnea (OSA) is a common comorbidity in bariatric surgery patients, with continuous pos itive airway pressure (CPAP) serving as a primary treatment. While bariatric surgery often results in significant weight loss and improvement in apnea severity, the roles of age, gender, and baseline daytime sleepiness—measured by the Epworth Sleepiness Scale (ESS)—in predicting CPAP adherence remain unclear. Methods: This retrospective chart study reviewed 140 patients evaluated at the Henry Ford Bariatric Clinic and referred to the Henry Ford Sleep Disorders and Research Center for preoperative sleep testing between April and August 2023. CPAP adherence, defined as any reported usage, was analyzed in rela tion to ESS scores, age, and gender. Results: Preliminary analyses revealed positive correlation between ESS scores and CPAP adherence, suggesting patients with higher daytime sleepiness are more likely to adhere to CPAP therapy. Older patients demonstrated higher adherence rates. Significant differences in adherence were also observed between genders, with male patients showing consistently higher adherence across all follow-up points. Conclusion: Age, gender, and baseline ESS appear to play significant roles in predicting CPAP adherence following bariatric surgery. These findings highlight the importance of tailoring postoperative CPAP management to demographic factors, with particular attention to younger and female patients who may benefit from additional adherence support.

Sleep Medicine

Chavez AG, **Xu TFY**, **Hirata M**, **Kalmbach D**, **Cheng PL**, **Drake C**, and **Pitts D**. Implementability of a Perinatal Sleep Clinic. *Sleep* 2025; 48:A565. Full Text

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Introduction: Sleep problems have been historically viewed as a normal feature of pregnancy, but a burgeoning literature high lights the high prevalence and morbidity of prenatal insomnia Half of pregnant women report speaking to their prenatal care provider about their sleep problems. However, care access is severely limited as most health systems do not have clearly iden tified clinics in which prenatal insomnia is managed. In 2023, Henry Ford Health (HFH) implemented the Perinatal Sleep Clinic (PSC), a telemedicine clinic co-directed by a clinical psychologist and obstetrician. As pregnant women with sleep disorders are not routinely treated in the HFH sleep clinic or behavioral health clinic, the PSC was intended to address an unmet patient need. The present study evaluated the implement ability of the PSC in a large health system. Methods: ~10,000 live births occur annually at HFH. The PSC launched to treat pregnant women with insomnia. We reviewed electronic medical records to describe patient throughput from January 2023 through November 2024. We surveyed 53 stake holders within and outside of HFH who had roles in health system leadership and/or clinical care in the areas of obstet rics-gynecology, maternal-fetal medicine, perinatal mental health, and/or sleep medicine. Surveys included the Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM). Scale scores range from 1-5 with higher scores indicating more favorable implementation ratings. Results: In 2 years, the PSC treated 110 pregnant women with insomnia. Among our surveyed stakeholders, 74.5% were employed by HFH. Stakeholders rated the PSC as highly accept able (AIM: 4.52±.67), highly appropriate (IAM: 4.61±.57), and highly feasible at HFH (FIM: 4.23±.68). Additionally, stake holders rated the clinic favorably for providing an unmet clini cal need (4.65±.52) and providing an important clinical service (4.65±.59). Most stakeholders (82.4%) indicated that the clinic should be hybrid, offering both telemedicine and in-person care options. Conclusion: As women increasingly seek help for their sleep dur ing pregnancy, clinic resources must be made available for these patients. Leadership and provider stakeholders supported the acceptability, appropriateness, and feasibility of the PSC (ide ally, as a hybrid clinic), thereby supporting its implementation in a large health system

Sleep Medicine

Corser B, Plante D, **Drake C**, Bogan R, Dauvilliers Y, Insana S, Seiden D, Nomikos G, Manuel M, Bauer E, Budur K, and Dayno J. EFFECT OF PITOLISANT ON SYMPTOMS OF IDIOPATHIC HYPERSOMNIA DURING AN OPEN-LABEL PERIOD IN A PHASE 3 CLINICAL TRIAL. *Sleep* 2025; 48:A376. Full Text

[Corser, Bruce; Drake, Christopher] Sleep Management Inst, Cincinnati, OH USA; [Plante, David] Univ Wisconsin Madison, Madison, WI 53706 USA; [Drake, Christopher] Henry Ford Hlth Syst, East Dundee, IL USA; [Bogan, Richard] Bogan Sleep Consultants, Columbia, SC USA; [Dauvilliers, Yves] Univ Montpellier, Dept Neurol,Guide Chauliac Hosp, Inst Neurosci Montpellier INM, Sleep Wake Disorders Ctr,INSERM, Montpellier, France; [Insana, Salvatore; Seiden, David; Nomikos, George; Manuel, Michelle; Bauer, Eric; Budur, Kumar; Dayno, Jeffrey] Harmony Biosci Holdings Inc, Plymouth Meeting, PA USA

Introduction: Idiopathic Hypersomnia (IH) is a rare and chronic neurological disorder. People with IH experience severe excessive daytime sleepiness (EDS), sleep inertia, and a multitude of adverse functional outcomes. Pharmacological treatments for IH are limited. Pitolisant is FDA approved for the treatment of EDS and cataplexy in adult patients and for excessive daytime sleepiness in pediatric patients ≥6 years with narcolepsy. Methods: The present analyses focused on an eight-week open-label period (OLP) that was part of a twelve-week dou ble-blind, placebo-controlled, randomized withdrawal phase 3 clinical trial to evaluate the safety and efficacy of pitolisant in adult patients with IH (NCT05156047). During the OLP, eli gible participants were titrated with pitolisant for three weeks (8.9 mg, 17.8 mg, and 35.6 mg), then began a three-week flexible dose period, and concluded with a two-week stable dose period. Efficacy measures included the Epworth Sleepiness Scale (ESS), Sleep Inertia Questionnaire (SIQ), Functional Outcomes of Sleep Questionnaire (FOSQ-10), Patient-Reported Outcomes Measurement Information System, Sleep Related Impairment (PROMIS-SRI), Idiopathic Hypersomnia Severity Scale (IHSS), Patient Global Impression of Severity of EDS (PGI-S), and Clinician Global Impression of Severity of IH (CGI-S). Efficacy measures were evaluated for change from OLP baseline to the end of the eight-week OLP. Results: Two hundred and thirteen patients (mean±SD age; 39.7±12.85 years; 79.3% female) were enrolled in the trial. There was a nominally statistically significant (P< 0.0001) group mean reduction in all efficacy measures from the OLP baseline to the end of the eight-week OLP (mean±SD): ESS (16.2±3.40, 8.7±5.04; delta=-7.6±5.12); SIQ (70.0±16.91, 52.8±19.86; delta=-18.0±19.14); FOSQ-10 (11.23±2.70, 13.72±3.56; delta=2.60±3.00); PROMIS-SRI (28.7±4.85, 21.6±6.58; delta=- 7.2±6.36); IHSS (33.3±7.48, 25.8±9.44; delta=-7.7±7.94); PGI-S (3.8±0.72, 2.8±0.96; delta=-1.1±1.07); and CGI-S (3.7±0.60, 2.6±0.89; delta=-1.1±0.87). Among the 173 patients who completed the OLP (81.2%), 144 (83.2%) of them achieved a ≥3-point reduction on their ESS score, and 136 (78.6%) achieved a ≥4-point reduction on their IHSS score. Conclusion: In an 8-week OLP of a phase 3 clinical trial in adult patients with IH, pitolisant demonstrated robust improvements in EDS, sleep inertia, and a multitude of functional outcomes. A large majority of patients exhibited clinically meaningful reduc tions in their EDS and IH symptoms.

Sleep Medicine

Dauvilliers Y, Plante D, Corser B, **Drake C**, Bogan R, Insana S, Seiden D, Nomikos G, Wilmsen K, Manuel M, Budur K, and Dayno J. Long-Term Safety and Effectiveness of Pitolisant Use in Adult Patients with Idiopathic Hypersomnia (IH). *Sleep* 2025; 48:A376-A377. Full Text

[Dauvilliers, Yves] Univ Montpellier, Gui De Chauliac Hosp, Sleep & Wake Disorders Ctr, Dept Neurol,INM,INSERM, Montpellier, France; [Plante, David] Univ Wisconsin Madison, Madison, WI USA; [Corser, Bruce] Sleep Management Inst, Cincinnati, OH USA; [Drake, Christopher] Henry Ford Hlth Syst, Candon, MI USA; [Budur, Kumar] Bogan Sleep Consultants, Columbia, SC USA; [Insana, Salvatore; Seiden, David; Nomikos, George; Wilmsen, Katie; Manuel, Michelle; Budur, Kumar; Dayno, Jeffrey] Harmony Biosci Holdings Inc, Plymouth Meeting, PA USA

Introduction: Pitolisant is being evaluated for use in adult patients with IH in two phase 3 clinical trials, a double-blind randomized withdrawal (DBRW) and an open-label extension (OLE). The present analyses focused on the safety and effective - ness of long-term administration of pitolisant in adult patients with IH across 13 months. The OLE study is ongoing. Methods: Open-label data were integrated across two con - tiguous phase 3 clinical trials (DBRW: NCT05156047; OLE: NCT05458128). Safety measures included

treatment-related treatment-emergent adverse events (TR-TEAEs). Effectiveness measures included the Epworth Sleepiness Scale (ESS); Idiopathic Hypersomnia Severity Scale (IHSS); Patient Reported Outcomes Measurement Information System, Sleep Related Impairment-8a (PROMIS-SRI); Patient Sleep Inertia Questionnaire (SIQ); Functional Outcomes of Sleep Questionnaire (FOSQ-10); Patient Global Impression of Severity of EDS (PGI-S); and Clinician Global Impression of Severity of IH (CGI-S). Effectiveness measures were assessed at baseline, Month 2, Month 4, Month 10, and Month 16. Results: The safety population included 213 patients who received at least one dose of pitolisant (mean±SD age, 39.7±12.85 years; 79.3% female). The median duration of pitolisant exposure was 39.14 weeks (range: 0.71-93.29 weeks) and the median maximum pitolisant dosage was 35.6 mg (median [range: 8.9-35.6 mg]). Among this population, 102 participants (47.9%) experienced a TR-TEAE; most frequent TR-TEAEs were headache (17.8%), insomnia (16.0%), and abnormal dreams (5.2%). The effective - ness population included 119 adult patients who enrolled in both trials (mean±SD age, 40.1±11.96 years; 79.8% female). Generally, the sample size remained stable across timepoints. All effectiveness measures demonstrated a nominally statistically sig - nificant reduction (P< 0.0001) from study baseline at every time - point. Effectiveness measures are reported as baseline mean±SD, and change from baseline across all timepoints (range: lowest, highest change across endpoints [mean±SD]): ESS, 16.6±2.99 (-8.4±4.46, -9.7±4.69); IHSS, 33.7±7.10 (-9.8±7.56, -13.4±8.66); PROMIS-SRI, 64.16±4.89 (-8.35±7.26, -10.11±5.56); SIQ, 71.8±17.14 (-21.2±17.21, -24.9±18.91); FOSQ-10, 11.14±2.77 (3.31±2.99, 4.24±3.07); PGI-S, 3.9±0.74 (-1.2±0.99, -1.4±0.95); and CGI-S, 3.6±0.60 (-1.2±0.89, -1.3±0.78). Conclusion: Pitolisant was well-tolerated, and the safety profile was consistent with the established safety profile for patients with narcolepsy. Pitolisant showed clinically meaningful and sustained improvements in multiple symptoms of IH across a >1-year dosing period

Sleep Medicine
Dauvilliers Y, Plazzi G, Plante D, Mignot E, **Roth T**, Sterkel A, Hartman D, Kong JNF, Accardi M, Saha S, and Im E. A Phase 2a, Double-blind, Placebo-controlled Study of ORX750 in Patients with Narcolepsy (type 1 and 2) and Idiopathic Hypersomnia: Study Design. *Sleep* 2025; 48:A373-A374. Full Text

[Dauvilliers, Yves] Univ Montpellier, Gui Chauliac Hosp, Inst Neurosci Montpellier INM, Sleep Wake Disorders Ctr,Dept Neurol,INSERM, Montpellier, France; [Plazzi, Guiseppe] Univ Modena & Reggio Emilia, Modena, Italy; [Plante, David] Univ Wisconsin Madison, Madison, WI USA; [Mignot, Emmanuel] Stanford Univ, Stanford, CA USA; [Roth, Thomas] Henry Ford Hlth Syst, Sleep Disorders & Res Ctr, Detroit, MI 48202 USA; [Sterkel, Amanda; Hartman, Deborah; Kong, Jennifer; Accardi, Mario; Saha, Saurabh] Centessa Pharmaceut, Boston, MA USA; [Im, Ellie] CENTESSA, Boston, MA USA

Introduction: Narcolepsy types 1 (NT1) and 2 (NT2), and idio pathic hypersomnia (IH) are rare, debilitating central disorders of hypersomnolence characterized by excessive daytime sleepi ness (EDS). None of the currently available therapies target the orexin system, which is a core element of wake-promoting cir cuitries and specifically, of NT1 pathology. ORX750 is a novel, investigational oral orexin-2 receptor (OX2R) agonist that demonstrated strong wake-promoting effects in acutely sleep-de prived healthy volunteers (ongoing phase 1 study). An ongoing phase 2a study, ORX750-0201 will evaluate the safety, tolerabil ity, efficacy, and PK of ORX750 in NT1, NT2, and IH patients. Methods: This phase 2a study is a randomized, double-blind, placebo-controlled, cross-over basket study with separate cohorts for NT1, NT2, and IH. Initial dosing will be 1 mg (NT1) and 2 mg (NT2 and IH) with sequential dose escalation/ de-escalation between cohorts. Within dosing cohorts, par ticipants will be randomized to one of two blinded treatment sequences and receive ORX750 for 4 weeks and placebo for 2 weeks (6-week treatment duration total) in a crossover design. Efficacy endpoints will include the Maintenance of Wakefulness Test (MWT), Epworth Sleepiness Scale (ESS), and weekly cat aplexy rate (NT1 only). Other exploratory assessments include measures of overall symptom improvement, sleep, cognition, attention, memory, and general health. Results: This study plans to complete 78 participants (n=18 NT1; n=24 NT2; n=36 IH), with three dose cohorts per disorder. This 6-week crossover study has >87.5 % power within each dos ing cohort to detect a 15 min change in mean sleep latency on the MWT relative to placebo (two-sided α=0.05). The study initiated with participating sites in the US, Canada, and EU. Data for all three disorders are expected in 2025. Conclusion: This study will evaluate the safety, tolerability, effi cacy, and PK of multiple doses of ORX750 for the first time in patients with NT1, NT2, and IH with results informing future clinical studies.

Sleep Medicine

Dauvilliers Y, Thorpy M, **Roth T**, Kushida C, Morse A, Harsh J, Ortiz L, and Gudeman J. CONSISTENT EFFICACY OF ONCE-NIGHTLY SODIUM OXYBATE ON DISRUPTED NIGHTTIME SLEEP IN PEOPLE WITH NARCOLEPSY. *Sleep* 2025; 48:A362-A363. Full Text

[Dauvilliers, Yves] Univ Montpellier, Gui de Chauliac Hosp, Sleep & Wake Disorders Ctr, Dept Neurol,Inst Neurosc Montpellier INM,INSERM, Montpellier, France; [Thorpy, Michael] Albert Einstein Coll Med, Bronx, NY USA; [Roth, Thomas] Henry Ford Hlth Syst, Sleep Disorders & Res Ctr, Detroit, MI USA; [Kushida, Clete] Stanford Univ, Sch Med, Stanford, CA USA; [Morse, Anne] Janet Weis Childrens Hosp, Med Geisinger Med Ctr, Geisinger Commonwealth Sch, Danville, PA USA; [Harsh, John] Colorado Sleep Inst, Boulder, CO USA; [Ortiz, Luis] Johns Hopkins All Childrens Hosp, Johns Hopkins Med Inst, St Petersburg, FL USA; [Gudeman, Jennifer] Avadel Pharmaceut, Dublin, Ireland

Introduction: Once-nightly sodium oxybate (ON-SXB; LUMRYZ™) demonstrated efficacy in treating narcolepsy symptoms, including disrupted nighttime sleep (DNS), in the phase 3 REST-ON trial (NCT02720744). This post hoc analysis assessed ON-SXB efficacy on DNS across various participant subgroups. Methods: Participants aged ≥16 years with narcolepsy type 1 (NT1) or 2 (NT2) were randomized 1:1 to ON-SXB (week 1, 4.5 g; weeks 2-3, 6 g; weeks 4-8, 7.5 g; weeks 9-13, 9 g) or pla cebo. Least squares mean differences (LSMDs) in changes from baseline for ON-SXB vs placebo for number of sleep stage shifts and nocturnal arousals as measured by polysomnography, as well as patient-reported sleep quality and refreshing nature of sleep, were compared among demographic (age, sex, race, body mass index [BMI] category), narcolepsy type (NT1/NT2), and concomitant alerting agent use subgroups from the modified intent-to-treat population (mITT;≥1 efficacy measurement after receiving the 6-g dose). Results: In the mITT population (ON-SXB, n=97; placebo, n=93), LSMDs for ON-SXB vs placebo demonstrated significant improvements from baseline (P< 0.001) in number of sleep stage shifts at week 13 (9 g) across all participant subgroups, including age (< 35, ≥35 years), sex (female, male), race (white, non-white), BMI (low [< 25 kg/m2], high [≥25 kg/m2]), narcolepsy type (NT1, NT2), and alerting agent/no alerting agent use. LSMDs were sig nificant in favor of ON-SXB 9 g vs placebo for change from base line in number of nocturnal arousals (P< 0.05) in all subgroups, except age ≥35 years. At week 13, ON-SXB was associated with significant improvement from baseline (P< 0.05) in visual ana logue scale (VAS) sleep quality compared with placebo across all subgroups, except non-white. All subgroups exhibited significant improvements (P≤0.01) in VAS refreshing nature of sleep with ON-SXB 9 g vs placebo, except NT2. Comparable trends were observed with the 6-g dose at week 3 and the 7.5-g dose at week 8. Conclusion: While the trial was not powered to test for subgroup differences, these post hoc analyses demonstrate the robust, con sistent efficacy of ON-SXB in treating DNS, including reducing nocturnal arousals and increasing refreshing nature of sleep, in patients with narcolepsy across various demographic and clini cal characteristics.

Sleep Medicine

Hirata M, **Afaneh H**, **Kapoor I**, **Kalmbach D**, **Reffi A**, **Jennings M**, **Cheng P**, **Ong J**, and **Drake C**. Trait Mindfulness Protects Against the Harmful Effects of Nocturnal Cognitive Arousal on Insomnia and Depression Symptoms in Pregnancy and Postpartum. *Sleep* 2025; 48:A246. Full Text

[Hirata, Mika; Kapoor, Ishana; Kalmbach, David] Henry Ford Sleep Res, Detroit, MI USA; [Afaneh, Heba; Jennings, Matthew] Henry Ford Hlth, Detroit, MI USA; [Reffi, Anthony; Drake, Christopher] Henry Ford Hlth Syst, Detroit, MI USA; [Cheng, Philip] Michigan State Univ Hlth Sci, Henry Ford Hlth, E Lansing, MI USA; [Ong, Jason] Nox Hlth, Alpharetta, GA USA

Introduction: Perinatal women are highly vulnerable to insom nia and depression. High cognitive arousal (e.g., worry, rumi nation) at night is a key risk factor for developing insomnia and depression during this period. However, mindfulness skills have been proposed to reduce risk for negative health outcomes by protecting individuals against the harmful effects of cognitive arousal. This prospective study tested whether trait mindfulness protects perinatal women against the harmful effects nocturnal cognitive arousal on insomnia and depression. Methods: Nine women (Age: 29.9±4.4y; Gestation at enroll ment: 26.7±1.0w) completed weekly health surveys for 4 months across late pregnancy and early postpartum.

Study outcomes included the revised cognitive and affective mindfulness scale (CAMS-R), pre-sleep arousal scale's cognitive factor (PSASC), insomnia severity index (ISI), and Edinburgh postnatal depres sion scale (EPDS). Linear mixed modeling was used to account for repeated measures and to test trait effects (between-person differences) and state effects (within-person changes) while con trolling for relevant covariates. Results: Lagged linear mixed modeling showed that women with high trait mindfulness reported lower levels of ISI (b=- 5.37, p=.032) and EPDS (b=-14.25, p<.001) across the next four months. However, within-person analyses showed higher state PSASC predicted higher levels of next-week ISI (b=1.95, p.030) and EPDS (b=1.28, p=.047). Mixed modeling also revealed significant moderation effects for CAMS-R*PSASC on future ISI (b=.01, p<.001) and EPDS (b=.002, p=.012) such that the magnitude of PSASC's effects on ISI and EPDS were smaller for women with high trait mindfulness. Indeed, insom nia- and depression-risk were lowest when women endorsed high CAMS-R and low PSASC (3.9% insomnia, 9.8% depression), whereas disease-risk was highest when women endorsed low CAMS-R and high PSASC (62.2% insomnia, 83.8% depression). Conclusion: Perinatal women with high trait mindfulness are protected against the harmful effects of high cognitive arousal on insomnia and depression, whereas women with low mindful ness are at higher risk for insomnia and depression when expe riencing high cognitive arousal. These prospective data support trait mindfulness as a critical protective factor against the devel opment of insomnia and depression during pregnancy and post partum. Interventions promoting mindfulness skills may help expecting moms sleep and feel better.

Sleep Medicine

Jennings M, **Treger M**, Zhou ER, and **Cheng PL**. Behavioral Insomnia Treatment Accessibility in the US: A Real-World Assessment of Cost, Location, and Availability. *Sleep* 2025; 48:A246. Full Text

[Jennings, Matthew; Treger, Marleigh] Henry Ford Hlth, Detroit, MI USA; [Zhou, Eric] Harvard Med Sch, Boston, MA USA; [Cheng, Philip] Michigan State Univ Hlth Sci, Henry Ford Hlth, E Lansing, MI USA

Introduction: Cognitive Behavioral Therapy for Insomnia (CBT-I) is the gold-standard treatment for insomnia disorder. There have been consistent calls to increase patient accessibil ity to CBT-I. However, there have been few studies of what the experience is for patients who are recommended CBT-I and seek community-based care. Even less attention has been paid to this experience in patients and communities with lower incomes and poorer insurance coverage. We sought to examine the real-world access to providers with CBT-I expertise. Methods: We contacted all clinicians listed on the Society of Behavioral Sleep Medicine's provider registry who met the fol lowing inclusion criteria: (1) US-based, (2) master's degree or above, and (3) eligible for state licensure. Initial data on treat ment modality, insurance coverage, session costs, waitlist times, and practice locations were collected through internet searches, and were supplemented by contacting providers as potential patients through a maximum of three emails, with follow-up phone calls used as needed. Practice addresses were used to generate census-tract income data to compare to the 2022 fami ly-of-four poverty line. Results: Data from N=240 CBT-I providers were collected, spanning 42 states. Of these, 92.1% (n=221) were accepting new patients, but only 56.3% (n=135) accepted insurance. Among CBT-I providers accepting new patients, initial session costs averaged $260.71 (SD=$91.81, mode=$250.00, range=$100.00- $530.00); subsequent session costs averaged $227.74 (SD=$76.50, mode=$250.00, range=$75.00-$500.00), and wait times averaged 51.1 days (SD=61.9, range=0-300, mode=7). Average household income in practice areas was $95,246 (SD=$52,622). Only 5.0% (n=12) of CBT-I providers accepting new patients operated in communities at or below the poverty line, and just 3.3% (n=8) accepted insurance. Among these providers, only one accepted Medicaid. Conclusion: This study underscores significant access disparities for behavioral insomnia treatment in the US, highlighting how high treatment costs and limited availability of CBT-I provid ers have disproportionate and negative impacts on lower-income populations and those with inadequate insurance coverage. A large proportion of CBT-I providers do not accept insurance, leaving 135 behavioral sleep providers to treat those millions of Americans with insomnia unable to afford private pay. Even with insurance, logistical barriers like provider location and nearly two-month wait times exacerbate insomnia care disparities.

Sleep Medicine

Kapoor I, **Treger M**, **Van Rossen V**, **Fellman-Couture C**, **Wernette E**, **Drake C**, and **Cheng PL**. Waking up to the Role of Occupational Prestige: Does Your Job Title Affect Your Sleep? *Sleep* 2025; 48(Supplement_1):A208-A209. Full Text

[Kapoor, Ishana; Van Rossen, Veronica; Fellman-Couture, Cynthia] Henry Ford Sleep Res, Detroit, MI USA; [Treger, Marleigh] Henry Ford Hlth, Detroit, MI USA; [Wernette, Elle; Drake, Christopher] Henry Ford Hlth Syst, Detroit, MI USA; [Cheng, Philip] Michigan State Univ Hlth Sci, Henry Ford Hlth, Detroit, MI USA

Introduction: Socioeconomic status (SES) is a robust risk fac tor for insomnia and is commonly measured with income and/ or education; however, these factors may better capture access to resources instead of social status (i.e., the “status” part of SES). One way to better capture social status may be through occu pational prestige, which reflects societal respect and status that comes with occupational title. We hypothesized occupational prestige would be significantly associated with sleep outcomes, specifically for insomnia severity and sleep reactivity (i.e., vulner ability to sleep disturbances). Methods: Participants (n = 524) completed a survey assessing occupational prestige (categorized by job title), income, and education. Jobs were classified into high, medium, or low pres tige using a validated ranking system. Only participants who were active in the workforce and had insomnia were included. The survey also included measures for insomnia severity (ISI), and sleep reactivity (FIRST). Data were analyzed using two ANOVAs with job prestige as the independent variable, and ISI and FIRST as the dependent variables. Results: Results revealed that sleep reactivity differed by occu pational prestige, $F(2,521) = 4.7$, $p < .01$. Higher-prestige occu pations showed lower sleep reactivity ($M = 22.6 \pm 6.3$) compared to low ($M = 24.9 \pm 6.0$) and middle-prestige ($M = 25.1 \pm 5.9$) occupations. Insomnia severity, however, did not differ by occu pational prestige. Conclusion: These findings suggest that while job prestige may not be associated with the severity of insomnia, it is associated with sleep reactivity. One potential explanation may be that higher-prestige occupations serve as a protective factor against stress, reducing sleep reactivity and leading to better sleep outcomes. This may be because individuals in higher prestige occupations are more likely to have greater self-esteem due to higher social status, or because higher prestige jobs often confer greater agency (e.g., these are often decision makers), there may also be greater internal locus of control. Additionally, lower prestige roles may involve unique stressors that exacerbate sleep disturbances. Future research should examine workplace stress and its impact on sleep across occupations to better understand SES influences and inform interventions and policies

Sleep Medicine

Korpole P, **Jaffery SH**, **Arcila-Londono X**, and **Bazan LF**. Description of Positive Airway Pressure Settings in Bulbar Onset Amyotrophic Lateral Sclerosis Patients Requiring Non-invasive Ventilation. *Am J Respir Crit Care Med* 2025; 211:1. Full Text

[Korpole, P.; Jaffery, S. H.; Arcila-Londono, X.; Bazan, L. F.] Henry Ford Hosp, Detroit, MI USA

Introduction : Amyotrophic Lateral Sclerosis (ALS) in general and bulbar onset ALS patients in particular are at high risk of developing respiratory failure secondary to neuromuscular weakness. Optimal Non-Invasive Positive Pressure Ventilation (NIPPV) settings are not clearly defined in this subgroup. Methods : A retrospective chart review study was designed to describe NIPPV settings in bulbar onset ALS patients who met initial compliance with NIPPV. Bulbar onset ALS patients were identified from a database including patients diagnosed with Motor Neuron Disease at Henry Ford Hospital from January 1, 2019 to December 31, 2023. Results : A total of 45 patients with bulbar onset ALS were identified and 37 patients were initiated on NIPPV therapy with 26 patients (70%) meeting compliance requirements. Amongst the compliant patients, 14 patients were initiated on Bilevel Positive Airway Pressure - Spontaneous Timed (BPAP-ST) mode and 12 patients on Volume Assured Pressure Support (VAPS) mode. At compliance, mean Positive Airway Pressure (PAP) therapy usage for more than or equal to 4 hours per 24 hours and mean duration of PAP therapy use per 24 hours in the BPAP-ST and VAPS groups was 88% and 5.6 hours versus 81.5% and 5.7 hours respectively. In the BPAP-ST group, mean values of PAP settings and data were as follows: Inspiratory PAP (IPAP) 10.6 cm water, Expiratory PAP (EPAP) 5.7 cm water, backup rate 8.8 breaths per minute, tidal volume 447.3 ml, respiratory rate 17 breaths per minute, minute

ventilation 7.5 liters per minute and Apnea Hypopnea Index (AHI) 5.4 per hour. In the VAPS group, mean values of PAP settings and data were as follows: target alveolar ventilation 4.2 liters per minute, back up rate 14 breaths per minute, minimum Pressure Support (PS) 4.6 cm water, maximum PS 13.9 cm water, EPAP 4.3 cm water, median IPAP 11.6 cm water, median EPAP 4.4 cm water, tidal volume 423.9 ml, respiratory rate 16.2 breaths per minute, minute ventilation 7.2 liters per minute and AHI 4.53 per hour. Conclusion : Both BPAP-ST and VAPS modes appear to be well tolerated in bulbar onset ALS patients requiring NIPPV. Further studies are required to analyze settings associated with NIPPV compliance in greater detail in bulbar onset ALS patients.

Sleep Medicine
Mahr G, **Reffi A**, **Jankowiak L**, **Moore D**, and **Drake C**. Emotional Dream Content of Acute Trauma Patients: Associations with Interpersonal Violence, Nightmares, and PTSD. *Sleep* 2025; 48:A509. Full Text

[Mahr, Greg; Jankowiak, Lily; Moore, David] Henry Ford Hlth, Detroit, MI USA; [Reffi, Anthony; Drake, Christopher] Henry Ford Hlth Syst, Candon, MI USA

Introduction: Dreams are involved in the processing of emotions and can serve as markers of emotional distress. The authors developed a rating scale for affect in dreams and applied it to an acute trauma population. Methods: We recruited 88 patients hospitalized within one week following traumatic injury (Mage = 39.53 ± 14.31 years, 67.0% male, 67.0% Black). Patients who recalled a dream since hospi talization recorded their dream (n = 43). An independent rater scored the dreams using a novel 33-item Affective Neuroscience Dream Rating Scale to indicate the presence of fear, rage, grief, seeking, care, play, and lust. We quantified the emotional valence of dreams by summing positive (seeking + care + play + lust) and negative emotions (fear + rage + grief) and explored their associations with interpersonal violence and clinical outcomes approximately one-month post-trauma. Results: The emotional valence of dreams across all patients was significantly more negative (M = 4.84 ± 2.91) than posi tive (M = 1.26 ± 1.16), p <.001. Experiencing negatively toned dreams was associated with increased odds of being hospitalized for interpersonal violence (OR = 1.45, p =.014, 95% CI = 1.08 – 1.96) and more severe acute stress symptoms (β = 0.36, p =.021), regardless of sex. Reporting more negatively toned dreams dur ing hospitalization prospectively predicted risk for trauma-re lated nightmares one month later (OR = 1.73, p =.045, 95% CI = 1.01 – 2.97), adjusting for time, and was prospectively associated with increased nightmare distress (r =.70, p <.001), night terrors (r =.37, p =.042), and PTSD status (r =.44, p =.033). The dreams of patients who went on to screen positive for PTSD one month after trauma were significantly more negative (M = 5.99) than patients without PTSD (M = 3.70), p =.038, ηp2 = 19, indicating a large effect. Conclusion: Negative affective tone in dreams immediately after trauma predicted subsequent nightmares and future PTSD and can provide a potential tool for assessing PTSD risk in acute trauma patients.

Sleep Medicine
McCray C, **Wernette E**, **Xu T**, **Ravindran S**, **Drake C**, and **Cheng P**. Exploring the Link Between Social Functioning and Depression Reduction in CBT-I. *Sleep* 2025; 48:A526. Full Text

[McCray, Cameron; Xu, Tiffany; Ravindran, Shruthi] Henry Ford Sleep Res, Detroit, MI USA; [Wernette, Elle; Drake, Christopher] Henry Ford Hlth Syst, Detroit, MI USA; [Cheng, Philip] Michigan State Univ Hlth Sci, Henry Ford Hlth, E Lansing, MI USA

Introduction: Cognitive-behavioral therapy for insomnia (CBT I) effectively treats insomnia and reduces depression symptom severity. However, research elucidating the mechanisms driving depression reduction via CBT-I is still underway. One underex plored mechanism may be social functioning. Prior research has shown that insomnia patients reduce their social activities, likely due to fatigue. As social functioning is important to mood reg ulation, this may also drive depressed mood. This study investi gated whether improvements in social functioning would predict reductions in depressive symptoms. Methods: Patients with insomnia disorder (N=1321) were ran domly assigned to digital CBT-I (dCBT-I, n=905) or a sleep education control (SE, n=416). Depression severity (QIDS) and social functioning (FSS and SNI) were evaluated at baseline and 1-year post-intervention. Social functioning was quanti fied along three

dimensions: 1) relationship strain, 2) quantity of supportive relationships, and 3) frequency of social interac tions. Change scores (post-treatment - baseline) were calculated for depression severity and social functioning. Linear regressions determined whether changes in social functioning predicted changes in depression symptom. Results: Regression analyses revealed that reduced relationship strain (β = -.361, p <.001), increased number of supportive rela tionships (β =.151, p <.001), and increased frequency of inter actions (β =.088, P <.001) following treatment were associated with improved depression symptoms. Furthermore, change in relationship strain was a significant moderator of the antidepres sant effect of dCBT-I (β =.262, p <.001); those who had greater reductions in relationship strain following treatment also showed greater improvements in depression. Conclusion: Results point to improved social functioning follow ing CBT-I as a potentially important factor in the antidepressant effect of insomnia treatment. This effect appears to be strongest with reduced relationship strain. Future research should explore how to optimize CBT-I to enhance social functioning and sup port, especially for patients with both depression and insomnia.

Sleep Medicine
Miller C, Bradley D, Wood I, **Willens D**, **Nair A**, **Brennan B**, **Bole S**, **Poisson L**, Hall S, Thomson G, **Hirata M**, **Kalmbach D**, and **Drake C**. Digital CBT for Insomnia Is Linked to Reductions in Healthcare Use in Real-world Settings at Henry Ford Health. *Sleep* 2025; 48:A236. Full Text

[Miller, Christopher; Bradley, Danielle; Wood, Ian; Hall, Shana; Thomson, Greig] Big Hlth, London, England; [Willens, David; Nair, Anupama; Brennan, Benjamin; Bole, Shane; Poisson, Laila] Henry Ford Hlth, Detroit, MI USA; [Hirata, Mika; Kalmbach, David] Henry Ford Sleep Res, Detroit, MI USA; [Drake, Christopher] Henry Ford Hlth Syst, Candon, MI USA

Introduction: Digital CBT-I offers a scalable solution for insomnia treatment, but evidence of its real-world adoption and impact in U.S. clinical settings is limited. This study evaluates the implementation and effects of digital CBT-I within a U.S. healthcare system, utilizing Normalization Process Theory to integrate it into clinical workflows. We compare healthcare utilization between patients who engaged with digital CBT-I and those who were offered but did not use it. Methods: Patients with insomnia were offered digital CBT-I via electronic and clinical workflows at the Internal Medicine and Sleep clinics within Henry Ford Health, Detroit, Michigan. Normalization Process Theory guided implementation. Electronic order rates and patient sign-ups assessed implemen tation success and workflow acceptability. Clinician training sessions and educational materials supported uptake. A propen sity-matched case-control design compared healthcare utilization rates between 340 digital CBT-I users and 340 matched controls, who were offered digital CBT-I but did not use it. We analyzed patient chart data and standardized time across patients. We evaluated the odds of medication fills and visits before and after. Results: A total of 340 patients utilizing digital CBT-I from treat ing practitioners were matched with 340 controls who did not. Digital CBT-I patients exhibited a 64% reduction in medication fills (for any condition) during the post-treatment period rela tive to before (p< 0.001), and were 53% less likely to fill insom nia-specific prescriptions compared to pre-treatment (p=0.013). Controls showed no significant changes. Time-varied logistic regression indicated that digital CBT-I patients had 37% higher odds of using outpatient services within the initial 30-60 days (p=0.048), but subsequently showed 28% lower odds at 120-150 days (p=0.041), and 41% lower odds at 150-180 days (p=0.039). Conclusion: Normalization Process Theory effectively facilitated the integration of digital CBT-I into clinical workflows, providing immediate access with minimal workflow disruptions. Training ses sions and ongoing clinician reminders promoted patient uptake of standard care for insomnia management. Findings indicate that dig ital CBT-I is associated with reduced medication fills and decreased odds of outpatient visits over time, suggesting its potential as an effective, scalable treatment for insomnia in clinical settings

Sleep Medicine
Ozeir S, **Belevender C**, **Bugazia S**, **Badhwar A**, **Shakaroun D**, **Carlin A**, **Roehrs T**, and **Skiba V**. PREDICTORS OF PAP ADHERENCE FOLLOWING BARIATRIC SURGERY IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA. *Sleep* 2025; 48:A585. Full Text

[Ozeir, Serene; Bugazia, Seif; Badhwar, Ankita; Shakaroun, Dania; Carlin, Arthur; Roehrs, Timothy; Skiba, Virginia] Henry Ford Hlth, Detroit, MI USA; [Belevender, Claire] Henry Ford Hosp, Detroit, MI USA

Introduction: Obstructive sleep apnea (OSA) frequently coexists with obesity, and positive airway pressure (PAP) therapy remains the gold standard for its treatment. Bariatric surgery is an effec tive intervention for significant weight loss, which can alter OSA severity and PAP adherence. This study investigates predictors of PAP adherence post-surgery, focusing on pre- and post-sur gery sleep clinic visits, apnea-hypopnea index (AHI), and refer ral source. Methods: A retrospective chart review was conducted on 140 patients evaluated at the Henry Ford Bariatric Clinic and referred to the Henry Ford Sleep Disorders and Research Center for sleep testing from April 2023 to August 2023. Data analysis included pre- and post-surgery PAP usage, number of sleep clinic visits, AHI, and referral source. Statistical methods, including ANOVA and correlation analysis, assessed the relationship between these factors and PAP adherence across 3, 6, 9, and 12 months post-operatively. Results: Significant predictors of PAP adherence included the number of post-operative sleep clinic visits and referral source. Patients with higher baseline AHI were more likely to adhere to PAP therapy at month 12. In addition, more frequent sleep medi cine clinic showed evidence of increased PAP therapy adherence. Referral source significantly influenced adherence patterns, with patients referred directly from bariatric clinics exhibiting greater compliance compared to referrals from primary care providers or other sources. Conclusion: Post-operative sleep clinic visits, referral source, and AHI are significant predictors of PAP adherence following bariatric surgery. These findings underscore the importance of structured follow-up care and referral pathways in promoting PAP adherence and improving long-term outcomes in OSA management.

Sleep Medicine

Ozeir S, **Belevender C**, **Korpole P**, **Jaziri M**, **McLellan B**, **Reffi A**, and **Bazan L**. Comparison of Time Interval to Obstructive Sleep Apnea Diagnosis in a Direct Referral Program versus Standard Care. *Sleep* 2025; 48:A586. Full Text

[Ozeir, Serene; Korpole, Pranay; Jaziri, Miriam; Mclellan, Beth; Bazan, Luisa] Henry Ford Hlth, Detroit, MI USA; [Belevender, Claire] Henry Ford Hosp, Detroit, MI USA; [Reffi, Anthony] HENRY FORD Hlth Syst, Detroit, MI USA

Introduction: A Direct Referral program was initiated at Henry Ford Health in 2015 to facilitate easier access and expedite sleep testing. The effectiveness of the Direct Referral program in com parison to standard care is unclear in terms of time interval to establish Obstructive Sleep Apnea (OSA) diagnosis. Methods: A retrospective chart review was conducted for patients referred for diagnostic sleep studies between September and December 2022 via the Direct Referral pathway versus a standard sleep clinic consult. Patients aged 18 years or older were included. Exclusion criteria included patients younger than 18 years and those participating in both pathways. Results: A total of 342 patients were evaluated for inclusion in the Direct Referral cohort, and 509 patients were assessed for the standard care cohort. Ultimately, 147 patients were included in the Direct Referral cohort, while 268 patients were included in the standard care cohort for final analysis. The mean time to confirm or rule out an OSA diagnosis was significantly shorter in the Direct Referral group compared to the standard care group (51 days vs. 105.6 days; p <.001). Conclusion: Time to inclusion or exclusion of OSA diagnosis was significantly shorter in the Direct Referral cohort compared to the standard care cohort.

Sleep Medicine

Plante D, Corser B, **Drake C**, Bogan R, Dauvilliers Y, Insana S, Seiden D, Nomikos G, Manuel M, Bauer E, Budur K, and Dayno J. Effect of Pitolisant on Idiopathic Hypersomnia Symptoms During a Double-Blind Withdrawal Period in a Phase 3 Trial. *Sleep* 2025; 48:A375-A376. Full Text

[Plante, David] Univ Wisconsin Madison, Madison, WI USA; [Corser, Bruce] Sleep Management Inst, Cincinnati, OH USA; [Drake, Christopher] Henry Ford Hlth Syst, Candon, MI USA; [Bogan, Richard] Bogan Sleep Consultants, Columbia, SC USA; [Dauvilliers, Yves] Univ Montpellier, Gui de Chauliac Hosp, Sleep & Wake Disorders Ctr, Dept Neurol,INSERM,Inst Neurosci Montpellier INM, Montpellier, France; [Insana, Salvatore; Seiden, David; Nomikos, George; Manuel, Michelle; Bauer, Eric; Budur, Kumar; Dayno, Jeffrey] Harmony Biosci Holdings Inc, Plymouth Meeting, PA USA

Introduction: Pitolisant is FDA approved for the treatment of excessive daytime sleepiness (EDS) or cataplexy in adult patients with narcolepsy and for the treatment of EDS in pediatric patients ≥6 years with narcolepsy. Given the adjacency between IH and narcolepsy and pharmacological treatments for IH are limited, the efficacy of pitolisant is being evaluated in adult patients with IH. Methods: The present analyses focused on a 4-week dou ble-blind randomized withdrawal period (DBRWP) within a 12-week phase 3 clinical trial to evaluate the safety and effi cacy of pitolisant in adult patients with IH (NCT05156047). Patients (213) initially received pitolisant for an 8-week open-la bel period (OLP) and then were assessed for their treatment response. Treatment responders (≥3-point reduction in their Epworth Sleepiness Scale [ESS] scores across the OLP) entered the DBRWP and were randomized to continue receiving dose matched pitolisant or placebo. Primary and key-secondary effi cacy measures included the ESS and the Idiopathic Hypersomnia Severity Scale (IHSS), respectively; change scores were evaluated from the end of the OLP to the end of the 4-week DBRWP for pitolisant compared with placebo. Results: Among the 173/213 patients who completed the OLP (81.2%), 139 (80.3%) of them were considered treatment responders and entered the DBRWP (mean±SD age: 39.9±11.91 years; 78.6% female). During the DBRWP the LSM difference (95% CI) in total score between the pitolisant and placebo treat ment groups was not statistically significant for the ESS (-0.85 [-2.24, 0.54]; P=0.228) and narrowly missed nominal statistical significance for the IHSS (-2.27 [-4.62, 0.08]; P=0.058). When statistically adjusting for the suspected placebo effect and sus pected regression to the mean, there was a nominally statistically significant difference between pitolisant and placebo on the ESS (-1.51 [-2.84, -0.18] P=0.026) and the IHSS (-3.20 [-5.49, -0.90] P=0.006). No new safety signals were observed. Conclusion: During the 4-week DBRWP, positive trends favor ing pitolisant were observed on the ESS and IHSS; however, they did not reach prespecified statistical significance. Ad hoc analyses showed nominally statistically significant improvements in ESS and IHSS. Pitolisant may offer a favorable benefit-risk profile and could be a potential treatment option for patients with IH.

Sleep Medicine

Pockrass A, **Treger M**, **Peeran I**, **Russell J**, **Wernette E**, **Drake C**, and **Cheng P**. Who Lasts Longer - Sleep Reactivity Predicts Duration of Night Shift Work. *Sleep* 2025; 48:A217-A218. Full Text

[Pockrass, Anna; Peeran, Izza] Henry Ford Sleep Res, Detroit, MI USA; [Treger, Marleigh] Henry Ford Hlth, Detroit, MI USA; [Russell, Jonny] Henry Ford Sleep Res Ctr, Detroit, MI USA; [Wernette, Elle; Drake, Christopher] Henry Ford Hlth Syst, Candon, MI USA; [Cheng, Philip] Michigan State Univ Hlth Sci, Henry Ford Hlth, Detroit, MI USA

Introduction: Around 80% of night shift workers experience cir cadian misalignment, leading to excessive sleepiness and decline of safety and work satisfaction. To address this, our team devel oped a mobile application, Arcashift, which tracks users' circa dian rhythms and makes personalized activity recommendations (i.e. when to avoid light, when to exercise, etc.) based on user goals (i.e. wake up earlier). While the app was built with patient i nput and has been tested in randomized controlled trial settings, the real-world user experience is not yet well-established. Methods: Night shift workers who habitually slept for less than 6 hours and presented with excessive sleepiness used Arcashift with pre mium access for 30 weeks (n = 28) in a hybrid type I effectiveness-im plementation trial. Upon completion of the implementation period, participants completed a user feedback survey in which participants rated overall experience and ease of use on a 5-point scale ranging from negative to positive and completed 6 short answer questions. Results: Among the users, 64% rated their overall experience as positive ("positive" or "somewhat positive") and 36% rated their experience as neutral. No users reported a negative ("negative" or "somewhat negative") experience. Eighty-two percent of users reported Arcashift was easy to use, whereas only 11% and 7% reported neutral and negative ease of use, respectively. Most liked features were the personalized recommendations (39%), the ease of inputting their work shifts and other obligations to the calendar (21%). The most common complaints were the app being unintui tive to use (11%) and the desire for more information about sleep in the app (14%). Other barriers included app glitches when enter ing shifts and other events into the calendar (7%). Conclusion: Participants generally appreciate the individualized approach of Arcashift. The app was well received but modifi cations may be needed to further improve the user experience. Future directions include the information about improving sleep in Arcashift being made more accessible to the users of the app, as

well as continuing to improve and providing great support to night shift workers in adapting to their schedules and decreasing their circadian misalignment.

Sleep Medicine
Ravindran S, **Treger M**, **Russell J**, **Coyne P**, **McCray C**, **Drake C**, Walch O, and **Cheng P**. User Experience of a Mobile Application to Reduce Circadian Misalignment in Night Shift Workers. *Sleep* 2025; 48:A385. Full Text

[Ravindran, Shruthi; Coyne, Paige; McCray, Cameron] Henry Ford Sleep Res, Detroit, MI USA; [Treger, Marleigh] Henry Ford Hlth, Detroit, MI USA; [Russell, Jonny] Henry Ford Sleep Res Ctr, Detroit, MI USA; [Drake, Christopher] Henry Ford Hlth Syst, Detroit, MI USA; [Walch, Olivia] Arcascope, Arlington, VA USA; [Cheng, Philip] Michigan State Univ Hlth Sci, Henry Ford Hlth, Detroit, MI USA

Introduction: Around 80% of night shift workers experience cir cadian misalignment, leading to excessive sleepiness and decline of safety and work satisfaction. To address this, our team devel oped a mobile application, Arcashift, which tracks users' circa dian rhythms and makes personalized activity recommendations (i.e. when to avoid light, when to exercise, etc.) based on user goals (i.e. wake up earlier). While the app was built with patient input and has been tested in randomized controlled trial settings, the real-world user experience is not yet well-established. Methods: Night shift workers who habitually slept for less than 6 hours and presented with excessive sleepiness used Arcashift with pre mium access for 30 weeks (n = 28) in a hybrid type I effectiveness-im plementation trial. Upon completion of the implementation period, participants completed a user feedback survey in which participants rated overall experience and ease of use on a 5-point scale ranging from negative to positive and completed 6 short answer questions. Results: Among the users, 64% rated their overall experience as positive ("positive" or "somewhat positive") and 36% rated their experience as neutral. No users reported a negative ("negative" or "somewhat negative") experience. Eighty-two percent of users reported Arcashift was easy to use, whereas only 11% and 7% reported neutral and negative ease of use, respectively. Most liked features were the personalized recommendations (39%), the ease of inputting their work shifts and other obligations to the calendar (21%). The most common complaints were the app being unintui tive to use (11%) and the desire for more information about sleep in the app (14%). Other barriers included app glitches when enter ing shifts and other events into the calendar (7%). Conclusion: Participants generally appreciate the individualized approach of Arcashift. The app was well received but modifi cations may be needed to further improve the user experience. Future directions include the information about improving sleep in Arcashift being made more accessible to the users of the app, as well as continuing to improve and providing great support to night shift workers in adapting to their schedules and decreasing their circadian misalignment.

Sleep Medicine
Reffi A, **Jankowiak L**, **Moore D**, Basarkod S, **Jovanovic T**, **Cheng PL**, Hsieh HF, and **Drake C**. Fear of Sleep Prospectively Predicts Nightmare Severity in Acute Trauma Patients Exposed to Community Violence. *Sleep* 2025; 48:A510. Full Text

[Reffi, Anthony; Drake, Christopher] Henry Ford Hlth Syst, Detroit, MI USA; [Jankowiak, Lily; Moore, David] Henry Ford Hlth, Detroit, MI USA; [Basarkod, Sattvik; Jovanovic, Tanja] Wayne State Univ, Detroit, MI USA; [Cheng, Philip] Henry Ford Hlth Michigan State Univ Hlth Sci, Detroit, MI USA; [Hsieh, Hsing-Fang] Univ Michigan, Ann Arbor, MI USA

Introduction: Fear of sleep engenders arousal at bedtime that can promote nightmares. Living in disadvantaged neighbor hoods with high rates of community violence may exacerbate fear of sleep and in turn increase nightmare risk. We tested fear of sleep among acute trauma patients as a prospective predic tor of nightmares, and whether exposure to community violence moderated this relationship. Methods: Patients hospitalized in the intensive care unit within one week following traumatic injury (N = 88; Mage = 39.53 ± SD 14.31, 67.0% male, 67.0% Black, 47.7% income ≤ $20,000). Patients completed the Fear of Sleep Inventory (FoSI) Short Form and a community violence questionnaire during hospital ization (T1; N = 88) and the Nightmare Disorder Index (NDI) approximately two months post-trauma (T2; n = 59). We com puted an NDI sum score as our outcome to indicate greater nightmare severity

(nightmare frequency and nightmare-re lated awakenings, distress, and impairment). Skin conductance response (SCR) was collected from a subsample of patients (n = 7) during the FoSI to preliminarily explore the psychophysiolog ical correlates of this scale. Results: Exposure to community violence exacerbated the pro spective effect of fear of sleep on future nightmare severity (β = 0.51, p =.039), such that relationship between fear of sleep at T1 a nd nightmare severity at T2 was strongest for patients reporting exposure to higher levels of community violence in the 90 days prior to hospitalization. SCR to the FoSI was correlated with greater exposure to community violence (r = 0.76, p =.048) and the following fear-of-sleep-related safety behaviors: "I stayed up late to avoid sleeping" (r = 0.87, p =.012) and "I tried to stay as alert as I could while lying in bed," though this relationship was nonsignificant (r = 0.74, p =.060). Conclusion: Acute trauma patients presenting with a fear of sleep may be at increased risk for posttraumatic nightmares during recovery, especially those living within neighborhoods marked by high levels of community violence. Preliminary results suggest fear of sleep and community violence exposure may share an association with sympathetic activation which, when elevated at bedtime, could increase nightmare production.

Sleep Medicine

Reffi A, **Moore D**, **Jankowiak L**, and **Drake C**. The Impact of Lifetime Trauma on Sleep Reactivity in Acute Trauma Patients: The Role of Victimization Traumas. *Sleep* 2025; 48:A228-A229. Full Text

[Reffi, Anthony; Drake, Christopher] Henry Ford Hlth Syst, Detroit, MI USA; [Moore, David; Jankowiak, Lily] Henry Ford Hlth, Detroit, MI USA

Introduction: Sleep reactivity is a vulnerability to sleep distur bance after stress that increases risk for insomnia and myriad negative health outcomes. Previous research shows life stress can heighten sensitivity of the sleep system, exacerbating sleep reac tivity. This study investigated the relationship between lifetime trauma exposure and sleep reactivity among patients hospital ized for acute trauma. Methods: We recruited 88 patients hospitalized in Detroit, MI within one week following traumatic injury (Mage = 39.53 ± 14.31, 67.0% male, 67.0% Black). Patients reported their lifetime exposure to traumatic events using the Life Events Checklist for DSM-5 (LEC-5). We summed all positive trauma exposures to compute a "trauma load" variable, with greater scores indi cating cumulative lifetime trauma experiences. Additionally, we computed three empirically derived clusters of trauma types previously shown to differentially correlate with mental health: Accidental/injury traumas (e.g. transportation accident), victimization traumas (e.g. physical assault), and predominant death threat traumas (containing mostly death-related traumas, e.g. assault with a weapon). Participants reported their sleep reactivity using the Ford Insomnia Response to Stress Test (FIRST) and insomnia using the Insomnia Severity Index (ISI). Results: Reactive sleepers (FIRST ≥ 20) reported significantly more traumatic life events (M number of events = 7.64 ± SD 3.72) than nonreactive sleepers (M number of events = 5.91 ± SD 4.12), p =.041. High sleep reactivity was uniquely associated with greater lifetime exposure to victimization trauma types ($F(1, 84,) = 4.22$, p =.043, $\eta p2$ =.048), adjusting for sex and insomnia (ISI ≥ 11). Specifically, 59.0% of patients with a his tory of physical assault had high sleep reactivity, whereas 41.0% had low sleep reactivity ($\chi 2 = 4.94$, p =.026). Similarly, 69.0% of patients with a history of sexual assault had high sleep reactivity, whereas only 31.0% had low sleep reactivity ($\chi 2 = 5.50$, p =.019). Conclusion: Acute trauma patients with high sleep reactivity report greater lifetime exposure to traumatic events, particularly physical and sexual assault. These results highlight the poten tial link between victimization traumas and increased sensitivity of the sleep system, independent of insomnia status, which may contribute to the development of insomnia and other negative health outcomes.

Sleep Medicine

Roehrs T, and **Roth T**. BzRA Hypnotic Receptor Specificity and Rebound Insomnia. *Sleep* 2025; 48:A238-A239. Full Text

[Roehrs, Timothy] Henry Ford Hlth, Detroit, MI USA; [Roth, Thomas] Henry Ford Hlth Syst, Sleep Disorders & Res Ctr, Detroit, MI USA

Introduction: Discontinuing hypnotics after chronic use remains a concern, which has never been directly tested in a controlled, blinded, prospective study using self-administration choice pro cedures. We report

on discontinuation predictors in a clinical trial in which persons with insomnia were instructed to stop tak ing medication after 6 months of nightly use. Methods:: Insomnia participants aged 23-61 yrs, (n=41, 36 females), with no other sleep disorders, unstable medical or psychiatric diseases or drug dependency completed the trial. Following a NPSG participants were randomized to zolpidem XR (12.5 mg), eszopiclone (3 mg), or placebo nightly for 6 months. After 6 months nightly use, over a 2-week discontinua tion, they were instructed to discontinue their hypnotic use, but if necessary, to self-administer either 1, 2, or 3 capsules of their assigned “blinded” medication (zolpidem XR 6.25 mg, 6.25 mg, placebo; eszopiclone 2 mg, 1 mg, placebo as capsules 1, 2 and 3 respectively; or 3 placebos). Sleep was recorded by actigraphy on a baseline week and during the two discontinuation weeks and scored for latency to sleep (LAT min), wake during sleep (WASO min), and sleep efficiency (SE %). Rebound insomnia was tested by comparing baseline nt 1 to discontinuation nts 1 & 2. Results: Over the 14 nights 21 participants took zero (51%) cap sules and among the 20 taking capsules the median total number chosen was 3. During the two-week discontinuation the BzRA receptor non-specific hypnotic, eszopiclone, was associated with a significantly greater (p<.005) number of capsule choices than the placebo group with the zolpidem group (BzRA receptor specific) not different than placebo. Compared to baseline, on discontinuation night 1 the eszopiclone group had greater WASO (i.e. rebound insomnia +10.2 +/-8.4 min), differing (p <.05) from the placebo (-9.3 +/-6.3 min) and zolpidem (-12.2+/8.5 min) groups which did not experience rebound insomnia. No rebound insomnia on discontinuation nt 2 in any of the three groups. Conclusion: Fifty-one percent discontinued 6-months of nightly hypnotic use. The BzRA receptor non-specific hypnotic group, eszopiclone, self-administered a greater number of capsules during the two-week discontinuation and experienced rebound insomnia on discontinuation night 1.

Sleep Medicine

Roth T, Ibrahim S, Morse A, Gudeman J, and Dauvilliers Y. Correlation Between Maintenance of Wakefulness Test and Epworth Sleepiness Scale Scores in REST-ON. *Sleep* 2025; 48:A373. Full Text

[Roth, Thomas] Henry Ford Hlth Syst, Sleep Disorders & Res Ctr, Detroit, MI USA; [Ibrahim, Sally] Univ Hosp Cleveland Med Ctr, Cleveland, OH USA; [Morse, Anne] Janet Weis Childrens Hosp, Geisinger Commonwealth Sch Med, Geisinger Med Ctr, Danville, PA USA; [Gudeman, Jennifer] Avadel Pharmaceut, Venissieux, France; [Dauvilliers, Yves] Univ Montpellier, Gui Chauliac Hosp, Sleep & Wake Disorders Ctr, INSERM,Inst Neurosci Montpellier INM,Dept Neurol, Montpellier, France

Introduction: Low-to-moderate strength correlations between Maintenance of Wakefulness Test (MWT) and Epworth Sleepiness Scale (ESS) scores have been reported in clinical trials in narcolepsy. This post hoc analysis of REST-ON (NCT02720744), which demon strated the efficacy of once-nightly sodium oxybate (ON-SXB; LUMRYZ™) for narcolepsy, assessed the correlation between mean sleep latency (MSL) on the MWT and ESS scores. Methods: REST-ON participants (age ≥16 years) with narco lepsy were randomized 1:1 to ON-SXB (week 1, 4.5 g; weeks 2-3, 6 g; weeks 4-8, 7.5 g; weeks 9-13, 9 g) or placebo. Pearson correlation coefficients assessed the relationship between MSL (min) on the MWT and ESS score by treatment arm in the modi fied intent-to-treat (mITT) population (≥1 efficacy measurement after receiving the 6-g dose) at baseline (pretreatment) and weeks 3 (6 g), 8 (7.5 g), and 13 (9 g). Results: In the mITT population (ON-SXB, n=97; placebo, n=93), respective baseline MSL (SD) on the MWT and baseline mean (SD) ESS score was 5.0 (3.1) and 16.6 (3.8) for ON-SXB and 4.7 (2.6) and 17.5 (4.1) for placebo. At baseline, no correla tion was observed between MSL on the MWT and ESS score for either arm (ON-SXB, r=0.015; placebo, r=–0.023). At weeks 3, 8, and 13, respective MSL (SD) was 13.1 (8.8), 14.5 (9.8), and 15.5 (9.8) minutes and respective ESS scores were 13.3 (5.9), 11.6 (6.1), and 10.4 (6.2) for ON-SXB; for placebo, MSL (SD) was 7.8 (5.9), 7.8 (6.3), and 9.4 (7.9) minutes, with ESS scores of 16.6 (4.6), 15.4 (5.3), and 14.9 (5.5). Moderate strength correlations between MSL on the MWT and ESS scores were observed in the ON-SXB arm (r=–0.419, –0.305, –0.394 at weeks 3, 8, 13, respectively). Weak correlations were observed in the placebo group (r= –0.193, –0.271, –0.181 at weeks 3, 8, 13, respectively). Conclusion: After initiating ON-SXB treatment, the correlation between MWT and ESS scores strengthened, suggesting that improved wakefulness enhances awareness of sleepiness levels in people with narcolepsy.

Sleep Medicine

Russell J, **Treger M**, **Kalmbach D**, **Drake C**, and **Cheng P**. Can Digital CBT-I Be as a Scalable Workplace Solution for Insomnia-Related Productivity Losses? *Sleep* 2025; 48(Supplement_1):A89. Full Text

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Introduction: Previous research demonstrated that insomnia significantly impairs work productivity, leading to substantial economic losses. Traditional Cognitive Behavioral Therapy for Insomnia (CBT-I) is effective in alleviating insomnia symp toms, but largely inaccessible due to the scarcity of trained pro viders and associated costs. Digital CBT-I (dCBT-I) offers a scalable and accessible solution, showing evidence in reducing insomnia severity. When investigating dCBT-I's effect on work productivity, existing studies have shown promise, but also have limitations, including homogeneous samples and insuffi cient follow-up data. This study examines whether dCBT-I can lead to meaningful improvements in overall work productivity. Methods: The 658 participants in this study met the DSM-5 cri teria for insomnia. Participants were randomized to complete six core sessions of dCBT-I (n=358), or receive six weekly emails of sleep education (n=300). Work productivity was measured using the Work Productivity and Activity Impairment Questionnaire specified to a specific health problem: insomnia (WPAI:SHP). The WPAI:SHP questionnaire was administered pre-treatment, post-treatment, and one-year follow up. Total work impairment was the primary outcome. Secondary analyses included presen teeism and absenteeism subscales. A meaningful improvement was operationalized as 15% improvement, which corresponds to 6 hours in a 40 hour work week. Results: Total work impairment was reduced 16.5% (b = -16.5 ± 2.7 SE, p <.001) more in the dCBT-I condition compared to the SE condition at post-treatment. At the one-year follow up, reduction in total work impairment remained 12.9% (b = -12.9 ± 2.8 SE, p <.001) greater than the SE condition. Sensitivity analysis indicated dCBT-I participants were 2.7 times more likely to achieve a 15% reduction in work impairment (95% CI [1.7, 4.3]) post-treatment. No significant effects were found for absenteeism in the secondary analysis, but participants in the dCBT-I group were 2.2 times more likely to achieve a 10% reduction in presenteeism (95% CI [1.4, 3.5]). Conclusion: This study demonstrates the potential for dCBT-I as a scalable solution to rescuing insomnia-related productiv ity losses. Our results demonstrated that dCBT-I may recover almost a full day of work productivity. Integrating dCBT-I into workplace occupational health programs may help companies recoup insomnia-related productivity losses while improving employees' sleep health.

Sleep Medicine

Thorpy M, Mundt J, Ibrahim S, Kushida C, Lavender M, Gudeman J, and **Roth T**. HYPNAGOGIC/HYPNOPOMPIC HALLUCINATION TYPES AMONG PARTICIPANTS WITH NARCOLEPSY TYPE 1 FROM THE PHASE 3 REST-ON TRIAL. *Sleep* 2025; 48:A361-A362. Full Text

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Introduction: Limited information is available to quantify hypnagogic/hypnopompic hallucination (HH) events people with nar colepsy (PWN) may experience. This post hoc analysis from the phase 3 REST-ON trial evaluated individual HH types. Methods: REST-ON (NCT02720744) participants (age ≥16 years) with narcolepsy were randomized 1:1 to once-nightly sodium oxybate (ON-SXB) (week 1, 4.5 g; weeks 2-3, 6 g; weeks 4-8, 7.5 g; weeks 9-13, 9 g) or placebo. HH events were assessed in participants with narcolepsy type 1. Modified intent-to-treat (mITT) population (≥1 efficacy measurement after 6-g dose) data were analyzed. Nocturnal HH types were evaluated via 6 yes/no questions and recorded in daily diaries. Daytime HHs were not assessed. Results: In the mITT population with HH at baseline (n=112 [ON-SXB, n=55; placebo n=57]), baseline mean [SD] number of HH events/day was 0.60 [0.35] and 0.66

[0.35] in the ON-SXB and placebo groups, respectively. Respective mean change from baseline (95% CI) in HH events/day to weeks 3, 8, and 13 was −0.16 (−0.21, −0.11), −0.28 (−0.37, −0.19), and −0.29 (−0.40, −0.18) with ON-SXB (all P< 0.001) and −0.14 (−0.20, −0.08), −0.18 (−0.26, −0.10), and −0.24 (−0.33, −0.14) with placebo (all P< 0.001). Participants chose from the following HH types: 1) feeling that shadows or objects are moving/distorting (total number of events with ON-SXB and placebo: 1693 and 2133), 2) feeling another presence in the room (1362 and 1839), 3) feeling that you are about to be attacked (655 and 1232), 4) feeling that you are flying through the air (543 and 1351), 5) feeling that you will soon fall into a hole (448 and 914), and 6) feeling caught in a fire (123 and 152). Of 12,455 HH events, 7762 (62%) were hypnagogic, and 4683 (38%) were hypnopompic. Conclusion: There were low baseline HH rates in REST-ON, and a strong placebo effect was observed. However, these data provide insight into the HH types participants experienced. Relevant to clinician-patient discussions, approximately half the number of events where participants felt like they were about to be attacked, flying through the air, and falling in a hole were reported with ON-SXB vs placebo.

Sleep Medicine

Treger M, **Pockrass A**, **Peeran I**, **Van Rossen V**, **Wernette E**, **Drake C**, Walch O, and **Cheng P**. Use of Apple Watch to Optimize Light Therapy and Reduce Circadian Misalignment for Night Shift Workers. *Sleep* 2025; 48:A383-A384. Full Text

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Introduction: Circadian misalignment can be alleviated with targeted light interventions. However, general “light at night” interventions do not account for shift workers’ variable circadian phases. Recently, our lab validated Apple Watch (AW) as a noninvasive means of predict ing circadian timing (i.e. dim light melatonin onset, DLMO). Here, we extend this by examining the clinical utility of AW in informing circadian interventions. We hypothesized the AW-informed group would result in higher rates of circadian alignment following treat ment vs the control (non-personalized) group. We also compared the magnitude of phase shifts between these interventions. Methods: Participants (N=46) were randomly assigned to either the AW or control group, and DLMO was measured before and after treatment. AW data (accelerometer and heart rate) was collected over 2 weeks and processed through a biomathemat ical model of the human circadian system to produce estimated DLMOs. Light therapy schedules were created from the corre sponding phase response curves and implemented with light boxes and blue-blocker glasses (at-home or in-lab) to induce phase shifts. Participants in the control group followed a non-personalized light schedule (light from 18:00 and 21:00; light avoidance from 04:00 and 10:00). Circadian alignment was operationalized as DLMO between 02:00 and 14:00, and a relative risk ratio was used to com pare the rate of circadian alignment between the two groups. Results: The rate of circadian alignment post-treatment was 2.6 times higher in the AW group (56.8%) compared to the control group (22.2%). Additionally, those in the AW group achieved phase delays that were 8.5-times greater than the control group (AW group: delay of 2.5 hours ± 5.0 SD; control group: 0.3 hours ± 4.0 SD). Conclusion: These findings support the use of AW to generate personalized light treatments. Accessible and effective circadian treatments are key to improving the safety of nightshift workers. In the future we aim to perform sensitivity analyses and compare the efficacy of personalized light interventions at-home versus in-lab, to establish the feasibility of prescribing personalized light therapy as an at-home treatment option.

Sleep Medicine

Van Rossen V, **Treger M**, **Kapoor I**, **Fellman-Couture C**, **Drake C**, and **Cheng P**. A Sound Approach: Is Digital Behavioral Insomnia Therapy Accessible for the Deaf Community? *Sleep* 2025; 48(Supplement_1):A256. Full Text

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Introduction: Prior research has demonstrated that digitally delivered CBT for Insomnia (dCBT-I) is highly effective for those who can access and complete treatment. However, there are significant accessibility challenges for many vulnerable pop ulations. Extant studies have focused on those with low socio economic (SES) resources and/or low digital health literacy; however, the accessibility of dCBT-I for people with hearing disabilities has not been well-established. This study conducted qualitative interviews with dCBT-I patients from various back grounds about treatment adherence and the addition of a nurse coach. Methods: Patients (n=263) had an initial telehealth consultation with the coach, then completed six consecutive weeks dCBT-I sessions via a mobile health application alongside sleep diaries which tracked sleep efficiency, sleep restriction, and time in bed. Patients received personalized feedback from the coach after each session and had the option of booking additional telehealth coaching sessions. Qualitative interviews were conducted with a subsample of patients to assess adherence across ability, SES, and treatment completion barriers and facilitators using the NIMHD framework. Results specifically pertinent to those with hearing disability are presented here. Results: While patients with hearing disabilities were able to suc cessfully complete the treatment, there were several barriers and facilitators named. Patients found that specific digital tools that are usually not available (e.g., chat box, live closed captioning) were integral to their ability to fully participate in the treatment. Patients with a hearing disability often relied on their own tools and strategies (e.g., translation services, microphones) to make the treatment recommendations feasible. Patients also noted that having a coach aided in treatment adherence, specifically refer encing the importance of receiving encouragement as an impor tant factor in their own treatment continuation. Conclusion: This feedback highlights the importance of aug menting dCBT-I with relevant tools and technology to increase accessibility to those with a hearing disability. Though the dig ital administration of CBT-I already has tools that increase accessibility compared to in-person treatment, those were not sufficient. Future research should further examine how imple mentation of dCBT-I can have greater equitable access for disa bled communities. Support (if any): R01HL159180 awarded to Dr. Philip Cheng.

Sleep Medicine

Wernette E, Walch O, **Drake C**, and **Cheng P**. Combining Wearables with Nearables: Using a Multi-Device Machine Learning Approach Improves Sleep Tracking at Home. *Sleep* 2025; 48:A192-A193. Full Text

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Introduction: Wearables have expanded access to sleep data, but proprietary algorithms are inaccurate and legacy actigraphy algorithms are outdated. Furthermore, legacy algorithms were trained on nighttime sleep, and only identify 50.3% of daytime sleep. This presents a unique challenge for night shift workers, who are prone to disordered sleep and need access to improved sleep measurement tools. We recently found machine learning (ML) algorithms using raw accelerometer and heart rate data from an Apple Watch could improve nighttime sleep tracking achieving up to 90% accuracy. However, wearables alone still do not capture environmental inputs needed to accurately clas sify sleep versus wake (e.g. sleep onset latency). We conducted a proof-of-concept study assessing the feasibility of a ML approach that combines inputs from nearables and a wearable to improve daytime sleep tracking at home. Methods: Researchers installed a curated sleep tracking system in participants' bedrooms to continuously monitor activity and the environment for 30 days. This included a presence sensor to detect presence in bed, a luxmeter to measure changes in ambi ent light, and a wireless light switch with smart light bulbs to track when lights were turned on and off. We also collected raw heart rate and accelerometer data from Apple Watches and raw accelerometer data from iPhones. Participants completed daily sleep diaries and a user experience questionnaire. Results: Preliminary results show our multi-device ML approach increases detection of daytime sleep by 43.4% in night shift workers. In nighttime sleepers, our ML approach achieves 93.7% sensitivity for sleep identification, while maintaining 97.2% specificity in wake classification. Participants report strong acceptance of the multi-device approach, with low per ceived intrusiveness (1.0 of 10) and high willingness to continue use (8.8 of 10). Conclusion: These findings support the feasibility of a multi-de vice ML approach for more accurate sleep tracking outside of the lab. We plan to expand this research to a larger sample of night shift workers to improve the precision of daytime sleep tracking, while assessing the sleep environment. Because our sleep tracking system

contains smart technology, we ultimately aim to help inform personalized interventions to the bedroom environment to improve sleep outcomes.

Surgery
Brown CS, Dualeh S, Osborne N, Albright J, Huang A, **Kabbani L**, Davis F, Aronow H, Kimball A, Laveroni E, Constantinou C, Mouawad NJ, and Henke P. Characterizing the Effect of Heparin Dose and Monitoring Activated Clotting Time on Postoperative Lower Extremity Bypass Outcomes. *J Vasc Surg* 2025; 81(6):e183. Full Text

Objectives: Intraoperative anticoagulation is essential for safe vascular occlusive control. Intravenous heparin is most commonly administered at a dose targeted to a measured intraoperative activated clotting time (ACT) of >250 seconds. The effects of heparin dosing or monitoring ACT on postoperative outcomes remains poorly characterized. Methods: Using data from a statewide quality improvement collaborative, we investigated rates of postoperative bleeding, arterial/graft thrombosis, major amputation, readmission and death among patients within 30 days after lower extremity bypass (LEB). We adjusted for patient clinical and sociodemographic factors, as well as procedural factors. In addition to descriptive statistics, we used a Bayesian random effects logistic regression model with non-informative prior to investigate the effect of heparin dosing and ACT monitoring, as well as an interaction effect between the two. Results: A total of 9030 patients undergoing LEB from 34 hospitals were included, among whom 190 (2.1%) experienced arterial/graft thrombosis, 152 (1.7%) postoperative bleeding, 824 (9.1%) 30-day amputation, 1029 (11.4%) 30-day readmission, and 42 (0.5%) 30-day mortality. Rates of ACT monitoring varied substantially across hospitals (12%-100%) with 4290 patients (47.5%) having ACT monitored intraoperatively. Heparin doses were slightly higher among patients in whom ACT was monitored, but neither heparin dose nor ACT monitoring were associated with postoperative thrombosis or bleeding (Fig 1). Intraoperative administration of protamine was associated with reduced postoperative bleeding (odds ratio [OR], 0.28; 95% confidence interval [CI], 0.17-0.46). Conclusions: There exists substantial variation in intraoperative heparin dose and monitoring of ACT across hospitals, but this variation is not associated with differences in postoperative outcomes. Future randomized studies targeting standardized intraoperative heparin dosing and ACT monitoring protocols may result in simplified care pathways without negatively affecting outcomes. [Formula presented]

Surgery
Chahrour M, **Chamseddine H**, **Shepard A**, **Nypaver T**, **Weaver M**, **Boules T**, Hoballah JJ, Aboul Hosn M, and **Kabbani L**. Endoscopic vein harvest is associated with worse but improving outcomes in infrainguinal bypass. *J Vasc Surg* 2025; 81(5):1183-1192. Full Text

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Objective: The impact of great saphenous vein harvest technique on infrainguinal bypass outcomes remains a matter of debate, with no robust evidence favoring a specific technique over the other. This study aims to compare the outcomes of open vein harvest (OVH) with endoscopic vein harvest (EVH) in patients undergoing infrainguinal bypass surgery. Methods: Patients who underwent an infrainguinal bypass from a femoral origin using a single-segment great saphenous vein between 2011 and 2023 were identified in the Vascular Quality Initiative infrainguinal bypass module. Only patients undergoing a bypass for peripheral artery disease were included, and those undergoing in-situ bypass were excluded. Patients were then classified according to their vein harvest technique into OVH and EVH groups. Three-to-one nearest-neighbor propensity score matching without replacement was performed to ensure balance of covariates between the two comparison groups. Kaplan-Meier and Cox regression analysis were used to estimate long-term event rates and evaluate the association of vein harvest technique with the primary outcomes of primary patency, primary-assisted patency, secondary patency, reintervention, amputation, and major adverse limb events, defined as the composite outcome of amputation and/or reintervention. Results: A total of 7929 patients who underwent OVH were matched to 2643 patients who underwent EVH. All baseline characteristics, demographics, and operative details were balanced after propensity score matching. EVH had a significantly lower rate of surgical site infections (1.8% vs 2.9%; P = .003), whereas other perioperative outcomes, including graft infection (P = .12), myocardial infarction (P

= .16), stroke (P = .13), and return to operating room (P = .14) were similar between the two groups. At 1-year follow-up, OVH patients had a significantly higher primary patency (71% vs 65%; P < .001), primary-assisted patency (86% vs 81%; P < .001), and secondary patency (90% vs 85%; P < .001), and significantly lower rates of amputation (6% vs 9%; P < .001), reintervention (20% vs 25%; P < .001), and major adverse limb events (25% vs 30%; P < .001) compared with EVH patients. The primary patency of EVH bypasses significantly increased from 59% to 70% between 2011 and 2020 (P = .042). Although OVH had a significantly higher primary patency compared with EVH in 2011 to 2012 (72% vs 59%; P = .006), this difference diminished over time, with no significant difference observed in the most recent interval (2019-2020) studied (73% vs 70%; P = .214). Conclusions: Although EVH is associated with a lower postoperative wound complication rate, OVH conferred superior long-term outcomes of patency, reintervention, and limb salvage over the study period. Nonetheless, EVH has demonstrated improvements in primary patency over the years, significantly narrowing the gap in this outcome between the two harvest methods.

Surgery

Chamseddine H, **Halabi M**, **Shepard A**, Hoballah JJ, **Nypaver T**, **Weaver M**, **Boules T**, **Kavousi Y**, **Onofrey K**, **Saleem H**, and **Kabbani L**. Real-World Comparison of Popliteal-Distal Bypass Versus Tibial Endovascular Therapy for Chronic Limb-Threatening Ischemia Secondary to Infrapopliteal Occlusive Disease. *J Vasc Surg* 2025; 81(6):e298. Full Text

Objective: Chronic limb-threatening ischemia (CLTI) secondary to infrapopliteal occlusive disease can be treated with surgical bypass or endovascular therapy (ET). The Bypass vs Angioplasty in Severe Ischemia of the Leg-2 (BASIL-2) trial demonstrated improved amputation-free survival (AFS) when ET was used as the initial treatment. However, most patients screened for the trial were deemed not eligible for randomization in BASIL-2. We aim to analyze real-world data to compare the outcomes of popliteal-distal bypass (PDB) vs tibial artery ET for isolated infrapopliteal occlusive disease. Methods: Patients undergoing PDB and tibial artery ET for CLTI were identified in the Vascular Quality Initiative between 2010 and 2023. Only bypasses using single-segment great saphenous vein from a popliteal inflow were included. Tibial artery ET included transluminal balloon angioplasty, atherectomy, and/or stenting of the tibial vessels; patients with a more proximal peripheral vascular intervention were excluded. Patients who underwent PDB were one-to-three propensity score matched to patients who underwent isolated tibial artery ET. Kaplan-Meier and Cox regression analyses were used to evaluate the long-term outcomes of primary patency, major amputation, reintervention, mortality, major adverse limb evens, and AFS. Results: A total of 3478 patients who underwent PDB were matched to 10,434 patients who underwent tibial artery ET. After matching, the two groups were similar in all demographics and preoperative characteristics (Table). PDB was associated with higher perioperative morbidity, including higher rates of myocardial infarction (2.7% vs 0.4%, P < .001), acute kidney injury (7.1% vs 1.4%, P < .001), surgical site infection (3.1% vs 1.0%, P < .001), and perioperative mortality (1.5% vs 0.9%, P = .002). At 1-year follow-up, PDB was associated with higher primary patency (73% vs 69%, P < .001) and lower major amputation (13% vs 16%, P = .003), lower reintervention (14% vs 17%, P = .026), lower major adverse limb events (26% vs 30%, P < .001), and lower mortality (14% vs 17%, P < .001) compared with tibial artery ET. PDB was also associated with significantly improved AFS (70% vs 64%, P < .001), reflecting a 17% reduction in the relative risk of amputation/death for PDB compared with tibial artery ET (Fig). Conclusions: Using real-world data, this study suggests that PDB has superior 1-year primary patency and AFS compared with isolated tibial artery ET. PDB is a more durable and effective revascularization strategy despite having higher perioperative morbidity and mortality. Consideration for both revascularization options, inclusive of great saphenous vein assessment, remains crucial in optimizing and improving the long-term outcomes of patients with CLTI secondary to infrapopliteal occlusive disease. [Formula presented] [Formula presented]

Surgery

Chamseddine H, **Halabi M**, **Shepard A**, **Nypaver T**, **Weaver M**, **Peshkepija A**, **Kavousi Y**, **Onofrey K**, and **Kabbani L**. Thoracic Endovascular Aortic Repair (TEVAR) for Aortic Dissection and Thoracic Aortic Aneurysms in Patients with Connective Tissue Disorders. *J Vasc Surg* 2025; 81(6):e210-e211. Full Text

Objectives: Open surgical repair continues to be the standard of care for treating aortic dissection and thoracic aortic aneurysms (TAAs) in patients with connective tissue disorders (CTDs). Data on the safety and durability of thoracic endovascular aortic repair (TEVAR) in this patient population remains limited. This study aims to evaluate the short to intermediate- term outcomes of TEVAR in patients with CTD. Methods: Patients with hereditary CTDs who underwent TEVAR for aortic dissection and TAA were identified in the Vascular Quality Initiative (VQI) between 2014 and 2024. CTDs included Marfan Syndrome, Loeys-Dietz Syndrome, and Ehlers-Danlos Syndrome. Kaplan-Meier and Cox regression analysis were used to evaluate the primary outcomes of aneurysmal degeneration, secondary aortic reintervention, dissection propagation, and survival. Aneurysmal degeneration was defined as a ≥5-mm increase in aortic diameter from baseline, whereas dissection propagation included either antegrade and/or retrograde dissection. Results: A total of 330 patients (209 males, 121 females) with a mean age 49 years were included. The most prevalent CTD was Marfan Syndrome (281 patients; 85%), followed by Loeys-Dietz (42 patients; 13%) and Ehlers-Danlos (7 patients; 2%). TEVAR was performed for dissection in 208 patients (63%) and for TAA in 122 patients (37%). The median maximum aortic diameter was 49 mm for dissection and 60 mm for TAA. Spinal cord ischemia and perioperative mortality were observed in 2% of patients. At 1-year follow-up, among patients treated for aortic dissection, aneurysmal degeneration was observed in 28% (18%-37%), dissection propagation in 8% (2%-13%), and secondary aortic reintervention in 28% (20%-35%) (Fig 1). For patients treated for TAAs, aneurysmal degeneration occurred in 20% (9%-30%) (Fig 2), dissection in 12% (0%-23%), and secondary aortic re-intervention in 27% (16%-37%). Survival rates at 1 and 2 years were 88% and 86%, respectively, for dissection, and 92% and 87%, respectively, for TAAs. Conclusions: TEVAR can be safely performed in patients with CTDs but carries a significant risk of short- to intermediate-term aortic-related complications. Reinterventions are frequent particularly within the first postoperative year. These findings suggest that TEVAR use in patients with CTDs should be restricted to emergency cases until improved and durable outcomes can be achieved. [Formula presented] [Formula presented]

Surgery

Chamseddine H, **Hamdan H**, **Halabi M**, **Kabbani L**, **Nypaver T**, **Weaver M**, **Peshkepija A**, **Kavousi Y**, **Onofrey K**, and **Shepard A**. Time Is Intestine: The Impact of Timely Intervention on Acute Mesenteric Ischemia Outcomes. *J Vasc Surg* 2025; 81(6):e5-e6. Full Text

Objectives: Acute mesenteric ischemia (AMI) is a highly morbid presentation associated with high perioperative mortality. Early diagnosis and prompt surgical revascularization are pivotal in reducing mortality and morbidity rates. This study investigates the impact of time from symptom onset to operative intervention in outcome determination in AMI patients. Methods: A single-center retrospective review of all patients who underwent revascularization for AMI at a quaternary medical center between 2014 and 2024 was performed. AMI was defined as acute symptom onset of ≤2 weeks duration. Patients with AMI secondary to aortic dissection were excluded. The optimal time threshold from symptom onset to intervention to achieve optimal outcomes was determined using receiver operating characteristic curves and the Youden index. Kaplan-Meier and Cox regression analysis were used to evaluate the long-term outcomes of survival, primary patency, reintervention, and AMI recurrence. Results: A total of 92 patients (35 males, 57 females) with a mean age of 67 years were included. Surgical interventions included open revascularization in 30% of patients, endovascular revascularization in 60%, and retrograde open mesenteric stenting in 10%. The median time from symptom onset to intervention was 48 hours. Demographics and baseline characteristics were similar between patients treated within 48 hours and those treated >48 hours from acute symptom onset (Table). Overall mortality was 24% at 30 days and 33% at 1 year. Patients undergoing revascularization >48 hours after acute symptom onset were more likely to be transferred from an outside hospital (76% vs 55%; P = .04), required greater bowel resection (97 cm vs 25 cm; P = .013), and had higher 30-day mortality (38% vs 14%; P = .010). One-year mortality was also higher in the patient population undergoing intervention >48 hours from symptom onset (45% vs 23%; P = .033) (Fig). Multivariate analysis revealed a 15% increase in the risk of 30-day mortality for each day of delayed intervention (odds ratio,1.15; 95% CI, 1.02-1.29; P = .019). Conclusions: Early recognition and prompt intervention are crucial in managing AMI and improving survival rates. The time to revascularization is an important factor which, when prolonged, leads to increased bowel loss, and higher short- and long-term mortality. Strategies to expedite diagnosis and treatment are needed to improve survival and recovery in patients with AMI. [Formula presented] [Formula presented]

Surgery

Chamseddine H, **Hamdan H**, **Halabi M**, **Shepard A**, **Nypaver T**, **Weaver M**, **Peshkepija A**, **Kavousi Y**, **Onofrey K**, and **Kabbani L**. Acute Mesenteric Ischemia: Does Etiology Influence Mortality and Recurrence? *J Vasc Surg* 2025; 81(6):e12-e13. Full Text

Objectives: Acute mesenteric ischemia (AMI) is a morbid condition associated with significant rates of operative mortality. This study investigates the impact of the underlying cause of AMI on outcomes and aims to identify key predictors of mortality. Methods: A retrospective review of all patients who underwent revascularization for AMI at a quaternary medical center between 2014 and 2024 was performed. AMI was defined as acute symptom onset of ≤2 weeks duration. Patients with AMI secondary to aortic dissection were excluded. Patients were categorized by AMI etiology into embolism and acute thrombosis. Kaplan-Meier and Cox regression analysis were used to evaluate the long-term outcomes of survival, primary patency, reintervention, and AMI recurrence. Multivariate logistic regression identified significant predictors of 30-day mortality. Results: Ninety-two patients (35 males, 57 females) with a mean age of 67 years were included. AMI etiologies were embolism (30%) and acute thrombosis (70%). Patients with acute thrombosis were more likely to have a history of smoking (91% vs 68%; P = .033), chronic obstructive pulmonary disease (34% vs 11%; P = .019), and chronic mesenteric ischemia (63% vs 4%; P < .001). They also more commonly presented with two-vessel disease compared to one-vessel disease (16% vs 0%; P = .013) and were more frequently treated with endovascular revascularization (80% vs 14%; P < .001). Mortality rates at 30 days (thrombosis 25% vs embolism 22%; P = .748) and mean bowel resection lengths (thrombosis 42 cm vs embolism 44 cm; P = .893) were similar between the two groups. At 1-year follow-up, thrombosis patients had lower primary patency (80% vs 94%; P = .008), higher rates of AMI recurrence (12% vs 6%; P = .05), and higher reintervention (21% vs 6%; P = .02) (Fig 1). Nonetheless, no difference in mortality was observed between the two groups (32% vs 34% P = .873) (Fig 2). Significant predictors of 30-day mortality were age, time from symptom onset to intervention, and lactate level at presentation (area under the receiver operating characteristic curve, 88%). Every 1-year increase in age increased mortality by 6% (odds ratio [OR], 1.06; 95% confidence interval [CI], 1.01-1.12; P = .049); every 1-day delay in intervention by 15% (OR 1.15; 95% CI, 1.03-1.44; P = .021); and every 1-unit increase in lactate by 27% (OR 1.27; 95% CI, 1.03-1.56; P = .029). Conclusions: In our institution, AMI etiology did not affect outcomes in terms mortality, morbidity, or extent of bowel resection. However, thrombotic AMI was associated with higher rates of AMI recurrence and reinterventions. Predictors of mortality included advancing age, time from symptom onset to intervention, and lactate levels on presentation. Prompt diagnosis and intervention remain key to survival in AMI. [Formula presented] [Formula presented]

Surgery

Chamseddine H, **Kabbani L**, and Hoballah JJ. Concomitant Suprainguinal Bypass With Infrainguinal Revascularization Procedures Are Safe and Effective in Combined Aortoiliofemoral Occlusive Disease. *J Vasc Surg* 2025; 81(6):e85. Full Text

Objectives: Extra-anatomical suprainguinal bypass (SIB) has traditionally been offered to patients with significant aortoiliac disease and concurrent hostile abdomens or advanced cardiopulmonary disease when an endovascular approach is not feasible. In the presence of aortoiliac and femoral occlusive disease requiring extra-anatomical SIB, simultaneous revascularization of the infrainguinal segment may be performed either through a concomitant infrainguinal bypass (IIB) or peripheral vascular intervention (PVI). This study aims to compare the safety and efficacy of the two approaches. Methods: Patients undergoing extra-anatomical SIB for CLTI were identified in the Vascular Quality Initiative between 2010 and 2020. Extra-anatomical SIB included axillofemoral bypass and crossover femoral-femoral bypass. Patients were classified into two groups: those receiving SIB with concomitant IIB (SIB+IIB), and those receiving SIB with concomitant infrainguinal PVI (SIB+PVI). Patients undergoing SIB+PVI were one-to-five propensity score matched to patients undergoing SIB+IIB. Kaplan Meier and Cox-regression analysis were used to evaluate the long-term outcomes of major amputation (above-ankle amputation) and mortality. Results: A total of 1310 patients (1107 males, 540 females) with a mean age of 67 years underwent SIB with concomitant infrainguinal revascularization. We matched 1310 (80%) patients who underwent SIB+IIB to 337 (20%) patients who underwent SIB+PVI. After matching, the two groups were

similar in all demographics and preoperative characteristics. The 30-day, 1-year, and 5-year mortality rates were 5%, 15% and 30% respectively. At the 1-year follow-up, the two groups had similar rates of major amputation (8% vs 7%; P = .307), reintervention (16% vs 13%; P = .160), and major adverse limb events (22% vs 20%; P = .179). No difference in long-term mortality was observed the two groups (P = .447) (Fig). Conclusions: This study demonstrates that concomitant infrainguinal revascularization during extra-anatomical SIB is a safe procedure that can be performed with similar efficacy using either IIB or PVI. Both approaches show comparable long-term outcomes in terms of limb salvage and mortality. Accordingly, these findings can be tailored based on individual patient characteristics and clinical considerations without compromising outcomes. [Formula presented]

Surgery

Halabi M, **Chamseddine H**, **Kabbani L**, **Nypaver T**, **Weaver M**, **Peshkepija A**, **Kavousi Y**, **Onofrey K**, and **Shepard A**. Cost Analysis of Open and Endovascular Interventions for Acute vs Chronic Limb Ischemia. *J Vasc Surg* 2025; 81(6):e231-e232. Full Text

Objectives: Acute limb ischemia (ALI) and chronic limb-threatening ischemia (CLTI) represent critical vascular diagnoses requiring resource intensive management through open or endovascular interventions. Although both diagnoses are reimbursed under the same diagnosis-related groups (DRGs), the costs associated with ALI and CLTI management remain poorly understood. This study aims to determine and compare the costs of both open and endovascular treatments for ALI and CLTI, providing insight on the economic challenges of treating these conditions. Methods: A retrospective review of all patients in a quaternary medical center who received treatment for ALI or CLTI between 2016 and 2020 was performed. Patients were identified using procedural codes for open and endovascular interventions. Exclusion criteria included trauma-related ischemia and incomplete cost data. Baseline demographics, treatment characteristics, and direct hospital costs, which include professional charges (physician management and surgery fees) and technical charges (facility fees, equipment costs, and consumables), were collected. Bivariate and multivariate regression analyses were performed to assess cost differences between ALI and CLTI. Results: A total of 494 patients were included in the analysis (ALI: n = 202; CLTI: n = 292). Patients with CLTI were older (74.6 vs 71.3 years; P = .484) and had more comorbidities including chronic kidney disease (26.7% vs 17.6%; P = .005), diabetes mellitus (57.1% vs 41.2%; P < .001), hypertension (82.9% vs 78.9%; P = .003), and hyperlipidemia (74.9% vs 59.3%; P = .003) (Table I). Patients with ALI demonstrated significantly higher costs compared with those with CLTI, driven by increased professional and technical charges. Professional charges, which include physician management and surgery fees, were higher for ALI patients ($25,269 vs $17,055; P < .001). Similarly, technical charges, encompassing facility fees, equipment costs, and consumables, were also higher ($152,880 vs $98,989; P < .001) (Table II). ALI was associated with longer lengths of stay (LOS) (9 days vs 6 days; P < .001), contributing to the higher costs across both treatment modalities. Open ALI procedures cost an average of $39,985 more than open CLTI procedures (P = .004), whereas endovascular ALI procedures cost $28,319 more than their CLTI counterparts (P = .015). Multivariate analysis confirmed that both endovascular (P = .004) and open (P = .008) ALI procedures were significantly more expensive than similar procedures for CLTI. Conclusions: ALI is associated with significantly higher costs than CLTI for both open and endovascular treatments. Higher professional and technical charges for ALI resulted from the need for multiple surgical interventions, prolonged operating room time, increased need for consumables, and extended LOS. The economic burden of ALI management highlights the need for coding and billing adjustments. [Formula presented] [Formula presented]

Surgery

Halabi M, **Chamseddine H**, **Shepard A**, **Nypaver T**, **Weaver M**, **Boules T**, **Peshkepija A**, **Kavousi Y**, **Onofrey K**, **Rteil A**, and **Kabbani L**. Outcomes of Carotid Stenting for Nonatherosclerotic Disease. *J Vasc Surg* 2025; 81(6):e285-e286. Full Text

Objective: Carotid artery stenting (CAS) is a well-recognized treatment for atherosclerotic carotid artery disease; recent studies have demonstrated that transcarotid artery revascularization (TCAR) is associated with lower risks of stroke and death compared with transfemoral CAS (tfCAS) in patients with atherosclerotic carotid stenosis. The comparative outcomes of these techniques in nonatherosclerotic

carotid diseases—dissection, trauma, and fibromuscular dysplasia (FMD)—however remain underexplored. This study aims to evaluate and compare the outcomes of tfCAS and TCAR in nonatherosclerotic carotid disease. Methods: Patients undergoing CAS for dissection, trauma, or FMD were identified in the Vascular Quality Initiative between 2016 and 2024. Demographics, procedural characteristics, and postoperative outcomes were compared between the two groups. Primary outcomes included stroke, death, and major adverse cardiovascular events (MACE) defined as a composite of stroke/myocardial infarction/death. Multivariate logistic regression was used to assess the differences in postoperative outcomes. Results: Among 818 patients (tfCAS: n = 590, TCAR: n = 228), TCAR patients were older (66.79 vs 58.35 years, P < .001), and had more hypertension (78.91% vs 64.2%, P < .001) and coronary artery disease (38.2% vs 25.8%, P < .001). Dissection was the most common etiology in both groups (TCAR: 78.5%, tfCAS: 79.5%), followed by trauma (TCAR: 8.8%, tfCAS: 8.8%) and FMD (TCAR: 12.7%, tfCAS: 9.7%). Intraoperatively, TCAR patients required slightly longer procedure times (75.5 minutes vs 69 minutes, P = .016). When comparing outcomes by etiology, there were no significant differences in stroke (P = .669) or MACE (P = .101) between the groups, while mortality was more common in trauma patients (trauma 7.1%, dissection 2.2%, FMD 1.2%, P = .017). When analyzing by procedure type, TCAR had significantly lower rates of MACE (2.2% vs 6.4%, P = .015) and death (0.4% vs 3.4%, P = .017), but a nonsignificant stroke advantage (1.3% vs 3.1%, P = .159). Multivariate analysis confirmed that TCAR was associated with a lower risk of MACE (odds ratio: 0.303, 95% confidence interval: 0.108-0.852, P = .024), but not stroke or death (Table). Conclusion: This study suggests that TCAR is associated with improved postoperative outcomes compared with tfCAS in patients with nonatherosclerotic carotid disease, notably in reducing MACE. These findings support the preferential use of TCAR in selected patients with nonatherosclerotic carotid artery disease. [Formula presented]

Surgery

Halabi M, **Chamseddine H**, **Shepard A**, **Rashid A**, **Nypaver T**, **Weaver M**, **Peshkepija A**, **Kavousi Y**, **Onofrey K**, and **Kabbani L**. Using Machine Learning to Predict Cerebral Hyperperfusion Following Carotid Revascularization. *J Vasc Surg* 2025; 81(6):e268-e269. Full Text

Objective: Cerebral hyperperfusion syndrome (CHS) is a rare but serious complication of carotid revascularization that may result in neurological dysfunction. Although the precise etiology of CHS remains unclear, this study aims to employ machine learning techniques to predict its occurrence to develop a comprehensive model identifying clinical features associated with this condition. Methods: Patients undergoing carotid artery stenting (CAS) and carotid endarterectomy (CEA) were identified in the Vascular Quality Initiative between 2005 and 2024. Preoperative and intraoperative variables were collected along with outcomes, including patient demographics and procedural details. Preoperative characteristics were assessed for the entire population, followed by stratification by procedure type to evaluate intraoperative characteristics. Machine learning models were developed to predict the occurrence of CHS. Feature importance was assessed using SHapley Additive exPlanations (SHAP) to identify key predictors, and model performance was evaluated using area under the receiver operating characteristic curve (AUCROC). Results: A total of 247,542 patients were analyzed, including 61,700 undergoing transcarotid artery revascularization (TCAR), 41,550 transfemoral CAS (tfCAS), and 144,292 CEAs. Preoperative characteristics were highly predictive of CHS (AUC = 0.97) across all revascularization modalities. Contralateral stenosis and coronary artery disease were the strongest risk factors, as indicated by high positive SHAP values (Fig. 1). Ipsilateral stenosis and emergency presentation also significantly increased CHS risk. Conversely, protective factors such as preoperative statin and ACE inhibitor use had negative SHAP values, reducing the risk of CHS. Intraoperative characteristics for CEA and TCAR were less predictive, with AUCs of 0.50 and 0.76, respectively. For CEA, shunt use and operative time were the most influential factors, with longer operative times associated with higher CHS risk. In TCAR, contrast volume and procedure time were the top predictors, with marginal associations to increased CHS risk. In contrast, tfCAS showed the strongest intraoperative predictive value (AUC = 0.98). Fluoroscopy time, procedure time, and contrast volume were the most significant contributors, with longer fluoroscopy times and higher contrast volumes markedly increasing the risk of CHS. Conclusions: Preoperative characteristics were highly predictive of CHS, whereas intraoperative predictors for TCAR and CEA had limited value. In contrast, tfCAS showed strong associations with procedural factors such as fluoroscopy time and contrast volume, highlighting its higher

risk for CHS. High-risk patients should avoid tfCAS, with alternative strategies such as TCAR or CEA being more appropriate to minimize CHS risk. [Formula presented] [Formula presented]

Surgery
Halabi M, **Chamseddine H**, **Shepard A**, **Rashid A**, **Nypaver T**, **Weaver M**, **Peshkepija A**, **Kavousi Y**, **Onofrey K**, and **Kabbani L**. TCAR versus tfCAS: Machine Learning Suggests That One is Safer, Faster, and Easier to Master. *J Vasc Surg* 2025; 81(6):e9-e10. Full Text

Objectives: This study aims to evaluate and compare the learning curves for transcarotid artery revascularization (TCAR) and transfemoral carotid artery stenting (tfCAS) based on procedural metrics and postoperative outcomes. Utilizing machine learning, we sought to identify procedural milestones, assess trends in operator performance, and explore the relationship between procedural proficiency and patient outcomes. Methods: Patients undergoing TCAR or tfCAS were identified using the Vascular Quality Initiative between 2005 and 2024. Physicians performing these procedures were assigned cumulative procedure counts by chronologically ordering their cases, enabling the analysis of operator experience over time. A machine learning model using neural network was implemented to predict how the risk of complications change with increasing procedure count. The learning curves for both TCAR and tfCAS were defined based on changes in the predicted probabilities of primary outcomes, which included stroke and major adverse cardiovascular events (MACE), comprising stroke, death, and myocardial infarction. Secondary outcomes included stroke/death and all-cause mortality. Procedural metrics, including contrast volume, fluoroscopy time, and operative time, were assessed to evaluate improvements in procedural efficiency over time. Results: The study included 48,536 TCAR and 37,561 tfCAS procedures, with an average of 20 TCAR procedures per operator and 16 tfCAS procedures per operator. MACE occurred at a rate 1.9% (2.4% symptomatic, 1.3% asymptomatic) for TCAR patients and 3.5% (4.5% symptomatic, 1.8% asymptomatic) for tfCAS patients. Among symptomatic patients, the rate of MACE was initially higher for tfCAS (5.01%) compared to TCAR (2.58%). While tfCAS showed a rapid decline early on, TCAR experienced a more gradual reduction. After the 50th procedure, the rates for both began to decline in parallel (Fig 1). The outcomes of stroke, death, and stroke/death followed similar downward trends. Asymptomatic patients displayed comparable patterns, but with overall lower rates of adverse events. Physician experience had a pronounced impact on procedural efficiency; for TCAR, the average procedure time (Fig 2) decreased from 79 minutes to 39 minutes, while for tfCAS, the reduction was less substantial (76 minutes to 56 minutes.) This improvement was mirrored by similar reductions in fluoroscopy time and contrast volume. Conclusions: TCAR consistently outperformed tfCAS, in both procedural and postoperative metrics. Notably, even the most experienced tfCAS operators achieved outcomes inferior to those of beginner TCAR operators. These findings highlight that TCAR is not only safer but easier to master. [Formula presented] [Formula presented]

Surgery
Kim J, **Tong M**, Rumore A, Tabriz M, Patel K, Delk I, Hassett L, Olson S, Ramos C, Schueler L, and Logan A. Utilization of Donor-Derived Cell-Free DNA (ddcfDNA) in Lung Transplant Recipients. *J Heart Lung Transplant* 2025; 44(4):S761. Full Text

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Purpose: The purpose of this study is to assess the utility of noninvasive monitoring with ddcfDNA in detecting acute rejection (AR), including acute cellular rejection (ACR) and antibody-mediated rejection (AMR). Methods: This is a single center, retrospective, observational, cohort analysis of lung transplant recipients. DdcfDNA samples were collected between 4/18/2022 and 7/11/2024 and included if patients had 3 or more samples and a corresponding transbronchial biopsy (TBBX). Samples were categorized based on biopsy results: stable, ACR, subclinical AMR, or AMR. Median and IQR, Wilcoxon sign-rank, and Friedman ANOVA tests were utilized. The primary outcome was to assess the trend of ddcfDNA before and after AR treatment. Secondary outcomes assessed the trend of FEV1 before and after AR treatment, and the correlation between ddcfDNA and change in FEV1. Results: Seventy patients were included. The median (IQR) of ddcfDNA at time of TBBX was 0.71 (0.32-1.1) in stable, 0.69 (0.2-1.1) in ACR, 0.43 in subclinical AMR, and 0.78 in AMR, $p< 0.05$. There were 50 episodes of biopsy-proven ACR

(62% were routine and 38% for-cause TBBX). The median ddcfDNA was noted to increase two-fold at time of ACR (pre-level 3) from the previous level (Figure 1). Among those treated, 97.2% received steroids and 2.8% received antithymocyte globulin (ATG). Of note, the patient who received ATG for steroid-refractory ACR had a ddcfDNA of 3.3% at time of ACR, a five-fold increase from their previous level. The mean FEV1 was 2.08 L before and 2.13 L after AR treatment. There was not a significant correlation between ddcfDNA and change in FEV1 in AR patients (rho= -0.036, p= 0.08). Conclusion: Trending ddcfDNA may provide a more useful tool as compared to a single value at time of ACR, as a doubling of median % ddcfDNA was noted at time of biopsy-proven acute rejection. A decrease back to pre-ACR ddcfDNA levels were also noted after treatment along with corresponding improvement in FEV1. [Formula presented]

Surgery

Koussa K, **Nassif G**, **Clark J**, **Langley K**, **Kanumuri D**, **Murphy E**, **Cools KS**, **Shah R**, and **Kwon DS**. From disadvantage to advantage: closing the care gap in tertiary health care for vulnerable groups. *HPB (Oxford)* 2025; 27:S127-S128. Full Text

Background: Lower socioeconomic status (SES) has consistently been linked to worse cancer outcomes, including higher mortality rates and lower survival probabilities. The Area Deprivation Index (ADI), a validated measure of neighborhood-level SES, captures these socioeconomic disparities and gives us a better understanding of how social determinants of health impact cancer care and outcomes. Our Multidisciplinary Pancreas Clinic – comprising nurse navigation, medical, surgical, radiation oncologists, psychologists, and nutritionists – aims to provide equitable and efficient care to all patient demographics in our integrated health system. We sought to explore the association between neighborhood disadvantage and time between initial diagnosis and first consultation in patients diagnosed with Pancreatic Ductal Adenocarcinoma (PDAC) as well as clinical tumor staging at diagnosis. Methods: A retrospective analysis of PDAC patients diagnosed between 2016 and 2024 was conducted. To measure neighborhood disadvantage, the cohort was categorized into ADI quartiles: Q1 (1-25), Q2 (26-50), Q3 (51-75) and Q4 (76-100) with 1 and 100 being the least and most disadvantaged groups, respectively. Associations between ADI and time to first consultation (in days) and clinical tumor staging (categorized into localized (Stages I&II) and advanced (Stages III&IV) were studied using Logistic and Linear Regression Models. Results: 551 patients were diagnosed with PDAC between 2016 and 2024. 43 patients had an ADI in Q1 (7.8%), 120 in Q2 (21.8%), 176 in Q3 (31.9%) and 212 in Q4 (38.5%). The mean age at diagnosis was 67.7 ± 10.2, the median ADI was 65, and the mean time to first consultation was 10.4 ± 6.3 days. 293 patients had localized disease at diagnosis (53.2%), while 258 had advanced disease (46.8%). In our institution, there was no significance in the time from diagnosis to consultation across the four quartiles of ADI. When evaluating ADI and its association with clinical stage at presentation, patients in Q4 (Adjusted OR: 0.51, 95% CI [0.26;0.98], p-value= 0.04) were less likely to present with advanced tumors when compared to those in Q1. Specifically, patients in Q1, Q2, Q3 and Q4 presented with stage IV disease in 34.9%, 28.3%, 25.0% and 22.2% respectively. Conclusion: Our data suggest that a dedicated multidisciplinary pancreas clinic in an integrated health care system can provide equitable access to care for patients newly diagnosed with PDAC. There was no difference in the time to first consultation, with results showing similar times for all ADI ranges and no statistical significance between the quartiles. These results highlight both the dedication of the healthcare team to provide equitable access to patients of all social determinants of health. Interestingly, we identified that patients who came from more disadvantaged neighborhoods (Q4) presented at earlier stages than those in Q1. Further analysis will be performed to assess such associations over time.

Surgery

Lisznyai E, **Moazzam Z**, **Jose J**, and **Okereke I**. Minimally Invasive Transabdominal Repair of a Massive Incarcerated Adult Bochdalek Hernia. *Am J Respir Crit Care Med* 2025; 211:1. Full Text

[Lisznyai, E.; Moazzam, Z.; Jose, J.; Okereke, I.] Henry Ford Hlth, Detroit, MI USA

Introduction: Bochdalek hernias are the most common form of congenital diaphragmatic hernia (CDH). While the majority of posterolateral diaphragmatic defects are identified in pediatric patients with respiratory distress, adult patients may remain asymptomatic until later in life. Symptomatic cases in

adults are rare and may present with vague respiratory and/or gastrointestinal symptoms. These large hernias may contain multiple intra-abdominal organs at risk for volvulus and strangulation, necessitating timely surgical repair. We present the case of a 73 year-old who underwent successful laparoscopic transabdominal repair of a massive, incarcerated Bochdalek hernia with patch placement. Case Presentation: The patient, a 73 year old male with an active lifestyle as a weightlifter and golfer, initially presented to his primary care physician with a 50-pound unintentional weight loss, poor appetite, dyspnea and fatigue. Computed tomography scan demonstrated a large left sided posterolateral diaphragmatic hernia containing the spleen, pancreatic tail, splenic flexure of the colon, small intestine and a large portion of stomach with mesoaxial volvulus (Fig 1A). After nasogastric decompression of the stomach, he was taken for urgent laparoscopic diaphragmatic hernia repair. Intraoperatively the transverse colon was adherent to the pleura, necessitating division of the gastrohepatic ligament and division of colonic attachments up to the splenic flexure. Once mobilized, the hernia contents were successfully reduced without injury to the spleen. The diaphragmatic defect measured 10 x 15 centimeters and was repaired using Gore Dual Mesh, which was secured to the diaphragm (Fig 1B). On postoperative day one, he tolerated clear liquids after a normal esophagram without leak or obstruction. He then tolerated full liquids on postoperative day two and was discharged to home. Conclusions: Traditionally, open repair of CDH was preferable in younger patients given lower recurrence rates when compared to minimally invasive (MIS) approaches. These repairs can be approached either through a transabdominal or transthoracic approach. MIS transabdominal repair with or without patch placement has more recently gained favor over open repair with comparable recurrence rates. Previous data may have been biased by patient complexity, surgeon preference and technical limitations. Overall, reduction and repair of massive diaphragmatic hernia defects can be achieved via a transabdominal MIS approach with durable results in select patients. Fig 1A. CT depicting large left sided diaphragmatic hernia containing stomach, small intestine, transverse colon, spleen and distal pancreas. 1B. Intraoperative photo of hernia defect with entire spleen in thoracic cavity. 1C. Dual Gore Mesh repair of hernia defect.

Surgery

Loor G, Fernandez R, Patel K, Belli E, Lee A, Smith M, Salerno C, Song T, Siddique A, Langer N, Kukreja J, **Nemeh H**, Hartwig M, Daneshmand M, Chan J, Schwartz G, Toyoda Y, Durham L, Ardehali A, Bush E, Suarez E, Hertz M, and Garcha P. Outcomes Associated with Lung Transplants Using Organ Care System (OCS) Lung in the United States. *J Heart Lung Transplant* 2025; 44(4):S190-S191. Full Text

Purpose: The Thoracic Organ Perfusion (TOP) registry captures prospective real-world data on OCS lung use in the US. The current study reports perioperative characteristics and survival outcomes associated with transplants using OCS lung. Methods: All patients in this study were consented for participation in the TOP registry. Our primary outcome of interest was one-year survival. In a secondary analysis, we compared outcomes associated with a center-specific OCS procurement model (direct acquisition group), and a third-party OCS procurement model [National Organ Care System Program (NOP) group]. Results: 467 lungs were instrumented on OCS and only 9 were turned down after OCS preservation yielding a donor utilization rate of 98.1% (458/467). A total of 458 OCS patients were included in the current analysis. Of all donors in this cohort, 20% were older than 55 years of age, 24% were from donation after circulatory death (DCD), 8% had a PaO2:FiO2 ratio <300mmHg prior to retrieval, and 9% had a significant smoking history (>20 pack year with recent smoking within 6 months). Recipients' mean age was 57.7 years old. Of all recipients, 11% were on ECMO prior to transplant, 35% had a lung allocation score >50, and 6% had a history of prior solid organ transplant. Average total cross clamp time was 619 min. 1-, 6- and 12-month survival was 97, 91, and 86%, respectively. There was no difference in survival between direct acquisition and NOP groups (p=0.28). Conclusion: The current analysis of transplant recipients in the TOP registry suggests that OCS lung was a safe preservation method for expanding the donor pool and extending cross-clamp times. NOP offers a safe alternative to facilitate procurement protocols and logistics. [Formula presented]

Surgery

Mahr G, **Reffi A**, **Jankowiak L**, **Moore D**, and **Drake C**. Emotional Dream Content of Acute Trauma Patients: Associations with Interpersonal Violence, Nightmares, and PTSD. *Sleep* 2025; 48:A509. Full Text

[Mahr, Greg; Jankowiak, Lily; Moore, David] Henry Ford Hlth, Detroit, MI USA; [Reffi, Anthony; Drake, Christopher] Henry Ford Hlth Syst, Candon, MI USA

Introduction: Dreams are involved in the processing of emotions and can serve as markers of emotional distress. The authors developed a rating scale for affect in dreams and applied it to an acute trauma population. Methods: We recruited 88 patients hospitalized within one week following traumatic injury (Mage = 39.53 ± 14.31 years, 67.0% male, 67.0% Black). Patients who recalled a dream since hospi talization recorded their dream (n = 43). An independent rater scored the dreams using a novel 33-item Affective Neuroscience Dream Rating Scale to indicate the presence of fear, rage, grief, seeking, care, play, and lust. We quantified the emotional valence of dreams by summing positive (seeking + care + play + lust) and negative emotions (fear + rage + grief) and explored their associations with interpersonal violence and clinical outcomes approximately one-month post-trauma. Results: The emotional valence of dreams across all patients was significantly more negative (M = 4.84 ± 2.91) than posi tive (M = 1.26 ± 1.16), p <.001. Experiencing negatively toned dreams was associated with increased odds of being hospitalized for interpersonal violence (OR = 1.45, p =.014, 95% CI = 1.08 – 1.96) and more severe acute stress symptoms (β = 0.36, p =.021), regardless of sex. Reporting more negatively toned dreams dur ing hospitalization prospectively predicted risk for trauma-re lated nightmares one month later (OR = 1.73, p =.045, 95% CI = 1.01 – 2.97), adjusting for time, and was prospectively associated with increased nightmare distress (r =.70, p <.001), night terrors (r =.37, p =.042), and PTSD status (r =.44, p =.033). The dreams of patients who went on to screen positive for PTSD one month after trauma were significantly more negative (M = 5.99) than patients without PTSD (M = 3.70), p =.038, ηp2 = 19, indicating a large effect. Conclusion: Negative affective tone in dreams immediately after trauma predicted subsequent nightmares and future PTSD and can provide a potential tool for assessing PTSD risk in acute trauma patients.

Surgery

Pansuriya S, **Hans S**, and **Polanco G**. Results of Open Repair of Giant Femoral Anastomotic Aneurysms. *J Vasc Surg* 2025; 81(6):e212. Full Text

Objectives: Open repair of giant femoral artery anastomotic aneurysms (FAAAs) can be a challenging operation, particularly in those with rupture and with recurrent anastomotic aneurysms. We report on the results of open repair of giant FAAAs and explore the use of technical maneuvers to assist in achieving successful outcomes. Methods: Among patients with open FAAA repairs, 16 (Group A) were identified with giant aneurysms (greater than 6.5 cm). During the same time interval, 69 patients underwent open repair of 3.5- to 6.4-cm FAAAs (Group B). The study was conducted from vascular registries of two teaching hospitals (2000-2024). Both groups were compared using Fisher Exact and Student t-test. Results: Both groups were similar in age and risk factors. Among 16 patients who underwent FAAA repairs for giant aneurysms (9 men), five presented with rupture, and 11 presented with local compressive symptoms. The diameter of FAAA was 6.5 to 8 cm in 10 patients and 8.1 to 9.5 cm in six patients. In patients with giant FAAAs, four had prior ipsilateral aortofemoral and contralateral aortoiliac graft for repair of abdominal aortic aneurysm; 11 had aortobifemoral graft for occlusive disease, and one had femoropopliteal graft for exclusion of popliteal aneurysm. Repair necessitated retroperitoneal exposure of the graft limb/external iliac artery (EIA) in five patients. Intraluminal control of deep femoral artery with number 5 or 6 arterial dilators was used in 14 repairs. Interposition prosthetic graft (8 mm) was used for repair from proximal common femoral artery to femoral artery bifurcation (n = 7), to deep femoral artery (n = 3), to the origin of lower extremity bypass (n = 2), and reimplantation of the deep femoral artery using a Carrell patch into the interposition graft (n = 4). One patient died following repair of a ruptured FAAA (6.2%) due to respiratory failure, and one had a late major amputation (above knee) approximately 1 year later due to occlusion of the femoral popliteal bypass. At a mean follow-up of 8.4 ± 2.6 years (range, 1-22 years), seven patients died; none were related to FAAA repair. No patient had a recurrence of FAAAs. Conclusions: Giant FAAAs appear later than conventional FAAAs following index operation. Repair of giant FAAAs as compared with conventional FAAA repair is associated with increased blood loss and operative time. Outcomes are similar in both groups. The proximal control of the graft limb/EIA in selective instances and the intraluminal control of deep femoral artery in all patients are technical aids to assist in satisfactory outcomes. [Formula presented]

Surgery

Reffi A, **Jankowiak L**, **Moore D**, Basarkod S, **Jovanovic T**, **Cheng PL**, Hsieh HF, and **Drake C**. Fear of Sleep Prospectively Predicts Nightmare Severity in Acute Trauma Patients Exposed to Community Violence. *Sleep* 2025; 48:A510. Full Text

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Introduction: Fear of sleep engenders arousal at bedtime that can promote nightmares. Living in disadvantaged neighbor hoods with high rates of community violence may exacerbate fear of sleep and in turn increase nightmare risk. We tested fear of sleep among acute trauma patients as a prospective predic tor of nightmares, and whether exposure to community violence moderated this relationship. Methods: Patients hospitalized in the intensive care unit within one week following traumatic injury (N = 88; Mage = 39.53 ± SD 14.31, 67.0% male, 67.0% Black, 47.7% income ≤ $20,000). Patients completed the Fear of Sleep Inventory (FoSI) Short Form and a community violence questionnaire during hospital ization (T1; N = 88) and the Nightmare Disorder Index (NDI) approximately two months post-trauma (T2; n = 59). We com puted an NDI sum score as our outcome to indicate greater nightmare severity (nightmare frequency and nightmare-re lated awakenings, distress, and impairment). Skin conductance response (SCR) was collected from a subsample of patients (n = 7) during the FoSI to preliminarily explore the psychophysiolog ical correlates of this scale. Results: Exposure to community violence exacerbated the pro spective effect of fear of sleep on future nightmare severity (β = 0.51, p =.039), such that relationship between fear of sleep at T1 a nd nightmare severity at T2 was strongest for patients reporting exposure to higher levels of community violence in the 90 days prior to hospitalization. SCR to the FoSI was correlated with greater exposure to community violence (r = 0.76, p =.048) and the following fear-of-sleep-related safety behaviors: “I stayed up late to avoid sleeping” (r = 0.87, p =.012) and “I tried to stay as alert as I could while lying in bed,” though this relationship was nonsignificant (r = 0.74, p =.060). Conclusion: Acute trauma patients presenting with a fear of sleep may be at increased risk for posttraumatic nightmares during recovery, especially those living within neighborhoods marked by high levels of community violence. Preliminary results suggest fear of sleep and community violence exposure may share an association with sympathetic activation which, when elevated at bedtime, could increase nightmare production.

Surgery

Reffi A, **Moore D**, **Jankowiak L**, and **Drake C**. The Impact of Lifetime Trauma on Sleep Reactivity in Acute Trauma Patients: The Role of Victimization Traumas. *Sleep* 2025; 48:A228-A229. Full Text

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Introduction: Sleep reactivity is a vulnerability to sleep distur bance after stress that increases risk for insomnia and myriad negative health outcomes. Previous research shows life stress can heighten sensitivity of the sleep system, exacerbating sleep reac tivity. This study investigated the relationship between lifetime trauma exposure and sleep reactivity among patients hospital ized for acute trauma. Methods: We recruited 88 patients hospitalized in Detroit, MI within one week following traumatic injury (Mage = 39.53 ± 14.31, 67.0% male, 67.0% Black). Patients reported their lifetime exposure to traumatic events using the Life Events Checklist for DSM-5 (LEC-5). We summed all positive trauma exposures to compute a “trauma load” variable, with greater scores indi cating cumulative lifetime trauma experiences. Additionally, we computed three empirically derived clusters of trauma types previously shown to differentially correlate with mental health: Accidental/injury traumas (e.g. transportation accident), victimization traumas (e.g. physical assault), and predominant death threat traumas (containing mostly death-related traumas, e.g. assault with a weapon). Participants reported their sleep reactivity using the Ford Insomnia Response to Stress Test (FIRST) and insomnia using the Insomnia Severity Index (ISI). Results: Reactive sleepers (FIRST ≥ 20) reported significantly more traumatic life events (M number of events = 7.64 ± SD 3.72) than nonreactive sleepers (M number of events = 5.91 ± SD 4.12), p =.041.

High sleep reactivity was uniquely associated with greater lifetime exposure to victimization trauma types (F(1, 84,) = 4.22, p =.043, ηp2 =.048), adjusting for sex and insomnia (ISI ≥ 11). Specifically, 59.0% of patients with a his tory of physical assault had high sleep reactivity, whereas 41.0% had low sleep reactivity (χ2 = 4.94, p =.026). Similarly, 69.0% of patients with a history of sexual assault had high sleep reactivity, whereas only 31.0% had low sleep reactivity (χ2 = 5.50, p =.019). Conclusion: Acute trauma patients with high sleep reactivity report greater lifetime exposure to traumatic events, particularly physical and sexual assault. These results highlight the poten tial link between victimization traumas and increased sensitivity of the sleep system, independent of insomnia status, which may contribute to the development of insomnia and other negative health outcomes.

Surgery

Said S, Alameddine D, Fischer U, Zwibelman H, **Kabbani L**, Kashyap VS, Tonnessen BH, Cardella J, Guzman RJ, and Ochoa Chaar CI. Antithrombotic Therapy in Patients With Isolated Peripheral Arterial Disease Undergoing Peripheral Vascular Interventions. *J Vasc Surg* 2025; 81(6):e56-e58. Full Text

Objectives: Comorbidities and procedural history can significantly influence the choice of antithrombotic therapy in patients undergoing peripheral vascular interventions (PVI) for peripheral arterial disease (PAD). The landscape of antithrombotic therapy is growing in complexity with paucity of trials dedicated to patients with PAD. This study assesses antithrombotic regimens in patients presenting with isolated PAD, without other comorbidities or procedural history that could affect antithrombotic management. Methods: The Vascular Quality Initiative PVI database was reviewed. Only patients with isolated PAD without history of cardiovascular or cerebrovascular disease, or other indications for antithrombotic therapy were included. Patients presenting with acute limb ischemia or chronic anticoagulation preoperatively were excluded. The characteristics and outcomes of patients discharged on factor Xa inhibitor plus single antiplatelet therapy (FXaI+SAPT) were compared to patients discharged on dual antiplatelet therapy (DAPT). Results: A total of 191,421 patients underwent PVI and 60% of patients were excluded because of competing indications for antithrombotic therapy. Isolated PAD constituted only 40% of the sample (n = 75,334) and exhibited extensive variations in the medications prescribed at discharge, totaling 40 unique combinations. The most common class combinations were DAPT (aspirin+P2Y12i) was used in 59% of patients, followed by SAPT (aspirin or P2Y12i) in 30%, FXaI+SAPT in 2.6%, and 5.5% were discharged without antithrombotic medication. Patients received FXaI+SAPT (n = 1914) were more likely to be younger (65 vs 67; P < .001) and African American (20% vs 18%; P < .001) compared to patients received DAPT (n = 43,807), but were less likely to have diabetes (40% vs 46%; P < .001) and chronic kidney disease (63% vs 70%; P < .001). Patients discharged on FXaI+SAPT were more likely to be treated for chronic limb-threatening ischemia compared to patients discharged on DAPT (71% vs 52%; P < .001). After 3:1 propensity matching, there were 5890 patients included in the analysis with no differences in baseline characteristics (Table). Patients received FXaI+SAPT had higher rates of thrombosis and embolism postoperatively and were less likely to be discharged home. Patients received FXaI+SAPT had higher rates of long-term reintervention and major amputation (Table). Kaplan-Meier curves showed a significantly lower overall survival, freedom from amputation, and MALE-free survival for patients receiving FXaI+SAPT compared to patients receiving DAPT upon discharge (Fig). Conclusions: Most patients with PAD undergoing PVI have competing indications for antithrombotic therapy. There is a wide variation in the antithrombotic regimens of patients with isolated PAD. DAPT seemed to be associated with better long-term outcomes compared to FXaI+SAPT for patients with isolated PAD undergoing PVI. [Formula presented] [Formula presented]

Surgery

Simanovski J, Crawley J, Ralph JL, Sleiman D, **Bryce K**, and Cruz E. Caring Beyond Measure: Scoping Review of the Experiences of Informal Caregivers of Lung Transplant Recipients. *J Heart Lung Transplant* 2025; 44(4):S322. Full Text

Purpose: Informal caregivers are essential in supporting patients after lung transplantation (LT). With a growing emphasis and recognition of the multiple demands placed on caregivers, the objective of this scoping review was to systematically map the literature surrounding informal caregiving experiences after LT and identify knowledge gaps. Methods: The protocol was developed a priori following guidelines for conducting scoping reviews recommended by Joanna Briggs Institute. Two health sciences librarians

developed the search strategy and searched multiple databases from January 2010 to January 2024 based on a combination of keywords and controlled vocabulary related to “caregiver” and “lung transplant recipients”. Using Covidence©, two independent reviewers screened titles and abstracts of the retrieved articles using the inclusion criteria for the review. Disagreements were resolved by a third reviewer before data extraction. Results: A total of 362 records were screened after the removal of duplicates. Among these, 16 sources met the inclusion criteria with 75% classified as full publications (n=12), 19% peer-reviewed conference abstracts (n=3), and a poster presentation (n=1). Most studies were based in North America (11/16 = 69%) with the remainder from Europe or Australia. Only 19% (3/16) of sources were published within the past 5 years. There were 7 qualitative studies (44%); 6 quantitative (38%); 2 mixed methods (13%); and 1 literature review. Informal caregivers described a wide variety of challenging experiences ranging from high levels of caregiver stress burden, psychological symptoms, knowledge deficits, handling multiple daily practicalities, and the need for more education and support. Positive aspects of the informal caregiver role include increased levels of life satisfaction, rewarding responsibilities, improved coping, and benefitting from mindful-based stress reduction, multi-media education programs, and hospitality houses. Conclusion: Informal caregivers remain an integral resource in supporting patients after LT. Unfortunately, the literature related to the informal caregiver experiences after LT is scarce and outdated, suggesting that additional studies are needed to further examine the topic, and design interventions to support this population.

Urology

Bertini A, Pozzi E, Belladelli F, Negri F, Corsini C, Raffo M, Malvestiti M, Oddo M, Birolini G, Matloob R, Boeri L, D'Arma A, **Abdollah F**, Montorsi F, and Salonia A. TEMPORAL TRENDS IN AGE AT PRESENTATION FOR PEYRONIE'S DISEASE PATIENTS: A 20-YEAR SINGLE-CENTER COHORT STUDY. *J Sex Med* 2025; 22:1. Full Text

[Bertini, A.; Pozzi, E.; Belladelli, F.; Negri, F.; Corsini, C.; Raffo, M.; Malvestiti, M.; Oddo, M.; Matloob, R.; D'arma, A.; Montorsi, F.; Salonia, A.] IRCCS Osped San Raffaele, Div Expt Oncol, Unit Urol, Milan, Italy; [Birolini, G.] Univ Vita Salute San Raffaele, Milan, Italy; [Boeri, L.] Fdn IRCCS Ca Granda Osped Maggiore, Dept Urol, Milan, Italy; [Montorsi, F.] Henry Ford Hlth Syst, VUI Ctr Outcomes Res Anal & Evaluat, Detroit, MI USA

Objectives: Peyronie’s disease (PD) is a common complaint even among young men, yet prevalence and risk factors of PD in these patients have been scantly analysed. We assessed sociodemographic and clinical characteristics of young men with new onset PD, highlighting changes over a 20-year period at a single tertiary referral centre. Methods: Data from 689 men presenting with PD at a single center were prospectively analysed. Comorbidities were scored with the Charlson Comorbidity Index (CCI). All patients completed the International Index of Erectile Function (IIEF) and Beck’s inventory for depression (BDI) at baseline. Patients were grouped into <40 vs. >40 years at first presentation. Univariable (UVA) Linear and Logistic regression models were fitted to explore changes in patterns of sociodemographic and clinical characteristics over a 19-yr period (2005-2024). Loess curve graphically displayed the association between age at first clinical visit and year of assessment. Results: Overall, median (IQR) age at presentation was 55 (44-62) years. 327 (47%) patients showed a CCI >2 and 33 (8.4%) patients reported at least one previous cardiovascular event. Of all, 144 (21%) men aged >40 at baseline. Younger patients had higher probability to be single persons (30% vs. 7.5%, $p < 0.001$) and active smoker (38% vs 20%, $p < 0.001$), reporting lower rates of CCI > 2 (4.2% vs. 59%, $p < 0.001$), arterial hypertension (2.5% vs. 45%, $p < 0.001$), cardiovascular events (0% vs. 10%, $p = 0.003$) and erectile dysfunction (ED) (50% vs. 64%, $p = 0.014$). Groups did not differ in median IIEF and BDI scores. At linear UVA, patients were younger (beta: -0.24, $p = 0.04$), with less comorbidities (beta: -0.03, $p = 0.005$), and lower IIEF-EF scores (beta: -0.33, $p = 0.02$) over the analyzed timeframe. At logistic UVA, patients evaluated for PD in recent years were more likely to be smokers (OR: 1.10, $p < 0.001$), to exercise more (OR: 1.06, $p < 0.001$) and report arterial hypertension (OR: 1.05, $p = 0.02$). Conclusions: Overall, one out of five patients seeking first medical help for PD was younger than 40 years, with a probability of assessing younger PD patients gradually increased over the last 20 years. Current findings confirm the severe impact of PD throughout ages.

Urology

Bertini A, Pozzi E, Corsini C, Belladelli F, Negri F, Raffo M, Matloob R, Boeri L, d'Arma A, **Abdollah F**, Montorsi F, and Salonia A. CLINICAL PREDICTORS OF RESPONSE TO PHOSPHODIESTERASE TYPE 5 INHIBITOR (PDE5IS) THERAPY IN PATIENTS WITH ERECTILE DYSFUNCTION: A PENILE HEMODYNAMIC STUDY. *J Sex Med* 2025; 22:2. Full Text

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Objectives: Phosphodiestrase-5 inhibitors (PDE5is) are the mainstay of treatment for erectile dysfunction (ED), yet the influence of patients' clinical characteristics and penile Color Doppler Duplex Ultrasounds (CDDU) parameters on PDE5is' efficacy have been poorly understood. We assesed the rates of and the predictors of PDE5is response in a cohort of ED men who underwent penile CDDU. Methods: Complete data from 175 consecutive men with new onset ED at a single academic center were prospectively collected. All patients underwent CDDU according to the internal protocol. Thereafter, patients were grouped into "nonresponders" and "responders" according to their response to PDE5is. All patients completed the International Index of Erectile Function-erectile function (IIEF-EF) domain, during initial assessment and after treatment assumption. Patients without any reported IIEF-EF improvement after PDE5is therapy (any) were categorized as "nonresponders". Univariable (UVA) and multivariate (MVA) logistic regression analyses tested the impact of patients' clinical characteristics and CDDU parameters on PDE5is response. Results: Of all, 119 (68%) patients depicted a response to PDE5is treatment. Median (IQR) age was 53 (41-60) years. Responders vs. nonresponders were more likely to be young (53 vs. 59 years, p = 0.006), reporting lower rates of arterial hypertension [29% vs. 48%, p = 0.01] and diabetes mellitus (DM) (6% vs. 16%, p = 0.02), higher median IIEF-EF score values (14 vs. 8, p = 0.005) and consequently a lower rate of severe ED (IIEF-EF = <11) (40% vs. 69%, p = 0.004), compared to the nonresponders. At UVA, older age (p = 0.006), arterial hypertension (p = 0.01), DM (p = 0.03) and higher median waist circumference (p = 0.05) values were significantly associated with a lower probability of PDE5is response. Among CDDU parameters, only patients with higher median Resistance Index (p = 0.03) were more likely to be responders at UVA. At MVA, men without arterial hypertension (OR: 0.28, p = 0.01) and those with higher median IIEF-EF scores (OR: 1.06, p = 0.04) had higher probability response to PDE5is. Conclusions: Our results outlined that none of the parameters assessed at the CDDU was an independent predictor of response to oral treatment for ED, showing that patients with arterial hypertension and more severe ED were less likely to respond to PDE5is.

Urology

Bertini A, Pozzi E, Negri F, Belladelli F, Corsini C, Raffo M, Malvestiti M, Oddo M, Folcia A, Birolini G, Boeri L, d'Arma A, **Abdollah F**, Montorsi F, and Salonia A. THE IMPACT OF EDUCATIONAL STATUS ON PATIENTS COMPLIANCE WITH PDE5IS: A COMPARATIVE CROSS-SECTIONAL REAL-LIFE STUDY. *J Sex Med* 2025; 22:2. Full Text

[Bertini, A.; Pozzi, E.; Negri, F.; Belladelli, F.; Corsini, C.; Raffo, M.; Malvestiti, M.; Oddo, M.; Folcia, A.; d'Arma, A.; Montorsi, F.; Salonia, A.] IRCCS Osped San Raffaele, Div Expt Oncol, Unit Urol, Milan, Italy; [Birolini, G.] Vita Salute San Raffaele, Milan, Italy; [Boeri, L.] Fdn IRCCS Ca Granda Osped Maggiore, Dept Urol, Milan, Italy; [Abdollah, F.] VUI Ctr Outcomes Researchm Anal & Evaluat, Henry Ford Hlth Syst, Detroit, MI USA

Objectives: The impact of educational status on patients' compliance regarding prescribed phosphodiesterase type 5 inhibitors (PDE5is) in men with erectile dysfunction (ED) has been scantly analysed. We investigated the impact of educational status on compliance with PDE5is in naïve men for PDE5is presenting with new-onset ED. Methods: Complete data from 1264 consecutive men presenting with new onset ED and naïve to PDE5is were prospectively analysed. Patients were grouped according to their educational status into low (elementary and/or secondary school education), mid (high school) and high (university degrees) educational levels. Baseline health significant comorbidities were scored with the Charlson Comorbidity Index (CCI). All patients have been prescribed with a PDE5i. Hence, all

patients completed the International Index of Erectile Function (IIEF), at baseline and after treatment discontinuation. Kaplan–Meier (KM) curves estimated the discontinuation free-survival (DFS) after stratification according to educational status. Univariable (UVA) and multivariate (MVA) Cox regression addressed the association between educational status and PDE5is' discontinuation. Results: Of all, 160 (13%), 573 (45%) and 531 (42%) individuals depicted low, mid and high educational status, respectively. Median (IQR) age and median (IQR) follow-up time were 51 (39-61) and 8.5 (5.9-11.3) years. Patients with higher educational levels were more likely to be younger (49 vs. 56 years, p < 0.001), reporting lower median BMI values (25 vs. 26.3 kg/m2, p < 0.001) and lower rates of CCI > = 2 (8.7% vs. 11%, p = 0.006), compared to their low educational level counterparts. No significant differences were found in terms of median duration of PDE5is assumption and IIEF-erectile function (IIEF-EF) across the groups. At KM, the lower the educational level the greater the adherence to the prescribed PDE5i (p = 0.02) (Fig. 1). Cox regression analysis, confirmed that older men (HR: 1.01, p = 0.02) and those with high educational level (HR: 1.90, p = 0.03) were more likely to discontinue PDE5is. Conclusions: Our findings suggest that the higher the edu cational level the greater the probability of PDE5is drop off. These results highlight a particular aspect of patients' compliance with PDE5is, enabling improvements in pharmacological management for ED.

Books and Book Chapters

Center for Health Policy and Health Services Research

Braciszewski JM, and Colby SM. Motivational interviewing for smoking cessation. In: Burke BL, Lundahl B, and Arkowitz H, eds. *Motivational interviewing in the treatment of psychological problems., 3rd ed.* The Guilford Press, US; 2025**:**206-228. Full Text