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# Henry Ford Health Publication List – September 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, and CINAHL during the month, and then imported into EndNote for formatting. There are 172 unique citations listed this month, including 139 articles and 33 conference abstracts.

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

**Note to authors: To help facilitate scholarly activity tracking, please include "Henry Ford Health" and your department/location in your author affiliation when submitting to a journal.**

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## Articles



## Conference Abstracts

## Articles

Administration

**Huang J**, **Doemer A**, **Siddiqui S**, **Shah M**, **Al Asadi A**, **DiCarlo A**, **Thind K**, **Moceri A**, **Scarpace L**, **Lee I**, and **Robin A**. Novel use of 3D printing for preoperative dose estimation in the first case of GammaTile spine implantation. *Brachytherapy* 2025; Epub ahead of print. PMID: 40992982. Full Text

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PURPOSE: For a patient who had two previous courses of external beam radiation therapy for rectosigmoid adenocarcinoma and presented with painful, recurrent disease in the sacrum, this study describes the first use of Cs-131 LDR GammaTile therapy outside of the brain and demonstrates a novel use of 3D printing for preoperative dose estimation. MATERIAL AND METHODS: A personalized 3D-printed model of the patient's spine was created using segmented MRI data, differentiating uninvolved bone, tumor, and thecal sac and nerve roots, with a Stratasys J5 MediJet® Printer. This model was used to simulate surgical resection and placement of dummy radioactive sources. A CT scan of the model facilitated preoperative dose calculations, including physical dose using Eclipse planning software and biologically effective dose (BED) using MIM Maestro software. The predicted dose was then compared to the postimplant dosimetry for the actual patient. RESULTS: For the relevant organ at risk (thecal sac), the max dose (D(0.035cc)) was calculated accurately within 8.0% for physical dose and within 10.0% for BED when comparing the dose estimated using our 3D-printed model and the patient's postimplant dosimetry. CONCLUSIONS: 3D printing can be used preoperatively to estimate dose to critical organs at risk for patients receiving surgical resection followed by Cs-131 LDR implantation in the spine and can be especially valuable in the context of reirradiation.

Allergy and Immunology

Gaberino CL, Segnitz RM, Dill-McFarland KA, Bacharier LB, Calatroni A, Gill MA, Stokes J, Liu AH, Cohen RT, Kumar R, Lang A, Khurana Hershey GK, Sherenian MG, **Zoratti EM**, Teach SJ, Kattan M, Becker PM, Togias A, Busse WW, Jackson DJ, and Altman MC. Mepolizumab alters gene regulatory networks of nasal airway type-2 and epithelial inflammation in urban children with asthma. *Nat Commun* 2025;16(1):8191. PMID: 40897727. Full Text

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Department of Pediatrics, Cincinnati Children's Hospital, Cincinnati, OH, USA.
Department of Medicine, Henry Ford Health System, Detroit, MI, USA.
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Department of Pediatrics, Columbia University, New York, NY, USA.
National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA.
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Mepolizumab (anti-IL5 therapy) reduces asthma exacerbations in urban children with exacerbation-prone eosinophilic asthma. We previously utilized nasal transcriptomics to identify inflammatory pathways (gene co-expression modules) associated with asthma exacerbations despite this therapy. In this study, we applied differential gene correlation analysis on these targeted gene co-expression modules to gain better insight into the treatment effects on correlation structure within gene networks. Mepolizumab treatment resulted in loss of correlation amongst eosinophil-specific genes but conservation and even strengthening of correlation amongst mast cell-specific genes, T2 cytokines, and airway epithelial inflammatory genes. Notably, mepolizumab induced significant gain in correlation of genes associated with multiple aspects of airway epithelial inflammation including those related to extracellular matrix production and nitric oxide synthesis, and this change was associated with a poor clinical response to mepolizumab. These findings highlight that using differential gene correlation analysis offers insight into the molecular regulatory effects of treatment on gene interactions and may lead to better understanding of disease mechanisms and therapeutic responses. ClinicalTrials.gov ID: NCT03292588.

Anesthesiology

Cortes-Mejía N, **Guerra-Londono JJ**, Feng L, Gloria-Escobar JM, Lillemoe HA, Ovsak G, and Cata JP. The impact of sugammadex versus neostigmine reversal on return to intended oncological therapy-related outcomes after breast cancer surgery: a retrospective cohort study. *Perioper Med (Lond)* 2025;14(1):92. PMID: 40898363. Full Text

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BACKGROUND: Early return to intended oncological therapy (RIOT) after cancer resection is a determinant for long-term oncological outcomes. Sugammadex is increasingly used to reverse the muscle relaxant effect of rocuronium during general anesthesia. It has been shown to improve early postoperative outcomes, but its impact on RIOT is unknown. This study tested the hypothesis that the administration of sugammadex during mastectomy for nonmetastatic breast cancer resection would be associated with better RIOT-related outcomes compared with neostigmine. METHODS:
Women ≥ 18 years who required mastectomy for nonmetastatic breast cancer resection from 2015 to 2022 were included in the retrospective study. They were grouped according to the administration of sugammadex or neostigmine. The study outcomes included time to RIOT, the incidence of RIOT at 90 and 180 days, length of hospital stay, and rate of 30-day hospital readmission. A multivariate analysis was conducted to test the association between sugammadex use and RIOT-related outcomes. RESULTS: Of 888 patients who met the study criteria, 319 received neostigmine and 569 received sugammadex. Sugammadex patients achieved RIOT at 90 days in 81.9% of the cases, whereas 70.8% of neostigmine patients were able to achieve RIOT ($P < 0.001$). Similar results were found for RIOT at 180 days (85.8% vs. 76.8%, respectively; $P < 0.001$). Sugammadex patients achieved RIOT faster than neostigmine patients (37 days, 95% CI: 35-41 days; $P < 0.001$). However, the multivariate analysis for RIOT initiation and time to RIOT did not show statistically significant differences. CONCLUSION: The administration of sugammadex, compared with neostigmine, is not associated with significant improvements in RIOT-related variables after breast cancer surgery.

Anesthesiology

Dykhouse G, Ngo ALT, **McKegg PC**, Spencer PB, Sayyed A, Manes TJ, Turnow M, and Long N. Epidemiology of Shoulder Dislocations in the United States From 1990 to 2019: A Temporal Study Using the Global Burden of Disease Database. *Cureus* 2025;17(8):e91146. PMID: 41018354. Full Text

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Introduction The shoulder joint is a common site for joint dislocation, with many individuals suffering from recurrent dislocations following treatment. The purpose of this study was to evaluate the epidemiology of shoulder dislocations in the United States from 1990 to 2019. Methods The Global Burden of Disease database was utilized to collect epidemiological data on shoulder dislocations in the United States (U.S.) from 1990 to 2019. These data included age-standardized rates of years lived with disability (YLDs), prevalence rates, and incidence rates per 100,000 people. Using the U.S. Census Bureau definitions, the data were stratified into four regions: the Northeast, Midwest, South, and West. Bartlett's test was used to assess whether the variance of the dataset was equal. Welch's ANOVA was performed to assess differences in YLDs, prevalence rates, and incidence rates between regions. Results From 1990 to 2019, there was an 8.69% decrease in mean YLDs, an 8.69% decrease in prevalence rates, and a 9.14% decrease in mean incidence rates of shoulder dislocations. Women experienced a 0.78% increase in mean YLDs, a 0.77% increase in mean prevalence rates, and a 0.27% increase in mean incidence rates of shoulder dislocation. Men experienced a 15.45% decrease in mean YLDs, a 15.45% decrease in mean prevalence rates, and a 15.82% decrease in mean incidence rate of shoulder dislocations. Regardless of region, men were more likely to experience a higher mean rate of YLDs (1.06 vs. 0.79, $p<0.001$), higher mean prevalence rates (17.16 vs. 12.70, $p<0.001$), and higher mean incidence rates (115.25 vs. 84.59, $p<0.001$) of shoulder dislocations. The West region experienced the highest mean rate of YLDs, the highest mean prevalence rates, and the highest mean incidence rates of shoulder dislocation. The Northeast region experienced the lowest mean rates of YLDs, mean prevalence rates, and mean incidence rates. Men experienced higher mean rates of YLDs, prevalence, and incidence of shoulder dislocations compared to women ($p<0.001$). Conclusion From 1990 to 2019, the U.S. witnessed a decline in mean YLDs, incidence, and prevalence rates for shoulder dislocations. This trend varied by gender, with men experiencing notable decreases across these metrics, while women saw slight increases. Overall, men consistently had higher rates of shoulder dislocations compared to women. Geographically, the Western region had the highest rates, whereas the Northeast had the lowest.

Behavioral Health Services/Psychiatry/Neuropsychology

Feldman N, Hibara A, Ye J, Macaranas A, Larkin P, **Hendrix E**, Aydinian T, Mittal L, Wiegartz P, Silbersweig D, and Liu CH. Postpartum anxiety: a state-of-the-art review. *Lancet Psychiatry* 2025; Epub ahead of print. PMID: 40907501. Full Text

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Although there has been increasing interest in the study of postpartum anxiety in recent years, it remains an emerging field. We present a state-of-the-art review of postpartum anxiety, with the aim of comprehensively surveying postpartum anxiety literature and presenting a synthesis of the complete body of knowledge around postpartum anxiety. We found an estimated global prevalence of 12·3% for postpartum anxiety. Postpartum anxiety is associated with primiparity and younger maternal age. Multiple screening tools are validated for use in postpartum anxiety, although none of these tools are validated for ongoing assessment. There are very few studies of pharmacotherapy in postpartum anxiety, but cognitive behavioural therapy has promising evidence. Postpartum anxiety is associated with altered offspring biology and mental health, as well as poor maternal psychological outcomes and quality of life. We review gaps in literature, particularly in our understanding of the biology and clinical features of postpartum anxiety, as well as the limitations of current screening tools. This Review should serve as a call to action towards a rigorous and coordinated study of postpartum anxiety.

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. Response to letter regarding maternal and fetal outcomes across hypertensive pregnancy subtypes. *Int J Cardiol Cardiovasc Risk Prev* 2025;27:200506. PMID: 41036184. Full Text

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Cardiology/Cardiovascular Research
**Aurora L**, **Gorgis S**, **Gandolfo C**, Sadiq O, Gakhal G, **Jacobsen G**, and **Ananthasubramaniam K**. Impact of routine repeat echocardiograms in patients hospitalized with acute decompensated heart failure without clear secondary cause. *Int J Cardiovasc Imaging* 2025; Epub ahead of print. PMID: 40897903. Full Text

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Transthoracic echocardiography (TTE) at the time of acute decompensated heart failure (ADHF) may reveal significant structural and hemodynamic abnormalities that can guide clinical management. However, the impact of routine repeat TTE in uncomplicated ADHF re-admissions is yet to be established. We studied patients with repeat TTE at the time of rehospitalization for ADHF to determine downstream clinical impact. In a single center retrospective study, 410 adult patients with 2 ADHF admissions within 1 year were studied. 185 patients met inclusion criteria. Demographics, key echocardiography parameters and clinical changes were collected between first and second TTE. The study population comprised predominantly of Caucasians (55.7%) and males (53%). Non-ischemic cardiomyopathy was the principal etiology of heart failure. Between first and second TTE, there were no statistically significant changes noted in left ventricular ejection fraction, right ventricular systolic pressure, right atrial pressure, E/e ratio, or diastolic function. Right ventricular function was noted to significantly worsen as seen on the second TTE ($p < 0.001$). Mitral and aortic regurgitation was noted to be less severe in the repeat TTE group ($p = 0.030$ and $p = 0.047$, respectively). The predominant impact of repeat TTE in rehospitalized ADHF patients was medication changes rather than significant interventions, such

as advanced imaging or invasive procedures. Our study demonstrates that clinicians should focus on reserving utilization of repeat TTE in uncomplicated ADHF readmissions to those not responding to standard medical optimization including diuresis. Major effect on downstream interventions and new diagnosis is not significantly impacted by repeating TTE.

Cardiology/Cardiovascular Research
**Engel Gonzalez P**, and Bortnick AE. Big MAC on the Interventional Menu. *J Soc Cardiovasc Angiogr Interv* 2025;4(8):103860. PMID: 41019897. Full Text

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Cardiology/Cardiovascular Research
Ghorbanzadeh A, Lane C, Al-Abcha A, Ortega-Macias A, Eleid M, **Wang DD**, George I, Kodali S, Tommaso CL, Krause P, Berger R, Palacios I, Makkar R, Satler L, Kaptzan T, Lewis B, Thaden J, Oh J, Hahn RT, Rihal C, and Guerrero M. Outcomes of Iatrogenic Atrial Septal Defect Closure After Transseptal Transcatheter Mitral Valve Replacement in the Mitral Implantation of Transcatheter Valves (MITRAL) Trial. *Struct Heart* 2025;9(10):100482. PMID: 40994662. Full Text

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BACKGROUND: The long-term hemodynamic consequences of iatrogenic atrial septum defect (iASD) after transseptal (TS) transcatheter mitral valve replacement (TMVR) are unknown. The objective of this study was to compare the clinical outcomes of patients who underwent iASD closure after TS TMVR in the MITRAL (Mitral Implantation of TRAnscatheter vaLves) trial. METHODS: The MITRAL trial enrolled high-surgical-risk patients with severe mitral annular calcification treated with valve-in-mitral annular calcification (ViMAC), failed surgical repair with annuloplasty ring treated with mitral valve-in-ring (MViR), or failed surgical mitral bioprosthesis treated with mitral valve-in-valve (MViV). RESULTS: Ninety-one patients were prospectively enrolled between February 2015 and December 2017, at 13 US sites (MViV = 30, MViR = 30, ViMAC = 31). Seventy-five of them were treated with TS access (MViV = 30, MViR = 30, and ViMAC = 15), of which 16 patients underwent iASD closure during or after the index procedure (MViV = 3, MViR = 7, ViMAC = 6). Closure of the iASDs was left to the operator's discretion, and the reason in most patients was the presence of large left-to-right shunt. Patients who underwent closure of iASD were a sicker population at baseline with more severe symptoms (87.5% with New York Heart Association functional class III-IV, compared to 81.4% in non-iASD closure group, $p = 0.02$), higher rate of recent heart failure hospitalization (68.8% vs. 30.5%; $p = 0.01$) and lower 6-minute walk test distance (110 m vs. 214 m; $p = 0.002$). These patients also had longer length of stay after TMVR compared with patients who did not undergo iASD closure (8 vs. 4 days, $p < 0.001$). Despite these differences at baseline and requiring longer hospital stays, there was no significant difference in mortality, New York Heart Association class, 6-minute walk test distance, or heart failure hospitalization at 5 years. CONCLUSIONS: Patients who underwent iASD closure were more symptomatic at baseline, had decreased functional exercise capacity and required longer length of stay after TMVR. Despite these differences at baseline, 5-year outcomes were similar between groups.

Cardiology/Cardiovascular Research

Hussain Y, Malhotra S, Sperry BW, Shu F, **Ananthasubramaniam K**, Desai U, Egolum U, Fernandez J, Freimer M, Mauricio E, Quan D, Small R, Capocelli K, Roblin S, Bender S, Jay PY, Yureneva E, and Zolty R. Impact of patisiran on polyneuropathy of hereditary transthyretin amyloidosis in patients with a V122I or T60A variant: a phase IV multicenter study. *Ann Med* 2025;57(1):2537347. PMID: 40974604. Full Text

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BACKGROUND: This study assessed the effectiveness and safety of patisiran in patients with V122I/T60A variant transthyretin (ATTRv) amyloidosis with polyneuropathy. These variants have been under-represented in previous trials of gene-silencing agents. METHODS: This was a multicenter, phase IV study conducted at 27 sites in the USA. Patients were ≥ 18 years, diagnosed with ATTRv amyloidosis with polyneuropathy and a documented V122I or T60A variant. Patisiran-treated patients were enrolled prospectively, ambispectively, and retrospectively. The primary endpoint was the proportion of patients with a stable or improved polyneuropathy disability (PND) score at 12 months vs. baseline. Safety was monitored throughout the trial. RESULTS: Sixty-seven patients were enrolled, of whom 58 received ≥ 1 dose of patisiran. In the efficacy population, 42/45 (93.3%) patients demonstrated stable or improved PND scores from baseline to Month 12. Patients also showed stable or improved quality of life, health status, autonomic symptoms, and cardiac function vs. baseline. Adverse events occurred in 13/42 (31.0%) patients in the prospective and ambispective cohorts; most were mild or moderate. No deaths or cardiac hospitalizations were considered related to patisiran. CONCLUSIONS: Patisiran demonstrated a consistent positive effect across multiple endpoints in patients with V122I/T60A ATTRv amyloidosis, including polyneuropathy manifestations.

Cardiology/Cardiovascular Research

Kandzari DE, **Alqarqaz M**, Nicholson WJ, Kearney KE, Buller CE, Cristea E, and Lansky AJ. Clinical Experience With a Novel Perfusion Balloon Catheter in Patients With Coronary Artery Perforation: Primary Results From the Ringer Clinical Study. *J Soc Cardiovasc Angiogr Interv* 2025;4(7):103575. PMID: 40933123. Full Text

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BACKGROUND: The Ringer perfusion catheter (Teleflex) features a novel design with a spiral-shaped inflatable balloon that approximates a hollow cylinder when inflated to manage hemorrhage associated with coronary artery perforation (CAP) during percutaneous coronary intervention while enabling distal

perfusion. METHODS: In a multicenter, prospective, single-arm study, the safety and efficacy of using the Ringer device in the treatment of CAP were assessed. The primary efficacy end point included successful Ringer delivery across the perforation site, angiographic confirmation of no extravasation with balloon inflation, and demonstration of antegrade coronary flow. The primary safety end point was freedom from device-related thrombosis and coronary dissection. Clinical and angiographic outcomes were independently adjudicated. RESULTS: Among 30 patients with CAP, lesion characteristics included: chronic total occlusion, 50%; severe calcification, 63.3%; lesion length 34.1 ± 23.4 mm. Ellis type II and III perforations occurred in 50% and 30% of patients, respectively. For all patients, the primary efficacy end point was 73.3% by intention to treat analysis. However, among the 26 patients with successful Ringer delivery across the perforation site, the primary end point was 84.6%. In this latter group, acute resolution of contrast extravasation was 84.6%, and maintenance of thrombolysis in myocardial infarction 2/3 antegrade flow during device inflation was 100%. No device-related safety events were observed. CONCLUSIONS: Treatment of CAP with a novel perfusion balloon catheter achieved favorable rates of deliverability and reduction in hemorrhage while maintaining antegrade flow. These results demonstrate that the Ringer perfusion catheter is a safe and effective method to manage CAP until definitive treatment is decided.

Cardiology/Cardiovascular Research

**Kheyrbek M**, **Alkehef Y**, **Alalwan Y**, **Mohamad N**, and **Mesiha N**. When Pain Puts Your Heart in the Fast Lane: A Case of Ventricular Tachycardia Induced by Pain From Rib Fracture. *Cureus* 2025;17(8):e90768. PMID: 40984896. Full Text

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Repetitive monomorphic ventricular tachycardia (RMVT) is the most common form of idiopathic ventricular tachycardia. It usually happens in patients with no history of cardiac disease. Many triggers have been described in the literature, specifically high catecholamine states such as surgery or acute illness. Here, we present a young patient with no past medical history who presented with acute onset right-sided upper back pain. An electrocardiogram (ECG) in the emergency room showed a wide QRS complex tachycardia with a left bundle branch morphology. The echocardiogram was significant for a reduced ejection fraction (EF) with severe global hypokinesis. She was evaluated by electrophysiology, who recommended initiating metoprolol tartrate, as the working diagnosis was thought to be RMVT. She underwent cardiac catheterization, which showed non-obstructive coronary artery disease (CAD). Upon further evaluation, she was found to have right-sided rib fractures that were not seen on the initial workup. Pain from the rib fracture was thought to be the triggering factor for her arrhythmia. Her tachycardia was resolved with beta blockers. The patient was discharged in a stable condition with electrophysiology follow-up for considering ablation.

Cardiology/Cardiovascular Research

Madder RD, Seth M, Sukul D, Yelavarthy P, **Pielsticker E**, Gribar J, Kumar S, Zainea M, Croce K, Shlofmitz E, Wanamaker B, and Gurm HS. Statewide Initiative to Increase Intracoronary Imaging Optimization in PCI: A Report From the BMC2 Registry. *J Soc Cardiovasc Angiogr Interv* 2025;4(7):103710. PMID: 40933111. Full Text

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BACKGROUND: This study assessed the temporal trend in intracoronary imaging (ICI)-guided percutaneous coronary intervention (PCI) concurrent with the implementation of a statewide quality improvement initiative to increase ICI use. METHODS: The Blue Cross Blue Shield of Michigan Cardiovascular Consortium implemented a formal initiative to increase ICI use for PCI optimization in the state of Michigan between 2020 and 2023. The initiative included focused education for physicians, reporting of comparative institution-level ICI use, and tracking of ICI use as a performance metric. The primary measure of interest was the use of ICI to optimize PCI. A hierarchical Bayesian regression model was created to assess the increase in ICI use over time. The year in which a PCI was performed was included as a variable in the model to delineate the impact of time on the odds of ICI use. RESULTS: Over the 5-year study period, a total of 140,739 PCIs were performed at 48 nonfederal hospitals in Michigan and represented the study population. A progressive and significant increase in ICI use to optimize PCI was observed from 7.3% in the first year to 44.0% in the fifth year of the study (P < .001 for trend). Significant increases in ICI use were observed for all key subgroups including PCI in left main disease (19.3% to 78.5%; P < .001), stent thrombosis (13.6% to 61.4%; P < .001), and in-stent restenosis (8.7% to 50.6%; P < .001). Each 1-year increase in time was associated with a significant increase in ICI use (adjusted odds ratio, 1.98; 95% credible interval, 1.95-2.00). CONCLUSIONS: Concurrent with a statewide quality improvement initiative, a significant increase in ICI use to optimize PCI was observed among patients undergoing PCI in the state of Michigan.

Cardiology/Cardiovascular Research

Magouliotis DE, Topcu AC, Estrada Mendoza RM, **Dabir RR**, Clark MJ, Pruitt AL, Pagani FD, and Yang B. A Statewide Quality Initiative to Promote Aortic Annular Enlargement: Leading An Evolving Paradigm Shift. *Ann Thorac Surg* 2025; Epub ahead of print. PMID: 40953788. Full Text

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BACKGROUND: Aortic annular enlargement (AAE) represents an important adjunct strategy during aortic valve replacement (AVR) enabling implantation of larger-size prosthesis to prevent patient-prosthesis mismatch. This study evaluates the results of a statewide quality improvement intervention (QII) to increase AAE adoption, including the novel "Y-incision" technique. METHODS: Using The Society of Thoracic Surgeons database, we identified patients undergoing AVR with or without AAE from January 2018 to December 2023, excluding emergent and endocarditis cases. A QII was initiated in September 2021 and again, May 2023 featuring wet-lab training in AAE techniques. Patients were categorized into pre-QII (before September 2021) and post-QII groups. Primary endpoints were AVR+AAE incidence and median prosthesis size; secondary endpoints included 30-day mortality, transfusions, and morbidity. Sensitivity analyses were performed on isolated AVR+AAE cases. RESULTS: Totally, 817 patients were included (pre-QII: 330; post-QII: 487) and 11.6% of the audited operative notes were reassigned to the QII "Y-incision" subgroup. Post-QII patients showed increased AVR+AAE incidence (7% vs. 19%; p<0.001), with isolated AVR+AAE cases rising from 8% to 23% (p<0.001). Median prosthesis size increased from 23 to 25 (p<0.001). "Y-incision" adoption rose significantly (20% vs. 70%; p<0.001), with more surgeons implementing the technique in the post-QII group (18 vs. 35). No significant differences were observed in secondary endpoints. Sensitivity analyses confirmed findings. CONCLUSIONS: A pilot

QII enhanced AAE adoption during AVR, leading to larger AV prosthesis size without a significant increase in morbidity/mortality. Future research should explore mid- and long-term benefits on patient outcomes, including quality of life and survival.

Cardiology/Cardiovascular Research

Mangner N, Sharma SK, O'Connor C, **Kaki A**, Dangas GD, Moses JW, Mahmud E, Tarantini G, Achenbach S, Pocock SJ, **O'Neill WW**, Grines CL, Lansky AJ, Wollmuth JR, Narula J, Karmpaliotis DI, Faraz HA, **Basir MB**, Bharadwaj AS, Ali ZA, Simonton C, Bilazarian SD, Kapur NK, Chapman RC, Bentley D, Popma JJ, Maehara A, Windecker S, and Stone GW. Mechanical circulatory support in high-risk elective PCI: rationale and design of the PROTECT IV trial. *EuroIntervention* 2025; Epub ahead of print. PMID: 41024656. Full Text

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Coronary artery disease (CAD) is the leading cause of heart failure with reduced ejection fraction (HFrEF). Coronary artery bypass grafting (CABG) improves long-term mortality in HFrEF. Percutaneous coronary intervention (PCI) is often performed as an alternative to CABG in patients at high surgical risk. However, in patients with HFrEF and limited myocardial reserve, PCI may result in haemodynamic instability, increasing risk and precluding optimal revascularisation. Mechanical circulatory support (MCS) during high-risk PCI may enhance haemodynamic stability during the procedure and enable complete revascularisation. We thus performed the PROTECT IV trial to determine whether PCI with routine use of the Impella CP microaxial flow pump improves early and late outcomes in patients with HFrEF and complex CAD compared with PCI with or without use of an intra-aortic balloon pump (IABP). PROTECT IV is a prospective, multicentre, randomised, parallel-controlled, open-label, superiority trial with an adaptive design. Patients with complex CAD and left ventricular ejection fraction ≤40% (n=1,252) deemed at excessive surgical risk for bypass grafting by the Heart Team will be randomised in a 1:1 ratio to PCI with Impella CP versus PCI with or without an IABP. The primary endpoint is the composite of all-cause death, stroke, myocardial infarction, unplanned clinically driven revascularisation, durable left ventricular assist device implant or heart transplant, or other hospitalisation for cardiovascular causes at 3-year

follow-up, with at least 1-year follow-up in all patients. Prespecified substudies will evaluate the impact of MCS on renal function, the procedural role of right heart catheterisation, and the utility of myocardial viability assessment. The PROTECT IV trial will determine whether routine MCS with Impella CP during high-risk PCI improves the prognosis of patients with complex CAD and HFrEF.

Cardiology/Cardiovascular Research
**McClellan B**, **Govil D**, **Sherman A**, and **Bradley C**. Early Recognition and Management of Arrhythmogenic Right Ventricular Cardiomyopathy in a Young Athlete: A Case Report Highlighting the Role of Multimodal Diagnosis and Preventive Implantable Cardioverter Defibrillator (ICD) Therapy. *Cureus* 2025;17(8):e90736. PMID: 40984939. Full Text

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Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) is a rare inherited cardiomyopathy marked by fibrofatty replacement of right ventricular (RV) myocardium, leading to electrical instability and increased risk for ventricular arrhythmias and sudden cardiac death (SCD). ARVC is typically inherited in an autosomal dominant pattern and often involves mutations in desmosomal proteins such as plakophilin-2 (PKP2). Clinical presentation can vary from asymptomatic to life-threatening arrhythmias, particularly among young athletes. This case emphasizes the importance of early detection and intervention in patients with ARVC. A 21-year-old previously healthy male presented with recurrent exertional syncope. Initial ECG demonstrated sinus rhythm with T-wave inversions in leads V1-V3. Coronary CT angiography and resting echocardiography were normal. However, the stress electrocardiogram revealed frequent premature ventricular complexes (PVCs) with a left bundle branch block morphology. Ambulatory event monitoring detected over 500 monomorphic PVCs in a 24-hour period. Cardiac MRI demonstrated mildly reduced RVEF (39%) with regional dyskinesia, meeting major diagnostic criteria per the 2010 Task Force Criteria for ARVC. Genetic testing confirmed a heterozygous pathogenic mutation (c.1689-1G>C) in the PKP2 gene. The patient was started on beta-blockers and underwent implantation of a single-chamber implantable cardioverter defibrillator (ICD) due to elevated arrhythmic risk. Post-implantation, the ICD successfully terminated three episodes of ventricular tachycardia, highlighting its life-saving role. This case underscores the necessity for a high index of suspicion when evaluating young patients with unexplained syncope or arrhythmias. Diagnosis of ARVC requires integration of clinical, electrocardiographic, imaging, and genetic data. Early diagnosis and prompt management, including activity modification, pharmacologic therapy, and ICD implantation, are critical to mitigating the risk of SCD. Genetic testing and vigilant follow-up remain essential components in the care of ARVC patients.

Cardiology/Cardiovascular Research
**Memon M**, Christenson RH, **Jacobsen G**, Apple FS, Singer AJ, Limkakeng AT, Jr., Peacock WF, deFilippi CR, **Miller JB**, and **McCord J**. Utility of N-Terminal Pro-B-Type Natriuretic Peptide -to-Troponin and BNP-to-Troponin Ratios for Differentiating Type 1 from Type 2 Myocardial Infarction: A HIGH-US Sub-Study. *Crit Pathw Cardiol* 2025; Epub ahead of print. PMID: 40997263. Full Text

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BACKGROUND: Differentiating type 1 myocardial infarction (T1-MI) from type 2 MI (T2-MI) remains a diagnostic challenge, even with the availability of high-sensitivity cardiac troponin assays. This study explored whether NT-proBNP, BNP, and their respective ratios to troponin could enhance the ability to distinguish between these MI subtypes. METHODS: As a HIGH-US sub-study, we examined data from

280 patients diagnosed with non-ST elevation myocardial infarction (172 with T1-MI and 108 with T2-MI). We assessed NT-proBNP, BNP, hs-cTnI, and their ratios as potential discriminative biomarkers. Diagnostic accuracy was evaluated using receiver operating characteristic (ROC) curves. RESULTS: NT-proBNP levels were markedly elevated in T2-MI patients compared to those with T1-MI (mean 10,327±12,923 vs 4,675±11,740 ng/L; P=0.006). Conversely, hs-cTnI concentrations were higher in T1-MI (1.4±5.1 vs 0.5±1.1 ng/L; P=0.030). Notably, the NT-proBNP-to-troponin ratio was more than three times greater in T2-MI cases (94,880±152,648 vs 24,209±78,727; P=0.007). NT-proBNP alone demonstrated fair discriminatory capacity (AUC 0.717, 95% CI 0.578-0.856), closely matching the NT-proBNP-to-troponin ratio (AUC 0.720, 95% CI 0.566-0.873). In contrast, BNP and the BNP-to-troponin ratio offered lower diagnostic values. Mean BNP levels were 505.4 ±576.6 ng/L for those with T2-MI and 437.1 ±738.8 ng/L for patients with T1-MI. BNP-to-troponin ratio showed a poor discrimination for the 2 MI types (AUC, 0.660; 95% CI, 0.532-0.789). CONCLUSIONS: Both NT-proBNP and its ratio to troponin show potential in differentiating T1-MI from T2-MI, reflecting distinct underlying pathophysiological processes. Given its comparable performance to the ratio, NT-proBNP alone may serve as a practical and cost-effective standalone marker. These findings support the hypothesis that incorporating NT-proBNP testing into routine clinical workflows may better informs the management of patients with suspected MI.

Cardiology/Cardiovascular Research
**Memon M**, **Sabra M**, and **Khan AA**. Precision in Action: Using Intracardiac Echocardiography for Targeted Removal of a Large Lead-Related Vegetation in a Patient With Infective Endocarditis. *J Arrhythm* 2025;41(5):e70192. PMID: 40950384. Full Text

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BACKGROUND: Lead-related infective endocarditis is a serious complication of implantable cardioverter-defibrillators (ICDs), especially in patients with advanced heart failure who are poor surgical candidates. Management of large lead-associated vegetations remains a clinical challenge. METHODS: We present the case of a 54-year-old woman with ischemic cardiomyopathy and recurrent ICD complications who developed bacteremia and infective endocarditis with vegetations on the aortic valve and a 1.5 × 1.3 cm mass on the right ventricular lead. Given her poor surgical candidacy due to worsening heart failure, a percutaneous approach was pursued. RESULTS: The patient underwent successful intracardiac echocardiography (ICE)-guided catheter-based vegetation removal using a vacuum-assisted aspiration system, followed by transvenous lead extraction. The procedure was well tolerated, and the patient demonstrated clinical improvement post intervention. CONCLUSIONS: This case illustrates the utility of ICE-guided percutaneous aspiration and lead extraction for managing large lead-related vegetations in patients with infective endocarditis who are not candidates for surgery.

Cardiology/Cardiovascular Research
**Obeidat L**, **Fadel R**, **Gupta K**, **Naimi A**, **Ronchetto E**, **Ama S**, **Helaly M**, **Malick A**, **Jamil D**, **Ananthasubramaniam K**, and **Azzo Z**. What is the Diagnostic Utility of Cardiac Magnetic Resonance Imaging in Unselected Patients with Premature Ventricular Contractions and Non-Sustained Ventricular Tachycardia? *Am J Cardiol* 2025; Epub ahead of print. PMID: 41016532. Full Text

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PURPOSE: Premature ventricular contractions (PVCs) and non-sustained ventricular tachycardia (NSVT) are common arrhythmias that may signal underlying structural heart disease (SHD). Cardiac magnetic resonance imaging (CMR) has emerged as a valuable tool for detecting myocardial abnormalities in this population. This study aimed to evaluate the diagnostic utility of CMR in patients with PVCs/NSVT and identify clinical predictors of pathologic late gadolinium enhancement (LGE). METHODS: We retrospectively reviewed patients who underwent CMR for PVCs or NSVT between 2012 and 2023 at a single health system. The primary outcome was the presence of pathologic LGE. Clinical data were extracted using ICD-10 codes, and cardiac sarcoidosis (CS) was adjudicated by a multidisciplinary team using WASOG criteria. RESULTS: Among 553 patients (mean age 61.1 ± 14.6 years; 40.7% female), pathologic LGE was identified in 214 (38.6%). Patients with LGE were older and had a greater burden of comorbidities. On multivariable analysis, independent risk factors for LGE included age (aOR 1.04, p=0.001), male sex (aOR 2.37, p<0.001), heart failure (aOR 2.53, p<0.001), and polymorphic PVCs (aOR 1.94, p=0.015). Among patients with LGE, 12.6% had highly probable CS. Other diagnoses included non-ischemic cardiomyopathy (53.7%), ischemic cardiomyopathy (11.7%), and idiopathic (34.6%). CONCLUSION: CMR frequently detects clinically significant myocardial abnormalities in patients with PVCs or NSVT, particularly in those with high-risk features. In this real-world study, nearly 40% of patients had LGE on CMR. An etiology was identified in one-third of these cases. These findings can inform patient selection for CMR in clinical practice to guide diagnosis, risk stratification, and management.

Cardiology/Cardiovascular Research
Odanovic N, **Engel Gonzalez P**, and Vora AN. Is Egg Ready to Leave the Nest and Fly? *J Soc Cardiovasc Angiogr Interv* 2025;4(8):103863. PMID: 41019895. Full Text

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Cardiology/Cardiovascular Research
Sedhom R, Omer M, Khedr M, Abramov D, Bharadwaj AS, Athar A, Prasad V, **Alaswad K**, **Basir MB**, Brilakis ES, and Megaly M. Characteristics and Outcomes of ST-Segment Elevation Myocardial Infarction due to Left Main Coronary Artery Stenosis. *Am J Cardiol* 2025; Epub ahead of print. PMID: 40992531. Full Text

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There is limited data on the incidence and outcomes of ST-segment elevation myocardial infarction (STEMI) due to the left main coronary artery (LMCA) lesions. We aimed to examine the trends and outcomes of STEMI due to LMCA lesions. The Nationwide Readmissions Database was utilized to identify hospitalizations with LMCA STEMI between January 2016 and December 2022. The primary outcome was all-cause in-hospital mortality during index admission. Among 1,528,764 weighted hospitalizations with STEMI from 2016 to 2022, 4,885 (0.3%) were due to LMCA lesions, of which 2,156 (44.1%) had cardiogenic shock (CS). The number of LMCA STEMI hospitalizations and the incidence of CS increased over time. Mechanical circulatory support was used in 78.8% of the patients with LMCA STEMI and CS, with intra-aortic balloon pump being the most common modality (63%). Impella utilization increased from 4.5% in Q1 2016 to 34% in Q4 2022. Revascularization was performed in 78.2% of cases, with percutaneous coronary intervention (PCI) being the most common revascularization modality (62.1%). Among those who had PCI, intravascular imaging (IVI) was used in 18.3%, with a significant increase from 9.6% in Q1 2016 to 26.3% in Q4 2022. All-cause in-hospital mortality was 25.5% and was significantly higher among CS patients (43.4% vs. 11.4%, P<0.001). In conclusion, the incidence of LMCA STEMI increased from 2016 to 2022 with nearly half of the patients developing CS. IVI use in LMCA PCI was low (18.3%) but increased over time. More than 1 in 4 patients with LMCA STEMI died during the index hospitalization.

Cardiology/Cardiovascular Research

Taggart C, Ferry AV, Chapman AR, Schulberg SD, Bularga A, Wereski R, Boeddinghaus J, Kimenai DM, Lowry MTH, Chew DP, Cullen L, Daniels LB, Devereaux PJ, French J, Gaggin HK, Huynh T, Jacquin L, Jaffe AS, Jernberg T, Koronowski R, McCarthy C, **McCord J**, Mamas MA, Mickley H, Morrow DA, Mueller C, Newby LK, Parsonage W, Raphael CE, Smer A, Smith SW, Sandoval Y, Smilowitz NR, White H, Eggers KM, Lindahl B, Thygesen K, and Mills NL. The assessment and management of patients with type 2 myocardial infarction: an international Delphi study. *Eur Heart J Qual Care Clin Outcomes* 2025; Epub ahead of print. PMID: 40905366. Full Text

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AIMS: Type 2 myocardial infarction due to myocardial oxygen supply-demand imbalance is associated with poor outcomes. There are no guidelines to inform care for these patients. The consensus on the assessment and management of type 2 myocardial infarction is gained. METHODS AND RESULTS: An international e-Delphi study including experts in type 2 myocardial infarction identified through systematic review was conducted. Participants were asked to describe their approach to (i) definition and diagnosis, (ii) risk stratification, (iii) assessment of coronary artery disease and cardiac function, (iv) specialty management, (v) treatment and secondary prevention, and (vi) communication and rehabilitation. Statements generated in round one were circulated, with consensus defined a priori as ≥70% agreement on a 5-point Likert scale. Where no consensus was reached, statements were amended and recirculated for a final round. The response rate was 56% (38/68), 54% (37/68), and 72% (49/68) in the first, second, and third rounds, respectively. Following the first round, 67 unique statements were generated across six domains. Overall, consensus was achieved on 64% (43/67) of statements. Consensus was achieved for 42% (5/12) of statements on the diagnosis of type 2 myocardial infarction, 75% (3/4) on risk stratification, 50% (9/18) on the assessment of coronary artery disease and cardiac function, 60% (6/10), on specialty management, 100% (9/9) on treatment and secondary prevention, and 79% (11/15) on communication and rehabilitation. CONCLUSION: Consensus was obtained across a number of domains for the assessment and management of patients with type 2 myocardial infarction. However, there was limited agreement amongst experts on the diagnostic criteria, which may benefit from refinement.

Cardiology/Cardiovascular Research

**Vuppuluri N**, and **Shakir A**. Synchronizing the Beat: The Art and Science of Intracardiac Device Implantation. *J Soc Cardiovasc Angiogr Interv* 2025;4(7):103717. PMID: 40933115. Full Text

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This is the case report of a 90-year-old woman with multiple prior valvular interventions and severe tricuspid regurgitation who underwent successful percutaneous tricuspid valve replacement with an EVOQUE bioprosthesis (Edwards Lifesciences). Despite initial success, she developed a right bundle branch block and high-degree atrioventricular block resulting in a traumatic syncopal episode, necessitating leadless pacemaker insertion. This case highlights the advancements in valvular interventions and intracardiac devices and the impact they have had in transforming the field of structural heart disease. We discuss the new challenges for interventionalists and electrophysiologists in device selection and the potential benefits of leadless pacemakers in patients with complex cardiac histories.

Cardiology/Cardiovascular Research

Wu C, Joseph S, Devireddy R, Kaldas M, Zlatopolsky M, **Qaqish O**, Gong YC, Blaceri S, Saad C, Harder WE, Saab FA, Kambhatla S, and Kondur A. A Systematic Analysis of Coronary to Pulmonary Artery Fistula and Its Associated Aneurysm in Adults. *Interdiscip Cardiovasc Thorac Surg* 2025;40(9). PMID: 40986421. Full Text

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OBJECTIVES: We conducted a systematic review to evaluate the clinical features, diagnosis, and treatment of coronary artery to pulmonary artery fistula (CPAF) and its associated aneurysms. METHODS: Our search encompassed MEDLINE/PubMed, Scopus, Google Scholar, and the Cochrane Collaboration Database from 1970 to 2025. RESULTS: A total of 461 cases were analysed. The volume of publications steadily increased after 2010. The left anterior descending coronary artery was the most common site of origin for CPAF. A total of 457 cases underwent coronary angiography confirming CPAF, with computed tomography coronary angiography being the most frequently used non-invasive imaging modality (190 cases, 41.2%). Stress tests were conducted in 78 cases (16.9%), revealing a coronary steal phenomenon associated with CPAF. Particularly, when comparing aneurysm CPAF to non-aneurysm CPAF, we found that older age is an independent risk factor for developing an aneurysm. For interventions, the symptomatic patients were more likely to close the fistula. We identified that 218 cases (49.7%) underwent surgical treatment, while 121 cases (27.6%) received percutaneous embolization. There were 8 reported deaths, resulting in a mortality rate of 1.8%. CONCLUSIONS: The clinical presentations of CPAF are often non-diagnostic. Computed tomography coronary angiography is the preferred method for visualizing the fistulas and their surrounding structures. Surgical treatment is beneficial in cases of aneurysm CPAF or with other surgical indications. Transcatheter closure of CPAF may be considered for selected individuals with favourable anatomy (PROSPERO Number CRD42025643603). CLINICAL REGISTRATION NUMBER: PROSPERO Number CRD42025643603.

Center for Health Policy and Health Services Research

**Lockhart E**, **Llamocca E**, **Kahn G**, **Loree A**, and Turner D. Social Determinants of Health and HIV Diagnosis Rates in U.S. Counties, Comparing Ending the Epidemic (EHE) and Non-EHE Priority Jurisdictions. *AIDS Behav* 2025; Epub ahead of print. PMID: 40920250. Full Text

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In the U.S., HIV diagnoses have remained steady over the past decade - despite the availability of condoms and pre-exposure prophylaxis. Factors such as adverse Social Determinants of Health (SDoH) may contribute to the sustained HIV diagnosis rate. This study sought to identify SDoH factors associated with HIV diagnosis rates in U.S. counties and between Ending the Epidemic (EHE) priority jurisdictions and non-EHE jurisdictions. We obtained county-level data from publicly available sources. We fit Poisson regression models to estimate associations between separate county-level SDoH factors and county-level HIV diagnosis rates among 344 U.S. counties and 82 EHE priority jurisdictions. Among all U.S. counties, five factors were associated with HIV diagnosis rates. In all U.S. counties, higher percent of renter-occupied housing with rent at least 30% of household income, percent of population with no health insurance, presence of medically underserved area, and percent of housing units that are overcrowded were associated with HIV diagnosis rates. For three factors (percent of populations with less than a high school education, Index of Dissimilarity, and number of social organizations), associations with HIV

diagnosis rates were significantly different between non-EHE and EHE priority jurisdictions. Future research should examine SDoH drivers of HIV diagnoses, including how they impact HIV prevention efforts. Long term, these efforts can help develop novel interventions to reduce HIV transmission.

Center for Health Policy and Health Services Research
Lopez-Arvizu C, Steelesmith DL, Hand BN, Huang R, Thompson AJ, **Llamocca EN**, Quinn BA, Fontanella CA, and Campo JV. Correlates of Deliberate Self-Harm in Youth With Autism and/or Intellectual Disability. *JAACAP Open* 2025;3(3):477-484. PMID: 40922768. Full Text

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OBJECTIVE: To identify correlates of deliberate self-harm (DSH) in youth with autism and/or intellectual disability (ID). METHOD: This retrospective longitudinal cohort analysis used claims data for youth ages 5 to 24 years continuously enrolled in Medicaid in a midwestern state for 6 months and diagnosed with autism and/or ID between 2010 and 2020 (N = 41,230). Cox proportional hazards regression examined associations between demographic and clinical variables and time to DSH for study cohorts with autism and/or ID. RESULTS: Autism was diagnosed in 34.3% of the sample, ID was diagnosed in 30.6%, and both autism and ID were diagnosed in 35.1%. Sample youth were predominantly male (73.4%) and had an internalizing (74.8%) or externalizing (62.1%) mental health condition. At least 1 DSH event was identified for 734 youths (2.6%) with autism and 686 youths (2.7%) with ID during follow-up. Increased risk of DSH was associated with older age; female sex; history of abuse or neglect; and co-occurring externalizing problems, internalizing problems, substance use, and thought problems for the autism cohort and ID cohort and with the presence of a chronic complex medical condition in the autism cohort. Risk of DSH was significantly lower for youth with moderate ID and youth eligible for Medicaid via disability and foster care. CONCLUSION: Risk factors for DSH in youth with autism and ID are similar to those in neurotypical youth and include increasing age, trauma, mental health conditions, substance use, and female sex. Clinician and consumer education regarding suicide risk and its correlates in youth with autism and ID warrants study.
This study of youth aged 5 to 24 enrolled in Ohio Medicaid found that 2.6% of youth with autism and 2.7% of youth with intellectual disabilities (ID) had at least one deliberate self-harm (DSH) event between 2010 and 2020. Youth who were older, female, had a history of abuse or neglect, and had co-occurring externalizing, internalizing, substance use, or thought problems, had increased risk for DSH. Risk of DSH was lower for youth with moderate ID and those eligible for Medicaid via disability and foster care.
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Center for Health Policy and Health Services Research
Metz VE, Palzes V, Binswanger IA, Altschuler A, Poulsen MN, **Ahmedani BK**, Andrade SE, Clark RE, Hechter RC, Horberg M, Sanchez K, Bailey SR, Stephens KA, Rubinstein AL, and Campbell CI. Risks for adverse events by sex and age after prescription opioid dose reduction. *Am J Prev Med* 2025;108085. Epub ahead of print. PMID: 40921304. Full Text

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INTRODUCTION: Prescription opioid dose reductions can raise the risk of adverse events for patients on long-term opioid therapy for non-cancer pain. Evidence on whether risks differ by age or sex is needed to support tailored clinical decision-making. METHODS: In 2024, a secondary analysis of an observational cohort study was conducted across 8 U.S. healthcare systems analyzing electronic health record and claims data from a prescription opioid registry (excluding buprenorphine prescriptions) between 1/1/2012 and 12/31/2018, including adults with stable prescription opioid use and a subsequent ≥2-month dose reduction period (n=60,040), yielding 600,234 dose reduction periods as the analytic sample. Differences in the association between dose reduction level (1-<15%, 15-<30%, 30-<100%, 100% from baseline) and potential adverse events (emergency department visits, opioid overdose, all-cause mortality, benzodiazepine prescription fills) in the month after dose reduction by sex and age group were examined by including interaction terms in logistic regression models. RESULTS: Of the 600,234 dose reduction periods, 346,733 were among women, with a mean age of 57.5 [SD=13.2] years for women and 56.7 [SD=12.1] years for men. Associations between dose reduction levels and potential adverse events did not differ significantly by sex, but differed by age for emergency department visits: patients 40-64 and ≥65 years with dose reductions of 30-<100% had lower odds compared to those aged 19-39 (adjusted ratio of odds ratios [aROR]=0.87, CI 0.80, 0.96; aROR=0.82, CI 0.74, 0.91; respectively). CONCLUSIONS: Patients under 40 may benefit from closer monitoring in the month after dose reduction, given their higher odds of an emergency department visit.

Center for Health Policy and Health Services Research
**Miller-Matero LR**, **Morris EP**, **Christopher B**, **Pappas C**, Chrusciel T, Salas J, Wilson L, Secrest S, Sullivan MD, Carpenter RW, Lustman PJ, **Ahmedani BK**, and Scherrer JF. Social Determinants of Health among Individuals Receiving Opioids for Pain Management. *Clin J Pain* 2025; Epub ahead of print. PMID: 41017040. Full Text

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OBJECTIVE: Individuals receiving opioids for pain management are at risk for negative outcomes. However, it is not clear whether social determinants of health (SDOH) predict outcomes a year after starting a prescription opioid. The purpose was to examine associations between SDOH with psychiatric-, pain-, and opioid-related outcomes at a 12-month follow-up. METHODS: Participants (N=783) with a new period of 30-90-day opioid use completed baseline and 12-month follow-up questionnaires regarding SDOH, depressive symptoms, pain severity, pain interference, and opioid use. Multivariate adjusted

models estimated the association between SDOH and outcomes. RESULTS: Participants had a mean age of 53.4 years (SD=11.9), 71.2% White race, and 69.9% women. Older age (OR=0.97; 0.95, 0.99) and Black race (OR=0.45; 0.27, 0.76) were inversely associated with depression, while being widowed/divorced/separated (OR=1.72; 1.01, 2.91) and lacking college education (OR=2.43; 1.25, 4.73) were positively associated with depression. Women (OR=1.56; 1.12, 2.18) and lower income (OR=2.09; 1.14, 3.85) were associated with greater odds of opioid use, while unemployment was associated with lower odds of opioid use at 12 months (OR=0.55; 0.34, 0.89). Older age (OR=0.95; 0.91, 0.99) was inversely associated with opioid use concerns while disability (OR=4.59; 1.60, 13.11) was positively associated. DISCUSSION: Several SDOH variables were associated with poorer functioning at baseline and 12-months after individuals were prescribed an opioid. It may be useful for clinicians to screen for SDOH to identify higher-risk individuals.

Clinical Quality and Safety

Branch-Elliman W, Chambers DA, Albin O, Batshon L, Castejon-Ramirez S, Cheng VC, Emetuche N, Datta R, Kamboj M, Krein SL, Staub M, Dassum SR, Rittmann B, Huang FS, Sreeramoju P, Stroever S, **Suleyman G**, Ting JY, Witt LS, Ziegler MJ, and Kwon JH. The life cycle of infection prevention and antimicrobial stewardship projects and interventions: the dynamic interplay of implementation and de-implementation science (Part I of II). *Infect Control Hosp Epidemiol* 2025;1-12. Epub ahead of print. PMID: 40926571. Full Text

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In Antimicrobial Stewardship and Infection Prevention and Control, programmatic goals often strive to achieve clinical benefit by practice change in the direction of doing less. Practically, this may include reducing the number of tests ordered, encouraging shorter and more narrow courses of antimicrobials, or discontinuing practices that are no longer contextually appropriate. Because promoting practice change in the direction of doing less is a critical aspect of day-to-day operations in Antimicrobial Stewardship and Infection Prevention and Control, the goals of this Society for Healthcare Epidemiology Research Committee White Paper are to provide a roadmap and framework for leveraging principles of implementation and de-implementation science in day-to-day practice. Part II of this series focuses on some practical case studies, including real-world examples of applied de-implementation science to promote discontinuation of practices that are ineffective, overused, or no longer effective.

Clinical Quality and Safety
Branch-Elliman W, Reyes Dassum S, Stroever S, Albin O, Batshon L, Castejon-Ramirez S, Cheng VC, Emetuche N, Datta R, Kamboj M, Krein SL, Staub M, Rittmann B, Scaggs Huang F, Sreeramoju P, **Suleyman G**, Ting JY, Witt LS, Ziegler MJ, and Kwon JH. Leveraging de-implementation science to promote infection prevention and stewardship: a roadmap and practical examples (Part II of II). *Infect Control Hosp Epidemiol* 2025;1-11. Epub ahead of print. PMID: 40926570. Full Text

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De-implementation of established practices is a common challenge in infection prevention and antimicrobial stewardship and a necessary part of the life cycle of healthcare quality improvement programs. Promoting de-implementation of ineffective antimicrobial use and increasingly of low-value diagnostic testing are cornerstones of stewardship practice. Principles of de-implementation science and the interplay of implementation and de-implementation are discussed in part I of this Society for Healthcare Epidemiology of America White Paper Series.In this second part of the series, we discuss a process for applying principles of de-implementation science in infection prevention and stewardship and then review some real-world examples and case studies, including a national blood culture shortage, contact precautions, and surgical and dental prophylaxis. We use these examples to demonstrate how barriers and facilitators can be mapped to evidence-informed implementation/de-implementation strategies to promote efforts to reduce low-value, ineffective, or out-of-date practices. These real-world examples highlight the need for infection prevention and stewardship programs to adapt to changing evidence, contexts, and conditions. Although barriers to practice change are often a bit different, de-implementation can sometimes be thought of as the implementation of a new program-but the new program aims to stop rather than start doing something.As the saying goes, sometimes less really is more. Medicine and public health have a strong action bias and a strong aversion to risk and uncertainty. Although our best intentions may point us to implementing more interventions, often, the best medicine instead dictates that we do less, or nothing at all. Leveraging principles of de-implementation science can help move healthcare in the right direction when interventions are low-value, ineffective, or no longer needed.

Clinical Quality and Safety

Guevara Núñez D, Morandini FN, **Suleyman G**, **Crooker K**, **Kaur J**, **Maki G**, Bocco JL, Fernández Do Porto D, **Zervos MJ**, Sola C, and Saka HA. Genomic Analysis and Virulence Features of Vibrio cholerae Non-O1/Non-O139 Harbouring CARB-Type β-Lactamases From Freshwater Bodies, Argentina. *Environ Microbiol Rep* 2025;17(5):e70181. PMID: 40997832. Full Text

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Vibrio cholerae is a globally distributed, free-living bacterium in aquatic ecosystems. While non-O1/non-O139 serogroups typically do not produce cholera toxin, they have the potential to cause diarrhoea. These strains may act as reservoirs of antibiotic resistance in rivers, lakes and oceans. Understanding their genetic resistance and virulence can shed light on their role in spreading antimicrobial resistance and their pathogenicity. In this study, we characterised 60 V. cholerae non-O1/non-O139 strains from 16 freshwater bodies located throughout the Province of Córdoba, Argentina. We found none of the strains carried cholera toxin and identified ampicillin resistance as the most prevalent phenotype. Whole genome sequencing revealed that all ampicillin-resistant strains (n = 10) carried CARB β-lactamases, leading to the identification of new CARB variants (CARB-59 to CARB-62) likely associated with the V. cholerae superintegron. Two strains were notably related and exhibited enhanced virulence due to an unusual genetic arrangement of the VPI-1 pathogenicity island, encoding both the toxin co-regulated pilus and a type VI secretion system cluster subclass i5, commonly found in non-cholera Vibrio species. These findings provide significant insights into the genetic diversity and virulent potential of ampicillin-resistant

environmental V. cholerae non-O1/non-O139 and enhance our understanding of the evolution of CARB β-lactamases within the species.

Dermatology
Burshtein J, Bunick CG, Vleugels RA, Armstrong AW, Golant AK, Schlesinger T, Strober BE, Song EJ, **Gold LS**, and Lebwohl M. Systemic Corticosteroid Use in Atopic Dermatitis: A Position Paper to Inform Safer Clinical Practice and Policy. *J Invest Dermatol* 2025; Epub ahead of print. PMID: 40914897. Full Text

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Dermatology
Callender VD, Alexis A, Desai SR, Jaleel T, **Lim HW**, Sarkar R, Taylor S, Andriessen A, Guénin S, Brown SG, 3rd, Burgess CM, Byrd AS, Cobb CBC, Dlova NC, Grimes PE, Heath CR, McMichael AJ, Miller-Monthrope Y, Okeke CAV, Weiss JS, Yoo JY, Akanji J, and Harvey VM. Beyond Fitzpatrick Skin Types: A Delphi Consensus on Key Considerations for a Universal Skin Typing Classification. *J Am Acad Dermatol* 2025; Epub ahead of print. PMID: 40902663. Full Text

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Dermatology
**Clark M**, **Wuennenberg J**, **Maghfour J**, **Jones B**, Grant-Kels JM, Jain M, **Ozog DM**, and **Kohli I**. Reflectance Confocal Microscopy for Monitoring Treatment Response in Superficial Basal Cell Carcinoma: Diagnostic Challenges Due to Scar Formation. *Clin Exp Dermatol* 2025; Epub ahead of print. PMID: 40920911. Full Text

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BACKGROUND: Reflectance confocal microscopy (RCM) criteria for in vivo diagnosis of unperturbed basal cell carcinoma (BCC) lesions have been validated and studies have reported high diagnostic sensitivity. However, a paucity of data remains regarding preservation or changes in RCM features after biopsy or treatment. OBJECTIVE: Prospectively image biopsy proven superficial BCC (sBCC) with RCM at baseline and 12 weeks post-treatment to determine clearance and identify any associated RCM features. METHODS: Ten subjects with biopsy proven sBCC completed this study. Clinical examination, dermoscopy, and RCM imaging were performed at baseline, prior to treatment, and 12 weeks post treatment with a 1064 Nd-YAG laser. Following treatment, RCM features were compared to clinical and histologic findings. RESULTS: Statistically significant changes in RCM features at baseline and follow-up included: tumor islands with hyperreflective aggregates, dark silhouettes, peripheral palisading, peritumoral clefting, and dermal inflammatory cells. Changes in nuclear streaming, fibrosis, and vasculature were not significant. LIMITATIONS: A limitation of this study is the small sample size. CONCLUSIONS: The features of nuclear streaming, fibrosis and dilated vessels may be observed during RCM imaging of biopsy proven BCC at baseline and post treatment, and should be cautiously interpreted. Additional studies are needed to further validate these findings.

Dermatology
**Gold LS**, Armstrong AW, Bissonnette R, Magnolo N, Vender RB, Sebastian M, Galimberti ML, Tsianakas A, Arnone M, Wallace P, Simon M, Riera-Monroig J, Gerdes S, Waibel J, Gonzalez-Cantero A, Schwarz B, Tada Y, Cecchini M, Ehst B, Kircik L, Kephart L, Reyes-Servin O, Edem BE, Campbell JH, Shen YK, Cresswell K, Li S, DeKlotz CMC, Nunes F, and Papp KA. Once-daily oral icotrokinra versus placebo and once-daily oral deucravacitinib in participants with moderate-to-severe plaque psoriasis (ICONIC-ADVANCE 1 & 2): two phase 3, randomised, placebo-controlled and active-comparator-controlled trials. *Lancet* 2025;406(10510):1363-1374. PMID: 40976249. Full Text

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BACKGROUND: Monoclonal antibodies targeting interleukin-23 and interleukin-12 are efficacious in treating plaque psoriasis but must be delivered via intravenous or subcutaneous injection. Here, we aimed to evaluate the efficacy and safety of icotrokinra (JNJ-77242113), a targeted oral peptide that selectively binds the interleukin-23 receptor, compared with both placebo and deucravacitinib in adults with moderate-to-severe plaque psoriasis. METHODS: The phase 3, randomised, double-blind, placebo-controlled and active-comparator-controlled ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2 trials, which are being done at 149 sites across 13 countries and 114 sites across 11 countries, respectively, randomly assigned (2:1:2 and 4:1:4, respectively) adults with moderate-to-severe plaque psoriasis diagnosed for at least 26 weeks (body-surface-area involvement ≤10%, Psoriasis Area and Severity Index [PASI] ≤12, and Investigator's Global Assessment [IGA] ≤3) to once-daily oral icotrokinra 200 mg, placebo, or deucravacitinib 6 mg; participants randomly assigned to placebo or deucravacitinib transitioned to icotrokinra at week 16 or week 24, respectively. Coprimary endpoints were proportions of participants achieving IGA 0 or 1 (clear or almost clear skin) with at least a two-grade improvement and at least 90% improvement in PASI (PASI 90) at week 16 with icotrokinra versus placebo. These studies are registered with ClinicalTrials.gov, NCT06143878 (ADVANCE 1) and NCT06220604 (ADVANCE 2), and are ongoing. FINDINGS: ICONIC-ADVANCE 1 enrolled participants from Jan 17, 2024, to May 24, 2024, and ICONIC-ADVANCE 2 enrolled participants from March 9, 2024, to June 13, 2024. Participants (ADVANCE 1: 774 of 988 patients screened; ADVANCE 2: 731 of 917 patients screened) were randomly assigned to icotrokinra (n=311 and 322), placebo (n=156 and 82), or deucravacitinib (n=307 and 327). All coprimary endpoints were met in both trials. Higher proportions of icotrokinra-treated versus placebo-treated participants achieved IGA 0 or 1 (ADVANCE 1: 213 [68%] of 311 vs 17 [11%] of 156, treatment difference 95% CI 58% [50-64]; ADVANCE 2: 227 [70%] of 322 vs seven [9%] of 82, 62% [53-69]; both p<0·0001) and PASI 90 (ADVANCE 1: 171 [55%] of 311 vs six [4%] of 156, treatment difference 95% CI 51% [44-57]; ADVANCE 2: 184 [57%] of 322 vs one [1%] of 82, 56% [48-62]; both p<0·0001) at week 16. Across studies, adverse event rates to week 16 were 303 (48%) of 632 and 136 (57%) of 237 with icotrokinra and placebo, respectively; the most common adverse events were nasopharyngitis (37 [6%] of 632 and 13 [5%] of 237) and upper respiratory tract infection (23 [4%] of 632 and eight [3%] of 237). To week 24, adverse event rates were lower than with icotrokinra (359 [57%] of 632) than deucravacitinib (411 [65%] of 634). INTERPRETATION: Icotrokinra showed superior clinical response rates versus placebo and deucravacitinib in phase 3 moderate-to-severe plaque psoriasis trials, with similar adverse event rates to

placebo. These findings suggest the potential of once-daily oral icotrokinra to provide robust efficacy and a favourable safety profile. FUNDING: Johnson & Johnson.

Dermatology

Haykal D, **Lim HW**, Dréno B, Schalka S, Berardesca E, Cartier H, and Passeron T. Beyond Sun Protection Factor: The Future of Personalized Photoprotection through Biomarkers, Artificial Intelligence, and Digital Twins. *J Invest Dermatol* 2025; Epub ahead of print. PMID: 40914896. Full Text

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Dermatology

Irvine AD, Prajapati VH, Guttman-Yassky E, Simpson EL, Papp KA, Blauvelt A, Chu CY, Hong HC, **Gold LFS**, de Bruin-Weller M, Bieber T, Kabashima K, Rosmarin D, Sancho C, Calimlim BM, Grada A, Yang Y, Wu X, Levy G, Raymundo EM, Teixeira HD, and Silverberg JI. Efficacy and Safety of Upadacitinib in Patients With Moderate-to-Severe Atopic Dermatitis: Phase 3 Randomized Clinical Trial Results Through 140 Weeks. *Am J Clin Dermatol* 2025; Epub ahead of print. PMID: 40900410. Full Text

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BACKGROUND: Upadacitinib is an oral selective Janus kinase inhibitor approved to treat moderate-to-severe atopic dermatitis (AD) in adults and adolescents; long-term efficacy and safety data beyond 1 year are needed. OBJECTIVE: The aim was to evaluate the long-term efficacy and safety of upadacitinib treatment through 140 weeks in patients with moderate-to-severe AD. METHODS: Measure Up 1 (MeUp1; NCT03569293), Measure Up 2 (MeUp2; NCT03607422), and AD Up (NCT03568318) are ongoing, phase 3, randomized clinical trials evaluating upadacitinib 15 mg (UPA15) and 30 mg (UPA30) in adults and adolescents with moderate-to-severe AD. This interim analysis evaluated efficacy and safety through week 140. At baseline, patients were randomized 1:1:1 to receive once-daily UPA15, UPA30, or placebo alone (MeUp1/2) or with concomitant topical corticosteroids (AD Up). At week 16, patients initially randomized to placebo were rerandomized 1:1 to UPA15 or UPA30. Skin and itch efficacy assessments included achievement of ≥ 75%/≥ 90%/100% improvement from baseline in Eczema Area and Severity Index (EASI 75/90/100), validated Investigator Global Assessment for AD score of clear/almost clear (vIGA-AD 0/1), and ≥ 4-point improvement from baseline in Worst Pruritus Numerical Rating Scale (ΔWP-NRS≥4). Safety assessments included incidence of treatment-emergent adverse events. RESULTS: A total of 2782 patients were randomized in MeUp1/2 or AD Up. Efficacy response rates, including optimal outcomes such as EASI 90 and WP-NRS score of 0/1, were sustained through week 140 in all three studies. At week 140, EASI 75 was achieved by 85.5%/90.5% (UPA15/UPA30; integrated MeUp1/2) and 81.5%/90.0% (UPA15/UPA30; AD Up) of patients, and vIGA-AD 0/1 was achieved by 56.6%/64.4% (UPA15/UPA30; integrated MeUp1/2) and 52.0%/56.8% (UPA15/UPA30; AD Up) of patients. Over 60% of patients across all three studies achieved ΔWP-NRS≥4 at week 140. Pooled safety data across all three studies demonstrated safety profiles consistent with 16-week and 52-week analyses. CONCLUSIONS: UPA15 and UPA30 with and without topical corticosteroids demonstrated robust, durable efficacy and a favorable safety profile through 140 weeks in adults and adolescents with moderate-to-severe AD. TRIAL REGISTRATION: Measure Up 1 (NCT03569293; https://clinicaltrials.gov/study/NCT03569293 ), Measure Up 2 (NCT03607422; https://clinicaltrials.gov/study/NCT03607422 ), and AD Up (NCT03568318; https://clinicaltrials.gov/study/NCT03568318 ).

Dermatology
**Ituarte BE**, Rosa-Nieves PM, Schissel M, Wysong A, and Lonowski SL. A Pilot Study of CO(2) Laser-Assisted Drug Delivery of Hyaluronidase for the Treatment of Scleroderma-Induced Microstomia. *J Am Acad Dermatol* 2025; Epub ahead of print. PMID: 41022328. Full Text

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Dermatology
Keddie SH, Griffiths CEM, Jemec GBE, Ezzedine K, Allen P, Ashcroft DM, Austin J, Bhose A, Bouazzi D, Breton VZ, Chang CY, Eleftheriadou V, Finken A, Kilmer J, Postigo JR, Rogers T, Saunte DML, Wright AK, **Lim HW**, and Flohr C. Grand Challenges for Skin Health Revisited: The International League of Dermatological Societies (ILDS) Skin Disease Atlases. *Br J Dermatol* 2025; Epub ahead of print. PMID: 41022647. Full Text

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Dermatology
**Levin EJ**, **Friedman BJ**, **Chaffins M**, and **Matthews NH**. Subcutaneous nodules and flexion contractures of the hands. *JAAD Case Rep* 2025;64:57-59. PMID: 40933631. Full Text

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Dermatology
**Maghfour J**, Meisenheimer J, and Kantor J. Cosmetic and functional outcomes of excisional surgical wounds healed by secondary intention: A systematic review. *JAAD Int* 2025;22:100-110. PMID: 40932884. Full Text

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BACKGROUND: Data regarding short-term and long-term cosmesis and functional outcomes of excisional surgical wounds healed by secondary intention healing (SIH) are limited. OBJECTIVE: To conduct a systematic review and assess the cosmetic and functional acceptability of SIH for acute excisional surgical wounds. METHODS: Full-text articles queried from PubMed and Embase databases between January 1964 and April 2024 with cosmetic outcome data of human subjects with acute surgical wounds healed by SIH were included. Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines were followed. RESULTS: A total of 1655 surgical wounds, of which 1518 (91.7%) healed by SIH, from 35 studies, were included in this review. The most frequent indication for SIH was a defect resulting from excision of nonmelanoma skin cancer (keratinocyte carcinoma), which was identified in 1439 (86%) of patients. Common sites for SIH included the nose (23.3%), periocular region (15.46%), and forehead (13.5%). The majority of wounds on the forehead, medial canthus, lower eyelid, nasal ala, cheeks, lips, postauricular area, and feet resulted in good to excellent cosmetic results, whereas those on the scalp, nasal dorsum, nasal tip, nasal sidewall, and chin yielded less acceptable cosmetic results. Given the baseline variability in cosmesis of primarily closed wounds in some anatomic locations, however, these data suggest the need for future prospective studies. SUMMARY: SIH may produce an acceptable cosmetic and functional outcome for selected defects and may be of clinical benefit in the appropriate setting. This must be weighed against the potentially improved cosmesis and more rapid healing seen with primarily closed defects.

Dermatology
**Maghfour J**, **Powers M**, **Wang A**, **Poisson L**, and Brian Jiang SI. Impact of clinical factors and surgical treatments on sebaceous carcinoma patients with and without Muir-Torre syndrome. *J Am Acad Dermatol* 2025; Epub ahead of print. PMID: 40902656. Full Text

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Dermatology
**Quiñonez RL**, **Mohammad TF**, and **Hamzavi I**. Hyperpigmentation After Melanocyte-Keratinocyte Transplantation Procedure in a Patient With Stable Vitiligo. *Dermatol Surg* 2025; Epub ahead of print. PMID: 40985533. Full Text

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Dermatology
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BACKGROUND: Melasma, an acquired hyperpigmentation disorder, affects individuals of all ethnicities. Its multifactorial aetiology, high recurrence rates and psychosocial impact complicate management and necessitate comprehensive, evidence-based recommendations. OBJECTIVES: The objective was to develop an international consensus on the diagnosis and management of melasma by synthesizing expert opinions and the latest scientific evidence. METHODS: This consensus was developed using a modified Delphi approach. A core group of two senior dermatologists who were experts in pigmentary disorders guided the process, and a diverse panel of 38 dermatologists with a special interest in pigmentary disorders from 11 countries (Australia, Brazil, France, India, Italy, Mexico, Philippines, South Africa, South Korea, Taiwan and the USA) participated in three rounds of surveys and discussions, under the aegis of the Pigmentary Disorders Society (PDS). A literature search of articles published between 2014 and 2024 identified key studies that were graded using the Oxford levels of evidence (2009). Consensus statements were drafted, refined and finalized based on expert feedback. Responses were assessed using a 5-point Likert scale, with predefined thresholds for high (≥75%), moderate (55%-74%) and low (<55%) agreement. RESULTS: The consensus development process started with 34 statements, and at the end of the third round of the Delphi process, 21, 4 and 1 statement reached high, moderate and low consensus, respectively. Key recommendations highlighted photoprotection with broad-spectrum sunscreens as essential, regulated and supervised use of hydroquinone-based triple combination creams as the gold standard, and alternatives such as topical azelaic acid, kojic acid and oral tranexamic acid. Adjunctive procedural therapies, such as chemical peels and microneedling, were suggested to enhance topical efficacy, while lasers were reserved for refractory cases. CONCLUSION: These recommendations aim to improve the outcomes of melasma patients globally by integrating expert opinion and evidence-based strategies. Future research should focus on evaluating emerging therapies and optimizing long-term maintenance strategies.
Melasma is a common skin condition that causes dark patches on the face. It affects people of all skin types and can have a major impact on confidence and quality of life. Treating melasma is challenging because it has many causes, tends to come back after treatment, and often requires a long-term plan. To help improve care, a group of international experts worked together with the Pigmentary Disorders Society (PDS) to develop clear recommendations for how to diagnose and manage melasma. The group included 40 dermatologists from 11 countries, and their advice was based on both published research and their clinical experience. The recommendations were created using a structured process to reach agreement on best practices. The experts agreed that daily sun protection with broad-spectrum sunscreen is essential for everyone with melasma. The most effective treatment remains hydroquinone-based triple combination creams, but these should only be used under medical supervision. Other options include topical agents such as azelaic acid and kojic acid, as well as oral tranexamic acid. Procedures like chemical peels and microneedling can be used alongside creams to improve results, while lasers should mainly be considered for patients who do not respond to other treatments. These international recommendations aim to help doctors provide more effective and consistent care for patients with melasma around the world. Further studies are needed to better understand new treatments and strategies for preventing relapses.
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Dermatology
Xu Z, Ding Y, Zhang C, Parsad D, Rodrigues M, Kumaran MS, Almutairi N, **Hamzavi I**, **Amin J**, Ghorbel HH, Xiang L, and Passeron T. Treatment of Acquired Dermal Macular Hyperpigmentation With Oral Isotretinoin: A Multi-Institutional Retrospective Study of 121 Cases. *Pigment Cell Melanoma Res* 2025;38(5):e70052. PMID: 40913266. Full Text

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The term acquired dermal macular hyperpigmentation (ADMH) was introduced to unify Riehl's melanosis (RM), lichen planus pigmentosus (LPP), and related entities. These are cosmetically distressing pigmentary disorders that pose therapeutic challenges. To investigate the efficacy and safety of oral isotretinoin in treating ADMH, we conducted a muticenter retrospective study of patients with ADMH treated with oral isotretinoin between 2014 and 2024. Patients from Australia, China, Europe, India, Middle East, North America, and North Africa were included. Patients lost to follow-up before two visits were excluded. The response was graded by a 5-point Investigator's Global Assessment (IGA) scale. A total of 121 patients were included. Most patients (64.5%) were treated with a dose of 20 mg/d for an average of 8 months. Oral isotretinoin improved the severity of pigmentation in all RM and 85 (90.4%) LPP patients, with 17 (63.0%) RM and 31 (33.0%) LPP patients achieving marked improvement. RM patients responded better than LPP patients ($p = 0.005$). Patients with localized lesions ($p = 0.0012$), disease duration of less than 5 years ($p = 0.046$ for RM, $p = 0.0272$ for LPP), Fitzpatrick skin phototypes III-VI ($p = 0.0081$), or longer duration of treatment ($p = 0.0178$) responded better. Oral isotretinoin appears to be a promising treatment modality for ADMH.

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: 40991495. 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
Zhao X, Hu SS, Lee WH, Zakrzewski JL, **Mi QS**, Rosenstein RK, Zang C, Ma X, and Xue HH. Single-cell multiomics identifies Tcf1 and Lef1 as key initiators of early thymic progenitor fate. *Sci Immunol* 2025;10(111):eadq8970. PMID: 40938954. Full Text

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Bone marrow-derived multipotent hematopoietic progenitors seed the thymus and generate early thymic progenitors (ETPs). However, the factors governing ETP formation remain poorly defined. Using single-cell RNA sequencing (scRNA-seq) and single-cell assay for transposase-accessible chromatin with sequencing (scATAC-seq), we dissected the heterogeneity of transcriptomic and chromatin accessibility landscapes in murine ETPs. Whereas Tcf1(-) ETPs exhibited higher proliferative capacity, Tcf1(+) ETPs appeared to be immediate, more robust precursors to T lineage-specified early thymocytes. Prethymic ablation of Tcf1 and its homolog Lef1 severely impaired ETP formation in vivo. Whereas ablating Tcf1 alone had limited impact, loss of both Tcf1 and Lef1 impaired transcriptional activation of Notch1 and Notch pathway effector molecules, including Hes1 and Hhex, accompanied by aberrantly induced B cell and myeloid gene programs. Acute deletion of both factors compromised Notch pathway, glycolysis, and T cell gene programs in emergent ETPs ex vivo. Thus, Tcf1 and Lef1 act upstream of the Notch pathway, functioning as prethymic initiators of ETP fate and intrathymic gatekeepers of ETP identity and T lineage potential.

Dermatology

Zou H, Teklehaimanot F, Seaba S, Bazzi M, Alkhouri F, **Boothby-Shoemaker W**, **Mansour M**, **Bardhi R**, Diaz C, and Daveluy S. Advocating for insurance coverage of keloids, alopecia, lupus, and sarcoidosis. *J Am Acad Dermatol* 2025; Epub ahead of print. PMID: 40907755. Full Text

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Diagnostic Radiology

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BACKGROUND: Sarcopenia of the psoas muscle and hypoalbuminemia indicate poor nutritional status, inflammation, and frailty in lung transplant (LT) candidates, correlating with worse post-transplant outcomes. METHODS: Retrospective study of LT recipients (2015-2023) examining the association of total psoas muscle area (TPA) and serum albumin with hospital stay, survival, and pulmonary function. RESULTS: One hundred thirty-two LT recipients (mean age 59.56 ± 10.65 years, BMI 26.73 ± 5.55 kg/m(2), 65% males), 95% underwent bilateral LT. Higher TPA was associated with shorter hospital and ICU stays ($p = 0.001$). Similarly, higher albumin levels were associated with reduced hospital and ICU stays ($p < 0.001$). Hospital survivors had higher TPA (17.5 ± 6.1 vs. 14.6 ± 5.2 cm(2), $p = 0.02$) and higher albumin levels (3.25 ± 0.73 vs. 2.75 ± 0.85 mg/dL, $p = 0.01$). Long-term survivors had higher TPA (17.8 ± 6.35 vs. 15.9 ± 5.51 cm(2), $p = 0.07$) and higher albumin levels (3.29 ± 0.75 vs. 2.97 ± 0.78 mg/dL, $p = 0.01$). On multivariate analysis, albumin and male gender remained independent predictors of hospital and long-term survival. TPA was positively associated with post-transplant pulmonary function based on FVC and FEV1 ($p < 0.001$), while albumin levels showed no association. CONCLUSION: In the present study of LT recipients, higher TPA and albumin levels were linked to shorter hospitalization, and albumin independently predicted survival. TPA, but not albumin, was associated with pulmonary function post-transplant.

Diagnostic Radiology

**Hayrapetyan H**, **Zhan Y**, and **Vummidi D**. Unusual Presentation of Acute Appendicitis: A Case Report of de Garengeot Hernia. *Cureus* 2025;17(8):e90397. PMID: 40978907. Full Text

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A de Garengeot hernia (DGH) is a rare anatomic variant involving the herniation of the appendix through the femoral canal. It is an uncommon surgical entity with diagnostic challenges. We report the case of a 63-year-old woman who presented with right inguinal region pain and swelling, in which preoperative ultrasound (US) and computed tomography (CT) identified the herniated, inflamed appendix within the canal of Nuck, which was intraoperatively found to be rather a femoral hernia. This rare case illustrates the characteristic imaging features of DGH and highlights the importance of early and accurate radiologic diagnosis for surgical planning and improved patient outcomes.

Diagnostic Radiology

Hruska CB, Hunt KN, Larson NB, **Miller PA**, Ellis RL, Shermis RB, Rauch GM, Conners AL, Gasal Spilde J, **Semaan DT**, **Siegal EC**, Zingula SN, **Mandava SR**, Martin TS, **Ahmed RK**, Whaley DH, Adrada BE, Gray LR, Mehta RA, Roll RJ, Redfern RE, O'Connor MK, and Rhodes DJ. Molecular Breast Imaging and Digital Breast Tomosynthesis for Dense Breast Screening: The Density MATTERS Trial. *Radiology* 2025;316(3):e243953. PMID: 40985829. Full Text

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Background Molecular breast imaging (MBI) relies on the functional uptake of a radiotracer, technetium 99m sestamibi, to reveal cancers that are occult on mammograms due to breast density. Purpose To assess the performance of screening MBI as a supplement to digital breast tomosynthesis (DBT) in women with dense breasts. Materials and Methods In this prospective, multiyear, multicenter trial from five sites, women with dense breasts were prospectively enrolled from 2017 to 2022 and underwent two annual screening rounds of DBT and MBI to assess the incremental cancer detection rate (CDR, reported as cancers per 1000 screenings) of supplemental MBI and to compare other performance metrics of DBT

and MBI. Results A total of 2978 participants were included. Participants had a mean age of 56.8 years ± 9.3 (SD) and a mean lifetime Tyrer-Cuzick risk of 12.0% ± 7.9 (SD). At year 1, the CDR was 5.0‰ (15 of 2978 participants) with DBT and 11.8‰ (35 of 2978 participants) with DBT plus prevalence screening MBI (incremental CDR, 6.7‰ [95% CI: 4.2, 10.6]; P < .001); the invasive CDR was 3.0‰ (nine of 2978 participants) with DBT and 7.7‰ (23 of 2978 participants) with DBT plus prevalence screening MBI (invasive incremental CDR, 4.7‰ [95% CI: 2.7, 8.1]; P < .001). At year 2, the CDR was 5.8‰ (15 of 2590 participants) with DBT and 9.3‰ (24 of 2590 participants) with DBT plus incidence screening MBI (incremental CDR, 3.5‰ [95% CI: 1.7, 6.8]; P = .001); the invasive CDR was 1.5‰ (four of 2590 participants) with DBT and 3.9‰ (10 of 2590 participants) with DBT plus incidence screening MBI (invasive incremental CDR, 2.3‰ [95% CI: 0.9, 5.3]; P = .048). The year 1 recall rate was 8.6% (255 of 2978 participants) with DBT and 17.9% (534 of 2978 participants) with DBT plus prevalence screening MBI (difference, 9.4% [95% CI: 8.4, 10.5]). The year 2 recall rate was 8.9% (231 of 2590 participants) with DBT and 13.8% (356 of 2590 participants) with DBT plus incidence screening MBI (difference, 4.8% [95% CI: 4.1, 5.7]). Twenty-nine participants had cancers detected only with MBI: 21 (72%) had invasive cancers (median size, 0.9 cm), 26 (90%) had node-negative cancers, and six (20%) had advanced cancers. The interval cancer rate was 0.7‰ (two of 2978 participants) in year 1 and 0.8‰ (two of 2590 participants) in year 2. Conclusion The addition of MBI to DBT screening increased invasive cancer detection by 2.5-fold and modestly increased the recall rate at the second screening round. © RSNA, 2025 See also the editorial by Fowler in this issue.

Diagnostic Radiology

**Turnbull J**, **Griepp DW**, **Caskey J**, **Alsalahi A**, **Desai S**, **Claus CF**, and **Griauzde J**. Middle Meningeal Artery Embolization: Poised to Become the Standard of Care for Chronic Subdural Hematoma. *World Neurosurg* 2025;124481. Epub ahead of print. PMID: 40953814. Full Text

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Emergency Medicine

Fahmy K, Chang E, and **Adams C**. Cervicogenic Headache. *Phys Med Rehabil Clin N Am* 2025. PMID: Not assigned. Full Text

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Cervicogenic headache (CGH) has proven to be an elusive diagnosis without the aid of diagnostic interventional procedures. This article highlights the key components of the clinical presentation and workup to aid the clinician in distinguishing CGH from its differential diagnoses. It also discusses the evidence and outcomes behind the treatment options to guide physicians when establishing a plan for patients. Fortunately, most cases will resolve with conservative care and physical therapy, but severe or chronic cases will likely require the expertise of an interventional spine physician or surgeon.

Emergency Medicine

**Gunaga S**, Carpenter CR, Kennedy M, Southerland LT, Lo AX, Lee S, **Swan K**, Mowbray F, Skains RM, Hogan TM, Casey MF, Ouchi K, George NR, de Wit K, Gettel CJ, Selman K, Ragsdale LC, Chary AN, van Oppen JD, Arendts G, Maddow CL, Hunold KM, Tyler KR, Khoujah D, Hwang U, and Liu S. A Model for Developing Subspecialty Clinical Practice Guidelines: The Geriatric Emergency Department Guidelines 2.0. *J Am Coll Emerg Physicians Open* 2025;6(6):100247. PMID: 41019914. Full Text

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The original consensus-based Geriatric Emergency Department (GED) Guidelines, published in 2014, established a framework of core principles for delivering high-quality, age-appropriate emergency care for older adults. In response to significant advances in geriatric emergency medicine research and evolving clinical priorities, we developed the GED Guidelines 2.0 to ensure continued relevance, clinical utility, and evidence-based rigor. This concept paper describes the systematic and iterative process undertaken to update the guidelines, including the formation of multidisciplinary working groups and the application of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology. Unlike the original GED Guidelines, our approach prioritized methodological transparency, formalized evidence grading, and consensus building grounded in systematic reviews and meta-analyses. We describe the identification, recruitment, and collaboration of multidisciplinary clinical and academic experts working together to improve the care of older adults in the emergency department. Through this multidisciplinary effort, key geriatric domains were selected, priority topics identified, and systematic reviews and meta-analyses conducted to generate a robust evidence base for future guideline and policy development. The GED Guidelines 2.0 represents the first emergency medicine (EM) subspecialty guideline effort to fully adopt the GRADE framework, offering a novel blueprint for future EM guideline development.

Emergency Medicine

Jiang JW, Ho SJ, Suttiratana SC, Topping CEW, Venkatesh AK, Owda R, Smith PJ, **Owda D**, and Khidir H. State-Level Variation in and Barriers to Medicaid Abortion Coverage. *JAMA Netw Open* 2025;8(9):e2530804. PMID: 40920379. Full Text

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IMPORTANCE: Approximately 35% of individuals seeking abortion care use Medicaid for health insurance. Although the Hyde Amendment restricts use of federal funds for most abortions, states can supplement coverage using state funds. Understanding the scope of abortion coverage across states and potential barriers to access may help address health care inequities and inform interventions. OBJECTIVE: To characterize state Medicaid abortion policies by conducting a qualitative analysis of publicly available state documents on Medicaid policy. DESIGN, SETTING, AND PARTICIPANTS: This qualitative study analyzed Medicaid abortion policies across all 50 states and the District of Columbia (hereinafter, states). Data were systematically collected from publicly available Medicaid documents and state websites from May 2023 to February 2024. MAIN OUTCOMES AND MEASURES: The main outcomes were key themes and descriptive statistics reporting on the scope of Medicaid abortion coverage and requirements for coverage across states, including documentation and procedures required of patients and physicians. Thematic analysis was performed to extract key themes found in abortion coverage policies, and descriptive statistics were used to show prevalence of identified themes across states. RESULTS: The analysis of 94 documents revealed 3 key themes. First, the scope of coverage across states was heterogeneous. Eighteen states aligned with the current wording of the Hyde Amendment, 10 states described life endangerment without use of current Hyde Amendment wording, 17 states outlined additional coverage for other specified conditions for abortions, 6 states covered all abortions, and 1 state's policy did not mention required federal coverage for rape or incest exceptions. Second, states imposed various patient restrictions and requirements with regard to abortion care coverage, with 22 states mandating reporting requirements for abortions due to rape or incest, along with other administrative hurdles for patients seeking care. Third, physicians were tasked with many responsibilities, such as determining eligibility for Medicaid abortion coverage and complying with documentation and administrative requirements. Thirty-eight states explicitly required physician certification and justification for clinical conditions warranting coverage. CONCLUSIONS AND RELEVANCE: The findings of this qualitative study of state Medicaid abortion policies suggest that there is substantial heterogeneity among states regarding the scope of Medicaid abortion coverage and that there are numerous obstacles for patients and physicians in accessing this coverage. This heterogeneity and burden may impose an additional layer of complexity to abortion access. Measures and policies that improve transparency, clarity, and efficiency may enhance access to essential abortion care for vulnerable populations.

Emergency Medicine

Li T, Huibregtse ME, Ely TD, van Rooij SJH, Lebois LAM, Webb EK, Jovanovic T, House SL, Bruce SE, Beaudoin FL, An X, Neylan TC, Clifford GD, Linnstaedt SD, 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, Datner EM, Pearson C, Peak DA, Merchant RC, Domeier RM, Rathlev NK, O'Neil BJ, Sergot P, Sanchez LD, Sheridan JF, Kessler RC, Koenen KC, Ressler KJ, McLean SA, Stevens JS, and Harnett NG. Childhood adversity is associated with longitudinal white matter changes after adulthood trauma. *Biol Psychiatry Cogn Neurosci Neuroimaging* 2025; Epub ahead of print. PMID: 40972945. Full Text

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BACKGROUND: Childhood adversity is associated with susceptibility to posttraumatic stress disorder (PTSD) in adulthood. PTSD and childhood adversity are linked to white matter microstructure, yet the role of white matter as a potential neural mechanism connecting childhood adversity to PTSD remains unclear. The present study investigated the potential moderating role of previous childhood adversity on longitudinal changes in white matter microstructure and posttraumatic stress symptoms following a recent traumatic event in adulthood. METHODS: As part of the AURORA Study, 114 recent trauma survivors completed diffusion weighted imaging at 2-weeks and 6-months after exposure. Participants reported on prior childhood adversity and PTSD symptoms at 2-weeks, 6-months, and 12-months post-trauma. We performed both region-of-interest (ROI) using fractional anisotropy (FA) and whole-brain correlational tractography using quantitative anisotropy (QA) analyses to index associations between white matter microstructure changes and prior adversity. RESULTS: ROI-based analyses did not identify significant associations between childhood adversity and changes in FA. Whole-brain correlational tractography revealed that greater childhood adversity moderated the QA changes within threat and visual processing tracts including the cingulum bundle and inferior fronto-occipital fasciculus (IFOF). QA changes within cingulum bundle and IFOF were associated with changes in PTSD symptoms between 2-weeks and 6-months. CONCLUSIONS: Our findings suggest temporal variability in threat and visual white matter tracts may be a potential neural pathway through which childhood adversity confers risk to PTSD symptoms after adulthood trauma. Future studies should take the temporal properties of white matter into consideration to better understand the neurobiology of childhood adversity and PTSD.

Emergency Medicine

**Memon M**, Christenson RH, **Jacobsen G**, Apple FS, Singer AJ, Limkakeng AT, Jr., Peacock WF, deFilippi CR, **Miller JB**, and **McCord J**. Utility of N-Terminal Pro-B-Type Natriuretic Peptide -to-Troponin and BNP-to-Troponin Ratios for Differentiating Type 1 from Type 2 Myocardial Infarction: A HIGH-US Sub-Study. *Crit Pathw Cardiol* 2025; Epub ahead of print. PMID: 40997263. Full Text

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BACKGROUND: Differentiating type 1 myocardial infarction (T1-MI) from type 2 MI (T2-MI) remains a diagnostic challenge, even with the availability of high-sensitivity cardiac troponin assays. This study explored whether NT-proBNP, BNP, and their respective ratios to troponin could enhance the ability to distinguish between these MI subtypes. METHODS: As a HIGH-US sub-study, we examined data from 280 patients diagnosed with non-ST elevation myocardial infarction (172 with T1-MI and 108 with T2-MI).

We assessed NT-proBNP, BNP, hs-cTnI, and their ratios as potential discriminative biomarkers. Diagnostic accuracy was evaluated using receiver operating characteristic (ROC) curves. RESULTS: NT-proBNP levels were markedly elevated in T2-MI patients compared to those with T1-MI (mean 10,327±12,923 vs 4,675±11,740 ng/L; P=0.006). Conversely, hs-cTnI concentrations were higher in T1-MI (1.4±5.1 vs 0.5±1.1 ng/L; P=0.030). Notably, the NT-proBNP-to-troponin ratio was more than three times greater in T2-MI cases (94,880±152,648 vs 24,209±78,727; P=0.007). NT-proBNP alone demonstrated fair discriminatory capacity (AUC 0.717, 95% CI 0.578-0.856), closely matching the NT-proBNP-to-troponin ratio (AUC 0.720, 95% CI 0.566-0.873). In contrast, BNP and the BNP-to-troponin ratio offered lower diagnostic values. Mean BNP levels were 505.4 ±576.6 ng/L for those with T2-MI and 437.1 ±738.8 ng/L for patients with T1-MI. BNP-to-troponin ratio showed a poor discrimination for the 2 MI types (AUC, 0.660; 95% CI, 0.532-0.789). CONCLUSIONS: Both NT-proBNP and its ratio to troponin show potential in differentiating T1-MI from T2-MI, reflecting distinct underlying pathophysiological processes. Given its comparable performance to the ratio, NT-proBNP alone may serve as a practical and cost-effective standalone marker. These findings support the hypothesis that incorporating NT-proBNP testing into routine clinical workflows may better informs the management of patients with suspected MI.

Emergency Medicine

Miller SM, **Jean Z**, Kyko JA, **Obeid I**, and **Buggia M**. Intensive Care Unit Liberation After Complete Left Anterior Descending Artery Occlusion: Unexpected Neurologic Recovery After a 53-Minute Cardiac Arrest. *Cureus* 2025;17(9):e91751. PMID: 40937019. Full Text

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Out-of-hospital cardiac arrest (OHCA) is associated with low survival and neurologic recovery rates, especially when return of spontaneous circulation exceeds 45 minutes. Additionally, neurologic prognostic indicators, such as absent brainstem reflexes and presence of alpha coma electroencephalogram (EEG) patterns, are typically associated with poor outcomes. This report outlines the case of a 48-year-old woman with a history of hypertension, dyslipidemia, and tobacco use who suffered an OHCA due to an acute left anterior descending artery occlusion. She experienced a total downtime of 53 minutes and required multiple rounds of defibrillation and advanced cardiac life support. Following successful percutaneous coronary intervention, her initial neurologic examination remained poor with absent brainstem reflexes, nonreactive pupils, and EEG findings consistent with severe encephalopathy. After 22 days in the hospital with minimal neurologic improvement, she was discharged to long-term care with a tracheostomy and percutaneous endoscopic gastrostomy tube. Two months after initial discharge, the patient unexpectedly returned to the hospital, demonstrating signs of cognitive recovery. During this second hospital stay, she was alert, followed commands, was able to communicate using a voice modulator, and passed a swallow study. This case illustrates a rare example of survival after prolonged OHCA and subsequent neurologic improvement following an initially guarded prognosis.

Emergency Medicine

Wongsripuemtet P, Ohnuma T, Temkin N, Barber J, Komisarow J, Manley GT, Hatfield J, Treggiari MM, Colton K, Sasannejad C, Chaikittisilpa N, Grandhi R, Laskowitz DT, Mathew JP, Hernandez A, James ML, Raghunathan K, **Miller JB**, Vavilala MS, and Krishnamoorthy V. Association of Preinjury Beta-Blocker Exposure With Brain Injury Biomarkers Following Traumatic Brain Injury. *J Neurosurg Anesthesiol* 2025; Epub ahead of print. PMID: 41024341. Full Text

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OBJECTIVE: Beta-blockers have been studied for their impact on traumatic brain injury (TBI). We aimed to examine the association of preinjury beta-blocker exposure with early brain injury biomarker levels and outcomes following TBI. METHODS: We retrospectively studied adults (≥40 y) participating in the Transforming Clinical Research and Knowledge in TBI (TRACK-TBI) study. The exposure was preinjury beta-blocker utilization. Primary outcome was blood-based brain injury biomarker levels on day 1 following injury. Secondary outcomes included biomarkers on days 3 and 5, hospital mortality, and the 6-month Glasgow Outcome Scale-Extended. Inverse probability-weighted models assessed the association between preinjury beta-blocker exposure, biomarker levels, and outcomes, stratified by TBI severity. RESULTS: A total of 1185 patients were included, with 101 on preinjury beta-blockers (BB+): 21 in the moderate/severe group and 80 in the mild TBI group. BB+patients were older than BB- in both mild (67 vs. 57 y, P<0.001) and moderate/severe TBI (64 vs. 56 y, P=0.003). Hypertension was more common in BB+patients (78% mild, 67% moderate/severe, P<0.001). Preinjury beta-blocker use was not associated with day 1 biomarker levels. The 6-month GOSE scores in the BB+ moderate/severe TBI were lower, but the effect was marginal (B= -1.20, 95% CI: -2.39 to -0.01, P=0.049). CONCLUSION: Our study did not find a clear association between preinjury beta-blocker exposure and day 1 blood-based brain injury biomarkers or clinical outcomes. These findings warrant confirmation in future studies with larger cohorts.

Endocrinology and Metabolism

Jha V, Bhadada SK, Pal R, Kharbanda C, and **Rao SD**. Personalizing denosumab therapy in postmenopausal Indian women with osteoporosis: predictive role of bone turnover markers and body mass index in determining dosing interval. *Osteoporos Int* 2025; Epub ahead of print. PMID: 41020995. Full Text

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This prospective study evaluated whether bone turnover markers (BTMs) and body mass index (BMI) can guide individualized denosumab dosing in postmenopausal Indian women with osteoporosis. Lower baseline β-CTX and BMI were independently associated with safe deferral of denosumab beyond 6 months, without increased fracture risk. These findings support a personalized, phenotype-based approach to denosumab therapy in low-turnover populations. PURPOSE: To evaluate whether baseline bone turnover markers (BTMs) and body mass index (BMI) can predict the safety and feasibility of extending the dosing interval of denosumab beyond six months in postmenopausal Indian women with osteoporosis. METHODS: In this prospective observational study, 56 postmenopausal women with DXA-confirmed osteoporosis were initiated on denosumab (60 mg subcutaneously).None of the participants had received prior anti-resorptive therapies. Several participants were on vitamin D supplementation, consistent with their high baseline serum 25-hydroxyvitamin D levels. Serum ß-CTX levels were measured at 6 months, guiding the timing of subsequent injections. Participants were classified into two groups: standard (dose at 6 months) and delayed (dose deferred beyond 6 months if ß-CTX <300 pg/mL). Baseline BTMs, BMI, and fracture outcomes were analysed. Multivariate logistic regression was used to identify predictors of delayed dosing. RESULTS: Twenty-eight women received delayed injections (median interval: 9.5 months). Compared to the standard group, the delayed group had significantly lower baseline ß-CTX levels (497 vs. 794 pg/mL; p < 0.001) and lower BMI (23.29 ± 2.77 vs. 25.59 ± 3.03 kg/m²; p = 0.005). Multivariate analysis showed both lower baseline ß-CTX (OR: 0.99; 95% CI: 0.98-1.00; p = 0.027) and lower BMI (OR: 0.60; 95% CI: 0.40-0.89; p = 0.012) independently predicted delayed denosumab administration. No new vertebral fractures were observed in either group during follow-up. CONCLUSIONS: Lower baseline bone turnover and lower BMI may help identify postmenopausal Indian

women in whom denosumab dosing can be safely deferred beyond six months. These findings are preliminary and do not establish long-term safety or efficacy; further studies with extended follow-up are needed before adopting extended dosing intervals in clinical practice.

Family Medicine
Korpal M, and **Jaddou N**. Downstream Outcomes of Elevated Prostate-Specific Antigen (PSA) Detected Through Routine Screening in Men Aged 55-70: A 10-Year Retrospective Study. *Cureus* 2025;17(8):e89931. PMID: 40951043. Full Text

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Introduction Prostate-specific antigen (PSA) screening remains a contentious issue due to its high sensitivity but low specificity. While elevated PSA can indicate prostate cancer, it may also result from benign conditions such as benign prostatic hyperplasia (BPH), prostatitis, or infection. The variability in downstream management following elevated PSA in nonspecialist outpatient settings is not well-characterized. Downstream management refers to clinical follow-up measures after elevated PSA results, including referral, biopsy, repeat testing, benign diagnoses, refusal, or no further evaluation. Objective This study aimed to assess the clinical outcomes following elevated PSA levels (≥4 ng/mL) identified through routine screening in men aged 55-70 years in a primary care clinic over a 10-year period. Methods We conducted a retrospective observational study at an independent outpatient clinic in Michigan, analyzing electronic health records (EHRs) from 2015 to 2024. A total of 1,258 men aged 55-70 who underwent routine PSA testing were included. Patients with known urologic conditions or prostate cancer were excluded. Among those with elevated PSA levels, downstream outcomes such as urology referrals, biopsy status, cancer detection, benign diagnoses, repeat testing, and loss to follow-up were evaluated using descriptive statistics. Results Of 1,258 screened patients, 127 (10.1%) had PSA levels ≥4 ng/mL. Among them, 44 (34.6%) underwent biopsy, with prostate cancer confirmed in 18 patients (40.9% of biopsied; 1.4% of total screened). The remaining 83 patients (65.4%) did not undergo biopsy: 13 normalized their PSA on repeat testing, 37 were diagnosed clinically with BPH, eight had other benign causes (e.g., urinary tract infection (UTI), prostatitis), 12 declined biopsy, and 13 were lost to follow-up. These findings reveal considerable heterogeneity in follow-up care and clinical decision-making. Conclusion In this real-world primary care setting, most men with elevated PSA were managed noninvasively, with a substantial proportion avoiding biopsy. Despite this, the cancer detection rate among biopsied individuals was significant. These results underscore the need for standardized follow-up protocols and decision-support frameworks to guide post-PSA screening management in outpatient environments.

Family Medicine
Korpal M, and **Jaddou N**. Improving Documentation and Follow-Up of Elevated Blood Pressure in a Family Clinic: A Quality Improvement Project. *Cureus* 2025;17(8):e89711. PMID: 40932951. Full Text

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Introduction Hypertension is a common and clinically significant condition frequently encountered in primary care. However, challenges such as poor documentation and inconsistent follow-up planning in many outpatient settings can result in suboptimal outcomes, increasing the risk of missed care opportunities. This quality improvement project aimed at improving documentation and follow-up planning for patients with elevated blood pressure (BP) (>140/90 mmHg) at a family clinic in Michigan. Objective This quality improvement project is aimed at improving documentation and follow-up planning for elevated BP readings in adult patients seen during outpatient visits from 33% to 70% over a three-week period in a family medicine clinic. Methods The project was conducted at an outpatient family medicine clinic over a three-week period from June 9 to June 27. Adult patients aged 18 years and older with elevated BP were included, and a total of 60 patient charts were reviewed during the intervention period. The intervention consisted of a daily review of patient charts to identify elevated BP, ensuring that follow-up plans such as

home BP monitoring, repeat BP checks, and lifestyle modification advice were documented in the electronic health record (EHR). Patients with elevated readings also received verbal counseling, and brief end-of-day team huddles were conducted to review documentation, and early in the cycle, brief staff education sessions were held to review the documentation standards. Data were collected through both EHR review and manual chart audits. A Plan-Do-Study-Act (PDSA) cycle was used to implement and evaluate the intervention. Results At baseline, only 33% (20 out of 60) of the patients with elevated BP had appropriate documentation and follow-up plan in the EHR. Following the three-week intervention, this increased to 80% (48 out of 60), surpassing the initial target of 70%. The documentation improvement was achieved using the iterative PDSA cycle approach, with adjustments made weekly to reinforce chart review, counselling, and end-of-day team huddles. Conclusion This quality improvement cycle led to a significant improvement in the documentation and follow-up plans, highlighting its importance in better management of hypertension. The intervention has been sustained in the daily clinic practice, with minor adjustments made to support long-term sustainability. This may also serve as a model for similar clinic-based quality improvement efforts.

Gastroenterology

Asrani SK, **Mellinger J**, Sterling S, Lucey MR, Bradley KA, Bhala N, Bray J, Chen PH, DiMartini A, Fernandez A, Ghadiali M, Haque LY, Khalili M, Lee B, Lin LA, Pillai AA, Satre DD, Sengupta S, Serper M, Simonetto D, Thiele M, Welsh J, Wu T, Zsohar J, and Shah VH. Reducing alcohol-associated liver disease burden in the general population. *Lancet Gastroenterol Hepatol* 2025; Epub ahead of print. PMID: 40976252. Full Text

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The prevalence of alcohol use disorder (AUD) and alcohol-associated liver disease (ALD) is rising. The National Institute on Alcohol Abuse and Alcoholism organised a multistakeholder workshop focused on reducing the burden of ALD. Decreasing ALD morbidity and mortality requires a multipronged approach, including increased population-based screening for AUD, early recognition of ALD, and multidisciplinary treatment. Recommended screening tools for alcohol use include the alcohol use disorders identification test for consumption (AUDIT-C). In patients with elevated AUDIT-C scores (AUDIT-C score of ≥3 points in women, ≥4 points in men), screening for fibrosis is recommended using non-invasive blood-based tests, such as the Fibrosis-4 index. Sequential testing using blood-based and imaging-based non-invasive liver disease assessment is preferred to blood-based tests alone to increase the positive predictive value of referral pathways. Screening, brief intervention, and referral to treatment are effective for reducing unhealthy alcohol use among adults who are not alcohol dependent. Integrated care models that

incorporate mental health treatment into general medical settings are crucial for AUD and ALD. Emerging care models, such as multidisciplinary ALD clinics and substance use navigators, can improve patient engagement and outcomes. Markers of success include a reduction in per capita alcohol consumption, declines in morbidity and mortality related to AUD and ALD, and a decrease in health-care costs.

Gastroenterology
Daugherty TT, Beas R, Hernandez L, Rajput M, and **Reyes Genere J**. Risk Factors for Readmissions in Patients Undergoing Endoscopic Drainage for Peripancreatic Fluid Collections. *Dig Dis Sci* 2025; Epub ahead of print. PMID: 40974533. Full Text

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BACKGROUND: Pancreatic fluid collections (PFCs) are a frequent complication following acute pancreatitis and often necessitate endoscopic cystogastrostomy (EC) for drainage. Despite high technical and clinical success rates, unplanned readmissions remain common. AIMS: This study aimed to evaluate readmission rates and identify associated risk factors in patients undergoing EC for PFCs. METHODS: We conducted a retrospective review of 100 patients who underwent EC for symptomatic PFCs between June 2016 and August 2021. Demographic data, clinical characteristics, procedural details, and outcomes were analyzed. Univariate and multivariate logistic regression were used to identify factors associated with unplanned readmissions. RESULTS: Clinical success was achieved in 95% of patients. However, 31% experienced unplanned readmissions, most commonly due to sepsis (47%), abdominal pain (28%), and gastrointestinal bleeding (14%). Univariate analysis identified intra-abdominal varices and paracolic gutter extension as significant risk factors. Multivariate analysis confirmed intra-abdominal varices as an independent predictor (OR 3.51, 95% CI 1.26-9.80, P = 0.016). Technical success was high (98%) with an overall adverse event rate of 14%. CONCLUSION: Unplanned readmissions are common after EC for PFCs, with intra-abdominal varices emerging as a key risk factor. Enhanced follow-up and risk stratification may improve patient outcomes and reduce healthcare burden.

Gastroenterology
Diaz LA, Thiele M, Louvet A, Lee BP, Ajmera V, Tavaglione F, Hsu CL, Huang DQ, Pose E, Bataller R, McClain C, **Mellinger J**, Tincopa M, Mitchell MC, Ratziu V, Rinella ME, Sarin SK, Shah VH, Szabo G, Wong VW, Bansal MB, Leggio L, Kamath PS, Krag A, Sanyal AJ, Arrese M, Arab JP, Anstee QM, Mathurin P, and Loomba R. Clinical trial design, biomarkers and end points in metabolic and alcohol-related liver disease. *Nat Rev Gastroenterol Hepatol* 2025; Epub ahead of print. PMID: 41006824. Full Text

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Metabolic and alcohol-related liver disease (MetALD) is a newly defined entity within the spectrum of steatotic liver disease, characterized by the interplay of cardiometabolic risk factors and alcohol consumption. The evolving epidemiology and complex pathophysiology of MetALD present unique challenges and opportunities for clinical trial design. Inclusion criteria should require simultaneous evidence of metabolic dysfunction (at least two cardiometabolic features) and verified quantifiable alcohol exposure recorded over the preceding 3-6 months. Traditional histological end points are limited by invasiveness, sampling error and interpretative variability. Thus, imaging modalities, serum-based fibrosis biomarkers and quantitative measures of alcohol intake are gaining relevance as non-invasive, reproducible and patient-centric end points aiming to improve trial feasibility. Furthermore, incorporating alcohol biomarkers, stratifying patients by metabolic risk factor burden, and using adaptive designs of trials might enhance the precision and generalizability of MetALD clinical trials. Although uncertainties remain regarding optimal patient selection criteria, event rates and the dynamic interplay between metabolic dysfunction and alcohol intake, ongoing research efforts aim to refine diagnostic criteria, standardize methodologies and validate novel end points. These advances will ultimately accelerate drug development, improve trial efficiency and foster interventions to treat MetALD.

Gastroenterology

**Faisal MS**, **Hasso M**, **Saleem A**, **Faisal MS**, and **Singla S**. Biliary Radiofrequency Ablation and Sphincterotomy Restenosis: A Unique Case of Biliary Obstruction. *ACG Case Rep J* 2025;12(9):e01824. PMID: 40927055. Full Text

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Biliary radiofrequency ablation is an emerging adjunctive and palliative therapy for patients with ampullary and biliary tumors. Given the high mortality for these malignancies, data on long-term complications are limited. We report a unique case of sphincterotomy restenosis causing biliary obstruction in a 98-year-old woman with a history of ampullary adenocarcinoma treated with papillectomy and biliary radiofrequency ablation (RFA). Endoscopic retrograde cholangiopancreatography revealed restenosis at the sphincterotomy site, managed successfully with repeat sphincterotomy and stenting. This case highlights sphincterotomy restenosis as a potential late complication of biliary RFA and emphasizes the need for awareness of delayed biliary obstruction in post-RFA patients.

Gastroenterology

Sanyal AJ, Reddy KR, **Brown KA**, Landis CS, Cullaro G, Huang X, Kelkar SS, Raina R, Corman S, Kebede N, Edmundson P, Jamil K, and Allegretti AS. Challenges in the Treatment of Hepatorenal Syndrome-Acute Kidney Injury: A US Chart Review of Treatment Patterns and Survival Outcomes. *JGH Open* 2025;9(9):e70255. PMID: 40958936. Full Text

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BACKGROUND: Treatments for hepatorenal syndrome with acute kidney injury (HRS-AKI) that are not FDA-approved have been widely used in the United States (US) with variable outcomes. This study describes the practice patterns, outcomes, and healthcare utilization around vasopressor use before terlipressin approval in 2022. METHODS: A retrospective chart review study was conducted at 10 US medical centers, assessing adult patients diagnosed with HRS-AKI between 2016 and 2019. The primary outcome was treatment response (change in serum creatinine [SCr] from the day of vasopressor treatment initiation to Day 14/vasopressor discontinuation). Secondary outcomes included overall and transplant-free survival, treatment patterns, and healthcare resource use. RESULTS: Of the 198 eligible patients, 129 and 69 had mild/moderate (SCr < 5 mg/dL, acute-on-chronic liver failure [ACLF] ≤ 2) and severe disease (SCr ≥ 5 mg/dL, ACLF > 2), respectively. The mean age was 57 years; 52.5% were males, and 71.2% were White. Alcohol-associated cirrhosis (53.5%) was the most common cause of cirrhosis. All 198 patients had a physician-diagnosed HRS-AKI, and only 30.3% met all International Club of Ascites (ICA)-HRS criteria. Most patients (85.4%) initiated treatment with midodrine and octreotide for a median of 7 days. The overall response rate (n = 157) was 20.3%. Median (95% CI) overall and transplant-free survival from vasopressor initiation was 48 (32-81) and 28 (19-36) days. Notably, 33.8% of patients died during hospitalization, and 31.3% required renal replacement therapy. CONCLUSION: Before 2022, hospitalized HRS-AKI patients experienced suboptimal treatment response with off-label treatments and poor survival. There remains an unmet need for safe and effective non-transplant treatments for hospitalized HRS-AKI patients in the United States.

Global Health Initiative

Guevara Núñez D, Morandini FN, **Suleyman G**, **Crooker K**, **Kaur J**, **Maki G**, Bocco JL, Fernández Do Porto D, **Zervos MJ**, Sola C, and Saka HA. Genomic Analysis and Virulence Features of Vibrio cholerae Non-O1/Non-O139 Harbouring CARB-Type β-Lactamases From Freshwater Bodies, Argentina. *Environ Microbiol Rep* 2025;17(5):e70181. PMID: 40997832. Full Text

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Vibrio cholerae is a globally distributed, free-living bacterium in aquatic ecosystems. While non-O1/non-O139 serogroups typically do not produce cholera toxin, they have the potential to cause diarrhoea. These strains may act as reservoirs of antibiotic resistance in rivers, lakes and oceans. Understanding their genetic resistance and virulence can shed light on their role in spreading antimicrobial resistance and their pathogenicity. In this study, we characterised 60 V. cholerae non-O1/non-O139 strains from 16 freshwater bodies located throughout the Province of Córdoba, Argentina. We found none of the strains carried cholera toxin and identified ampicillin resistance as the most prevalent phenotype. Whole genome sequencing revealed that all ampicillin-resistant strains (n = 10) carried CARB β-lactamases, leading to the identification of new CARB variants (CARB-59 to CARB-62) likely associated with the V. cholerae superintegron. Two strains were notably related and exhibited enhanced virulence due to an unusual genetic arrangement of the VPI-1 pathogenicity island, encoding both the toxin co-regulated pilus and a type VI secretion system cluster subclass i5, commonly found in non-cholera Vibrio species. These findings provide significant insights into the genetic diversity and virulent potential of ampicillin-resistant environmental V. cholerae non-O1/non-O139 and enhance our understanding of the evolution of CARB β-lactamases within the species.

Hematology-Oncology

Adhikari SD, **Steele NG**, **Theisen B**, Wang J, and Cui Y. SPACE: Spatially variable gene clustering adjusting for cell type effect for improved spatial domain detection. *Nucleic Acids Res* 2025;53(18). PMID: 40985765. Full Text

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Recent advances in spatial transcriptomics (ST) have significantly deepened our understanding of biology. A primary focus in ST analysis is to identify spatially variable genes (SVGs) which are crucial for downstream tasks like spatial domain detection. Spatial domains reflect underlying tissue architecture and distinct biological processes. Traditional methods often use a set number of top SVGs for this purpose, and embedding these SVGs simultaneously can confound unrelated spatial signals, dilute weaker patterns, leading to obscured latent structure. Instead, grouping SVGs and getting low-

dimensional embedding within each group preserves specific patterns, reduces signal mixing, and enhances the detection of diverse structures. Furthermore, classifying SVGs is akin to identifying cell-type marker genes, offering valuable biological insights. The challenge lies in accurately categorizing SVGs into relevant clusters, aggravated by the absence of prior knowledge regarding the number and spatial gene patterns. Here, we propose SPACE, a framework that classifies SVGs based on their spatial patterns by adjusting for shared cell-type confounding effects, to improve spatial domain detection. This method does not require prior knowledge of gene cluster numbers, spatial patterns, or cell type information. Both simulation and real data analyses demonstrate that SPACE is an efficient and promising tool for ST analysis.

Hematology-Oncology

**Arena CJ**, **El-Tatari B**, **Lovric K**, **Greenlee SB**, **Kenney RM**, **Gadgeel SM**, **Patterson K**, **Shallal AB**, **Alangaden GJ**, **Davis SL**, and **Veve MP**. Is Shorter Better in Oncology Patients, Too? A Retrospective Cohort Study of Short- Versus Long-Course Antibiotic Therapy for Uncomplicated Infections in Solid Tumor Patients Receiving Care in Ambulatory Oncology Clinics. *Open Forum Infect Dis* 2025;12(9):ofaf505. PMID: 40908971. Full Text

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This retrospective cohort study evaluated short- versus long-course antibiotics for uncomplicated infections in ambulatory solid tumor patients. Among 303 patients, outcomes were similar between groups, including infection recurrence, treatment delays, and adverse events. Short-course therapy was not associated with worse outcomes, suggesting it may be a viable alternative.

Hematology-Oncology

Kyei I, Bea VJ, Gyan KK, Adjei E, Stonaker B, Bekele M, Abebe E, Davis M, Boakye A, Boateng R, Elemento O, Aitpillah F, Alebachew H, Jibril A, Chen Y, Taiwo E, **Bensenhaver J**, **Walker E**, **Ali H**, Oppong J, Ginter P, Nalwoga H, Kalungi S, Ebughe G, Ezeome ER, Jackson K, Bonsu EO, Momoh A, Martini R, Demaria S, Yates C, Balogun OD, Louie C, Manohar J, Bediako Y, Boaitey GA, Fondjo LA, Iloanusi N, Okoye I, Adinku M, Ankomah K, Dally C, Rockefeller E, **Susick L**, Obong-Ekanem I, Greenspun BC, Daba SA, **Schwartz T**, Robine N, Chen S, Carrot-Zhang J, Amazu S, **Jiagge E**, Acheamfour OK, Patino S, Malik M, Ju T, Siegel B, Martin IK, Mills C, Phillip J, Kalu CO, Joseph C, Peters F, Stromain A, Olusina B, Nwokoro O, Lasebikan N, Udosen J, Nwagbara V, Carpten J, Fisseha S, Johnson T, Awuah B, and Newman LA. Oncologic Anthropology and the African Diaspora: Twenty-Year Anniversary Report, International Center for the Study of Breast Cancer Subtypes (ICSBCS). *Ann Surg Oncol* 2025; Epub ahead of print. PMID: 40914775. Full Text

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The International Center for the Study of Breast Cancer Subtypes (ICSBCS) has played a vital role in defining and overcoming many inequities that exist in breast cancer treatment and outcome on a global basis through capacity-building programs that improve the management of breast cancer patients across the African diaspora. ICSBCS activities also fill critical gaps in disparities research related to the genetics of ancestry. Over the past 20 years, ICSBCS teams have spearheaded landmark studies documenting the relevance of genetic African ancestry to breast cancer risk, while also improving the quality of care delivered to patients in diverse communities. Herein, the achievements and future goals of this international, multi-institutional breast cancer research and outreach program are summarized.

Hematology-Oncology
**Masters S**, **Kim S**, **Moses E**, **McManaman A**, **Ghimire B**, and **Goyert G**. Stage IV Pancreatic Adenocarcinoma in Pregnancy. *Matern Fetal Med* 2025. PMID: Not assigned. Full Text

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Hematology-Oncology
Xie A, **Steele NG**, and Cui Y. gwSPADE: gene frequency-weighted reference-free deconvolution in spatial transcriptomics. *Nucleic Acids Res* 2025;53(18). PMID: 41002029. Full Text

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Most spatial transcriptomics (ST) technologies (e.g. 10× Visium) operate at the multicellular level, where each spatial location often contains a mixture of cells with heterogeneous cell types. Thus, effective deconvolution of cell type compositions is critical for downstream analysis. Although reference-based deconvolution methods have been proposed, they depend on the availability of reference data, which may not always be accessible. Additionally, within a deconvolved cell type, cellular heterogeneity may still exist, requiring further deconvolution to uncover finer structures for a better understanding of this complexity. Here, we present gwSPADE, a gene frequency-weighted reference-free SPAtial DEconvolution method for ST data. gwSPADE requires only the gene count matrix and utilizes appropriate weighting schemes within a topic model to accurately recover cell type transcriptional profiles and their proportions at each spatial location, without relying on external single-cell reference information. In various simulations and real data analyses, gwSPADE demonstrates scalability across various platforms and shows superior performance over existing reference-free deconvolution methods such as STdeconvolve.

Hematology-Oncology

Yang JC, Lu S, Hayashi H, Felip E, Spira AI, Girard N, Kim YJ, Lee SH, Ostapenko Y, Danchaivijitr P, Liu B, Alip A, Korbenfeld E, Mourão Dias J, Besse B, Passaro A, Lee KH, Xiong H, How SH, Cheng Y, Chang GC, Yoshioka H, Thomas M, Nguyen D, Ou SI, Mukhedkar S, Prabhash K, D'Arcangelo M, Alatorre-Alexander J, Vázquez Limón JC, Alves S, Stroyakovskiy D, Peregudova M, Şendur MAN, Yazici O, Califano R, Gutiérrez Calderón V, de Marinis F, Kim SW, **Gadgeel SM**, Owen S, Xie J, Sun T, Mehta J, Venkatasubramanian R, Ennis M, Fennema E, Daksh M, Roshak A, Man J, Knoblauch RE, Bauml JM, Baig M, Shah S, Sethi S, and Cho BC. Overall Survival with Amivantamab-Lazertinib in EGFR-Mutated Advanced NSCLC. *N Engl J Med* 2025; Epub ahead of print. PMID: 40923797. Full Text

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BACKGROUND: Previous results from this phase 3 trial showed that progression-free survival among participants with previously untreated EGFR (epidermal growth factor receptor)-mutated advanced non-small-cell lung cancer (NSCLC) was significantly improved with amivantamab-lazertinib as compared with osimertinib. Results of the protocol-specified final overall survival analysis in this trial have not been reported. METHODS: We randomly assigned, in a 2:2:1 ratio, participants with previously untreated EGFR-mutated (exon 19 deletion or L858R substitution), locally advanced or metastatic NSCLC to receive amivantamab-lazertinib, osimertinib, or lazertinib. Overall survival (assessed in an analysis of the time from randomization to death from any cause) in the amivantamab-lazertinib group as compared with the osimertinib group was a key secondary end point. Additional end points included safety. RESULTS: A total of 429 participants each were assigned to receive amivantamab-lazertinib or osimertinib. Over a median follow-up of 37.8 months, amivantamab-lazertinib led to significantly longer overall survival than osimertinib (hazard ratio for death, 0.75; 95% confidence interval, 0.61 to 0.92; P = 0.005); 3-year overall survival was 60% and 51%, respectively. At the clinical cutoff date, 38% of participants in the

amivantamab-lazertinib group and 28% in the osimertinib group were still receiving the assigned treatment. Adverse events of grade 3 or higher were more common with amivantamab-lazertinib (in 80% of participants) than with osimertinib (in 52%), particularly skin-related events, venous thromboembolism, and infusion-related events; these findings were consistent with the established safety profile of each treatment. No new safety signals were observed with additional follow-up. CONCLUSIONS: Amivantamab-lazertinib led to significantly longer overall survival among participants with previously untreated EGFR-mutated advanced NSCLC than osimertinib but was associated with an increased risk of adverse events of grade 3 or higher. (Funded by Janssen Research and Development; MARIPOSA ClinicalTrials.gov number, NCT04487080.).

Infectious Diseases
**Akon MO**, **Kenney RM**, **Everson NA**, **VanDorf S**, **Suleyman G**, **Tibbetts RJ**, **Shallal AB**, and **Veve MP**. A little nudge goes a long way: assessing the impact of a microbiology nudge comment on narrow-spectrum antibiotic use in uncomplicated Streptococcus pneumoniae bloodstream infections. *Antimicrob Steward Healthc Epidemiol* 2025;5(1):e230. PMID: 40989659. Full Text

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Narrow-spectrum antibiotic prescribing (ampicillin IV or penicillin IV) was compared before and after implementing an interpretive microbiology comment for uncomplicated Streptococcus pneumoniae bloodstream infections. The postintervention group was associated with 4-fold increased odds of de-escalation to narrow-spectrum antibiotics (adjusted odds ratio, 4.66; 95% confidence interval, 1.97-11.00).

Infectious Diseases
**Arena CJ**, **El-Tatari B**, **Lovric K**, **Greenlee SB**, **Kenney RM**, **Gadgeel SM**, **Patterson K**, **Shallal AB**, **Alangaden GJ**, **Davis SL**, and **Veve MP**. Is Shorter Better in Oncology Patients, Too? A Retrospective Cohort Study of Short- Versus Long-Course Antibiotic Therapy for Uncomplicated Infections in Solid Tumor Patients Receiving Care in Ambulatory Oncology Clinics. *Open Forum Infect Dis* 2025;12(9):ofaf505. PMID: 40908971. Full Text

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This retrospective cohort study evaluated short- versus long-course antibiotics for uncomplicated infections in ambulatory solid tumor patients. Among 303 patients, outcomes were similar between groups, including infection recurrence, treatment delays, and adverse events. Short-course therapy was not associated with worse outcomes, suggesting it may be a viable alternative.

Infectious Diseases
**Arena CJ**, **Everson NA**, **Kenney RM**, **Brar I**, **Gudipati S**, **Yared N**, Davis SL, and **Veve MP**. A cross-sectional analysis of doxyPEP use and outcomes in Michigan, United States. *Int J STD AIDS* 2025; Epub ahead of print. PMID: 40953601. Full Text

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Background: In 2024, national guidance was issued for doxycycline post-exposure prophylaxis (doxy-PEP) to prevent bacterial sexually transmitted infections (STIs). The study purpose was to evaluate doxy-PEP use in patients with increased risk of STI exposure at a large, urban health system. Methods: IRB-exempt study of adult patients with clinic encounters for increased risk of STI exposure and testing for N. gonorrhoeae, C. trachomatis, and T. pallidum from 01/01/2023-31/10/2024. Patients were identified using ICD-10 code Z20.XX and STI testing. Doxy-PEP prescription utilization was evaluated after a dedicated doxy-PEP order was implemented with appropriate patient counseling instructions. The primary outcome was the proportion of doxy-PEP prescriptions utilized in at-risk patients; secondary outcomes were utilization of the dedicated doxy-PEP order and abnormal STI testing within 3-months of the doxy-PEP prescription. Results: 4234 high-risk sexual patient encounters were documented; 7.37% of patients received a doxy-PEP prescription. Of these, 29.5% were ordered utilizing a dedicated doxy-PEP order. Most patients who received a doxy-PEP prescription were Black (96.6%), men (92.6%), with a median (IQR) age of 29 (24-37) years, and had private/commercial insurance (42%). One patient had abnormal syphilis testing within 3-months of doxy-PEP prescription. Conclusions: These findings highlight doxy-PEP underutilization and the need for broader provider engagement and advanced antimicrobial stewardship interventions.

Infectious Diseases

Branch-Elliman W, Chambers DA, Albin O, Batshon L, Castejon-Ramirez S, Cheng VC, Emetuche N, Datta R, Kamboj M, Krein SL, Staub M, Dassum SR, Rittmann B, Huang FS, Sreeramoju P, Stroever S, **Suleyman G**, Ting JY, Witt LS, Ziegler MJ, and Kwon JH. The life cycle of infection prevention and antimicrobial stewardship projects and interventions: the dynamic interplay of implementation and de-implementation science (Part I of II). *Infect Control Hosp Epidemiol* 2025;1-12. Epub ahead of print. PMID: 40926571. Full Text

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In Antimicrobial Stewardship and Infection Prevention and Control, programmatic goals often strive to achieve clinical benefit by practice change in the direction of doing less. Practically, this may include reducing the number of tests ordered, encouraging shorter and more narrow courses of antimicrobials, or discontinuing practices that are no longer contextually appropriate. Because promoting practice change in the direction of doing less is a critical aspect of day-to-day operations in Antimicrobial Stewardship and Infection Prevention and Control, the goals of this Society for Healthcare Epidemiology Research Committee White Paper are to provide a roadmap and framework for leveraging principles of implementation and de-implementation science in day-to-day practice. Part II of this series focuses on some practical case studies, including real-world examples of applied de-implementation science to promote discontinuation of practices that are ineffective, overused, or no longer effective.

Infectious Diseases
Branch-Elliman W, Reyes Dassum S, Stroever S, Albin O, Batshon L, Castejon-Ramirez S, Cheng VC, Emetuche N, Datta R, Kamboj M, Krein SL, Staub M, Rittmann B, Scaggs Huang F, Sreeramoju P, **Suleyman G**, Ting JY, Witt LS, Ziegler MJ, and Kwon JH. Leveraging de-implementation science to promote infection prevention and stewardship: a roadmap and practical examples (Part II of II). *Infect Control Hosp Epidemiol* 2025;1-11. Epub ahead of print. PMID: 40926570. Full Text

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De-implementation of established practices is a common challenge in infection prevention and antimicrobial stewardship and a necessary part of the life cycle of healthcare quality improvement programs. Promoting de-implementation of ineffective antimicrobial use and increasingly of low-value diagnostic testing are cornerstones of stewardship practice. Principles of de-implementation science and the interplay of implementation and de-implementation are discussed in part I of this Society for Healthcare Epidemiology of America White Paper Series.In this second part of the series, we discuss a process for applying principles of de-implementation science in infection prevention and stewardship and then review some real-world examples and case studies, including a national blood culture shortage, contact precautions, and surgical and dental prophylaxis. We use these examples to demonstrate how barriers and facilitators can be mapped to evidence-informed implementation/de-implementation strategies to promote efforts to reduce low-value, ineffective, or out-of-date practices. These real-world examples highlight the need for infection prevention and stewardship programs to adapt to changing evidence, contexts, and conditions. Although barriers to practice change are often a bit different, de-implementation can sometimes be thought of as the implementation of a new program-but the new program aims to stop rather than start doing something.As the saying goes, sometimes less really is more. Medicine and public health have a strong action bias and a strong aversion to risk and uncertainty. Although our best intentions may point us to implementing more interventions, often, the best medicine instead dictates that we do less, or nothing at all. Leveraging principles of de-implementation science can help move healthcare in the right direction when interventions are low-value, ineffective, or no longer needed.

Infectious Diseases

Guevara Núñez D, Morandini FN, **Suleyman G**, **Crooker K**, **Kaur J**, **Maki G**, Bocco JL, Fernández Do Porto D, **Zervos MJ**, Sola C, and Saka HA. Genomic Analysis and Virulence Features of Vibrio cholerae Non-O1/Non-O139 Harbouring CARB-Type β-Lactamases From Freshwater Bodies, Argentina. *Environ Microbiol Rep* 2025;17(5):e70181. PMID: 40997832. Full Text

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Vibrio cholerae is a globally distributed, free-living bacterium in aquatic ecosystems. While non-O1/non-O139 serogroups typically do not produce cholera toxin, they have the potential to cause diarrhoea. These strains may act as reservoirs of antibiotic resistance in rivers, lakes and oceans. Understanding their genetic resistance and virulence can shed light on their role in spreading antimicrobial resistance and their pathogenicity. In this study, we characterised 60 V. cholerae non-O1/non-O139 strains from 16

freshwater bodies located throughout the Province of Córdoba, Argentina. We found none of the strains carried cholera toxin and identified ampicillin resistance as the most prevalent phenotype. Whole genome sequencing revealed that all ampicillin-resistant strains (n = 10) carried CARB β-lactamases, leading to the identification of new CARB variants (CARB-59 to CARB-62) likely associated with the V. cholerae superintegron. Two strains were notably related and exhibited enhanced virulence due to an unusual genetic arrangement of the VPI-1 pathogenicity island, encoding both the toxin co-regulated pilus and a type VI secretion system cluster subclass i5, commonly found in non-cholera Vibrio species. These findings provide significant insights into the genetic diversity and virulent potential of ampicillin-resistant environmental V. cholerae non-O1/non-O139 and enhance our understanding of the evolution of CARB β-lactamases within the species.

Infectious Diseases

Oladipo PM, **Tibbetts RJ**, Sivertsen A, **Barger JM**, Bruvold TS, Fite A, Sims M, **Zervos M**, Jomaa A, and Ram JL. New diagnostic methods for Escherichia marmotae and the first report of its identification in clinical isolates in North America. *Front Microbiol* 2025;16:1664775. PMID: 40980316. Full Text

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BACKGROUND: Genomic sequences of E. marmotae and E. coli differ by 10%. Discovered as an environmental "cryptic clade" of Escherichia, E. marmotae also occurs in human infections. Microbiological and MALDI-TOF-MS methods frequently misidentify E. marmotae as E.coli. Our goal was to develop methods that reliably distinguish E. marmotae from E. coli to improve therapeutic decisions and treatments. METHODS: A Taqman PCR method was developed to distinguish E. marmotae from E. coli based on genomic sequences of uidA, uidB, and a positive control targeting adk in E. marmotae and E. coli. MALDI-TOF-MS spectra were obtained for environmental and clinical isolates using a bioMérieux VITEK MALDI-TOF-MS system. RESULTS: UidA- and uidB species-specific PCR amplified DNA from E. marmotae with 100% specificity, and not from E. coli or other Escherichia species. The Biomérieux VITEK MALDI-TOF-MS consistently misidentified E. marmotae as E. coli, with median IVD confidence scores for both E. marmotae and E. coli of 99.9%; however, RUO scores for E. marmotae (median 0%) were significantly lower ($P < 0.0001$) than for E. coli (median = 87.4%). The spectral peak between m/z 7,250 to 7,280 consistently occurred between 7,260 and 7,268 in E. marmotae and only between 7,268 and 7,280 in E. coli, with no overlap ($p < 0.001$). Application of these spectral criteria to 176 clinical isolates revealed the first identification of a E. marmotae isolate from a human infection in North America. The isolate had originally been diagnosed as E. coli based on a 99.1% IVD confidence score. This first North American clinical isolate was confirmed as E. marmotae by Taqman-PCR and whole genome sequencing. This isolate had numerous antibiotic resistance gene markers and unlike most clinical E. coli, this E. marmotae isolate lacked motility at 37°C. CONCLUSION: Clinical tests based on these methods of differentiating E. marmotae and E. coli may assist in determining the prevalence of this emerging pathogen and making therapeutic decisions.

Internal Medicine

Ahmad M, Sikandar A, Aziz A, Bachar Al Sumodi W, **Hans A**, and Usman M. Cardiovascular Benefits of Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists in Type 2 Diabetes Mellitus With Atherosclerotic Cardiovascular Disease: A Systematic Review of Randomized Controlled Trials. *Cureus* 2025;17(8):e89514. PMID: 40918811. Full Text

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This systematic review evaluates the cardiovascular effects of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) in adults with type 2 diabetes mellitus (T2DM) and established atherosclerotic cardiovascular disease, chronic kidney disease, or heart failure (HF). A comprehensive literature search across four major databases identified eight eligible studies, including randomized controlled trials and prespecified or pooled post-hoc analyses. The findings demonstrate consistent cardiovascular benefits of GLP-1 RAs, particularly semaglutide and exenatide, with notable reductions in major adverse cardiovascular events, cardiovascular mortality, and HF-related outcomes. Mechanistically, these benefits may be attributed to anti-inflammatory effects, improved endothelial function, and metabolic improvements such as weight loss and blood pressure reduction. Despite some heterogeneity across subgroups and study designs, the overall evidence supports the integration of GLP-1 RAs into cardiovascular risk management for patients with T2DM.

Internal Medicine

**Alkhafaji A**, **Govil D**, **Shaya F**, and **Ather A**. Lifting the Veil: Delayed Diagnosis of Sheehan Syndrome Unmasked by Adrenal Crisis. *JCEM Case Rep* 2025;3(10):luaf190. PMID: 40895498. Full Text

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We report a 28-year-old woman with refractory hypoglycemia, hypotension, and profound fatigue found to have panhypopituitarism secondary to Sheehan syndrome. Although she had a remote history of postpartum hemorrhage marked by agalactia and secondary amenorrhea, her diagnosis was delayed until she developed an adrenal crisis in the setting of acute pyelonephritis. Comprehensive endocrine testing confirmed secondary adrenal insufficiency, central hypothyroidism, hypogonadotropic hypogonadism, and lactotroph failure; Magnetic resonance imaging demonstrated a partially empty sella consistent with remote pituitary infarction. Prompt initiation of stress-dose glucocorticoids and thyroid hormone led to rapid hemodynamic stabilization and resolution of hypoglycemia. This case underscores the importance of early recognition of subtle hypopituitarism signs-particularly postpartum lactation failure-and the need to consider endocrine etiologies in critical care presentations that mimic septic shock.

Internal Medicine

Alsakarneh S, Khalifa A, Almasaid S, **Aburumman R**, Kilani Y, Khalid Z, Numan L, Dahiya DS, Karagozian R, and Helzberg JH. Sex, racial, and ethnic disparities in United States liver transplantation clinical trials. *World J Hepatol* 2025;17(9):110384. PMID: 41024882. Full Text

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BACKGROUND: Regulatory agencies are increasingly recognizing that minority trial representation is inadequate, contributing to healthcare disparities. The scope of minority population disparities in clinical trial participation remains unclear, as previous studies have compiled enrollment data from published trials, which frequently do not report participant race and ethnicity. AIM: To evaluate sex, racial and ethnic inequities in liver transplantation (LT) trials participation in the United States. METHODS: We used data from completed United States liver transplant clinical trials registered and reported on the National Institute of Health (NIH) website (clincaltrials.gov). Demographic data, including race, ethnicity, sex, and age were collected. To make inferences to a larger population, 95%CIs were computed for estimates in each demographic group using the Wilson method for binomial proportions. We also computed the simultaneous 95%CIs by applying a Bonferroni correction to reflect the multinomial distribution of race proportions. The numbers and percentages of racial/ethnic minority and female individuals compared with United States census data from 2010 and 2018. Secondary outcome measures were inclusion by trial funding source and year of completion. RESULTS: A total of 69 United States based clinical trials involving 6990 participants were included in the analysis. Of these, 35 trials (51%) were randomized, and 26 (38%) were conducted across multiple United States regions. All trials reported sex, while 42 (61%) reported race and 27 (39%) reported ethnicity. Compared to United States census data, Asian individuals were overrepresented (9.3%; 95%CI: 8.1%-10.5%), whereas African American (7.8%; 95%CI: 6.7%-8.9%) and American Indian or Alaska Native individuals (0.4%; 95%CI: 0.1%-0.6%) were underrepresented. The proportion of White participants (75.9%; 95%CI: 74.1%-77.7%) was consistent with census estimates. Hispanic participants were underrepresented (13.3%; 95%CI: 12.2%-14.5%) regardless of the census year referenced. In industry-sponsored trials, Asian representation was three times higher than in the general population (15%). NIH funded trials showed overrepresentation of White participants (83.8%) and underrepresentation of Black participants (4.1%) relative to census data. Women comprised 31.1% of all participants (95%CI: 30.0%-32.2%), indicating underrepresentation. Among trials that reported racial data, 62 (90%) did not include participants of American Indian or Alaska Native, Native Hawaiian, or Pacific Islander descent. CONCLUSION: Our analysis indicates that women, African Americans, and Hispanic individuals are underrepresented in LT clinical trials compared to the general United States population. These results highlight the need for regulatory initiatives aimed at enhancing the inclusion of historically marginalized racial and ethnic groups in clinical research.

Internal Medicine

Aref A, **Sheffeh J**, **Sheffeh MA**, Aggarwal N, Banno F, Alkhero M, and Rana K. Esophageal Hematoma Following Transcatheter Edge-to-Edge Repair of the Mitral Valve: A Rare Complication of Transesophageal Echocardiography. *ACG Case Rep J* 2025;12(9):e01822. PMID: 40933198. Full Text

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Transesophageal echocardiography is commonly used to guide structural cardiac interventions but carries a risk of esophageal injury. We present a 79-year-old woman who underwent a Transcatheter Edge-to-Edge Repair of the mitral valve and developed an esophageal hematoma. Clinical course was complicated by intractable gastrointestinal bleeding and sepsis due to acute cholecystitis. She did not survive despite aggressive measures. Our case demonstrates the potential severity of transesophageal echocardiography-related complications, especially in patients with predisposing factors such as esophageal diverticula and anticoagulation use.

Internal Medicine

**Arena CJ**, **El-Tatari B**, **Lovric K**, **Greenlee SB**, **Kenney RM**, **Gadgeel SM**, **Patterson K**, **Shallal AB**, **Alangaden GJ**, **Davis SL**, and **Veve MP**. Is Shorter Better in Oncology Patients, Too? A Retrospective Cohort Study of Short- Versus Long-Course Antibiotic Therapy for Uncomplicated Infections in Solid Tumor Patients Receiving Care in Ambulatory Oncology Clinics. *Open Forum Infect Dis* 2025;12(9):ofaf505. PMID: 40908971. Full Text

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This retrospective cohort study evaluated short- versus long-course antibiotics for uncomplicated infections in ambulatory solid tumor patients. Among 303 patients, outcomes were similar between groups, including infection recurrence, treatment delays, and adverse events. Short-course therapy was not associated with worse outcomes, suggesting it may be a viable alternative.

Internal Medicine
Bahar AR, Bahar Y, Rabib A, Manasrah N, **Onal F**, Bolaji O, Abidov A, and Alraies MC. Implementation of Intravascular Coronary Lithotripsy in the United States: Social Determinants of Health. *JACC Adv* 2025;4(10 Pt 2):102099. PMID: 40897137. Full Text

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BACKGROUND: Disparities in health care access persist in cardiovascular interventions. Coronary lithotripsy, a novel treatment for calcified coronary lesions, shows variability in utilization by sociodemographic factors. OBJECTIVES: This study examines the impact of sex, race, income, and hospital characteristics on lithotripsy use in the United States. METHODS: Using the 2021 Nationwide Inpatient Sample, patients undergoing percutaneous coronary intervention were identified. Lithotripsy was defined by the International Classification of Diseases-10th Revision codes. Multivariable logistic regression assessed the impact of sociodemographic factors, adjusting for comorbidities and hospital characteristics. Outcomes were compared using propensity score matching, with $P < 0.05$ considered significant. RESULTS: Of 261,260 percutaneous coronary intervention patients, 1,000 (0.38%) underwent lithotripsy. Adjusted analyses revealed that women were less likely to receive lithotripsy than men (adjusted OR [aOR]: 0.65; 95% CI: 0.53-0.79; $P < 0.001$). African American patients had lower odds of receiving lithotripsy than Whites (aOR: 0.66; 95% CI: 0.48-0.93; $P = 0.016$). Medicaid patients were less likely to receive lithotripsy (aOR: 0.20; 95% CI: 0.11-0.36; $P < 0.001$) compared to Medicare beneficiaries. Higher-income quartiles increased odds of receiving lithotripsy compared to lower quartiles (aOR: 1.38-1.6; $P < 0.05$). Regional disparities were noted, with lower use in the South (aOR: 0.66; 95% CI: 0.47-0.94; $P = 0.022$). CONCLUSIONS: Disparities in lithotripsy utilization persist, driven by sex, race, insurance status, income, and geographic region. These findings emphasize the need for targeted interventions to promote equitable access to advanced cardiovascular therapies. While some disparities may reflect differences in disease prevalence, persistent inequities in treatment allocation warrant further investigation.

Internal Medicine
Bakht D, Arham M, Rashid Z, Amir M, Nasir Z, Naqvi MZ, Tahir M, Khalil M, Gulzar E, Haris HM, Bakht K, Dad A, **Tareen H**, and Awais MN. Reduced Versus Full-Dose Direct Oral Anticoagulants for Venous Thromboembolism in Cancer Patients: A Systematic Review and Meta-Analysis. *EJHaem* 2025;6(5):e70155. PMID: 41000253. Full Text

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BACKGROUND: Venous thromboembolism (VTE) is a serious complication in cancer patients, with malignancy increasing the risk significantly. Direct oral anticoagulants (DOACs) have emerged as a convenient alternative to traditional therapies, though optimal dosing remains uncertain. METHODS: We performed a systematic review and meta-analysis on three studies. A comprehensive literature search was performed on PubMed, Embase, the Cochrane Library, and ScienceDirect till April 2025. Analysis was carried out on RevMan 5.4. The risk of bias was assessed via RoB 2.0. RESULTS: A total of three studies with 2416 participants were identified, including 1495 patients in the reduced-dose group and 1232 patients in the full-dose group. No significant difference was observed in recurrent VTE (OR 0.70, 95% CI 0.45-1.09, p = 0.11) or recurrent symptomatic VTE (OR 0.96, 95% CI 0.50-1.84, p = 0.91). However, reduced-dose DOACs were associated with a significantly lower incidence of incidental VTE (OR 0.31, 95% CI 0.14-0.69, p = 0.004). The reduced-dose group also had a lower incidence of CRNMB plus major bleeding (OR 0.69, 95% CI 0.55-0.88, p = 0.002). CONCLUSIONS: In terms of venous thromboembolism, bleeding events, and all-cause mortality, reduced-dose DOACs demonstrated a safety profile that was either superior or comparable to that of full-dose DOACs. TRIAL REGISTRATION: The authors have confirmed clinical trial registration is not needed for this submission.

Internal Medicine
**Faisal MS**, **Hasso M**, **Saleem A**, **Faisal MS**, and **Singla S**. Biliary Radiofrequency Ablation and Sphincterotomy Restenosis: A Unique Case of Biliary Obstruction. *ACG Case Rep J* 2025;12(9):e01824. PMID: 40927055. Full Text

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Biliary radiofrequency ablation is an emerging adjunctive and palliative therapy for patients with ampullary and biliary tumors. Given the high mortality for these malignancies, data on long-term complications are limited. We report a unique case of sphincterotomy restenosis causing biliary obstruction in a 98-year-old woman with a history of ampullary adenocarcinoma treated with papillectomy and biliary radiofrequency ablation (RFA). Endoscopic retrograde cholangiopancreatography revealed restenosis at the sphincterotomy site, managed successfully with repeat sphincterotomy and stenting. This case highlights sphincterotomy restenosis as a potential late complication of biliary RFA and emphasizes the need for awareness of delayed biliary obstruction in post-RFA patients.

Internal Medicine
**Garg A**, **Aldaoud N**, **Khan W**, and **Kulairi ZI**. Intraparenchymal Anaplastic Meningioma With Isolated Motor Deficits. *Cureus* 2025;17(8):e89822. PMID: 40937245. Full Text

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This case report describes a 62-year-old female with a history of gastroesophageal reflux disease and irritable bowel syndrome who presented with progressively worsening left-sided weakness and gait instability of two weeks' duration. A CT of the head without contrast revealed a 3.7 × 3.6 cm right frontal lobe mass with vasogenic edema and significant midline shift. A subsequent brain MRI with and without contrast demonstrated a 5.8 × 4.6 × 4.2 cm intra-axial, aggressive-appearing mass centered posteriorly within the right frontotemporal lobe, with extensive surrounding edema and local mass effect. The patient underwent surgical resection via craniotomy, with subsequent resolution of focal deficits. Histopathology confirmed an anaplastic meningioma, WHO Grade III, despite the fact that meningiomas are typically extra-axial tumors. This case underscores that high-grade meningiomas, although rare, can present in unexpected ways and at unpredictable sites, creating diagnostic challenges. It also emphasizes the importance of timely neurosurgical intervention to improve the chances of recovery.

Internal Medicine

**McClellan B**, **Govil D**, **Sherman A**, and **Bradley C**. Early Recognition and Management of Arrhythmogenic Right Ventricular Cardiomyopathy in a Young Athlete: A Case Report Highlighting the Role of Multimodal Diagnosis and Preventive Implantable Cardioverter Defibrillator (ICD) Therapy. *Cureus* 2025;17(8):e90736. PMID: 40984939. Full Text

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Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) is a rare inherited cardiomyopathy marked by fibrofatty replacement of right ventricular (RV) myocardium, leading to electrical instability and increased risk for ventricular arrhythmias and sudden cardiac death (SCD). ARVC is typically inherited in an autosomal dominant pattern and often involves mutations in desmosomal proteins such as plakophilin-2 (PKP2). Clinical presentation can vary from asymptomatic to life-threatening arrhythmias, particularly among young athletes. This case emphasizes the importance of early detection and intervention in patients with ARVC. A 21-year-old previously healthy male presented with recurrent exertional syncope. Initial ECG demonstrated sinus rhythm with T-wave inversions in leads V1-V3. Coronary CT angiography and resting echocardiography were normal. However, the stress electrocardiogram revealed frequent premature ventricular complexes (PVCs) with a left bundle branch block morphology. Ambulatory event monitoring detected over 500 monomorphic PVCs in a 24-hour period. Cardiac MRI demonstrated mildly reduced RVEF (39%) with regional dyskinesia, meeting major diagnostic criteria per the 2010 Task Force Criteria for ARVC. Genetic testing confirmed a heterozygous pathogenic mutation (c.1689-1G>C) in the PKP2 gene. The patient was started on beta-blockers and underwent implantation of a single-chamber implantable cardioverter defibrillator (ICD) due to elevated arrhythmic risk. Post-implantation, the ICD successfully terminated three episodes of ventricular tachycardia, highlighting its life-saving role. This case underscores the necessity for a high index of suspicion when evaluating young patients with unexplained syncope or arrhythmias. Diagnosis of ARVC requires integration of clinical, electrocardiographic, imaging, and genetic data. Early diagnosis and prompt management, including activity modification, pharmacologic therapy, and ICD implantation, are critical to mitigating the risk of SCD. Genetic testing and vigilant follow-up remain essential components in the care of ARVC patients.

Internal Medicine

**Memon M**, Christenson RH, **Jacobsen G**, Apple FS, Singer AJ, Limkakeng AT, Jr., Peacock WF, deFilippi CR, **Miller JB**, and **McCord J**. Utility of N-Terminal Pro-B-Type Natriuretic Peptide -to-Troponin and BNP-to-Troponin Ratios for Differentiating Type 1 from Type 2 Myocardial Infarction: A HIGH-US Sub-Study. *Crit Pathw Cardiol* 2025; Epub ahead of print. PMID: 40997263. Full Text

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BACKGROUND: Differentiating type 1 myocardial infarction (T1-MI) from type 2 MI (T2-MI) remains a diagnostic challenge, even with the availability of high-sensitivity cardiac troponin assays. This study explored whether NT-proBNP, BNP, and their respective ratios to troponin could enhance the ability to distinguish between these MI subtypes. METHODS: As a HIGH-US sub-study, we examined data from 280 patients diagnosed with non-ST elevation myocardial infarction (172 with T1-MI and 108 with T2-MI). We assessed NT-proBNP, BNP, hs-cTnI, and their ratios as potential discriminative biomarkers. Diagnostic accuracy was evaluated using receiver operating characteristic (ROC) curves. RESULTS: NT-proBNP levels were markedly elevated in T2-MI patients compared to those with T1-MI (mean

10,327±12,923 vs 4,675±11,740 ng/L; P=0.006). Conversely, hs-cTnI concentrations were higher in T1-MI (1.4±5.1 vs 0.5±1.1 ng/L; P=0.030). Notably, the NT-proBNP-to-troponin ratio was more than three times greater in T2-MI cases (94,880±152,648 vs 24,209±78,727; P=0.007). NT-proBNP alone demonstrated fair discriminatory capacity (AUC 0.717, 95% CI 0.578-0.856), closely matching the NT-proBNP-to-troponin ratio (AUC 0.720, 95% CI 0.566-0.873). In contrast, BNP and the BNP-to-troponin ratio offered lower diagnostic values. Mean BNP levels were 505.4 ±576.6 ng/L for those with T2-MI and 437.1 ±738.8 ng/L for patients with T1-MI. BNP-to-troponin ratio showed a poor discrimination for the 2 MI types (AUC, 0.660; 95% CI, 0.532-0.789). CONCLUSIONS: Both NT-proBNP and its ratio to troponin show potential in differentiating T1-MI from T2-MI, reflecting distinct underlying pathophysiological processes. Given its comparable performance to the ratio, NT-proBNP alone may serve as a practical and cost-effective standalone marker. These findings support the hypothesis that incorporating NT-proBNP testing into routine clinical workflows may better informs the management of patients with suspected MI.

Internal Medicine

**Memon M**, **Sabra M**, and **Khan AA**. Precision in Action: Using Intracardiac Echocardiography for Targeted Removal of a Large Lead-Related Vegetation in a Patient With Infective Endocarditis. *J Arrhythm* 2025;41(5):e70192. PMID: 40950384. Full Text

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BACKGROUND: Lead-related infective endocarditis is a serious complication of implantable cardioverter-defibrillators (ICDs), especially in patients with advanced heart failure who are poor surgical candidates. Management of large lead-associated vegetations remains a clinical challenge. METHODS: We present the case of a 54-year-old woman with ischemic cardiomyopathy and recurrent ICD complications who developed bacteremia and infective endocarditis with vegetations on the aortic valve and a 1.5 × 1.3 cm mass on the right ventricular lead. Given her poor surgical candidacy due to worsening heart failure, a percutaneous approach was pursued. RESULTS: The patient underwent successful intracardiac echocardiography (ICE)-guided catheter-based vegetation removal using a vacuum-assisted aspiration system, followed by transvenous lead extraction. The procedure was well tolerated, and the patient demonstrated clinical improvement post intervention. CONCLUSIONS: This case illustrates the utility of ICE-guided percutaneous aspiration and lead extraction for managing large lead-related vegetations in patients with infective endocarditis who are not candidates for surgery.

Internal Medicine

**Obeidat L**, **Fadel R**, **Gupta K**, **Naimi A**, **Ronchetto E**, **Ama S**, **Helaly M**, **Malick A**, **Jamil D**, **Ananthasubramaniam K**, and **Azzo Z**. What is the Diagnostic Utility of Cardiac Magnetic Resonance Imaging in Unselected Patients with Premature Ventricular Contractions and Non-Sustained Ventricular Tachycardia? *Am J Cardiol* 2025; Epub ahead of print. PMID: 41016532. Full Text

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PURPOSE: Premature ventricular contractions (PVCs) and non-sustained ventricular tachycardia (NSVT) are common arrhythmias that may signal underlying structural heart disease (SHD). Cardiac magnetic resonance imaging (CMR) has emerged as a valuable tool for detecting myocardial abnormalities in this population. This study aimed to evaluate the diagnostic utility of CMR in patients with PVCs/NSVT and identify clinical predictors of pathologic late gadolinium enhancement (LGE). METHODS: We retrospectively reviewed patients who underwent CMR for PVCs or NSVT between 2012 and 2023 at a single health system. The primary outcome was the presence of pathologic LGE. Clinical data were extracted using ICD-10 codes, and cardiac sarcoidosis (CS) was adjudicated by a multidisciplinary team using WASOG criteria. RESULTS: Among 553 patients (mean age 61.1 ± 14.6 years; 40.7% female), pathologic LGE was identified in 214 (38.6%). Patients with LGE were older and had a greater burden of comorbidities. On multivariable analysis, independent risk factors for LGE included age (aOR 1.04, p=0.001), male sex (aOR 2.37, p<0.001), heart failure (aOR 2.53, p<0.001), and polymorphic PVCs (aOR 1.94, p=0.015). Among patients with LGE, 12.6% had highly probable CS. Other diagnoses included non-ischemic cardiomyopathy (53.7%), ischemic cardiomyopathy (11.7%), and idiopathic (34.6%). CONCLUSION: CMR frequently detects clinically significant myocardial abnormalities in patients with PVCs or NSVT, particularly in those with high-risk features. In this real-world study, nearly 40% of patients had LGE on CMR. An etiology was identified in one-third of these cases. These findings can inform patient selection for CMR in clinical practice to guide diagnosis, risk stratification, and management.

Internal Medicine

Patel T, Kharat M, John JD, Panchal H, **Sardarova N**, Misra G, **Ahmed M**, and Millis RM. Early diagnosis and tailored treatment in atypical idiopathic thrombocytopenic purpura: A CARE compliant case report. *Medicine (Baltimore)* 2025;104(36):e44263. PMID: 40922302. Full Text

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RATIONALE: Idiopathic thrombocytopenic purpura (ITP) is a hematological disorder characterized by a decrease in platelet count due to increased destruction or decreased production. Although the pathophysiology and etiology remain largely unknown, understanding the typical and atypical presentations of ITP is crucial for early diagnosis and effective management. This case report highlights the rationale behind a comprehensive approach for the diagnosis and treatment of ITP, especially in cases with atypical presentations. PATIENT CONCERNS: A 45-year-old woman presented with a mucocutaneous petechial rash spreading over the ocular and oral areas of the face, accompanied by similar manifestations in the limbs. While petechiae are a hallmark of ITP, the initial widespread distribution and specific involvement of these extensive mucocutaneous areas were considered atypical presentation patterns in this case. She also reported moderate gum bleeding, epistaxis, and spontaneous

ecchymosis of the oral mucosa. These symptoms suggested a potential platelet disorder. DIAGNOSES: Based on the clinical presentation and laboratory findings, the diagnosis of ITP was made. The patient's symptoms and laboratory results were consistent with the typical features of ITP, including a decreased platelet count, petechiae, and manifestations of bleeding. INTERVENTIONS: A thorough history and physical examination were conducted to rule out other potential causes of thrombocytopenia, including infections, medications, and underlying autoimmune diseases. Laboratory tests, including complete blood count, peripheral blood smear, and coagulation profile, were performed to assess platelet count, morphology, and clotting function. The diagnosis was initially followed by conservative management. Later on, the patient was also treated with corticosteroids and then intravenous immunoglobulin. OUTCOMES: The patient responded well to intravenous immunoglobulin, thereby demonstrating the effectiveness of the treatment. She was then discharged with maintenance doses of corticosteroids and a close follow-up schedule. LESSONS: This case report illustrates the importance of recognizing the diverse presentations of ITP, including its atypical manifestations. Early diagnosis and effective management are crucial for improving patient outcomes. A comprehensive approach, including thorough history, physical examination, and laboratory tests, is essential for the accurate diagnosis and effective treatment of ITP.

Internal Medicine

**Qureshi MA**, Amir M, Bakht D, Ali K, Asif A, Bakht K, Sarmad M, Tahir M, Shahid A, Rehmani M, Awais MN, Haseeb S, Bokhari SFH, and Ali MKB. Assessing the risk factors of permanent pacemaker implantation following mitral valve surgery: A systematic review and meta-analysis. *Medicine (Baltimore)* 2025;104(36):e44232. PMID: 40922347. Full Text

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BACKGROUND: Mitral valve surgery is a widely performed intervention for the treatment of various mitral valve pathologies. Postoperative conduction disturbances may necessitate permanent pacemaker (PPM) implantation. This study aims to identify and quantify patient-related, cardiovascular, procedural risk factors, and risk score-based predictors of PPM implantation following mitral valve surgery. METHODS: The conduct of this systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses reporting guidelines. A systematic literature search was performed across PubMed, Cochrane Library, Google Scholar, and Embase, including studies published from inception until September 2024. Statistical analyses were conducted using RevMan 5.4 software. RESULTS: The meta-analysis included 8 studies totaling 39,634 patients (PPM: 3417; no PPM: 36,217) and revealed multiple significant predictors of postoperative PPM implantation. Among demographics, advanced age (mean difference [MD] 3.54; P < .00001) and female sex (odds ratio [OR] 1.19; P < .00001) were found as independent risk factors. Comorbidities included hypertension (OR 1.71, P < .00001), diabetes (OR 1.96, P < .00001), renal disease (OR 1.96, P < .00001), preexisting atrial fibrillation (OR 1.82, P < .00001), prior stroke (OR 1.57, P < .00001), chronic lung disease (OR 1.38, P < .00001), peripheral vascular disease (OR 2.03, P = .01), and smoking history (OR 1.19, P < .0001). Cardiovascular predictors comprised mitral stenosis (OR 1.77, P <.00001), prior cardiac surgery (OR 1.48, P = .0002), New York Heart Association class III/IV (OR 1.38, P = .005), and New York Heart Association class I (OR 0.64, P = .03). Procedural factors showed longer cardiopulmonary bypass time (MD 9.89, P < .00001) and aortic cross-clamp duration (MD 11.96, P < .00001) increasing risk, along with concomitant atrial fibrillation ablation (OR 1.34, P = .002). Increased society of thoracic surgeons' mortality risk (MD 1.14%, P = .04) and EuroScore (MD 2.16, P = .0005), both effectively predicted PPM need. CONCLUSION: This meta-analysis represents the first comprehensive evaluation of risk factors associated with PPM implantation in patients undergoing mitral valve surgery. Several significant risk factors have been identified, warranting further research to validate and expand upon these findings.

Internal Medicine

Shahzil M, Hasan F, Qureshi AA, Jamil Z, Kashif T, **Faisal MS**, Arif TB, **Chaudhary AJ**, Farooq U, Ali H, and Levenick JM. Efficacy and Safety of Linaclotide as an Adjunct to Polyethylene Glycol in Bowel Preparation: A Meta-Analysis. *J Dig Dis* 2025; Epub ahead of print. PMID: 40955723. Full Text

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OBJECTIVES: Linaclotide, a guanylyl cyclase-C agonist, may enhance efficacy and tolerability when combined with polyethylene glycol (PEG) for bowel preparation. This meta-analysis evaluated linaclotide plus PEG versus PEG alone for bowel preparation prior to colonoscopy. METHODS: Randomized controlled trials (RCTs) including adults undergoing colonoscopy that compared linaclotide plus PEG with PEG alone for bowel preparation were identified via database search up to March 2024. Statistical analysis was performed in RevMan Web using random-effects models. RESULTS: Eleven RCTs were analyzed. Adequate bowel preparation rate was comparable (risk ratio [RR] 1.01, 95% confidence interval [CI] 0.98-1.04; I(2) = 23%), as was cecal intubation rate (RR 1.01, 95% CI 1.00-1.01). Subgroup analyses showed that compared with 3-L PEG alone, 2-L PEG plus linaclotide was non-inferior, while 3-L PEG plus linaclotide was superior regarding bowel preparation adequacy (RR 1.11, 95% CI 1.01-1.23) and total Boston Bowel Preparation Scale (BBPS) score (mean difference 0.44, 95% CI 0.04-0.85). Right and left colon BBPS scores were also higher with linaclotide. Polyp detection rate improved significantly in the 3-L PEG plus linaclotide subgroup (RR 1.78, 95% CI 1.32-2.40), whereas adenoma detection rate and withdrawal time were comparable. Linaclotide reduced abdominal pain, bloating, nausea, and sleep disturbance, and increased willingness to repeat colonoscopy. CONCLUSIONS: Linaclotide with PEG provides comparable overall bowel cleansing to PEG alone while reducing adverse events and improving patient acceptance. Importantly, 2-L PEG plus linaclotide was non-inferior compared with 3-L PEG, whereas 3-L PEG plus linaclotide showed superiority over 3-L PEG alone, supporting its use in low-volume bowel preparation strategies.

Internal Medicine

**Sheffeh MA**, du Fay de Lavallaz J, Magana AE, Siontis KC, and Liang JJ. Trends and Disparities in Ventricular Tachycardia-Related Mortality According to Cardiomyopathy Type in the United States. *J Cardiovasc Electrophysiol* 2025; Epub ahead of print. PMID: 41017393. Full Text

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BACKGROUND: Recent data show increased ventricular tachycardia (VT) related mortality. We aimed to investigate the trends and disparities of VT-related mortality according to cardiomyopathy subtypes. METHODS: Mortality and demographic data were obtained from the CDC Wide-ranging Online Data for Epidemiologic Research database between 1999 and 2020. VT-related mortality was defined as the underlying cause of death and ischemic cardiomyopathy (ICM) or nonischemic cardiomyopathy (NICM) as the contributing cause of death. The direct method of standardization was utilized to estimate age-adjusted mortality rates (AAMRs). Temporal trends were evaluated using log-linear regression models. RESULTS: A total of 15 888 deaths were related to both VT and ICM, and 16 777 were due to both VT and NICM. There was a significant increase in VT and ICM-related mortality between 2006 and 2020 with

an APC of +1.38% ($p < 0.05$). Similarly, VT and NICM-related mortality increased between 2008 and 2020 with an APC of +0.60% ($p < 0.05$). ICM had a higher AAMR in males [6.23 (6.12-6.34)], Whites [3.49 (3.43-3.54)], Hispanics [2.11 (1.95-2.26)], and the Midwest region [3.73 (3.61-3.85)] compared to NICM. In contrast, NICM had a higher AAMR in females [1.57 (1.52-1.61)], Black or African Americans [5.02 (4.84-5.20)], and the South region [3.10 (3.03-3.18)]. p for all trend < 0.05. CONCLUSIONS: Real-world data show significant differences in VT-related mortality according to cardiomyopathy subtypes with prominent sex, race, and regional disparities. Clinical and public health strategies are needed to address inequities and improve outcomes.

Internal Medicine

**Singh B**, Kalra S, Khanna T, Kohli I, Kumar V, Sohal A, and Sejpal D. The Prevalence of Various Autoimmune Comorbidities in Patients with Inflammatory Bowel Disease. *Epidemiologia (Basel)* 2025;6(3). PMID: 40981083. Full Text

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Introduction: Patients with inflammatory bowel disease (IBD) are at increased risk of developing other autoimmune disorders due to possible shared genetic, environmental, and immunological mechanisms. While autoimmune diseases are frequently observed in patients with IBD, data quantifying their inpatient prevalence and their association with outcomes such as mortality remain limited. Methods: National Inpatient Sample (NIS) 2016-2020 and International Classification of Diseases 10th Version, Clinical Modification (ICD-10-CM) diagnosis codes were used to identify patients with IBD and autoimmune conditions. A multivariate logistic regression analysis to identify an association between various autoimmune diseases and various IBDs was performed. Results: The study population included 141,478,025 patients. An association was found between 24 autoimmune conditions and IBD. Conclusions: Our study identified autoimmune comorbidities that are more prevalent in IBD patients. We found that polymyositis, AIHA, ITP, and thrombotic microangiopathy are associated with a higher risk of in-hospital mortality. Psoriasis and hypothyroidism are associated with a lower risk of in-hospital mortality. Further studies are needed to explore the mechanisms responsible.

Nephrology

Hidalgo LG, Madill-Thomsen KS, Reeve J, Mackova M, Gauthier P, Demko Z, Prewett A, Lee M, Alhamad T, Anand S, Arnol M, Baliga R, Banasik M, Blosser CD, Bobba S, Brennan D, Bromberg J, Budde K, Chamienia A, Chow K, Ciszek M, Costa N, Dęborska-Materkowska D, Debska-Ślizień A, Domański L, 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, Kumar D, Lan J, Lowe D, Mazurkiewicz J, Miglinas M, Moinuddin I, Mueller T, Myślak M, Naumnik B, Pączek L, **Patel A**, Perkowska-Ptasińska A, Piecha G, Poggio E, Bloudíčkova SR, Regele H, Schachtner T, Shojai S, Sikosana MLN, Slatinská J, Smykal-Jankowiak K, Haler Ž V, Viklicky O, Vucur K, Weir MR, Wiecek A, Zaky Z, and Halloran PF. Improving the histologic detection of donor-specific antibody-negative antibody-mediated rejection in kidney transplants. *Am J Transplant* 2025; Epub ahead of print. PMID: 40854490. Full Text

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Emerging treatments for antibody-mediated rejection (ABMR, NEJM391 (2):122-132) have increased the importance of ABMR detection when donor-specific antibody (DSA) is negative. We addressed this issue in the Trifecta-Kidney study (ClinicalTrials.gov #NCT04239703) using 3 centralized tests in 690 kidney transplant biopsies: DSA (One Lambda Inc), blood donor-derived cell-free DNA (dd-cfDNA, Prospera™ test, Natera, Inc), and molecular biopsy assessment (MMDx). We used an "AutoBanff 2022" algorithm to model the impact of alternative DSA interpretations on the histologic diagnosis of DSA-negative ABMR following Banff guidelines, including agreement with dd-cfDNA and molecular ABMR. Lowering MFI cutoffs for DSA positivity did not improve the detection of DSA-negative ABMR. However, simply calling all DSA as positive allowed the Banff 2022 guidelines to identify 46% more ABMR cases with no measurable conventional DSA, and per net reclassification improvement increased agreement between histologic diagnoses and both dd-cfDNA (P = 7.72E-7) and molecular ABMR (P = 7.69E-7). New ABMR cases were as strongly positive for dd-cfDNA and molecular ABMR as those found using the conventional DSA interpretation. A validation set analysis using INTERCOMEX study data (ClinicalTrials.gov NCT#01299168) confirmed these findings and found that the new DSA-negative ABMR cases identified by calling all DSA-positive had the same risk for graft loss as those found with conventional DSA interpretation. Trifecta-Kidney Study ClinicalTrials.gov #NCT04239703.

Nephrology

Obeidat AE, **Mahfouz RT**, Shah PK, Kozai LA, Darweesh MR, Mansour MM, Yassine AA, Kuwada SK, and Chang CH. Potential impact of aortic stenosis diagnosis on mortality and other in-hospital complications in patients with pancreatic cancer undergoing pancreaticoduodenectomy. *Porto Biomed J* 2025;10(5):e302. PMID: 40933723. Full Text

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BACKGROUND: Patients with aortic stenosis undergoing noncardiac surgery pose a dilemma to physicians as they are at an increased risk for complications. This study aims to investigate the effect of aortic stenosis on mortality and other complications in patients with pancreatic cancer undergoing pancreaticoduodenectomy. METHODS: We investigated patients with pancreatic cancer undergoing pancreaticoduodenectomy between 2016 and 2019 using the National Inpatient Sample database. The study population was divided based on the presence or absence of aortic stenosis. Multivariate logistic regression analyses were performed to determine factors associated with in-hospital mortality and other complications. RESULTS: Of the 16,150 patients with pancreatic cancer who underwent pancreaticoduodenectomy, 165 patients were diagnosed with aortic stenosis. The mean age of patients with aortic stenosis was significantly higher. Patients with aortic stenosis had a significantly higher in-hospital mortality, occurrence of cardiac arrest, and ICU admission compared with patients without aortic stenosis. There was no difference in mechanical ventilation, hospital charges, and length of stay between the two groups. CONCLUSIONS: Aortic stenosis was found to be associated with higher in-hospital mortality and worse outcomes in patients with pancreatic cancer undergoing pancreaticoduodenectomy. Preoperative risk stratification and a multidisciplinary approach to perioperative management, among other measures, should be considered to improve outcomes.

Neurology

**Wang L**, **Lu X**, **Szalad A**, **Zhang Y**, **Li Y**, **Lu M**, **Kemper A**, **Liu Z**, **Liu XS**, **Chopp M**, and **Zhang ZG**. Engineered miR-214 enriched Schwann cell-derived extracellular vesicles amplify therapeutic efficacy for peripheral neuropathy in T2D mice. *Front Cell Neurosci* 2025;19:1649830. PMID: 40950414. Full Text

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Extracellular vesicles (EVs) derived from healthy Schwann cells (SC-EVs) ameliorate peripheral neuropathy in diabetic mice and rescue sciatic nerve function in Schwann cell Dicer knockout mice in part via SC-EV cargo miRNAs. Among these miRNAs, miR-214 repairs nerve damage. The present study investigated whether engineered SC-EVs with elevated miR-214 (214-EVs), further amplify the therapeutic effect of naïve SC-EVs (naïve-EVs) on reducing diabetic peripheral neuropathy (DPN) in a mouse model of high-fat diet (HFD)-streptozotocin (STZ) induced type 2 diabetes. Compared to naïve-EVs, 214-EVs significantly improved motor and sensory nerve conduction velocity of the sciatic nerve and thermal latency, which were associated with increased intraepidermal nerve fiber density, axonal diameter, and myelin thickness in the sciatic nerve. Quantitative RT-PCR and Western blot analyses of sciatic nerve tissues showed that, compared to naïve-EVs, 214-EVs significantly increased miR-214 levels and downregulated axonal inhibitory protein PTEN and the myelination inhibitory protein cJUN. Furthermore, 214-EVs markedly suppressed neuroinflammation by decreasing CD68 + macrophages and inactivating the TLR4/NF-κB signaling pathway. Collectively, our findings demonstrate that miR-214-

enriched SC-EVs are superior to naïve-EVs to ameliorate DPN and represent a promising EV-based therapeutic strategy.

Neurology
Zaganas I, Tsiverdis I, Kokosali E, Litso I, Drakos M, Skoula I, Zabetakis A, Mathioudakis L, Mastorodemos V, and **Mitsias P**. Study of the NOTCH3 Gene Reveals the First CADASIL Cases in Crete and a Novel Pathogenic Variant. *Brain Behav* 2025;15(9):e70789. PMID: 40999599. Full Text

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BACKGROUND: NOTCH3 gene variants are associated with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). In this study we aimed to examine the presence of pathogenic NOTCH3 variants in individuals with suspected CADASIL on the Greek island of Crete. This represents the first report of CADASIL patients in Crete. METHODS: We reviewed the medical records of the University Hospital of Heraklion and identified three patients with the clinical diagnosis of CADASIL. In these patients pathogenic NOTCH3 variants were identified through targeted or whole-exome sequencing (WES). RESULTS: A novel heterozygous variant in exon 4 of the NOTCH3 gene (p.Cys206Trp; NM_000435.3:c.618C>G) was found in a 67-year-old woman who suffered from recurrent ischemic strokes, cognitive impairment, depression, and headache, as well as her son, who presented with headache, anxiety disorder, and insomnia. Brain MRI for both patients revealed white matter disease, including the anterior temporal lobes. The characteristics of this variant (a Cys-related variant in the epidermal growth factor repeats area) support its pathogenicity. We also identified a 72-year-old patient affected by CADASIL and carrying a previously described p.Arg607Cys (NM_000435.3:c.1819C>T) NOTCH3 variant. CONCLUSIONS: This report extends the geographic and genotypic spectrum of pathogenic NOTCH3 variants and documents the first CADASIL cases on the island of Crete, Greece.

Neurosurgery
Falowski S, Ali R, Sweet J, Mackel C, Kesarwani R, Arle J, Larkin MB, Pinckard-Dover HN, Stone L, Nerison C, Ben Haim S, Rosenow J, Viswanathan A, Petersen E, Lad N, **Schwalb J**, and Raslan A. Technical and Clinical Overview: Spinal Cord Stimulation. *Neuromodulation* 2025; Epub ahead of print. PMID: 41003458. Full Text

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INTRODUCTION: Spinal cord stimulation (SCS) has evolved from simple systems with limited waveforms and electrode configurations to modern, complex systems developed to exert specific effects on the central nervous system. The growth in this space has focused on improving therapy delivery, enhancing

tolerance, increasing longevity, and expanding indications. MATERIALS AND METHODS: Members of the American Association of Neurological Surgeons/Congress of Neurological Surgeons Pain Section evaluate current technologies on the market to define the state of implants and devices. The study also discusses each manufacturer's scientific evidence and waveforms, in addition to reviewing their current publications and support data. RESULTS: The SCS devices of all Food and Drug Administration-approved companies are reviewed, including Medtronic, Abbott, Boston Scientific, Saluda, Biotronik, and Nevro. CONCLUSION: Technology and innovation are evolving rapidly in the field of spinal neuromodulation space. Clinical trials providing level 1 evidence have followed suit and indicated the superiority of this therapy to medical management in treating patients with different painful conditions.

Neurosurgery

Harland TA, Ku A, Topp G, Prabhala T, Bandlamuri S, Thiets R, Figueroa F, Ortiz S, Boulos A, and **Entezami P**. Platelet function testing does not predict hemorrhage progression in mild traumatic brain injury. *J Clin Neurosci* 2025;142:111647. PMID: 40992201. Full Text

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BACKGROUND: Antiplatelet medications are frequently assumed to increase the risk of radiographic progression following traumatic intracranial hemorrhage (ICH), influencing guidelines that recommend prolonged observation and repeat imaging. However, antiplatelet use does not uniformly result in functional platelet inhibition, and the clinical relevance of therapeutic response remains unclear. METHODS: We conducted a retrospective cohort study of adult patients with traumatic ICH and a Glasgow Coma Scale (GCS) score of 13-15 who were on antiplatelet therapy and underwent platelet function testing (VerifyNow PRU or PFA) on admission. Patients were classified as therapeutic or non-therapeutic based on test thresholds. All patients received follow-up CT imaging within 24 h. Clinical variables and outcomes, including radiographic progression, surgical intervention, and mortality, were compared between groups. A sensitivity analysis excluded patients with hematocrit <30 % or platelet count <100,000. RESULTS: A total of 239 patients were included: 190 in the non-therapeutic group and 49 in the therapeutic group. Radiographic progression occurred in 17.6 % of patients overall, with no significant difference between therapeutic and non-therapeutic groups (20.4 % vs. 16.8 %; p = 0.53). Surgical intervention (p = 0.57) and mortality (p = 0.38) rates were similarly low and comparable. Sensitivity analyses confirmed these findings (p = 0.81). CONCLUSIONS: Therapeutic platelet inhibition was not associated with increased risk of radiographic or clinical worsening in patients with mild traumatic ICH. These findings challenge current assumptions regarding antiplatelet risk and suggest that platelet function testing may have limited utility in this setting. These findings support the need to reevaluate current guidelines and validate risk stratification approaches through prospective multicenter studies.

Neurosurgery

**Huang J**, **Doemer A**, **Siddiqui S**, **Shah M**, **Al Asadi A**, **DiCarlo A**, **Thind K**, **Moceri A**, **Scarpace L**, **Lee I**, and **Robin A**. Novel use of 3D printing for preoperative dose estimation in the first case of GammaTile spine implantation. *Brachytherapy* 2025; Epub ahead of print. PMID: 40992982. Full Text

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PURPOSE: For a patient who had two previous courses of external beam radiation therapy for rectosigmoid adenocarcinoma and presented with painful, recurrent disease in the sacrum, this study describes the first use of Cs-131 LDR GammaTile therapy outside of the brain and demonstrates a novel use of 3D printing for preoperative dose estimation. MATERIAL AND METHODS: A personalized 3D-printed model of the patient's spine was created using segmented MRI data, differentiating uninvolved bone, tumor, and thecal sac and nerve roots, with a Stratasys J5 MediJet® Printer. This model was used to simulate surgical resection and placement of dummy radioactive sources. A CT scan of the model facilitated preoperative dose calculations, including physical dose using Eclipse planning software and biologically effective dose (BED) using MIM Maestro software. The predicted dose was then compared to the postimplant dosimetry for the actual patient. RESULTS: For the relevant organ at risk (thecal sac), the max dose (D(0.035cc)) was calculated accurately within 8.0% for physical dose and within 10.0% for BED when comparing the dose estimated using our 3D-printed model and the patient's postimplant dosimetry. CONCLUSIONS: 3D printing can be used preoperatively to estimate dose to critical organs at risk for patients receiving surgical resection followed by Cs-131 LDR implantation in the spine and can be especially valuable in the context of reirradiation.

Neurosurgery
**Suhail H**, Rahman MA, Yadab MK, **Gonawala S**, **deCarvalho A**, **Ewing JR**, **Snyder J**, and **Ali MM**. A novel HPβCD-Cu(DDC)(2) delivery system in patient derived orthotopic xenograft targeting MGMT-mediated temozolomide resistance in glioblastoma. *Sci Rep* 2025;15(1):32869. PMID: 40998915. Full Text

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The uniform lethality of glioblastoma (GBM) with a survival of less than 2 years despite best available therapy is attributed to treatment resistance due to DNA repair mechanisms that drive disease relapse and tumor heterogeneity. One prognostic factor identified as a reliable biomarker for GBM sensitivity to temozolomide (TMZ) and radiotherapy (RT) is the overexpression of O(6)-methylguanine-methyl-transferase (MGMT) enzyme. Patients with active MGMT were found to receive little benefit from TMZ and RT. They represent a group of great unmet need with no treatment options that significantly improve survival. Recently, several preclinical and clinical studies suggest that the alcohol aversion drug, disulfiram (DSF), inhibited MGMT and improved the efficacy of TMZ in GBM when combined with copper (Cu). However, phase II trial showed that there was no significant survival benefit from oral Cu/DSF. Nevertheless, the major limitation of oral Cu/DSF has been delivery of fragile DSF to the in vivo system. To address this limitation, we developed a novel delivery system using 2-hydroxypropyl beta cyclodextrin (HPβCD) encapsulating the Cu complex of DSF's active metabolite, diethyldithiocarbamic acid (DDC). It was determined that HPβCD stabilized Cu(DDC)(2). In vitro cell culture study revealed that HPβCD-Cu(DDC)(2) inhibited MGMT through the ubiquitin-proteasome pathway. Inhibition of MGMT activity in cell cultures vastly increased the alkylation-induced DNA double-strand breaks, cytotoxicity, and the levels of apoptotic markers like histone family member X (γ-H2AX), JNK-P and cleavage of Poly [ADP-ribose] polymerase 1 (PARP-1). Preliminary intravenous delivery of HPβCD-Cu(DDC)(2) in combination with TMZ in an MGMT-positive patient derived orthotopic xenograft (PDOX) model demonstrated tumor size regression. HPβCD-Cu(DDC)(2) targets MGMT-145-cysteine and its unique cytotoxic mechanism circumvents MGMT-mediated TMZ resistance. This novel delivery system shows promise for overcoming MGMT-mediated resistance in GBM, offering a potential new therapeutic strategy.

Neurosurgery
**Turnbull J**, **Griepp DW**, **Caskey J**, **Alsalahi A**, **Desai S**, **Claus CF**, and **Griauzde J**. Middle Meningeal Artery Embolization: Poised to Become the Standard of Care for Chronic Subdural Hematoma. *World Neurosurg* 2025;124481. Epub ahead of print. PMID: 40953814. Full Text

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Obstetrics, Gynecology and Women's Health Services

**Masters S**, **Kim S**, **Moses E**, **McManaman A**, **Ghimire B**, and **Goyert G**. Stage IV Pancreatic Adenocarcinoma in Pregnancy. *Matern Fetal Med* 2025. PMID: Not assigned. Full Text

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Obstetrics, Gynecology and Women's Health Services

Prasad N, Chaturvedi S, Singh H, **Udumula MP**, Rawat A, Jeyakumar M, Jaiswal A, Kumar S, and Agarwal V. Peritoneal Dialysis -Associated Fibrosis: Emerging Mechanisms and Therapeutic Opportunities. *Front Pharmacol* 2025;16:1635624. PMID: 40918510. Full Text

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Peritoneal Dialysis (PD) requires a healthy and functional peritoneal membrane for adequate ultrafiltration and fluid balance, making it a vital treatment for patients with end-stage renal disease (ESRD). The spectrum of PD-associated peritoneal fibrosis encompasses a diverse range of collective mechanisms: peritoneal fibrogenesis, epithelial to mesenchymal transition (EMT), peritonitis, angiogenesis, sub-mesothelial immune cells infiltration, and collagen deposition in the sub-mesothelial compact zone of the membrane that accompany deteriorating membrane function. In this narrative review, we summarize the repertoire of current knowledge about the structure, function, and pathophysiology of the peritoneal membrane, focusing on biomolecular mechanisms and signalling pathways that potentiate the development and progression of peritoneal fibrosis. The article suggests future directions that could enhance our comprehension of the relationship between peritoneal membrane dysfunction and its fibrosis to elucidate the promising targets for therapeutic interventions. A thorough understanding of early events in pathophysiology closely associated with the inflammatory events in peritoneal fibrosis is the logical starting point for identifying new targets rather than concentrating on more downstream effects. Biomarkers are essential for monitoring the progression of peritoneal fibrosis and evaluating the effectiveness of therapeutic interventions. Biomarkers are evolving in concert with new targets and novel agents, and biomarker outcomes offer a means of monitoring the peritoneal membrane's health. Recent approaches to reducing the etiologies of peritoneal membrane dysfunction, the impact of fibroblast switch, and peritoneal membrane events perturbing fibroblast function are explored and suggest using unique, effective therapeutic strategies to target peritoneal fibrosis and associated complications.

Ophthalmology and Eye Care Services

Sethi D, Mohiddin O, Kelleher C, Kasetty VM, **Kumar N**, **Desai UR**, and **Hamad A**. Syphilis Uveitis: A Case of Occam's Razor, Hickam's Dictum, and Crabtree's Bludgeon. *Cureus* 2025;17(8):e89329. PMID: 40918778. Full Text

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This report discusses a case of diagnosing neurosyphilis in a non-classical presentation with confounding test results needing a deliberate and multidisciplinary diagnostic approach. A 38-year-old immunocompetent male presented with uveitis and a skin rash. Although serology was positive for syphilis (rapid plasma reagin 1:128), it was also positive for tuberculosis, and a dermatology consult identified the rash as psoriasis, creating a complex diagnostic picture. Based on a high suspicion of ocular syphilis, the patient received intravenous penicillin, which led to the complete resolution of his ocular symptoms and a serologically confirmed cure. This case of an ophthalmic masquerading disease was complicated by misleading clinical signs and a coexisting positive serology, serving as a reminder to maintain a broad differential diagnosis and be systematic in workup and management in order to optimize clinical outcomes.

Orthopedics/Bone and Joint Center
Balach T, **Guthrie ST**, Schroeder N, and Socci A. Are We Choosing and Training the Best Surgeons? *J Bone Joint Surg Am* 2025; Epub ahead of print. PMID: 40906795. Full Text

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The U.S. orthopaedic surgery residency match is among the most competitive in medicine; in 2024, 40% of applicants were unmatched. This drives applicants to differentiate themselves, while residency programs aim to evaluate candidates holistically. In order to understand the process that is used to select and educate the best surgeons, we examined medical student advising, the role of national organizations, and programmatic practices for resident selection. Effective career advising is essential for attracting and supporting highly qualified applicants. Exposure through preclinical courses, clerkships, and accessible mentorship enhances interest in orthopaedics among applicants with an array of experiences, skills, and backgrounds. National initiatives (e.g., the Orthopaedic Residency Information Network [ORIN]) provide centralized resources to address disparities in information access, although further standardization and consolidation are needed. Collaboration among national stakeholders is necessary to ensure fairness in the match process and to attract the best applicants. Initiatives like preference signaling have shown promise, increasing interview rates at preferred programs and better aligning applicants with residency opportunities. However, barriers such as limited access to research, costly away rotations, and expensive applications disproportionately affect underrepresented groups, highlighting the need for systemic changes. Resident selection practices must evolve to counter the inefficiencies and biases. Holistic review processes, structured interviews, and mission-driven scoring can improve alignment with program values. Programs must consider their setting and their population and also consider applicants who demonstrate an understanding of, and have an interest in caring for, that community. Improving orthopaedic residency selection requires collaborative efforts across organizations, advisors, and programs to refine processes and ensure the selection and training of those who will advance clinical orthopaedics and the science of orthopaedic surgery and also meet the needs of all patient populations.

Orthopedics/Bone and Joint Center
**Best BJ**, **Khan U**, **Weaver MJ**, **Puri S**, **Rababa I**, and **Afsari A**. The Motown Corkscrew: A Simple Method for Extraction of an Embedded Intra-Articular Foreign Body. *JBJS Case Connect* 2025;15(3). PMID: 40966361. Full Text

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CASE: A 17-year-old boy presented after a gunshot wound; computed tomography showed a comminuted posterior-wall acetabular fracture and a bullet 90% embedded. Through a Ganz surgical

dislocation, a standard 2.5 mm drill bit was advanced 8 to 10 mm into the projectile, its flutes functioning as a self-tapping screw to rock and extract the bullet en bloc, followed by trochanteric osteotomy fixation. He regained painless full activity by 2 months; 33-month imaging confirmed durable union with no osteolysis. CONCLUSION: The "Motown Corkscrew" technique provides a cost-neutral, controlled method to remove bone-embedded intra-articular bullets while preserving articular structures.

Orthopedics/Bone and Joint Center
**Gaudiani MA**, **Nerys-Figueroa J**, **Jurayj A**, **Wager SG**, **Kadakolh H**, **Hamade H**, **Hodson N**, **Kasto J**, **Makhni EC**, **Mahylis JM**, and **Muh SJ**. Young age, female sex, smoking, and worse area deprivation index associated with prolonged postoperative opioid use after rotator cuff repair. *Shoulder Elbow* 2025; Epub ahead of print. PMID: 40951910. Full Text

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BACKGROUND: Oral opioid analgesia is commonly used for postoperative pain control in arthroscopic rotator cuff repair (RCR). Concerns about opioid side effects and potential abuse persist. This study aimed to identify risk factors for prolonged opioid use (POU) after RCR and assess its impact on patient-reported outcomes. METHODS: A retrospective chart review included patients over 18 years old who underwent primary arthroscopic RCR and had at least one preoperative and postoperative patient-reported outcomes measurement information system (PROMIS) score. POU was defined as at least one opioid prescription refill more than 30 days postoperatively. Demographic characteristics, clinical outcomes, and PROMIS scores up to one year postoperatively were collected. RESULTS: A total of 318 patients were included, and 38 had POU. Logistic regression identified opioid refill within 30 days after surgery, younger age, female sex, smoking, higher area deprivation index, and higher preoperative PROMIS depression score was associated with POU. Patients with POU had higher reoperation rates (15.8% vs. 5.4%; P = 0.015) and worse PROMIS pain interference and PROMIS upper extremity scores postoperatively. CONCLUSION: Risk factors for POU after arthroscopic RCR include younger age, female sex, smoking, depression, higher area deprivation, and early opioid refill. POU correlated with higher reoperation rates and poorer postoperative outcomes.

Orthopedics/Bone and Joint Center
Ketelaar E, McDonald M, and **Dietz J**. Periprosthetic Humeral Shaft Fracture about Total Elbow Arthroplasties Managed with Medial and Lateral Femoral Strut Allografts and Implant Retention: A Case Report. *J Orthop Case Rep* 2025;15(9):240-244. PMID: 40936861. Full Text

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INTRODUCTION: Expanding indications for total elbow arthroplasty in recent years have led to increased occurrence of complications, such as periprosthetic elbow fracture, which can occur in up to 12% of cases. Several management options for periprosthetic elbow fracture have been suggested in literature; however, there is currently no accepted guideline for treatment. CASE REPORT: We present two cases of periprosthetic humerus fractures without implant loosening multiple years after the index procedures. They were treated with open reduction internal fixation (ORIF) utilizing a plate with medial and lateral cortical strut femoral allografting with implant retention. CONCLUSION: Two cases of periprosthetic humerus fractures about total elbow arthroplasties were successfully treated with ORIF with medial and lateral cortical strut augmentation. Treatment for periprosthetic elbow fractures should be tailored to each patient based on factors, such as stability of implant, bone stock, and patient goals.

Orthopedics/Bone and Joint Center
**Lizzio VA**, **James CL**, **Kasto JK**, **Sanii RY**, and **Muh SJ**. Fulfillment of patients' expectations for reverse total shoulder arthroplasty for the treatment of rotator cuff tear arthropathy using the Exactech Equinoxe Platform. *J Shoulder Elbow Surg* 2025; Epub ahead of print. PMID: 40835106. Full Text

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BACKGROUND: Despite the increasing use of reverse total shoulder arthroplasty (rTSA), there remain limited data regarding perioperative expectations and fulfillment of expectations for patients undergoing rTSA for rotator cuff tear arthropathy (CTA). Thus, the purpose of this study was to determine the proportion of expectations that are fulfilled following rTSA and to determine which patient characteristics are associated with fulfillment of expectations at 2-year follow-up. METHODS: Preoperatively, patients completed the Hospital for Special Surgery's Shoulder Surgery Expectation Survey, American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form (ASES), visual analog scale (VAS) for pain, and a Single Assessment Numeric Evaluation (SANE) score for the affected shoulder. At 2-year follow-up, patients were asked to what extent each of their corresponding preoperative expectations that they had previously cited as "very important" were now fulfilled, and again completed the patient-reported outcomes. Demographic and range of motion (ROM) data were also collected. RESULTS: Seventy-seven patients met all inclusion criteria and were included in this study. The expectations most frequently cited as being "very fulfilled" postoperatively were improvement in self-care (75%), improvement in ability to drive and put on seatbelt (77%), and relief of daytime pain (73%). Eighty-one percent of patients cited improvement in shoulder ROM as an important expectation preoperatively, but only 53% reported that this expectation was "very fulfilled" postoperatively. Patients with better postoperative ASES scores ($P < .001$), better VAS scores ($P < .001$), and better SANE scores ($P < .001$) compared with the average patient had a greater proportion of expectations fulfilled. CONCLUSIONS: Patients undergoing rTSA for CTA had greatest fulfillment of expectations for improvement in self-care, ability to drive, and relief of daytime pain at 2-year follow-up. Relatively few patients reported fulfillment of expectations for shoulder ROM. Better postoperative ASES, VAS, and SANE scores correlated with greater fulfillment of expectations. It is important to understand traditional objective metrics considered for success to surgeons may not be the same as a patient's perspective. Using this information, surgeons can better tailor their preoperative discussions with patients to appropriately manage expectations.

Orthopedics/Bone and Joint Center

Salazar DH, DiCaprio M, **Braman J**, Denduluri SK, Plancher KD, and Fishman FG. Health-Care Leadership and Orthopaedic Surgeons: Exploring the Value of an Advanced Degree. *J Bone Joint Surg Am* 2025; Epub ahead of print. PMID: 40906821. Full Text

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As the field of health care continues to evolve, it requires physician leaders who are not only clinically strong but also knowledgeable in business, public health, health-care administration, and medical law. In this article, we investigate the benefits and challenges of pursuing advanced graduate-level education for orthopaedic surgeons. Advanced training can assist clinicians in the development of leadership skills and career advancement opportunities and deepen their understanding of the modern complexities of health-care systems. Key takeaways include the importance of strategic thinking, emotional intelligence, and the ability to navigate complex health-care environments. The decision to pursue an advanced degree should align with an individual's career goals and personal circumstances. Advanced degrees and leadership programs may provide the requisite competencies and valuable tools for physicians to lead effectively in an increasingly dynamic health-care environment.

Otolaryngology – Head and Neck Surgery

Bui L, Espinoza V, Giang HA, Schiffer LP, Do P, Ngu P, Vu C, Tiro J, **Adjei Boakye E**, Phillips SM, Brandt H, Berry E, Tran S, Macdonald E, Khuc C, Nguyen J, Vuong T, and Vu M. U.S. Vietnamese Parents' Perceptions of Different Approaches for Confirming Adolescent HPV Vaccination Records in Research Studies. *Health Expect* 2025;28(5):e70448. PMID: 41020406. Full Text

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BACKGROUND: The United States (U.S.) Vietnamese communities face a high burden of HPV-related cancer rates; they also have low HPV vaccination coverage. HPV vaccination is a safe, effective tool to prevent HPV-related cancers, particularly when administered during adolescence. Understanding Vietnamese parents' perspectives on the acceptability of different HPV vaccination status verification methods can improve the implementation of community-based research interventions to improve HPV vaccine coverage in this population. OBJECTIVE: We assessed their perceptions of three HPV vaccination status confirmation methods: medical records, vaccination card photographs, and self-reported surveys. DESIGN: We conducted interviews with Vietnamese parents of adolescents ages 9-18, healthcare providers, and community leaders (n = 34). We used an inductive thematic analysis approach with four qualitative coders. RESULTS: Preferences for confirming vaccination status were split almost equally among each method. Key drivers of these preferences included privacy concerns, autonomy, efforts required from parents, digital literacy, and data accuracy. DISCUSSION: These findings suggest offering multiple confirmation options to accommodate diverse preferences and enhance the effectiveness of HPV vaccination promotion strategies in this population. PUBLIC CONTRIBUTION: Community involvement was integral to the design, implementation of this project, and writing of the manuscript. The study team partnered with a community organization that works closely with the U.S. Vietnamese population and Vietnamese healthcare providers. The group met regularly to discuss participant recruitment strategies and study instruments. Lived experiences from parents of adolescents, community leaders, and healthcare providers were included in the production of this manuscript to guide the interpretation of preferences for vaccination confirmation methods.

Otolaryngology – Head and Neck Surgery

**Grewal JS**, and **John RC**. Spontaneous Mandible Regeneration After Segmental Resection in a Pediatric Patient With Ameloblastoma. *J Craniofac Surg* 2025; Epub ahead of print. PMID: 40982890. Full Text

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BACKGROUND: The purpose of this case report is to highlight the understated regenerative potential of the pediatric mandible, which favors early aggressive management and delayed secondary reconstruction of the mandible in the management of ameloblastoma, a well-known pathology. METHODS: This is a case of an otherwise healthy 12-year-old girl presented with complaints of loose teeth and right facial swelling. An orthopantogram was obtained, which revealed a unilocular radiolucent lesion of the right mandible. The lesion was biopsied to be plexiform ameloblastoma, and the patient underwent segmental mandibulectomy and temporary reconstruction with custom reconstruction mandibular bar with future plans for microvascular reconstruction. RESULTS: Patient was followed postoperatively with serial orthopantograms and 3-dimensional computed tomography at 17 months that revealed progressive mandibular regeneration avoiding need for further reconstruction. CONCLUSIONS: Delayed reconstruction of the mandible in the pediatric population can be minimized with early aggressive management of a solid ameloblastoma. The ideal environment for regeneration of the mandible should be

taken into consideration during treatment planning: the absence of infection, rigid fixation, patient age, and an intact periosteum.

Otolaryngology – Head and Neck Surgery
**Grewal JS**, Wax MK, and Ducic Y. Secondary Free Flap Reconstruction of the Maxilla Following Obturator Failure. *J Craniofac Surg* 2025; Epub ahead of print. PMID: 40951981. Full Text

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BACKGROUND: In patients with acquired maxillary defects, obturators are often effective, but some fail, necessitating further surgery, typically via free flap reconstruction. Long-term functional outcomes in these cases are underreported. This study examines the outcomes of secondary free flap reconstruction in patients who failed obturator use, focusing on enteral and tracheostomy tube dependence, dental implantation rates, and complications. METHODS: This retrospective cohort study included patients who were initially planned for maxillary reconstruction with an obturator but were unable to retain it due to mechanical issues, not financial constraints. RESULTS: Seventy-one patients were included. There were no flap losses. Postoperatively, 98.6% (70 patients) underwent tracheostomy decannulation, 90.1% (64 patients) tolerated an oral diet, and 49.3% (35 patients) received successful dental implants. Postoperative complications occurred in 11.3% (8 patients). CONCLUSIONS: Secondary free flap reconstruction yields favorable outcomes in patients with failed obturators, improving tracheostomy dependence, diet tolerance, and dental implantation success. Financial considerations may influence flap choice.

Otolaryngology – Head and Neck Surgery
**Oslin KA**, **Wilson CP**, and **Craig JR**. Maxillary Sinus Antrochoanal Polyp Recurrence Following Surgery in Adults: A Systematic Review. *Laryngoscope* 2025; Epub ahead of print. PMID: 40944545. Full Text

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OBJECTIVE: Antrochoanal polyps (ACPs) are cystic non-neoplastic lesions that most commonly originate from the maxillary sinus and may extend posteriorly through the choana. Transnasal endoscopic removal is preferred for symptomatic ACPs. ACPs can recur after surgical removal, and while a 15% recurrence rate was published in a systematic review on pediatric ACPs, this has not been well-established in adults. The purpose of this systematic review was to determine the recurrence rate of maxillary sinus ACPs following surgical resection in adults. DATA SOURCES: A systematic review was conducted on ACP resection using Medline, Embase, and Web of Science databases from 1946 to July 2025. REVIEW METHODS: After excluding duplicate and non-English articles, 395 abstracts were screened, and 63 articles were selected for full-text review. Articles were included if they were original studies that reported recurrence rates after surgical resection of maxillary sinus ACPs in patients ≥ 16 years old. Articles were excluded if study populations had minimum follow-up of less than 6 months or mean follow-up of less than 12 months. RESULTS: After full-text review, 16 studies met inclusion criteria with 439 patients being utilized for analyses. Mean age was 33.8 years and 39.7% were female. Endoscopic middle meatal antrostomy with ACP removal was performed in 80.8% of cases. Following surgery, patients experienced an overall recurrence rate of 9% (95% CI: 6%-14%), with a mean follow-up of 36.8 months. CONCLUSION: ACPs recurred in about 9% of adults following surgical resection. Further research is needed to determine whether certain patient factors and surgical techniques are associated with ACP recurrence.

Otolaryngology – Head and Neck Surgery
Tham T, Kim AH, Wilensky J, Tsang C, Giannaris PS, Wang BY, Panara K, Christian Z, Kuan EC, Papagiannopoulos P, Tajudeen B, **Eide JG**, **Craig JR**, Kshirsagar RS, Locke TB, Ahn S, Oh EJ, Fastenberg JH, Chaskes MB, Pollack AZ, Har-El G, Workman AD, Kohanski MA, Douglas J, Adappa ND,

Palmer JN, and Tong CCL. Frontal Sinus Inverted Papilloma: Surgical Challenges and Outcomes of a Multi-Institutional Cohort. *Laryngoscope* 2025; Epub ahead of print. PMID: 40899433. Full Text

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OBJECTIVES: Inverted papilloma (IP) is typically a benign sinonasal tumor with a propensity to recur. The surgical treatment of IP arising from the frontal sinus is complicated by proximity to the orbit and skull base. The objective of this study is to describe the surgical challenges when managing this disease and report treatment outcomes in a multicenter cohort. METHODS: A retrospective review was performed on frontal sinus IP resected from 1993 to 2023. Demographic and clinicopathologic data, complications, surgical approach, and outcomes were analyzed. RESULTS: Ninety-eight patients (60 males, 38 females) were identified. Mean age was 59 years, with a median follow-up of 44 months. Histopathologic evaluation identified 13 lesions with carcinoma in situ or invasive carcinoma (13.3%). Bilateral involvement was found in 28 patients (28.6%). Overall, 17 patients (17.3%) had recurrent disease with a median recurrence time of 29.2 months. Fourteen patients (14.3%) underwent staged procedures, with a median time to the second procedure of 7.7 months. Twenty-three patients (23.5%) presented with skull base dehiscence on perioperative imaging. Skull base dehiscence had a significant effect on intraoperative cerebrospinal fluid leak (OR 9.1, 95% CI 3.0-27.4 $p < 0.001$). CONCLUSION: Frontal sinus IP is commonly attached at the skull base and associated with skull base dehiscence, CSF leak, and often requires operative repair and staged procedures. Complete tumor removal can be challenging and may necessitate a combined open and endoscopic approach. Careful surgical planning and close follow-up in the postoperative period are essential for disease control. LEVEL OF EVIDENCE: Level 4.

Pathology and Laboratory Medicine

Adhikari SD, **Steele NG**, **Theisen B**, Wang J, and Cui Y. SPACE: Spatially variable gene clustering adjusting for cell type effect for improved spatial domain detection. *Nucleic Acids Res* 2025;53(18). PMID: 40985765. Full Text

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Recent advances in spatial transcriptomics (ST) have significantly deepened our understanding of biology. A primary focus in ST analysis is to identify spatially variable genes (SVGs) which are crucial for downstream tasks like spatial domain detection. Spatial domains reflect underlying tissue architecture and distinct biological processes. Traditional methods often use a set number of top SVGs for this purpose, and embedding these SVGs simultaneously can confound unrelated spatial signals, dilute weaker patterns, leading to obscured latent structure. Instead, grouping SVGs and getting low-dimensional embedding within each group preserves specific patterns, reduces signal mixing, and enhances the detection of diverse structures. Furthermore, classifying SVGs is akin to identifying cell-type marker genes, offering valuable biological insights. The challenge lies in accurately categorizing SVGs into relevant clusters, aggravated by the absence of prior knowledge regarding the number and spatial gene patterns. Here, we propose SPACE, a framework that classifies SVGs based on their spatial patterns by adjusting for shared cell-type confounding effects, to improve spatial domain detection. This method does not require prior knowledge of gene cluster numbers, spatial patterns, or cell type information. Both simulation and real data analyses demonstrate that SPACE is an efficient and promising tool for ST analysis.

Pathology and Laboratory Medicine

**Akon MO**, **Kenney RM**, **Everson NA**, **VanDorf S**, **Suleyman G**, **Tibbetts RJ**, **Shallal AB**, and **Veve MP**. A little nudge goes a long way: assessing the impact of a microbiology nudge comment on narrow-spectrum antibiotic use in uncomplicated Streptococcus pneumoniae bloodstream infections. *Antimicrob Steward Healthc Epidemiol* 2025;5(1):e230. PMID: 40989659. Full Text

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Narrow-spectrum antibiotic prescribing (ampicillin IV or penicillin IV) was compared before and after implementing an interpretive microbiology comment for uncomplicated Streptococcus pneumoniae bloodstream infections. The postintervention group was associated with 4-fold increased odds of de-escalation to narrow-spectrum antibiotics (adjusted odds ratio, 4.66; 95% confidence interval, 1.97-11.00).

Pathology and Laboratory Medicine

Kogler V, Pagano MB, Fontaine MJ, Azimi V, **Brancamp R**, Cataife G, Covington M, Delaney M, Eichbaum Q, Jacquot C, Kutner JM, Lu W, Saifee NH, Shan H, Thibodeaux SR, Wali JA, Yeh A, Yokoyama APH, Yunce M, and Ziman A. Serologic Characteristics and Clinical Significance of Non-ABO Red Blood Cell Antibodies in Hematopoietic Stem Cell Transplant. The BEST Collaborative Study. *Transplant Cell Ther* 2025; Epub ahead of print. PMID: 40998264. Full Text

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Transfusion Medicine, Department of Pathology and Laboratory Medicine, David Geffen School of Medicine at UCLA, Los Angeles, California, USA.
The Biomedical Excellence for Safer Transfusion (BEST) Collaborative.

BACKGROUND: ABO-incompatible hematopoietic stem cell transplant (HSCT) has a number of well-established complications including hemolysis, delayed RBC engraftment, pure red cell aplasia (PRCA), and transfusion dependence. However, the clinical significance of non-ABO RBC antibodies in allogeneic HSCT remains insufficiently explored. OBJECTIVE: The aim of this study is to characterize the prevalence, incidence, and clinical implications of non-ABO RBC auto- and alloantibodies in the HSCT population. STUDY DESIGN: This international, multicenter, retrospective study analyzed HSCT 2010-2021 across nine U.S. and one Brazilian academic centers. This study focused on immunohematologic findings in recipients of allogeneic HSCTs, excluding hemoglobinopathies. RBC antibodies were evaluated pre-HSCT and 100 days post-HSCT. Hemolysis was assessed by labs and confirmed by a two-physician review of the medical records. Descriptive statistics and regression analysis were performed. IRB approval and data use agreements were obtained at each center. RESULT: Study analysis included a total of 8896 transplants. The majority of transplants utilized apheresis collections (78.0%), were matched unrelated (41.6%), involved a non-myeloablative conditioning regimen (51.2%), and were ABO-compatible (56.7%). The prevalence of non-ABO antibodies pre-HSCT, including auto-, alloantibodies, and passive transfer of anti-D, was 4.0% (n=355). The majority of these were alloantibodies (77.5%), followed by warm autoantibodies (7.3%) and both alloantibodies and warm-reactive autoantibodies (6.5%). De-novo antibody formation post-HSCT occurred in 1.5% (n=135). The most frequent pre-HSCT alloantibody specificities were in the Rh blood group system (46%), followed by Kell (17%) and Kidd (13%). The incidence of anti-D in RhD-mismatched transplant was 1% (n=8) for RhD-positive recipients with RhD-negative donors, and 0.2% (n=2) for RhD-negative recipients with RhD-positive donors. Myeloproliferative neoplasms and myelodysplastic syndromes had the highest rate of antibodies pre- and post-HSCT. Hemolysis was observed in 24 cases (antibodies present pre-HSCT) and 15 de-novo cases post-HSCT. Pure red cell aplasia was not observed in any of these cases. The presence of non-ABO RBC antibodies was associated with higher RBC transfusions, but not platelet transfusions; engraftment of neutrophils and platelets were not affected by the presence of RBC antibodies. CONCLUSION: The current study reports on a low prevalence of RBC antibodies, including allo- and autoantibodies, in HSCT patients during the peri-transplant period, with a rate of 4% for those with pre-existing antibodies prior to transplant and 1% for the de-novo antibody formation post-transplant. They are associated with a low risk of mild to moderate hemolysis, but increased RBC transfusions. Comprehensive immunohematology data should be incorporated into HSCT databases for improved risk assessment, monitoring, and management.

Pathology and Laboratory Medicine

Oladipo PM, **Tibbetts RJ**, Sivertsen A, **Barger JM**, Bruvold TS, Fite A, Sims M, **Zervos M**, Jomaa A, and Ram JL. New diagnostic methods for Escherichia marmotae and the first report of its identification in clinical isolates in North America. *Front Microbiol* 2025;16:1664775. PMID: 40980316. Full Text

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BACKGROUND: Genomic sequences of E. marmotae and E. coli differ by 10%. Discovered as an environmental "cryptic clade" of Escherichia, E. marmotae also occurs in human infections. Microbiological and MALDI-TOF-MS methods frequently misidentify E. marmotae as E.coli. Our goal was to develop methods that reliably distinguish E. marmotae from E. coli to improve therapeutic decisions and treatments. METHODS: A Taqman PCR method was developed to distinguish E. marmotae from E. coli based on genomic sequences of uidA, uidB, and a positive control targeting adk in E. marmotae and E. coli. MALDI-TOF-MS spectra were obtained for environmental and clinical isolates using a bioMérieux VITEK MALDI-TOF-MS system. RESULTS: UidA- and uidB species-specific PCR amplified DNA from E. marmotae with 100% specificity, and not from E. coli or other Escherichia species. The Biomérieux VITEK MALDI-TOF-MS consistently misidentified E. marmotae as E. coli, with median IVD confidence scores for both E. marmotae and E. coli of 99.9%; however, RUO scores for E. marmotae (median 0%) were significantly lower ($P < 0.0001$) than for E. coli (median = 87.4%). The spectral peak between m/z 7,250 to 7,280 consistently occurred between 7,260 and 7,268 in E. marmotae and only between 7,268 and 7,280 in E. coli, with no overlap ($p < 0.001$). Application of these spectral criteria to 176 clinical isolates revealed the first identification of a E. marmotae isolate from a human infection in North America. The isolate had originally been diagnosed as E. coli based on a 99.1% IVD confidence score. This first North American clinical isolate was confirmed as E. marmotae by Taqman-PCR and whole genome sequencing. This isolate had numerous antibiotic resistance gene markers and unlike most clinical E. coli, this E. marmotae isolate lacked motility at 37°C. CONCLUSION: Clinical tests based on these methods of differentiating E. marmotae and E. coli may assist in determining the prevalence of this emerging pathogen and making therapeutic decisions.

Pathology and Laboratory Medicine

**Palathingal Bava E**, **W LA**, and **S BG**. A rare case of in situ follicular B-cell neoplasm involving sebaceous lymphadenoma. *J Hematop* 2025;18(1):43. PMID: 40960713. Full Text

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In situ follicular neoplasia (ISFN) is characterized by a monoclonal proliferation of BCL2-positive B cells harboring the translocation t(14;18)(q32;q21). These cells are confined to follicle centers and are usually identified incidentally, with a very low risk of progression to follicular lymphoma. Sebaceous lymphadenoma is a rare, benign salivary gland tumor, most commonly arising in the parotid gland, and is histologically defined by solid epithelial nests and cysts with sebaceous differentiation in a hyperplastic lymphoid stroma. We report an unusual case of ISFN arising within a sebaceous lymphadenoma. To the best of our knowledge, this association has not previously been reported.

Pathology and Laboratory Medicine

**Wang L**, **Lu X**, **Szalad A**, **Zhang Y**, **Li Y**, **Lu M**, **Kemper A**, **Liu Z**, **Liu XS**, **Chopp M**, and **Zhang ZG**. Engineered miR-214 enriched Schwann cell-derived extracellular vesicles amplify therapeutic efficacy for peripheral neuropathy in T2D mice. *Front Cell Neurosci* 2025;19:1649830. PMID: 40950414. Full Text

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Extracellular vesicles (EVs) derived from healthy Schwann cells (SC-EVs) ameliorate peripheral neuropathy in diabetic mice and rescue sciatic nerve function in Schwann cell Dicer knockout mice in part via SC-EV cargo miRNAs. Among these miRNAs, miR-214 repairs nerve damage. The present study investigated whether engineered SC-EVs with elevated miR-214 (214-EVs), further amplify the therapeutic effect of naïve SC-EVs (naïve-EVs) on reducing diabetic peripheral neuropathy (DPN) in a mouse model of high-fat diet (HFD)-streptozotocin (STZ) induced type 2 diabetes. Compared to naïve-EVs, 214-EVs significantly improved motor and sensory nerve conduction velocity of the sciatic nerve and

thermal latency, which were associated with increased intraepidermal nerve fiber density, axonal diameter, and myelin thickness in the sciatic nerve. Quantitative RT-PCR and Western blot analyses of sciatic nerve tissues showed that, compared to naïve-EVs, 214-EVs significantly increased miR-214 levels and downregulated axonal inhibitory protein PTEN and the myelination inhibitory protein cJUN. Furthermore, 214-EVs markedly suppressed neuroinflammation by decreasing CD68 + macrophages and inactivating the TLR4/NF-κB signaling pathway. Collectively, our findings demonstrate that miR-214-enriched SC-EVs are superior to naïve-EVs to ameliorate DPN and represent a promising EV-based therapeutic strategy.

Pharmacy

**Akon MO**, **Kenney RM**, **Everson NA**, **VanDorf S**, **Suleyman G**, **Tibbetts RJ**, **Shallal AB**, and **Veve MP**. A little nudge goes a long way: assessing the impact of a microbiology nudge comment on narrow-spectrum antibiotic use in uncomplicated Streptococcus pneumoniae bloodstream infections. *Antimicrob Steward Healthc Epidemiol* 2025;5(1):e230. PMID: 40989659. Full Text

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Narrow-spectrum antibiotic prescribing (ampicillin IV or penicillin IV) was compared before and after implementing an interpretive microbiology comment for uncomplicated Streptococcus pneumoniae bloodstream infections. The postintervention group was associated with 4-fold increased odds of de-escalation to narrow-spectrum antibiotics (adjusted odds ratio, 4.66; 95% confidence interval, 1.97-11.00).

Pharmacy

**Arena CJ**, **El-Tatari B**, **Lovric K**, **Greenlee SB**, **Kenney RM**, **Gadgeel SM**, **Patterson K**, **Shallal AB**, **Alangaden GJ**, **Davis SL**, and **Veve MP**. Is Shorter Better in Oncology Patients, Too? A Retrospective Cohort Study of Short- Versus Long-Course Antibiotic Therapy for Uncomplicated Infections in Solid Tumor Patients Receiving Care in Ambulatory Oncology Clinics. *Open Forum Infect Dis* 2025;12(9):ofaf505. PMID: 40908971. Full Text

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This retrospective cohort study evaluated short- versus long-course antibiotics for uncomplicated infections in ambulatory solid tumor patients. Among 303 patients, outcomes were similar between groups, including infection recurrence, treatment delays, and adverse events. Short-course therapy was not associated with worse outcomes, suggesting it may be a viable alternative.

Pharmacy

**Arena CJ**, **Everson NA**, **Kenney RM**, **Brar I**, **Gudipati S**, **Yared N**, Davis SL, and **Veve MP**. A cross-sectional analysis of doxyPEP use and outcomes in Michigan, United States. *Int J STD AIDS* 2025; Epub ahead of print. PMID: 40953601. Full Text

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Background: In 2024, national guidance was issued for doxycycline post-exposure prophylaxis (doxy-PEP) to prevent bacterial sexually transmitted infections (STIs). The study purpose was to evaluate doxy-PEP use in patients with increased risk of STI exposure at a large, urban health system. Methods: IRB-exempt study of adult patients with clinic encounters for increased risk of STI exposure and testing for N. gonorrhoeae, C. trachomatis, and T. pallidum from 01/01/2023-31/10/2024. Patients were identified using ICD-10 code Z20.XX and STI testing. Doxy-PEP prescription utilization was evaluated after a dedicated doxy-PEP order was implemented with appropriate patient counseling instructions. The primary outcome was the proportion of doxy-PEP prescriptions utilized in at-risk patients; secondary outcomes were utilization of the dedicated doxy-PEP order and abnormal STI testing within 3-months of the doxy-PEP prescription. Results: 4234 high-risk sexual patient encounters were documented; 7.37% of patients received a doxy-PEP prescription. Of these, 29.5% were ordered utilizing a dedicated doxy-PEP order. Most patients who received a doxy-PEP prescription were Black (96.6%), men (92.6%), with a median (IQR) age of 29 (24-37) years, and had private/commercial insurance (42%). One patient had abnormal syphilis testing within 3-months of doxy-PEP prescription. Conclusions: These findings highlight doxy-PEP underutilization and the need for broader provider engagement and advanced antimicrobial stewardship interventions.

Pharmacy

**Martirosov AL**, **Griebe K**, and **Hameed AA**. Enhancing Pulmonary Care in Older Adults: The Vital Role of Healthcare Providers in Managing Age-Related Challenges and Medication Access. *Clin Geriatr Med* 2025. PMID: Not assigned. Full Text

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Pharmacy

Mohammednoor M, Mubarak Osman AME, **Hamad S**, Abdelhalim Ismail FI, Elsharief Mohammed Elamien MEY, Mohamed Gamareldin EE, and Rahman MH. Impact of Inhaled Corticosteroids on Osteoporosis in Chronic Obstructive Pulmonary Disease (COPD): A Systematic Review. *Cureus* 2025;17(8):e89201. PMID: 40895651. Full Text

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Inhaled corticosteroids (ICS) are commonly prescribed for chronic obstructive pulmonary disease (COPD) management, but their long-term use has been associated with potential adverse effects on bone health, including osteoporosis and fractures. This systematic review aimed to evaluate the impact of ICS on osteoporosis and fracture risk in COPD patients by synthesizing evidence from observational and clinical studies. A comprehensive literature search was conducted across PubMed, Web of Science, Scopus, Embase, and the Cochrane Library, following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Studies were screened for eligibility based on predefined inclusion criteria, and data were extracted using a standardized form. The Newcastle-Ottawa Scale (NOS) was employed to assess the risk of bias in included studies. Due to heterogeneity in study designs and outcome measures, a narrative synthesis was performed, focusing on key themes such as dose-response relationships, fracture risk, and the influence of ICS duration. Eleven studies were included, revealing mixed findings on the association between ICS use and bone health outcomes. While some studies reported a dose-dependent increase in osteoporosis incidence and fracture risk, others found no significant association or even protective effects in specific subgroups. High-dose and long-term ICS use were consistently linked to greater risks, particularly in vulnerable populations such as elderly and female patients. The methodological quality of studies varied, with most demonstrating low to moderate risk of

bias. This review highlights the complex relationship between ICS use and bone health in COPD patients, emphasizing the importance of individualized treatment approaches. While ICS remain essential for COPD management, clinicians should consider bone-protective strategies in high-risk patients, particularly those on long-term or high-dose regimens. Future research should standardize exposure and outcome definitions to facilitate more robust quantitative synthesis.

Pharmacy
Roye-Azar M, Prater M, **Giuliano C**, and **Kale-Pradhan PB**. The Combination of Aztreonam-Avibactam in Multidrug-Resistant Gram-Negative Infections. *Ann Pharmacother* 2025; Epub ahead of print. PMID: 40947426. Full Text

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OBJECTIVE: Aztreonam-avibactam (ATM-AVI) is used for difficult-to-treat gram-negative infections. The objective of this review is to analyze the pharmacology, safety, and clinical application of ATM-AVI. DATA SOURCES: PubMed, Embase, and ClinicalTrials.gov were searched using the terms aztreonam avibactam, PF-06947387, Emblaveo, and ATM-AVI. STUDY SELECTION AND DATA EXTRACTION: Articles written in English and published from January 1, 1985, to June 10, 2025, that related to pharmacology, safety, clinical trials, and clinical application of ATM-AVI were reviewed. DATA SYNTHESIS: The ATM-AVI has shown similar efficacy to comparator antibiotics in complicated intra-abdominal infection (cIAI) and hospital/ventilator-acquired pneumonia (HAP/VAP). The REVISIT trial showed cIAI clinical cure rates of 76.4% and 74% for the ATM-AVI and meropenem groups, respectively (treatment difference 2.4% [95% confidence interval, CI = -7.4 to 13.0]). For HAP/VAP, clinical cure rates were 45.9% and 41.7% for the ATM-AVI and meropenem groups, respectively (treatment difference 4.3% [95% CI = -15.1 to 23.1]). The ATM-AVI was generally well tolerated, with hepatic adverse effects being the most commonly reported.Relevance to patient care and clinical practice comparison to existing drugs:The ATM-AVI has demonstrated clinical efficacy for the treatment of cIAI. However, its role needs to be further studied for other infections such as HAP/VAP, urinary tract, and other serious infections. Pharmacoeconomic analysis may be needed to assess the cost-benefit impact in the United States. CONCLUSION: The ATM-AVI may be an alternative option for the treatment of cIAI and other complicated gram-negative infections. Further studies are needed to delineate the role of ATM-AVI in clinical practice.

Pharmacy
**Sunshine N**, **Kenney RM**, **Everson NA**, **Arena CJ**, **Eriksson E**, **Church BM**, **Manteuffel J**, and **Veve MP**. Impact of an Interruptive Alert on the Number of Women Receiving CDC-Recommended Therapy for Trichomoniasis. *J Pharm Technol* 2025; Epub ahead of print. PMID: 40936794. Full Text

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Background: The 2021 Centers of Disease Control and Prevention (CDC) sexually transmitted infection treatment guidelines recommend a 7-day course of metronidazole or single-dose tinidazole for women with trichomoniasis due to improved patient outcomes compared with single-dose metronidazole therapy. A health system antimicrobial stewardship program implemented an interruptive electronic health record (EHR) alert to promote optimal trichomoniasis prescribing when nonrecommended treatment is ordered. Objective: To determine the impact of an interruptive EHR alert on optimal trichomoniasis prescribing for women. Methods: This was an institutional review board-approved, single pretest, posttest quasi-experiment of women ≥15 years with a microbiologically confirmed Trichomonas vaginalis infection from 10/2023 to 12/2023 (preintervention) and 10/2024 to 12/2024 (postintervention). An EHR alert was implemented 9/2024 that notifies prescribers that single-dose metronidazole 2 g is not recommended and suggests CDC-recommended treatments. The primary outcome was the proportion of single-dose metronidazole 2 g orders before and after EHR alert implementation. A secondary cross-sectional

evaluation of all alerts triggered from 10/2024 to 12/2024 was performed and included the number of alerts, location of alert, and provider response. Results: A total of 285 patients were included, 49.8% pre-intervention and 50.2% postintervention. Metronidazole 2 g was prescribed for 8.45% of pre-intervention and 2.80% of postintervention patients (P = 0.038). The clinical support alert fired 102 times for 75 patients during the 3-month postimplementation period. The alert was associated with a change in intended prescription to a metronidazole 7-day course in greater than 60% of patients over 3 months. Conclusion: The implementation of an interruptive alert was associated with high acceptance and improved prescribing for women treated for trichomoniasis.

Podiatry

Behme S, Zhou S, **Brown A**, and Rothenberg GM. Acid-fast bacilli staining for nonhealing ulcers: a case report of cutaneous Mycobacterium chelonae infection. *Wounds* 2025;37(7):264-268. PMID: 40801883. Full Text

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BACKGROUND: Cutaneous infections due to nontuberculous mycobacteria (NTM) are rare, and they can be challenging to treat, often requiring prolonged therapy with multiple antibiotics. Although recent literature challenges the idea of routine acid-fast bacilli (AFB) testing in diabetic foot infections, this report presents a case of Mycobacterium chelonae (M chelonae) infection in a patient with nonhealing ulceration. CASE REPORT: A 64-year-old female with no history of immunocompromise and no recent surgical history presented with a rapidly growing ulceration despite appropriate antibiotic therapy based on routine aerobic culture results. After AFB cultures were obtained, she was found to have NTM infection with M chelonae, and the ulceration was healed without recurrence after treatment for 4 months with linezolid and clarithromycin. CONCLUSION: This case highlights the potential inoculation of M chelonae, even in immunocompetent patients without known inoculation injury, and it highlights the value of AFB cultures in patients who do not progress with standard wound care therapies and routine aerobic cultures.

Public Health Sciences

**Aurora L**, **Gorgis S**, **Gandolfo C**, Sadiq O, Gakhal G, **Jacobsen G**, and **Ananthasubramaniam K**. Impact of routine repeat echocardiograms in patients hospitalized with acute decompensated heart failure without clear secondary cause. *Int J Cardiovasc Imaging* 2025; Epub ahead of print. PMID: 40897903. Full Text

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Transthoracic echocardiography (TTE) at the time of acute decompensated heart failure (ADHF) may reveal significant structural and hemodynamic abnormalities that can guide clinical management. However, the impact of routine repeat TTE in uncomplicated ADHF re-admissions is yet to be established. We studied patients with repeat TTE at the time of rehospitalization for ADHF to determine downstream clinical impact. In a single center retrospective study, 410 adult patients with 2 ADHF admissions within 1 year were studied. 185 patients met inclusion criteria. Demographics, key echocardiography parameters and clinical changes were collected between first and second TTE. The study population comprised predominantly of Caucasians (55.7%) and males (53%). Non-ischemic cardiomyopathy was the principal etiology of heart failure. Between first and second TTE, there were no statistically significant changes noted in left ventricular ejection fraction, right ventricular systolic pressure, right atrial pressure, E/e ratio, or diastolic function. Right ventricular function was noted to significantly worsen as seen on the second TTE ($p < 0.001$). Mitral and aortic regurgitation was noted to be less severe in the repeat TTE group ($p = 0.030$ and $p = 0.047$, respectively). The predominant impact of repeat

TTE in rehospitalized ADHF patients was medication changes rather than significant interventions, such as advanced imaging or invasive procedures. Our study demonstrates that clinicians should focus on reserving utilization of repeat TTE in uncomplicated ADHF readmissions to those not responding to standard medical optimization including diuresis. Major effect on downstream interventions and new diagnosis is not significantly impacted by repeating TTE.

Public Health Sciences
Bertini A, Cirulli GO, **Stephens A**, Finocchiaro A, Viganò S, Lughezzani G, Buffi N, Ficarra V, Salonia A, Briganti A, Montorsi F, Sood A, **Rogers C**, and **Abdollah F**. Reply to 'Comment on Bertini et al.: area deprivation and PSA screening disparities' and 'Comment on socioeconomic disparities in prostate cancer screening: the impact of the Area Deprivation Index on PSA screening frequency'. *BJU Int* 2025; Epub ahead of print. PMID: 40905572. Full Text

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Public Health Sciences
Bertini A, **Stephens A**, Finocchiaro A, Viganò S, Dinesh A, Guivatchian E, Cusmano N, Lughezzani G, Buffi N, Sorce G, Ficarra V, Briganti A, Salonia A, Montorsi F, Sood A, **Rogers C**, and **Abdollah F**. Association of area of deprivation index with magnetic resonance imaging (MRI) utilization for prostate cancer detection: results from a contemporary North American population. *World J Urol* 2025;43(1):584. PMID: 41021031. Full Text

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PURPOSE: Since the use of Magnetic Resonance Imaging (MRI) in the initial diagnostic evaluation for prostate cancer (PCa) has considerable costs, there is concern that socioeconomic barriers may result in MRI underutilization. We examined the relationship between socioeconomic factors, measured by the Area Deprivation Index (ADI), and MRI utilization in PCa diagnostic setting using a contemporary North American population. METHODS: We included all the patients aged > 40 years with a confirmed PSA > 3 ng/mL at Henry Ford Health (HFH) between 2018 and 2022. 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 socio-economic disadvantage. MRI and biopsy status were defined as undergoing these procedures within 6 and 9 months, respectively, from their first PSA > 3 ng/mL in the time period. Univariable (UVA) and multivariable (MVA) Logistic regression models tested the impact of ADI on prostate MRI or biopsy utilization. RESULTS: We included 18,827

patients who had a PSA > 3 ng/mL, 3759 (20%) of whom were Non-Hispanic Black. Overall, 679 (3.6%) and 1672 (8.8%) of these individuals underwent prostatic MRI and prostate biopsy, respectively. Median (IQR) age and ADI percentile were 68 (62-74) years and 58 (38-79), respectively. Patients who received MRI were more likely to be younger (66 vs. 68, p = 0.006), Non-Hispanic Black [28.0% (95%CI: 24.7%-31.5%) vs. 19.7% (95% CI 19.1%-20.3%), p < 0.0001] and to undergo PSA test in more recent median years (2021 vs. 2019, p < 0.0001), compared to those who did not undergo MRI. When stratifying the population by ADI quintiles, men in the fifth (most deprived) quintile were less likely to receive MRI (3.1% vs. 5.9%, p < 0.001), compared to those in the first (most affluent) quintile. At logistic MVA, patients living in more deprived neighborhoods (higher ADI percentile) were less likely to receive MRI before PCa diagnosis (OR: 0.90, p < 0.001). Specifically, for an increase in ADI percentile of 10 units, the relative odds of receiving MRI decreased by 10%. CONCLUSIONS: Although the overall utilization of prostate MRI remains low in this real-world study, men living in more socioeconomically deprived areas were significantly less likely to undergo MRI before PCa diagnosis. Our findings underscore the need for targeted interventions to ensure a more equitable access to advanced diagnostic tools.

Public Health Sciences

Bertini A, **Tylecki A**, **Stephens A**, Finocchiaro A, Viganò S, Cusmano N, Dinesh A, Guivatchian E, Lughezzani G, Buffi N, Di Trapani E, Ficarra V, Briganti A, Salonia A, Montorsi F, Sood A, **Rogers C**, and **Abdollah F**. Socioeconomic Disparities in Prostate Cancer Presentation: The Impact of ADI on Prostate Cancer Stage at Diagnosis. *Clin Genitourin Cancer* 2025;23(6):102418. PMID: 40961906. Full Text

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OBJECTIVES: To investigate the impact of socioeconomic deprivation, as measured by Area Deprivation Index (ADI), on PCa stage at diagnosis in a North-American statewide cohort. METHODS: The Michigan Department of Health and Human Services (MDHHS) was queried to identify men aged ≥30 with a confirmed diagnosis of PCa at prostate biopsy between 2004 and 2022. An ADI score was assigned to each patient based on their residential census block group. Individuals were further categorized into quartiles, where the fourth 1 (ADI 75-100) represented those living in the most deprived areas. Logistic regression analysis tested the impact of ADI on diagnosis with NCCN high-risk PCa (T3-T4 or PSA >20 ng/ml or ISUP GG ≥4) or metastatic PCa (N1 or M1) at presentation. RESULTS: We included 78018 patients, 17% of whom were Non-Hispanic Black (NHB). Median (IQR) age was 66 (59-72) years. Patients in the most disadvantage quartile (Q4) were more likely to be NHB (40.1% vs. 5.4%), had higher proportion with PSA>20 ng/ml (10.6 % vs. 5.1%), GG≥4 (55.4% vs. 53.1%), clinical T ≥ 3 (4% vs. 3%)

and metastasis (3.3% vs. 1.8%) at diagnostic presentation, compared to those in the least disadvantaged quartile (Q1) (all P < .0001). At MVA, for each 10-unit increase in ADI percentile, the relative odds of being diagnosed with NCCN high-risk and metastatic PCa increases by 2% (95% CI, 1.01-1.02) and 4% (95% CI, 1.02-1.05), respectively. Moreover, when compared to NHW men, NHB men had a 1.16 (95% CI, 1.12-1.22) and a 1.52-fold (95% CI, 1.38-1.68) higher relative odds of being diagnosed with NCCN high-risk PCa and metastatic PCa, respectively (P < .001). CONCLUSIONS: Living in more deprived areas was associated with higher relative odds of newly diagnosed PCa with unfavorable features. Our study underscores the silent barrier that socioeconomic deprivation poses to cancer early diagnosis and echo the call for tailored interventions to bridge this gap.

Public Health Sciences

**Budhathoki N**, Koroma MI, Cheng CI, Inungu JN, and Mumford V. Factors associated with colorectal cancer screening among U.S. adults: A cross-sectional study using NHIS 2023 data. *Electron J Gen Med* 2025;22(5). PMID: Not assigned. Full Text

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Introduction: Colorectal cancer (CRC) remains a leading cause of cancer-related mortality in the USA. Although early detection via screening significantly reduces morbidity and mortality, national uptake rates remain suboptimal, particularly among underserved populations. Understanding the multifaceted factors influencing CRC screening adherence is essential for guiding targeted public health interventions. Objective: This study used a nationally representative sample to identify demographic, socioeconomic, and behavioral factors associated with CRC screening adherence among U.S. adults aged 45-75 years. Methods: A cross-sectional analysis was conducted using the 2023 national health interview survey (NHIS) data. Adults aged 45-75 years who reported CRC screening history were included. The primary outcome was up-to-date screening per U.S. Preventive Services Task Force guidelines. Independent variables were guided by Andersen and Davidson's behavioral model of health services use and included demographic characteristics, socioeconomic status, and healthcare access. Multivariable logistic regression analyses were conducted using weighted survey procedures. Results: The study showed that 68.2% of the adults were up-to-date with CRC screening. Screening rates increased with age and education and were higher among individuals with health insurance and a regular source of care. Compared to non-Hispanic whites, minority groups, particularly Hispanic, non-Hispanic Black, and non-Hispanic Other, exhibited lower screening rates. Access to care, including insurance coverage and a usual care provider, emerged as the strongest predictors of adherence. Individuals who lacked U.S. citizenship, insurance, or faced transportation and cost-related barriers were significantly less likely to be screened. Conclusion: Disparities in CRC screening persist, especially among younger adults, racial/ethnic minorities, and the socioeconomically disadvantaged. Expanding insurance coverage and strengthening provider engagement are key drivers to improve screening uptake.

Public Health Sciences

Bui L, Espinoza V, Giang HA, Schiffer LP, Do P, Ngu P, Vu C, Tiro J, **Adjei Boakye E**, Phillips SM, Brandt H, Berry E, Tran S, Macdonald E, Khuc C, Nguyen J, Vuong T, and Vu M. U.S. Vietnamese Parents' Perceptions of Different Approaches for Confirming Adolescent HPV Vaccination Records in Research Studies. *Health Expect* 2025;28(5):e70448. PMID: 41020406. Full Text

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BACKGROUND: The United States (U.S.) Vietnamese communities face a high burden of HPV-related cancer rates; they also have low HPV vaccination coverage. HPV vaccination is a safe, effective tool to prevent HPV-related cancers, particularly when administered during adolescence. Understanding Vietnamese parents' perspectives on the acceptability of different HPV vaccination status verification methods can improve the implementation of community-based research interventions to improve HPV vaccine coverage in this population. OBJECTIVE: We assessed their perceptions of three HPV vaccination status confirmation methods: medical records, vaccination card photographs, and self-reported surveys. DESIGN: We conducted interviews with Vietnamese parents of adolescents ages 9-18, healthcare providers, and community leaders (n = 34). We used an inductive thematic analysis approach with four qualitative coders. RESULTS: Preferences for confirming vaccination status were split almost equally among each method. Key drivers of these preferences included privacy concerns, autonomy, efforts required from parents, digital literacy, and data accuracy. DISCUSSION: These findings suggest offering multiple confirmation options to accommodate diverse preferences and enhance the effectiveness of HPV vaccination promotion strategies in this population. PUBLIC CONTRIBUTION: Community involvement was integral to the design, implementation of this project, and writing of the manuscript. The study team partnered with a community organization that works closely with the U.S. Vietnamese population and Vietnamese healthcare providers. The group met regularly to discuss participant recruitment strategies and study instruments. Lived experiences from parents of adolescents, community leaders, and healthcare providers were included in the production of this manuscript to guide the interpretation of preferences for vaccination confirmation methods.

Public Health Sciences

Chapman LE, Hall MS, Foster A, Baird DD, Harmon QE, Wright RO, Landero JA, Heffron R, Wise LA, **Wegienka G**, Geller RJ, Wesselink AK, Schildroth S, Hall JE, Tokar EJ, and Upson K. Estrogen-containing contraceptive use and blood lead concentrations in a cohort of premenopausal individuals. *Environ Res* 2025;122935. Epub ahead of print. PMID: 41015173. Full Text

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After exposure, toxic metal lead is stored in the skeleton and is mobilized to systemic circulation with bone turnover. Given the bone-conserving properties of estrogen, we investigated whether current use of estrogen-containing contraception is associated with lower blood lead concentrations. We conducted a cross-sectional analysis using enrollment data from the Study of Environment, Lifestyle & Fibroids (SELF), a cohort of 1693 Black women ages 23-35 years enrolled in years 2010-2012. The study population was restricted to non-users of injectable hormonal contraception with questionnaire data on

hormonal contraceptive use and laboratory data on whole blood lead concentrations (n=1549). The geometric mean blood lead concentrations for current users of estrogen-containing contraception and non-users were 0.41 µg/dl (95% CI: 0.39-0.43) and 0.51 µg/dl (95% CI: 0.50-0.52), respectively. After adjusting for age, education, current smoking status, alcohol consumption, recency of injectable contraceptive hormone use, and recent birth using a multivariable linear regression model to estimate the percent difference in blood lead concentrations, current use of estrogen-containing contraception was associated with an 11% lower blood-lead concentrations (95% CI: -16%, -5%). In exploratory analyses considering contraceptive type, current combined oral contraceptive users (n=187) had 10% lower blood lead concentrations (95% CI: -16%, -4%) and contraceptive vaginal ring/transdermal patch users (n=33) had 18% lower blood lead concentrations (95% CI: -29%, -5%) compared with non-users. Given the known toxic effects of lead and the common use of estrogen-containing contraception, further research is warranted to confirm our observation of lower blood lead concentrations with current use of estrogen-containing contraception.

Public Health Sciences

Ditonno F, Veccia A, Bignante G, Wu Z, Wang L, **Abdollah F**, **Stephens A**, Simone G, Tuderti G, Lee R, Eun DD, Correa AF, De Cobelli O, Ferro M, Porpiglia F, Amparore D, Checcucci E, Tufano A, Contieri R, Perdonà S, Bhanvadia R, Margulis V, Brönimann S, Singla N, Porter J, Ghodoussipour S, Minervini A, Mari A, Lambertini L, Ghoreifi A, Nativ OF, Gonzalgo ML, Sidhom D, Sundaram CP, Ben-David R, Eraky A, Mehrazin R, Yoshida T, Kinoshita H, Dehghanmanshadi A, Rais-Bahrami S, Meagher MF, Puri D, Derweesh IH, Moghaddam FS, Djaladat H, Bertolo R, Autorino R, and Antonelli A. Radical nephroureterectomy vs kidney sparing surgery for upper tract urothelial carcinoma in solitary kidney patients: a multi-institutional analysis of the ROBUUST 2.0 registry. *World J Urol* 2025;43(1):534. PMID: 40897892. Full Text

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PURPOSE: Radical nephroureterectomy (RNU) for upper tract urothelial carcinoma (UTUC) in solitary kidney patients is a rare and underreported scenario. This study aims to compare the outcomes of UTUC solitary kidney patients becoming anephric after RNU to those of patients undergoing kidney-sparing surgery (KSS). METHODS: Data from patients with a solitary kidney were retrieved from the ROBUUST 2.0 database, a global, multicenter registry containing data on patients who underwent curative surgery for UTUC. Baseline patient demographics, disease characteristics, and surgical features were compared between RNU and KSS. Kaplan-Meier methods were used to estimate recurrence-free survival (RFS), metastasis-free survival (MFS), cancer-specific survival (CSS), and overall survival (OS) in patients undergoing RNU, with 3-year and 5-year cutoffs applied. RESULTS: Thirty-nine patients (76.5%) underwent RNU, whereas 12 (23.5%) underwent KSS. Despite a comparable preoperative renal function, the distribution of CKD stages differed significantly between the groups ($p = 0.019$). Despite a similar rate of postoperative complications, patients undergoing RNU experienced a significantly higher median LOS ($p < 0.001$). Among RNU patients, OS was 83.9%, CSS was 96.9%, RFS was 71.8%, and MFS was 84.4% at the 3-year follow-up. After 5 years post-surgery, OS was 73.4%, CSS was 83.1%, RFS was 59.9%, and MFS was 78.5% in the same cohort. CONCLUSIONS: UTUC solitary kidney patients undergoing RNU or KSS face a substantial perioperative burden. Despite these challenges, our cohort demonstrated favorable oncological outcomes comparable to those reported in the existing literature.

Public Health Sciences

**Franco-Palacios DJ**, Franco-Palacios CR, **Crowley S**, **Allenspach LL**, **Stagner L**, **Corrales JP**, **Olexsey K**, **Waynick L**, **Simanovski J**, Bhatti H, **Laier R**, **Myszenski A**, **Wang Y**, **Lu M**, and **Song T**. Effect of Total Psoas Muscle Area and Serum Albumin on Outcomes After Lung Transplantation. *Clin Transplant* 2025;39(9):e70308. PMID: 40932471. Full Text

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BACKGROUND: Sarcopenia of the psoas muscle and hypoalbuminemia indicate poor nutritional status, inflammation, and frailty in lung transplant (LT) candidates, correlating with worse post-transplant outcomes. METHODS: Retrospective study of LT recipients (2015-2023) examining the association of total psoas muscle area (TPA) and serum albumin with hospital stay, survival, and pulmonary function. RESULTS: One hundred thirty-two LT recipients (mean age 59.56 ± 10.65 years, BMI 26.73 ± 5.55 kg/m(2), 65% males), 95% underwent bilateral LT. Higher TPA was associated with shorter hospital and ICU stays ($p = 0.001$). Similarly, higher albumin levels were associated with reduced hospital and ICU stays ($p < 0.001$). Hospital survivors had higher TPA (17.5 ± 6.1 vs. 14.6 ± 5.2 cm(2), $p = 0.02$) and higher albumin levels (3.25 ± 0.73 vs. 2.75 ± 0.85 mg/dL, $p = 0.01$). Long-term survivors had higher TPA (17.8 ± 6.35 vs. 15.9 ± 5.51 cm(2), $p = 0.07$) and higher albumin levels (3.29 ± 0.75 vs. 2.97 ± 0.78 mg/dL, $p = 0.01$). On multivariate analysis, albumin and male gender remained independent predictors of hospital and long-term survival. TPA was positively associated with post-transplant pulmonary function based on FVC and FEV1 ($p < 0.001$), while albumin levels showed no association. CONCLUSION: In the present study of LT recipients, higher TPA and albumin levels were linked to shorter hospitalization, and albumin independently predicted survival. TPA, but not albumin, was associated with pulmonary function post-transplant.

Public Health Sciences

Kyei I, Bea VJ, Gyan KK, Adjei E, Stonaker B, Bekele M, Abebe E, Davis M, Boakye A, Boateng R, Elemento O, Aitpillah F, Alebachew H, Jibril A, Chen Y, Taiwo E, **Bensenhaver J**, **Walker E**, **Ali H**, Oppong J, Ginter P, Nalwoga H, Kalungi S, Ebughe G, Ezeome ER, Jackson K, Bonsu EO, Momoh A, Martini R, Demaria S, Yates C, Balogun OD, Louie C, Manohar J, Bediako Y, Boaitey GA, Fondjo LA, Iloanusi N, Okoye I, Adinku M, Ankomah K, Dally C, Rockefeller E, **Susick L**, Obong-Ekanem I, Greenspun BC, Daba SA, **Schwartz T**, Robine N, Chen S, Carrot-Zhang J, Amazu S, **Jiagge E**,

Acheamfour OK, Patino S, Malik M, Ju T, Siegel B, Martin IK, Mills C, Phillip J, Kalu CO, Joseph C, Peters F, Stromain A, Olusina B, Nwokoro O, Lasebikan N, Udosen J, Nwagbara V, Carpten J, Fisseha S, Johnson T, Awuah B, and Newman LA. Oncologic Anthropology and the African Diaspora: Twenty-Year Anniversary Report, International Center for the Study of Breast Cancer Subtypes (ICSBCS). *Ann Surg Oncol* 2025; Epub ahead of print. PMID: 40914775. Full Text

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The International Center for the Study of Breast Cancer Subtypes (ICSBCS) has played a vital role in defining and overcoming many inequities that exist in breast cancer treatment and outcome on a global

basis through capacity-building programs that improve the management of breast cancer patients across the African diaspora. ICSBCS activities also fill critical gaps in disparities research related to the genetics of ancestry. Over the past 20 years, ICSBCS teams have spearheaded landmark studies documenting the relevance of genetic African ancestry to breast cancer risk, while also improving the quality of care delivered to patients in diverse communities. Herein, the achievements and future goals of this international, multi-institutional breast cancer research and outreach program are summarized.

Public Health Sciences

**Maghfour J**, **Powers M**, **Wang A**, **Poisson L**, and Brian Jiang SI. Impact of clinical factors and surgical treatments on sebaceous carcinoma patients with and without Muir-Torre syndrome. *J Am Acad Dermatol* 2025; Epub ahead of print. PMID: 40902656. Full Text

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Public Health Sciences

**Memon M**, Christenson RH, **Jacobsen G**, Apple FS, Singer AJ, Limkakeng AT, Jr., Peacock WF, deFilippi CR, **Miller JB**, and **McCord J**. Utility of N-Terminal Pro-B-Type Natriuretic Peptide -to-Troponin and BNP-to-Troponin Ratios for Differentiating Type 1 from Type 2 Myocardial Infarction: A HIGH-US Sub-Study. *Crit Pathw Cardiol* 2025; Epub ahead of print. PMID: 40997263. Full Text

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BACKGROUND: Differentiating type 1 myocardial infarction (T1-MI) from type 2 MI (T2-MI) remains a diagnostic challenge, even with the availability of high-sensitivity cardiac troponin assays. This study explored whether NT-proBNP, BNP, and their respective ratios to troponin could enhance the ability to distinguish between these MI subtypes. METHODS: As a HIGH-US sub-study, we examined data from 280 patients diagnosed with non-ST elevation myocardial infarction (172 with T1-MI and 108 with T2-MI). We assessed NT-proBNP, BNP, hs-cTnI, and their ratios as potential discriminative biomarkers. Diagnostic accuracy was evaluated using receiver operating characteristic (ROC) curves. RESULTS: NT-proBNP levels were markedly elevated in T2-MI patients compared to those with T1-MI (mean 10,327±12,923 vs 4,675±11,740 ng/L; P=0.006). Conversely, hs-cTnI concentrations were higher in T1-MI (1.4±5.1 vs 0.5±1.1 ng/L; P=0.030). Notably, the NT-proBNP-to-troponin ratio was more than three times greater in T2-MI cases (94,880±152,648 vs 24,209±78,727; P=0.007). NT-proBNP alone demonstrated fair discriminatory capacity (AUC 0.717, 95% CI 0.578-0.856), closely matching the NT-proBNP-to-troponin ratio (AUC 0.720, 95% CI 0.566-0.873). In contrast, BNP and the BNP-to-troponin ratio offered lower diagnostic values. Mean BNP levels were 505.4 ±576.6 ng/L for those with T2-MI and 437.1 ±738.8 ng/L for patients with T1-MI. BNP-to-troponin ratio showed a poor discrimination for the 2 MI types (AUC, 0.660; 95% CI, 0.532-0.789). CONCLUSIONS: Both NT-proBNP and its ratio to troponin show potential in differentiating T1-MI from T2-MI, reflecting distinct underlying pathophysiological processes. Given its comparable performance to the ratio, NT-proBNP alone may serve as a practical and cost-effective standalone marker. These findings support the hypothesis that incorporating NT-proBNP testing into routine clinical workflows may better informs the management of patients with suspected MI.

Public Health Sciences

Nance N, Gilsanz P, Karter AJ, Finertie H, Schmittdiel JA, An J, Adams AS, Oshiro C, **Cassidy-Bushrow AE**, Krahe-Dombrowski S, Yassin M, Lin S, Izadian K, O'Connor PJ, and Neugebauer R. GLP-1RA comparative effectiveness against dementia onset relative to other antidiabetic medications in a large, multi-site cohort of patients with type 2 diabetes. *Alzheimers Dement* 2025;21(9):e70621. PMID: 40952016. Full Text

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INTRODUCTION: To address gaps in current research, this study aims to compare the impact of exposure to glucagon-like peptide-1 receptor agonists (GLP-1RA) versus sodium-glucose cotransporter 2 inhibitors (SGLT2i), dipeptidyl peptidase 4 inhibitors (DPP4i), and sulfonylureas (SU) on reducing the risk of dementia, using a rigorous targeted learning causal inference approach. METHODS: Using clinical and claims data from four diverse US health-care systems, we emulated three two-arm trials contrasting sustained treatment with GLP-1RA versus SGLT2i, DPP4i, and SU on dementia diagnosis. We included diabetes patients aged ≥ 60 years who initiated medication between 2014 and 2022. We estimated cumulative risk differences at 2.5 years. RESULTS: In Cohort 1, there was no evidence of differential dementia risk between sustained exposure to GLP1-RA versus SGLT2i (adjusted risk difference [aRD] -0.001, 95% confidence interval [CI] -0.004, 0.001). In Cohorts 2 and 3, GLP-1RA was associated with reduced risk of dementia diagnosis compared to DPP4i and SU, respectively (aRD -0.013, 95% CI -0.017, -0.009; aRD -0.016, 95% CI -0.018, -0.015). DISCUSSION: Rigorous causal inference analysis suggests that sustained exposure to GLP-1RA may modestly reduce risk of dementia, compared to DPP4i or SU exposure-but not compared to SGLT2i. HIGHLIGHTS: We researched the comparative effects of diabetes medications on dementia. We studied a large, diverse observational cohort of patients with diabetes in the United States. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) may modestly reduce risk of dementia compared to dipeptidyl peptidase 4 inhibitor or sulfonylurea exposure. GLP-1RAs do not show evidence of dementia risk reduction compared to sodium-glucose cotransporter 2 inhibitors. Physicians may consider this when making prescription decisions with patients.

Public Health Sciences

**Oslin KA**, **Wilson CP**, and **Craig JR**. Maxillary Sinus Antrochoanal Polyp Recurrence Following Surgery in Adults: A Systematic Review. *Laryngoscope* 2025; Epub ahead of print. PMID: 40944545. Full Text

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OBJECTIVE: Antrochoanal polyps (ACPs) are cystic non-neoplastic lesions that most commonly originate from the maxillary sinus and may extend posteriorly through the choana. Transnasal endoscopic removal is preferred for symptomatic ACPs. ACPs can recur after surgical removal, and while a 15% recurrence rate was published in a systematic review on pediatric ACPs, this has not been well-established in adults. The purpose of this systematic review was to determine the recurrence rate of maxillary sinus ACPs following surgical resection in adults. DATA SOURCES: A systematic review was conducted on ACP resection using Medline, Embase, and Web of Science databases from 1946 to July 2025. REVIEW

METHODS: After excluding duplicate and non-English articles, 395 abstracts were screened, and 63 articles were selected for full-text review. Articles were included if they were original studies that reported recurrence rates after surgical resection of maxillary sinus ACPs in patients ≥ 16 years old. Articles were excluded if study populations had minimum follow-up of less than 6 months or mean follow-up of less than 12 months. RESULTS: After full-text review, 16 studies met inclusion criteria with 439 patients being utilized for analyses. Mean age was 33.8 years and 39.7% were female. Endoscopic middle meatal antrostomy with ACP removal was performed in 80.8% of cases. Following surgery, patients experienced an overall recurrence rate of 9% (95% CI: 6%-14%), with a mean follow-up of 36.8 months. CONCLUSION: ACPs recurred in about 9% of adults following surgical resection. Further research is needed to determine whether certain patient factors and surgical techniques are associated with ACP recurrence.

Public Health Sciences

**Santana-Garces MA**, Wagner AL, Harapan H, and Lu Y. Role of universal and targeted recommendations for vaccines for sexually transmitted infections in the USA, China and Indonesia: a cross-sectional study. *BMJ Public Health* 2025;3(2):e001897. PMID: 40959837. Full Text

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BACKGROUND: Vaccines for sexually transmitted infections (STIs) are in development and little is known about their future acceptance. The type of recommendations released by National Immunisation Technical Advisory Groups could influence vaccine uptake. This study aims to understand how universal and targeted wording affects theoretical acceptance to vaccines for four common STIs (chlamydia, gonorrhoea, syphilis and genital herpes) in the USA, China and Indonesia. We also aim to understand how universal and targeted wording may influence acceptance among those who engage in high-risk sexual behaviours. METHODS: A total of 1941 adults between the ages of 18 and 45 were included in the final sample. For each country, the sample was stratified by sexual behaviours, then the proportion of those who accepted each vaccine under universal or targeted wording was reported. $\chi(2)$ tests were used to assess differences, and the likelihood of vaccine acceptance was represented using prevalence ratios (PRs) from Poisson regression models. RESULTS: Overall, vaccine acceptance for each STI and in every country sampled tended to be lower among those who received targeted wording compared with universal wording. Previous knowledge of STIs significantly affected vaccine acceptance. In the USA, there was significant interaction between recommendation wording type and having heard of the STI; individuals who had previously heard of STIs were more likely to accept an STI vaccine, and that this acceptance varied significantly based on whether they received a universal (PR: 1.30, 95% CI: 1.05 to 1.62) versus targeted recommendation (PR: 2.45, 95% CI: 1.69 to 3.56). CONCLUSIONS: Our results are important for future vaccine recommendations as vaccine hesitancy and refusal are on the rise globally. Thus, wording and education surrounding sexual health and STIs are factors that influence decision-making. Our research also highlights the importance of appealing to certain high-risk groups and providing informative language when releasing vaccine recommendations.

Public Health Sciences

Singh R, Pierce CB, Makker K, Jacobson L, Jensen ET, Vaidya R, Gogcu S, Sanderson K, South AM, Thompson A, Perng W, Perrin EM, **Cassidy-Bushrow AE**, Dunlop AL, Dabelea D, Ferrara A, Hedderson MM, Zhu Y, Karagas M, Camargo CA, Jr., Hockett CW, Aris IM, McEvoy CT, Ganiban JM, Farzan S, Serrano-Gonzalez M, Carnell S, Geiger SD, Zhao Q, and O'Shea TM. Association of Maternal Prepregnancy BMI With Offspring Cardiometabolic Outcomes in Childhood. *Obesity (Silver Spring)* 2025; Epub ahead of print. PMID: 40976645. Full Text

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OBJECTIVE: This study aimed to evaluate associations of maternal prepregnancy BMI with offspring BMI and blood pressure in childhood, specifically for infants born preterm. METHODS: In this observational cohort study of children in the Environmental Influences on Child Health Outcomes (ECHO) Cohort, we utilized four levels of maternal prepregnancy BMI and child BMI. Children were categorized as being born extremely, very, or moderately preterm; late preterm; or term. RESULTS: In total, 13,810 children from 44 ECHO cohorts were included in these analyses. After adjusting for maternal education, maternal age at delivery, and singleton birth, a monotonic dose relationship was noted between child BMI z-scores and maternal prepregnancy BMI level. For child blood pressure outcomes, only extremely preterm children born to mothers with healthy weight and obesity and very/moderately preterm children born to mothers with healthy weight had higher odds of elevated blood pressure/hypertension compared with their term counterparts. CONCLUSIONS: High maternal prepregnancy BMI was associated with a stepwise increase in offspring BMI in childhood. Preterm children had a higher probability of elevated blood

pressure/hypertension than term children. These findings highlight a possible window of opportunity to modify lifestyles and behavior of at-risk children prior to adolescence to positively impact adolescent cardiometabolic health.

Public Health Sciences

Thompson D, Visness CM, Wood RA, O'Connor GT, Robison RG, Hershey GKK, Kercsmar CM, Chambliss J, Liu AH, **Johnson C**, Lovinsky-Desir S, Bacharier LB, Gern JE, Jackson DJ, Busse WW, Gergen PJ, Teach SJ, and Rastogi D. Associations between body weight, asthma burden, and T2 inflammation among under-resourced children. *Ann Allergy Asthma Immunol* 2025; Epub ahead of print. PMID: 41022283. Full Text

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BACKGROUND: Overweight/obesity is a risk factor for asthma, particularly in under-resourced children, and contributes to higher disease burden. T2 inflammation, a key characteristic of asthma endotypes, has been inconsistently associated with burden of obesity-related asthma, which may be due to limited overlap between different T2 features, including elevated total serum IgE, eosinophilia, and allergen sensitization. OBJECTIVE: To investigate the effects of different T2 features on association of overweight/obesity with asthma burden in under-resourced children. METHODS: Among 2,160 children ages 6-20 years from four Inner-City Asthma Consortium cohorts, we investigated the association of overweight/obesity with asthma burden (unscheduled visits, hospitalizations, exacerbations, asthma control, and pulmonary function), and the effect of T2 features (total IgE higher than age-specific cutoffs, total eosinophils >300 cells/ul, or sensitization to ≥2 allergens) on the association. RESULTS: The odds (OR (95% CI)) of unscheduled visits was higher among those with overweight/obesity (1.35 (1.04-1.75)) and allergen sensitization (1.35 (1.02-1.80)), hospitalizations was higher among those with elevated total IgE (2.17 (1.27-3.69)) and eosinophilia (2.80 (1.56-5.21)), and poor asthma control was higher among those with elevated total IgE (1.27 (1.09-1.41)). Overweight/obesity and all T2 features were associated with lower FEV1/FVC ratio. There was no synergistic or clinically significant mediating influence of any of T2 features on the association of overweight/obesity with asthma burden. CONCLUSION: Among under-resourced children with asthma, overweight/obesity and T2 inflammation are largely independently associated with unscheduled visits and pulmonary function deficits. T2 inflammation, but not overweight/obesity, is associated with poor control and hospitalizations.

Public Health Sciences

**Wang L**, **Lu X**, **Szalad A**, **Zhang Y**, **Li Y**, **Lu M**, **Kemper A**, **Liu Z**, **Liu XS**, **Chopp M**, and **Zhang ZG**. Engineered miR-214 enriched Schwann cell-derived extracellular vesicles amplify therapeutic efficacy for peripheral neuropathy in T2D mice. *Front Cell Neurosci* 2025;19:1649830. PMID: 40950414. Full Text

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Extracellular vesicles (EVs) derived from healthy Schwann cells (SC-EVs) ameliorate peripheral neuropathy in diabetic mice and rescue sciatic nerve function in Schwann cell Dicer knockout mice in part via SC-EV cargo miRNAs. Among these miRNAs, miR-214 repairs nerve damage. The present study investigated whether engineered SC-EVs with elevated miR-214 (214-EVs), further amplify the therapeutic effect of naïve SC-EVs (naïve-EVs) on reducing diabetic peripheral neuropathy (DPN) in a mouse model of high-fat diet (HFD)-streptozotocin (STZ) induced type 2 diabetes. Compared to naïve-EVs, 214-EVs significantly improved motor and sensory nerve conduction velocity of the sciatic nerve and thermal latency, which were associated with increased intraepidermal nerve fiber density, axonal diameter, and myelin thickness in the sciatic nerve. Quantitative RT-PCR and Western blot analyses of sciatic nerve tissues showed that, compared to naïve-EVs, 214-EVs significantly increased miR-214 levels and downregulated axonal inhibitory protein PTEN and the myelination inhibitory protein cJUN. Furthermore, 214-EVs markedly suppressed neuroinflammation by decreasing CD68 + macrophages and inactivating the TLR4/NF-κB signaling pathway. Collectively, our findings demonstrate that miR-214-enriched SC-EVs are superior to naïve-EVs to ameliorate DPN and represent a promising EV-based therapeutic strategy.

Pulmonary and Critical Care Medicine

**Franco-Palacios DJ**, Franco-Palacios CR, **Crowley S**, **Allenspach LL**, **Stagner L**, **Corrales JP**, **Olexsey K**, **Waynick L**, **Simanovski J**, Bhatti H, **Laier R**, **Myszenski A**, **Wang Y**, **Lu M**, and **Song T**. Effect of Total Psoas Muscle Area and Serum Albumin on Outcomes After Lung Transplantation. *Clin Transplant* 2025;39(9):e70308. PMID: 40932471. Full Text

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BACKGROUND: Sarcopenia of the psoas muscle and hypoalbuminemia indicate poor nutritional status, inflammation, and frailty in lung transplant (LT) candidates, correlating with worse post-transplant outcomes. METHODS: Retrospective study of LT recipients (2015-2023) examining the association of total psoas muscle area (TPA) and serum albumin with hospital stay, survival, and pulmonary function. RESULTS: One hundred thirty-two LT recipients (mean age 59.56 ± 10.65 years, BMI 26.73 ± 5.55 kg/m(2), 65% males), 95% underwent bilateral LT. Higher TPA was associated with shorter hospital and ICU stays ($p = 0.001$). Similarly, higher albumin levels were associated with reduced hospital and ICU stays ($p < 0.001$). Hospital survivors had higher TPA (17.5 ± 6.1 vs. 14.6 ± 5.2 cm(2), $p = 0.02$) and higher albumin levels (3.25 ± 0.73 vs. 2.75 ± 0.85 mg/dL, $p = 0.01$). Long-term survivors had higher TPA (17.8 ± 6.35 vs. 15.9 ± 5.51 cm(2), $p = 0.07$) and higher albumin levels (3.29 ± 0.75 vs. 2.97 ± 0.78 mg/dL, $p = 0.01$). On multivariate analysis, albumin and male gender remained independent predictors of hospital and long-term survival. TPA was positively associated with post-transplant pulmonary function based on FVC and FEV1 ($p < 0.001$), while albumin levels showed no association. CONCLUSION: In the present study of LT recipients, higher TPA and albumin levels were linked to shorter hospitalization, and albumin independently predicted survival. TPA, but not albumin, was associated with pulmonary function post-transplant.

Pulmonary and Critical Care Medicine

**Martirosov AL**, **Griebe K**, and **Hameed AA**. Enhancing Pulmonary Care in Older Adults: The Vital Role of Healthcare Providers in Managing Age-Related Challenges and Medication Access. *Clin Geriatr Med* 2025. PMID: Not assigned. Full Text

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Pulmonary and Critical Care Medicine

Miller RJ, Chrissian AA, Kheir F, Shafiq M, Chua AT, Navani N, Almeida FA, Alraiyes AH, Bain PA, Bellinger CR, Chao CH, Cheng GZ, Cloyes R, **Diaz-Mendoza J**, DiBardino DM, Folch E, Frye LK, Gesthalter YB, Gildea TR, Goyal A, Heskett KM, Holden VK, Liberman M, Manley C, Meena NK, Oberg CL, Pannu JK, Pickering EM, Senitko M, Shepard JO, Vandemoortele T, Mehta AC, and Yasufuku K. American Association for Bronchology and Interventional Pulmonology (AABIP) Evidence-Based Guidelines on Bronchoscopic Diagnosis and Staging of Lung Cancer. *J Bronchology Interv Pulmonol* 2025;32(4). PMID: 41024606. Full Text

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BACKGROUND: Lung cancer remains a predominant cause of cancer-related deaths worldwide, and there are notable geographic and institutional differences in both diagnostic and staging approaches. To address this, the American Association for Bronchology and Interventional Pulmonology (AABIP) convened a multidisciplinary committee to craft evidence-based and evidence-informed recommendations for diagnosing peripheral pulmonary nodules and performing convex probe endobronchial ultrasound (CP-EBUS)-guided mediastinal staging. METHODS: A modified Delphi method guided the creation and refinement of 9 Population, Intervention, Comparator, Outcome (PICO) questions. A systematic literature review, updated through March 2023, served as the basis for drafting recommendations. The panel used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach to assess the quality of evidence and relied on National Institute for Health and Care Excellence (NICE) language to express the strength of each recommendation. Where suitable, meta-analyses were completed; otherwise, systematic reviews and consensus among experts provided the evidence for guidance. RESULTS: Nine recommendations were ultimately proposed: 6 were supported by meta-analyses and 3 by systematic reviews. The topics include comparing diagnostic yield and complication rates between peripheral bronchoscopy and transthoracic needle biopsy, the use of multiple biopsy instruments and the role of rapid on-site evaluation (ROSE) during peripheral bronchoscopy, and best practices for CP-EBUS-guided mediastinal staging. Several critical considerations emerged, such as lesion size, evolving technologies in bronchoscopy, and the importance of both available resources and local expertise. CONCLUSION: These guidelines aim to standardize and streamline recommendations for the bronchoscopic diagnosis and staging of lung cancer. Since rapid technological progress and observational data play significant roles in this field, ongoing research and evidence updates will be vital to refining best practices. Clinicians are advised to tailor these recommendations according to local circumstances, the unique needs of their patients, and any new findings as they develop.

Radiation Oncology

**AlKhatib S**, Akbarov K, Hande V, Ciraj-Bjelac O, and Abdel-Wahab M. Radiotherapy Resources in Central Asia: An International Atomic Energy Agency Update. *JCO Glob Oncol* 2025;11:e2500271. PMID: 40971756. Full Text

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PURPOSE: Radiation therapy is crucial in cancer treatment. However, low- and middle-income countries (LMICs), including Central Asia (Kazakhstan, Uzbekistan, Turkmenistan, Kyrgyzstan, Tajikistan), face increasing challenges because of limited radiation oncology resources, compounded by diverse health care systems and vast geography. METHODS: A longitudinal, registry-based review analyzed the state of radiation oncology resources in Central Asia to assess current conditions and future needs, considering projected regional growth. Data were sourced from the Directory of Radiotherapy Centres (DIRAC) and GLOBOCAN 2020. A simple linear regression evaluated the relationship between machine capacity rate and Gross National Income (GNI) per capita. RESULTS: As of 2022, the region has 75 megavoltage machines and 35 brachytherapy (BT) units, with all but two being high-dose rate BT. The number of megavoltage units per million population varies, ranging from 0.1 to 0.2 in Tajikistan, Kyrgyzstan, and Uzbekistan, and it is 2.3 in Kazakhstan. A significant correlation between GNI per capita and machine capacity was found ($R(2) = 0.89$, $P = .014$), indicating that higher GNI correlates with increased machine

capacity. By 2030, a minimum of 115 megavoltage machines will be needed to meet demand, but only 75 are available as of 2022. CONCLUSION: While progress has been made, there remain significant challenges to ensuring equitable access to radiation therapy across Central Asia, underscoring the need for additional resources to meet growing demands.

Radiation Oncology
Dykstra MP, Regan SN, Yin HM, **McLaughlin PW**, Zaki M, Mislmani M, Miller SR, 2nd, **Narayana V**, Kendrick D, Khadija M, Dryden D, Litzenberg DW, Mietzel M, Heimburger DK, Schipper M, Jackson WC, and Dess RT. Androgen Deprivation Therapy Practice Patterns in High-Risk Prostate Cancer Treated With Definitive Radiotherapy: Prospective Results From a Statewide Quality Consortium. *JCO Oncol Pract* 2025;Op2500489. Epub ahead of print.:. PMID: 41004692. Full Text

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PURPOSE: The 2022 AUA/ASTRO guidelines recommend 18-36 months of androgen deprivation therapy (ADT) with definitive radiotherapy for localized, high-risk prostate cancer. The STAMPEDE M0 trial supports intensification with androgen receptor pathway inhibitors (ARPIs) for patients with ≥2 cT3/T4, Grade Group [GG] 4-5, prostate-specific antigen (PSA) ≥40 ng/mL, or cN1. Given advances in imaging, risk stratification, and treatment delivery, we characterized contemporary practice patterns using prospective data from the Michigan Radiation Oncology Quality Consortium (MROQC). METHODS: Patients enrolled in MROQC with intact, high-risk M0/N0-1 prostate cancer were included. Clinical information, including intended ADT duration and ARPI use, was prospectively collected. The primary outcome was intended guideline-concordant ADT (GC-ADT, ≥18 months). Multivariable analyses (MVA) assessed associations between clinical factors and GC-ADT recommendations. We compared the adoption of ARPI with standard therapies before and after the publication of STAMPEDE M0. Facility-level variability was evaluated using a mixed-effects model, with the treatment site as a random intercept. RESULTS: Between June 2020 and November 2024, 553 patients across 26 centers were included: cT3/4 (13.3%), cN1 (19.9%), GG 4-5 (75.0%), and PSA ≥20 ng/mL (40.0%). Overall, 91.3% were recommended ADT, with 67.0% being guideline-concordant. On MVA, GC-ADT was significantly associated with cN1 (odds ratio [OR], 2.94 [95% CI, 1.44 to 5.99]), GG (GG4 OR, 6.23 [95% CI, 2.85 to 13.62]; GG5 OR, 9.45 [95% CI, 4.46 to 20.06]), and PSA ≥40 (OR, 3.64 [95% CI, 1.22-10.87]). Facility-level variability persisted in the MVA ($P < .0001$). Among the 27.9% who met meeting STAMPEDE criteria, ARPI recommendations increased from 0% prepublication to 23.2% afterward. CONCLUSION: Within a statewide quality consortium, guideline-concordant ADT recommendations occurred in two thirds of patients, with ARPI intensification in under 25% among STAMPEDE-eligible patients. These findings highlight the need for individualized ADT strategies and collaborative efforts to standardize high-quality care.

Radiation Oncology
**Huang J**, **Doemer A**, **Siddiqui S**, **Shah M**, **Al Asadi A**, **DiCarlo A**, **Thind K**, **Moceri A**, **Scarpace L**, **Lee I**, and **Robin A**. Novel use of 3D printing for preoperative dose estimation in the first case of GammaTile spine implantation. *Brachytherapy* 2025; Epub ahead of print. PMID: 40992982. Full Text

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PURPOSE: For a patient who had two previous courses of external beam radiation therapy for rectosigmoid adenocarcinoma and presented with painful, recurrent disease in the sacrum, this study describes the first use of Cs-131 LDR GammaTile therapy outside of the brain and demonstrates a novel use of 3D printing for preoperative dose estimation. MATERIAL AND METHODS: A personalized 3D-printed model of the patient's spine was created using segmented MRI data, differentiating uninvolved bone, tumor, and thecal sac and nerve roots, with a Stratasys J5 MediJet® Printer. This model was used to simulate surgical resection and placement of dummy radioactive sources. A CT scan of the model facilitated preoperative dose calculations, including physical dose using Eclipse planning software and biologically effective dose (BED) using MIM Maestro software. The predicted dose was then compared to the postimplant dosimetry for the actual patient. RESULTS: For the relevant organ at risk (thecal sac), the max dose (D(0.035cc)) was calculated accurately within 8.0% for physical dose and within 10.0% for BED when comparing the dose estimated using our 3D-printed model and the patient's postimplant dosimetry. CONCLUSIONS: 3D printing can be used preoperatively to estimate dose to critical organs at risk for patients receiving surgical resection followed by Cs-131 LDR implantation in the spine and can be especially valuable in the context of reirradiation.

Radiation Oncology

Kyei I, Bea VJ, Gyan KK, Adjei E, Stonaker B, Bekele M, Abebe E, Davis M, Boakye A, Boateng R, Elemento O, Aitpillah F, Alebachew H, Jibril A, Chen Y, Taiwo E, **Bensenhaver J**, **Walker E**, **Ali H**, Oppong J, Ginter P, Nalwoga H, Kalungi S, Ebughe G, Ezeome ER, Jackson K, Bonsu EO, Momoh A, Martini R, Demaria S, Yates C, Balogun OD, Louie C, Manohar J, Bediako Y, Boaitey GA, Fondjo LA, Iloanusi N, Okoye I, Adinku M, Ankomah K, Dally C, Rockefeller E, **Susick L**, Obong-Ekanem I, Greenspun BC, Daba SA, **Schwartz T**, Robine N, Chen S, Carrot-Zhang J, Amazu S, **Jiagge E**, Acheamfour OK, Patino S, Malik M, Ju T, Siegel B, Martin IK, Mills C, Phillip J, Kalu CO, Joseph C, Peters F, Stromain A, Olusina B, Nwokoro O, Lasebikan N, Udosen J, Nwagbara V, Carpten J, Fisseha S, Johnson T, Awuah B, and Newman LA. Oncologic Anthropology and the African Diaspora: Twenty-Year Anniversary Report, International Center for the Study of Breast Cancer Subtypes (ICSBCS). *Ann Surg Oncol* 2025; Epub ahead of print. PMID: 40914775. Full Text

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The International Center for the Study of Breast Cancer Subtypes (ICSBCS) has played a vital role in defining and overcoming many inequities that exist in breast cancer treatment and outcome on a global basis through capacity-building programs that improve the management of breast cancer patients across the African diaspora. ICSBCS activities also fill critical gaps in disparities research related to the genetics of ancestry. Over the past 20 years, ICSBCS teams have spearheaded landmark studies documenting the relevance of genetic African ancestry to breast cancer risk, while also improving the quality of care delivered to patients in diverse communities. Herein, the achievements and future goals of this international, multi-institutional breast cancer research and outreach program are summarized.

Radiation Oncology

Mudgal M, **Bhatnagar AR**, Kumar Vasudevan A, Priya Gajendiran A, Gondhi V, Balaji S, Murugan SK, and Gunasekaran K. The Impact of Pulmonary Hypertension on Hospitalization Risk in Adults with Respiratory Syncytial Virus Infection. *Biomedicines* 2025;13(9). PMID: 41007832. Full Text

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Background/Objectives: Respiratory syncytial virus (RSV) infection can lead to significant complications, particularly among those with underlying cardiovascular and pulmonary complications. Patients with pulmonary hypertension (PH) are susceptible to clinical deterioration triggered by respiratory infections due to their limited cardiopulmonary reserve. This study aimed to assess the risk of hospitalization in RSV-infected adults with and without PH. Methods: We conducted a retrospective cohort study using the research network TriNetX to assess the risk of hospitalization in a cohort of patients with RSV infection, comparing those with and without PH. Propensity score matching was performed for demographic variables and RSV risk factors between the two cohorts. The risk of hospitalization was expressed as an adjusted odds ratio (aOR) with a 95% confidence interval (CI). Results: There were 193,256 patients in the RSV with PH cohort and 2,843,714 in the RSV without PH cohort (all aged >18 years). The mean age of the RSV with PH cohort was 68.2 ± 15.3 years, 50.6% were females, 64% were white, and 64.2% were

group 2 PH. The RSV with PH cohort was at an increased risk of hospitalization (aOR 1.89, 95% CI 1.87-1.92, p-value 0.02). There was a significant risk (aOR 1.29, 95% CI 1.27-1.32) for the composite outcome of hospitalization-related complications between the two cohorts. Comorbid conditions (diabetes, cardiovascular disease, chronic lung disease, and chronic kidney disease) increased the risk of hospitalization in the RSV with PH group, with the biggest effect noted with underlying cardiovascular disease. Similarly, those with group 2 PH had a higher risk of hospitalization compared to the other PH groups. Remarkably, all PH groups demonstrated increased hospitalization risk compared to the RSV without PH cohort. Conclusions: We found that patients >18 years of age with PH and RSV infection were at an increased risk of hospitalization, with subsequently higher rates of RSV-infection-related complications. All PH groups had a higher hospitalization risk compared to the RSV without PH cohort, likely denoting PH as an independent risk factor for worse RSV-infection-related outcomes. RSV vaccination, therefore, may benefit all age groups of patients with PH.

Radiation Oncology

Runge CL, Lyness JA, Gillison ML, Adelstein DJ, Harari PM, Ringash J, Geiger JL, Krempl GA, Blakaj DM, Bates JE, Galloway TJ, Jones CU, Gensheimer MF, Dunlap NE, Phan J, Caudell JJ, Pennington JD, Torres-Saavedra PA, Yom SS, Le QT, and **Movsas B**. Self-Perceived Hearing Outcomes With Radiation and Cisplatin or Radiation and Cetuximab for Patients With Human Papilloma Virus (HPV)-Positive Oropharyngeal Cancer-Results From NRG Oncology RTOG 1016. *Int J Radiat Oncol Biol Phys* 2025; Epub ahead of print. PMID: 40829719. Full Text

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Cleveland Clinic Foundation, Cleveland, Ohio.
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University Health Network-Princess Margaret Hospital, Toronto, Ontario, Canada.
University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma.
Ohio State University Comprehensive Cancer Center, Columbus, Ohio.
Emory University Hospital Midtown, Atlanta, Georgia.
Fox Chase Cancer Center, Philadelphia, Pennsylvania.
Sutter Medical Center Sacramento, Roseville, California.
Stanford Cancer Institute Palo Alto, Stanford, California.
The James Graham Brown Cancer Center at University of Louisville, Louisville, Kentucky.
Moffitt Cancer Center, Tampa, Florida.
Southeast Clinical Oncology Research Consortium NCORP, Winston-Salem, North Carolina.
Biometric Research Program, National Cancer Institute, Bethesda, Maryland (This work was performed while employed by NRG Oncology, Philadelphia, Pennsylvania).
UCSF Medical Center-Mount Zion, San Francisco, California.
Henry Ford Cancer Institute, Detroit, Michigan.

PURPOSE: RTOG 1016 was a noninferiority phase 3 trial comparing the efficacy of radiation with either cisplatin (RT + Cis) or cetuximab (RT + Cetux) for patients with Humman Papillomavirus (HPV)+ oropharyngeal cancer (OPC). Perceived hearing handicap was included as a patient-reported outcome (PRO) secondary endpoint. The primary hypothesis was that perceived hearing handicap would be greater for patients receiving RT + Cis compared with RT + Cetux. METHODS AND MATERIALS: Perceived hearing handicap was measured at baseline, end of treatment, and 3, 6, and 12 months posttreatment using the Hearing Handicap Inventory for Adults Screening Version (HHIA-S), a 10-item self-assessment questionnaire designed to measure patients' reactions to their hearing loss. Mixed ordinal logistic models were used to determine the treatment effect on HHIA-S scores and handicap categories (2-sided $\alpha = 0.05$). RESULTS: The PRO substudy included 375 eligible patients. No significant differences in patient/tumor characteristics were found between patients who participated in the HHIA-S study versus those excluded. For total HHIA-S scores and social and emotional subscales, RT + Cetux had significantly lower (ie, better) scores from end of treatment. Change score from baseline to end of treatment for RT + Cis (4.32; 95% confidence interval [CI], 2.57-6.07]) was greater than RT + Cetux (0.08;

95% CI, -1.15 to 1.31). For hearing handicap category, RT + Cis had a significantly higher percentage of mild/moderate and severe cases at the end of treatment (32%) compared with RT + Cetux (20%) (P < .0001). Adjusted conditional odds of higher self-perceived hearing handicap category for RT + Cis compared with RT + Cetux was 3.73 (95% CI, 2.10-6.62). CONCLUSION: Patients have significantly worse self-perceived hearing handicap after receiving RT + Cis treatment than with RT + Cetux. This was consistent across time through 1 year posttreatment. These findings inform hearing-related outcomes for patients with HPV-associated OPC and indicate the need for ototoxicity monitoring with RT + Cis treatment.

Radiation Oncology
Tang LL, Huang CL, Lin SJ, Le QT, O'Sullivan B, Yom SS, Huang SH, Chan AW, Lee N, Pan JJ, Mejia MBA, Ahn YC, Wong KCW, McDowell L, Orlandi E, Friborg J, Chen YP, Yasuda K, Kodaira T, Whitley AC, King AD, Prajogi GB, Hahn E, Lin JC, Kiyota N, Lee V, Ji PJ, Hitchcock Y, Hoebers F, Blanchard P, Moon SH, Wan Ishak WZ, Harrington KJ, Yang KY, Colevas AD, Lee A, Hu CS, Rosenthal D, **Siddiqui F**, Langendijk JA, Lang JY, Yi JL, Shen LF, Li JB, Liu LZ, Lee AWM, Mai HQ, Yang MK, Sun Y, Chua MLK, and Ma J. Target volume delineation of the neck for radiotherapy in nasopharyngeal carcinoma: CSTRO, CACA, CSCO, HNCIG, ESTRO, and ASTRO guidelines and contouring atlas. *Lancet Oncol* 2025;26(9):e488-e498. PMID: 40907527. Full Text

The Chinese Society for Therapeutic Radiology Oncology, the Chinese Anti-Cancer Association, the Chinese Society of Clinical Oncology, the Head and Neck Cancer International Group, the European Society for Radiotherapy and Oncology, and the American Society for Radiation Oncology collaboratively developed evidence-based guidelines and a comprehensive contouring atlas for neck target volume delineation in nasopharyngeal carcinoma. These guidelines address five key challenges in modern radiotherapy practice: margin design of clinical target volume; nodal target volume delineation after induction chemotherapy; delineation of equivocal nodes evident on imaging; low-risk clinical target volume delineation based on regional stepwise extension patterns; and modifications for anatomical boundaries of lymphatic areas. Developed through a rigorous systematic review and expert appraisal process by a panel of 50 international, multidisciplinary members from 17 countries and regions, these guidelines incorporate the latest advances in nasopharyngeal carcinoma diagnosis and treatment. They reflect contemporary therapeutic concepts and elaborate on current practice variations. These guidelines aim to standardise global practice, substantially improving consistency and reducing variability in nasopharyngeal carcinoma radiotherapy target delineation.

Radiation Oncology
Tang LL, Huang CL, Lin SJ, Le QT, O'Sullivan B, Yom SS, Huang SH, Chan AW, Lee N, Pan JJ, Mejia MBA, Ahn YC, Wong KCW, McDowell L, Orlandi E, Friborg J, Chen YP, Yasuda K, Kodaira T, Whitley AC, King AD, Prajogi GB, Hahn E, Lin JC, Kiyota N, Lee V, Ji PJ, Hitchcock Y, Hoebers F, Blanchard P, Moon SH, Wan Ishak WZ, Harrington KJ, Yang KY, Colevas AD, Lee A, Hu CS, Rosenthal D, **Siddiqui F**, Langendijk JA, Lang JY, Yi JL, Shen LF, Li JB, Liu LZ, Lee AWM, Mai HQ, Yang MK, Sun Y, Chua MLK, and Ma J. Primary target volume delineation for radiotherapy in nasopharyngeal carcinoma: CSTRO, CACA, CSCO, HNCIG, ESTRO, and ASTRO guidelines and contouring atlas. *Lancet Oncol* 2025;26(9):e477-e487. PMID: 40907526. Full Text

The Chinese Society for Therapeutic Radiology Oncology, the Chinese Anti-Cancer Association, the Chinese Society of Clinical Oncology, Head and Neck Cancer International Group, the European Society for Radiotherapy and Oncology, and the American Society for Radiation Oncology jointly developed evidence-based guidelines and a contouring atlas for primary target volume delineation for radiotherapy in nasopharyngeal carcinoma. The guidelines systematically address three crucial challenges: margin design of clinical target volumes; target volume delineation after induction chemotherapy; and low-risk clinical target volume delineation based on local stepwise extension patterns. Based on a comprehensive systematic review and critical appraisal by an international multidisciplinary panel of 50 nasopharyngeal carcinoma specialists from 17 countries and regions, these guidelines are in keeping with advances in nasopharyngeal carcinoma diagnosis and treatment, embodying contemporary treatment concepts, and elaborating on the differences in practice. These guidelines aim to support global clinical practice in

radiotherapy target volume delineation, substantially enhancing homogeneity and reducing variability in nasopharyngeal carcinoma target delineation.

Sleep Medicine

Aggarwal B, Gao Y, Alfini A, Azarbarzin A, Anafi RC, Glazer Baron K, Bautch VL, Bowles N, Broussard JL, Brown M, **Cheng P**, Cook SH, Cortese R, Fernandez FX, Galis Z, Johnson DA, Jelic S, Lipton JO, Lutsey PL, Miao Q, Ordovas JM, Prather AA, Swirski FK, Tasali E, Vargas I, Grandner MA, and Lloyd-Jones D. Sleep and circadian rhythms in cardiovascular resilience: mechanisms, implications, and a Roadmap for research and interventions. *Nat Rev Cardiol* 2025; Epub ahead of print. PMID: 40968347.
Full Text

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The interaction between sleep, circadian rhythms and cardiovascular resilience is a crucial yet underexplored research area with important public health implications. Disruptions in sleep and circadian rhythms exacerbate hypertension, diabetes mellitus and obesity, conditions that are increasingly prevalent globally and increase the risk of cardiovascular disease. A National Heart, Lung, and Blood Institute workshop examined these connections, as well as the emerging concept of cardiovascular resilience as a dynamic and multifaceted concept spanning molecular, cellular and systemic levels across an individual's lifespan. The workshop emphasized the need to expand the focus from solely understanding whether and how sleep and circadian rhythm disturbances contribute to disease, to also exploring how healthy sleep and aligned circadian rhythms can increase cardiovascular resilience. To develop a Roadmap towards this goal, workshop participants identified key knowledge gaps and research opportunities, including the need to integrate biological, behavioural, environmental and societal factors in

sleep and circadian health with cardiovascular research to identify therapeutic targets. Proposed interventions encompass behavioural therapies, chronotherapy, lifestyle changes, organizational policies and public health initiatives aimed at improving sleep and circadian health for better cardiovascular outcomes. Future cross-disciplinary research and translation of discoveries into public health strategies and clinical practices could improve cardiovascular resilience across the lifespan in all populations.

Surgery

**Chamseddine H**, **Halabi M**, **Shepard A**, **Kabbani L**, and **Onofrey K**. Limb salvage using Pounce LP mechanical thrombectomy system after failed open and percutaneous thromboembolectomy. *J Vasc Surg Cases Innov Tech* 2025;11(6):101935. PMID: 40979408. Full Text

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Mechanical thrombectomy devices have limited efficacy in organized subacute and chronic thrombi and face challenges in small-caliber distal vessels. The Pounce LP Thrombectomy System (Surmodics) is a fully percutaneous, purely mechanical thrombectomy device designed to overcome these limitations. We report the case of an 83-year-old female presenting to an out-of-state hospital with acute limb ischemia secondary to a right external iliac artery occlusion. Despite percutaneous mechanical thrombectomy with an aspiration thrombectomy device and subsequent open Fogarty balloon thromboembolectomy for distal embolization, her ischemia worsened, and a below-knee amputation was recommended. Upon transfer to our institution, she had sensorimotor deficits, distal ischemic changes, and occlusions of the anterior tibial, posterior tibial, and peroneal arteries at the level of the midcalf. Mechanical thrombectomy using the Pounce LP device successfully removed organized thrombus and restored multiphasic inline flow to the peroneal artery and its communicating branch, which subsequently fed into the distal posterior tibial artery and the plantar vessels. The patient ultimately underwent a successful transmetatarsal amputation, achieving limb salvage.

Surgery

**Franco-Palacios DJ**, Franco-Palacios CR, **Crowley S**, **Allenspach LL**, **Stagner L**, **Corrales JP**, **Olexsey K**, **Waynick L**, **Simanovski J**, Bhatti H, **Laier R**, **Myszenski A**, **Wang Y**, **Lu M**, and **Song T**. Effect of Total Psoas Muscle Area and Serum Albumin on Outcomes After Lung Transplantation. *Clin Transplant* 2025;39(9):e70308. PMID: 40932471. Full Text

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BACKGROUND: Sarcopenia of the psoas muscle and hypoalbuminemia indicate poor nutritional status, inflammation, and frailty in lung transplant (LT) candidates, correlating with worse post-transplant outcomes. METHODS: Retrospective study of LT recipients (2015-2023) examining the association of total psoas muscle area (TPA) and serum albumin with hospital stay, survival, and pulmonary function. RESULTS: One hundred thirty-two LT recipients (mean age 59.56 ± 10.65 years, BMI 26.73 ± 5.55 kg/m(2), 65% males), 95% underwent bilateral LT. Higher TPA was associated with shorter hospital and ICU stays ($p = 0.001$). Similarly, higher albumin levels were associated with reduced hospital and ICU stays ($p < 0.001$). Hospital survivors had higher TPA (17.5 ± 6.1 vs. 14.6 ± 5.2 cm(2), $p = 0.02$) and higher albumin levels (3.25 ± 0.73 vs. 2.75 ± 0.85 mg/dL, $p = 0.01$). Long-term survivors had higher TPA (17.8 ± 6.35 vs. 15.9 ± 5.51 cm(2), $p = 0.07$) and higher albumin levels (3.29 ± 0.75 vs. 2.97 ± 0.78 mg/dL, $p = 0.01$). On multivariate analysis, albumin and male gender remained independent predictors of hospital and long-term survival. TPA was positively associated with post-transplant pulmonary function based on FVC and FEV1 ($p < 0.001$), while albumin levels showed no association. CONCLUSION: In the present study of LT recipients, higher TPA and albumin levels were linked to

shorter hospitalization, and albumin independently predicted survival. TPA, but not albumin, was associated with pulmonary function post-transplant.

Surgery

Hidalgo LG, Madill-Thomsen KS, Reeve J, Mackova M, Gauthier P, Demko Z, Prewett A, Lee M, Alhamad T, Anand S, Arnol M, Baliga R, Banasik M, Blosser CD, Bobba S, Brennan D, Bromberg J, Budde K, Chamienia A, Chow K, Ciszek M, Costa N, Dęborska-Materkowska D, Debska-Ślizień A, Domański L, 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, Kumar D, Lan J, Lowe D, Mazurkiewicz J, Miglinas M, Moinuddin I, Mueller T, Myślak M, Naumnik B, Pączek L, **Patel A**, Perkowska-Ptasińska A, Piecha G, Poggio E, Bloudíčkova SR, Regele H, Schachtner T, Shojai S, Sikosana MLN, Slatinská J, Smykal-Jankowiak K, Haler Ž V, Viklicky O, Vucur K, Weir MR, Wiecek A, Zaky Z, and Halloran PF. Improving the histologic detection of donor-specific antibody-negative antibody-mediated rejection in kidney transplants. *Am J Transplant* 2025; Epub ahead of print. PMID: 40854490. Full Text

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Emerging treatments for antibody-mediated rejection (ABMR, NEJM391 (2):122-132) have increased the importance of ABMR detection when donor-specific antibody (DSA) is negative. We addressed this issue in the Trifecta-Kidney study (ClinicalTrials.gov #NCT04239703) using 3 centralized tests in 690 kidney transplant biopsies: DSA (One Lambda Inc), blood donor-derived cell-free DNA (dd-cfDNA, Prospera™ test, Natera, Inc), and molecular biopsy assessment (MMDx). We used an "AutoBanff 2022" algorithm to model the impact of alternative DSA interpretations on the histologic diagnosis of DSA-negative ABMR following Banff guidelines, including agreement with dd-cfDNA and molecular ABMR. Lowering MFI cutoffs for DSA positivity did not improve the detection of DSA-negative ABMR. However, simply calling all DSA as positive allowed the Banff 2022 guidelines to identify 46% more ABMR cases with no measurable conventional DSA, and per net reclassification improvement increased agreement between histologic diagnoses and both dd-cfDNA (P = 7.72E-7) and molecular ABMR (P = 7.69E-7). New ABMR cases were as strongly positive for dd-cfDNA and molecular ABMR as those found using the conventional DSA interpretation. A validation set analysis using INTERCOMEX study data (ClinicalTrials.gov NCT#01299168) confirmed these findings and found that the new DSA-negative ABMR cases identified by calling all DSA-positive had the same risk for graft loss as those found with conventional DSA interpretation. Trifecta-Kidney Study ClinicalTrials.gov #NCT04239703.

Surgery
**Oki R**, **Rocha I**, **Al-Juburi S**, **Rajendran L**, **Kerby E**, **Mohamed A**, **Al-Kurd A**, **Nassar A**, **Kim DY**, **Yoshida A**, **Abouljoud M**, and **Nagai S**. The Individual Impact of Machine Perfusion on Liver and Kidney on Donor Expansion in Simultaneous Liver and Kidney Transplantation. *Transpl Int* 2025;38:14807. PMID: 40994627. Full Text

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Machine perfusion (MP) use for both organs can increase organ usage in simultaneous liver and kidney transplantation (SLKT). We analyzed 6,956 SLKT performed between 2015 and 2024 using the United Network for Organ Sharing database. The primary outcomes were the 1-year graft survival for kidney and liver. Donor types and MP use for liver and/or kidney were captured and associations with outcomes were evaluated. SLKT from Donation after circulatory death donors (DCD) increased from 4.5% in 2015 to 16% in 2023. The median Kidney Donor Profile Index (KDPI) has increased from 23% in 2015 to 28% in 2023. MP use for kidney and liver also increased from 21% to 51% and 0%-17%, respectively. KDPI >85% was an independent risk factor of 1-year kidney graft failure in the no kidney MP group [HR 2.03, 95% CI 1.20-3.44, p = 0.009], but not in the kidney MP group. DCD was found to be an independent risk factor of 1-year liver graft failure in the no liver MP group [HR 1.56, 95% CI 1.19-2.03, p = 0.001], but not in the liver MP group. MP for both organs may contribute to expanding the donor pool for SLKT without compromising post-transplant outcomes.

Surgery
**Singh JP**, **Aleissa M**, **Chitragari G**, **Drelichman ER**, **Mittal VK**, and **Bhullar JS**. Uncovering the role of microbiota and fecal microbiota transplantation in Crohn's disease: Current advances and future hurdles. *World J Methodol* 2025;15(4):106148. PMID: 40900872. Full Text

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Crohn's disease (CD) is an idiopathic, chronic, and recurrent inflammatory condition of the gastrointestinal tract. Recent studies suggest a potential role of gut microbiota in CD, particularly dysbiosis-an imbalance in gut bacteria. While dysbiosis is consistently observed in CD, it remains uncertain whether it is a cause or a consequence of the disease. Given its association with CD, the therapeutic potential of fecal microbiota transplantation (FMT) has been explored. This review examines the role of gut microbiota in CD, evaluates the therapeutic potential of probiotics and FMT, and highlights current research findings and limitations. Key studies on the relationship between gut dysbiosis, probiotics, and FMT in CD were analyzed, with a focus on randomized trials, meta-analyses, and clinical observations. Dysbiosis is a consistent feature of CD, but its causative role remains unclear. Probiotics, prebiotics, and synbiotics have shown no efficacy in inducing or maintaining remission in CD. FMT shows potential as a therapeutic option for CD, but its efficacy remains inconsistent and inconclusive. The variability in outcomes, including diminished effects over time despite repeated FMT, underscores the need for larger, well-controlled trials. Only one randomized controlled trial (RCT) has compared FMT with sham transplantation, but the sample size was very small. Other studies are limited by factors such as small sample sizes, lack of control groups, short follow-up periods, and inconsistent methodologies, making it challenging to draw definitive conclusions. While gut dysbiosis likely plays a role in CD pathogenesis, its causative role remains uncertain. Current evidence does not support FMT as a reliable treatment for inducing or maintaining remission in CD, though it appears generally safe. Larger, standardized, RCTs are necessary to clarify the therapeutic role of FMT in CD management.

Surgery

Ward KR, **Bui J**, Bondarenko I, Chang A, Lagisetty K, Lin J, Ekeke CN, Odell DD, and Reddy RM. Improved outcomes with robotic-assisted laparoscopic paraesophageal hernia repairs compared with laparoscopic and transthoracic approaches: A single high-volume institution experience. *JTCVS Open* 2025;26:255-265. PMID: 40923072. Full Text

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OBJECTIVES: Laparoscopic (lap) paraesophageal hernia repair has excellent short-term outcomes but higher long-term recurrence rates compared with the transthoracic repair. We hypothesized that the robotic-assisted lap (robot) approach would have similarly good short-term outcomes as lap, but also lower recurrence rates. METHODS: A retrospective study of prospectively collected data was performed for paraesophageal hernia repairs at a single high-volume quaternary hospital from July 2018 to September 2022. Outcomes analyzed included 2-year postoperative radiographic recurrence (Rad), Society of Thoracic Surgeons-defined radiographic recurrence (STS-rad), symptomatic recurrence (Sx), and perioperative outcomes. Lap, robot, and transthoracic groups were compared using univariate, multivariate, and propensity score analysis. RESULTS: Among 207 cases (52 lap, 90 robot, and 65 transthoracic), robot was lower than lap (odds ratio [OR], 0.13-0.17; P < .01) and similar to transthoracic (OR, 0.79-1.02; P > .05) in univariate and multivariate analyses. STS-rad was similar between approaches across analyses, apart from robot being higher than transthoracic on propensity score analysis (OR, 1.83; P < .01). Robotic Sx recurrence was lower in robot compared with lap across analyses (OR, 0.40-0.50; P < .001). Median length of stay was 2 days for robot and lap, significantly shorter than transthoracic (median, 5 days; P < .01). Fewer postoperative complications occurred in robot compared with transthoracic (OR, 0.19-0.21; P < .01). Reoperation and endoscopic intervention were lower in robot compared with lap (OR, 0.09-0.12; P < .01 and OR, 0.32-0.40; P < .05). CONCLUSIONS: Robotic paraesophageal hernia repairs had generally lower 2-year recurrence and reoperation than lap and shorter hospital stays and fewer immediate complications than transthoracic.

Surgery

Xie A, **Steele NG**, and Cui Y. gwSPADE: gene frequency-weighted reference-free deconvolution in spatial transcriptomics. *Nucleic Acids Res* 2025;53(18). PMID: 41002029. Full Text

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Most spatial transcriptomics (ST) technologies (e.g. 10× Visium) operate at the multicellular level, where each spatial location often contains a mixture of cells with heterogeneous cell types. Thus, effective deconvolution of cell type compositions is critical for downstream analysis. Although reference-based deconvolution methods have been proposed, they depend on the availability of reference data, which may not always be accessible. Additionally, within a deconvolved cell type, cellular heterogeneity may still exist, requiring further deconvolution to uncover finer structures for a better understanding of this complexity. Here, we present gwSPADE, a gene frequency-weighted reference-free SPAtial DEconvolution method for ST data. gwSPADE requires only the gene count matrix and utilizes appropriate weighting schemes within a topic model to accurately recover cell type transcriptional profiles and their proportions at each spatial location, without relying on external single-cell reference information. In various simulations and real data analyses, gwSPADE demonstrates scalability across various platforms and shows superior performance over existing reference-free deconvolution methods such as STdeconvolve.

Urology
Bertini A, Cirulli GO, **Stephens A**, Finocchiaro A, Viganò S, Lughezzani G, Buffi N, Ficarra V, Salonia A, Briganti A, Montorsi F, Sood A, **Rogers C**, and **Abdollah F**. Reply to 'Comment on Bertini et al.: area deprivation and PSA screening disparities' and 'Comment on socioeconomic disparities in prostate cancer screening: the impact of the Area Deprivation Index on PSA screening frequency'. *BJU Int* 2025; Epub ahead of print. PMID: 40905572. Full Text

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Urology
Bertini A, **Stephens A**, Finocchiaro A, Viganò S, Dinesh A, Guivatchian E, Cusmano N, Lughezzani G, Buffi N, Sorce G, Ficarra V, Briganti A, Salonia A, Montorsi F, Sood A, **Rogers C**, and **Abdollah F**. Association of area of deprivation index with magnetic resonance imaging (MRI) utilization for prostate cancer detection: results from a contemporary North American population. *World J Urol* 2025;43(1):584. PMID: 41021031. Full Text

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PURPOSE: Since the use of Magnetic Resonance Imaging (MRI) in the initial diagnostic evaluation for prostate cancer (PCa) has considerable costs, there is concern that socioeconomic barriers may result in MRI underutilization. We examined the relationship between socioeconomic factors, measured by the Area Deprivation Index (ADI), and MRI utilization in PCa diagnostic setting using a contemporary North American population. METHODS: We included all the patients aged > 40 years with a confirmed PSA > 3 ng/mL at Henry Ford Health (HFH) between 2018 and 2022. 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 socio-economic disadvantage. MRI and biopsy status were defined as undergoing these procedures within 6 and 9 months, respectively, from their first PSA > 3 ng/mL in the time period. Univariable (UVA) and multivariable (MVA) Logistic regression models tested the impact of ADI on prostate MRI or biopsy utilization. RESULTS: We included 18,827 patients who had a PSA > 3 ng/mL, 3759 (20%) of whom were Non-Hispanic Black. Overall, 679 (3.6%) and 1672 (8.8%) of these individuals underwent prostatic MRI and prostate biopsy, respectively. Median (IQR) age and ADI percentile were 68 (62-74) years and 58 (38-79), respectively. Patients who received MRI were more likely to be younger (66 vs. 68, p = 0.006), Non-Hispanic Black [28.0% (95%CI: 24.7%-31.5%) vs. 19.7% (95% CI 19.1%-20.3%), p < 0.0001] and to undergo PSA test in more recent median years (2021 vs. 2019, p < 0.0001), compared to those who did not undergo MRI. When stratifying the population by ADI quintiles, men in the fifth (most deprived) quintile were less likely to receive MRI (3.1% vs. 5.9%, p < 0.001), compared to those in the first (most affluent) quintile. At logistic MVA, patients living in more deprived neighborhoods (higher ADI percentile) were less likely to receive MRI before PCa diagnosis (OR: 0.90, p < 0.001). Specifically, for an increase in ADI percentile of 10 units, the relative odds of receiving MRI decreased by 10%. CONCLUSIONS: Although the overall utilization of prostate MRI remains low in this real-world study, men living in more socioeconomically deprived areas were significantly less likely to undergo MRI before PCa diagnosis. Our findings underscore the need for targeted interventions to ensure a more equitable access to advanced diagnostic tools.

Urology

Bertini A, **Tylecki A**, **Stephens A**, Finocchiaro A, Viganò S, Cusmano N, Dinesh A, Guivatchian E, Lughezzani G, Buffi N, Di Trapani E, Ficarra V, Briganti A, Salonia A, Montorsi F, Sood A, **Rogers C**, and **Abdollah F**. Socioeconomic Disparities in Prostate Cancer Presentation: The Impact of ADI on Prostate Cancer Stage at Diagnosis. *Clin Genitourin Cancer* 2025;23(6):102418. PMID: 40961906. Full Text

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OBJECTIVES: To investigate the impact of socioeconomic deprivation, as measured by Area Deprivation Index (ADI), on PCa stage at diagnosis in a North-American statewide cohort. METHODS: The Michigan Department of Health and Human Services (MDHHS) was queried to identify men aged ≥30 with a confirmed diagnosis of PCa at prostate biopsy between 2004 and 2022. An ADI score was assigned to each patient based on their residential census block group. Individuals were further categorized into quartiles, where the fourth 1 (ADI 75-100) represented those living in the most deprived areas. Logistic regression analysis tested the impact of ADI on diagnosis with NCCN high-risk PCa (T3-T4 or PSA >20 ng/ml or ISUP GG ≥4) or metastatic PCa (N1 or M1) at presentation. RESULTS: We included 78018 patients, 17% of whom were Non-Hispanic Black (NHB). Median (IQR) age was 66 (59-72) years. Patients in the most disadvantage quartile (Q4) were more likely to be NHB (40.1% vs. 5.4%), had higher proportion with PSA>20 ng/ml (10.6 % vs. 5.1%), GG≥4 (55.4% vs. 53.1%), clinical T ≥ 3 (4% vs. 3%) and metastasis (3.3% vs. 1.8%) at diagnostic presentation, compared to those in the least disadvantaged quartile (Q1) (all P < .0001). At MVA, for each 10-unit increase in ADI percentile, the relative odds of being diagnosed with NCCN high-risk and metastatic PCa increases by 2% (95% CI, 1.01-1.02) and 4% (95% CI, 1.02-1.05), respectively. Moreover, when compared to NHW men, NHB men had a 1.16 (95% CI, 1.12-1.22) and a 1.52-fold (95% CI, 1.38-1.68) higher relative odds of being diagnosed with NCCN high-risk PCa and metastatic PCa, respectively (P < .001). CONCLUSIONS: Living in more deprived areas was associated with higher relative odds of newly diagnosed PCa with unfavorable features. Our study underscores the silent barrier that socioeconomic deprivation poses to cancer early diagnosis and echo the call for tailored interventions to bridge this gap.

Urology
Biasatti A, Soputro NA, Porpiglia F, Perdonà S, **Abdollah F**, Nelson R, **Rogers C**, Zhao LC, Ghazi A, Challacombe B, Eden C, Mattei A, Fankhauser CD, Breda A, Rocco B, Montorsi F, Briganti A, Pellegrino AA, Mottrie A, De Groote R, Haese A, Graefen M, Moschovas MC, Patel V, Simone G, Galfano A, Secco S, Bertolo R, Pandolfo SD, Pansadoro V, Carvalho FLF, Joseph JV, Ramadan M, Shakuri-Rad J, Yuh B, Nix J, Lee DI, Rais-Bahrami S, Hemal S, Eltemamy M, Beksac AT, Schwen Z, Su LM, Buscarini M, Palese M, Tewari A, Wiklund P, Cherullo EE, Vourganti S, Linehan JA, Wu Z, Stifelman M, Ahmed M, Mehrazin R, Badani K, Link RE, Crivellaro S, Kaouk J, and Autorino R. The current landscape of single-port robotic surgery in urology. *Nat Rev Urol* 2025; Epub ahead of print. PMID: 40897917. Full Text

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The advent of the purpose-built da Vinci single-port robotic platform marks a pivotal advancement in minimally invasive urological surgery. Designed to overcome the ergonomic and technical limitations of prior single-site approaches, the single-port system enables complex procedures through a single incision, with enhanced dexterity, optimized use of confined spaces and improved cosmetic and peri-operative outcomes. The single-port system has been increasingly used across a wide range of urological indications, including robot-assisted radical prostatectomy, partial nephrectomy, nephroureterectomy and reconstructive surgeries such as pyeloplasty and ureteral re-implantation. Innovative access strategies, such as the single-port transvesical and low anterior access approaches, have facilitated regionalized and multi-quadrant surgeries without the need for repositioning or robot re-docking. These advances have translated into reduced morbidity, faster recovery and increased feasibility of opioid-sparing, same-day discharge protocols. As surgical expertise deepens and technology evolves, the single-port robotic platform stands as a refinement of minimally invasive surgery, and also as a potential paradigm shift in urological practice.

Urology
Ditonno F, Veccia A, Bignante G, Wu Z, Wang L, **Abdollah F**, **Stephens A**, Simone G, Tuderti G, Lee R, Eun DD, Correa AF, De Cobelli O, Ferro M, Porpiglia F, Amparore D, Checcucci E, Tufano A, Contieri R, Perdonà S, Bhanvadia R, Margulis V, Brönimann S, Singla N, Porter J, Ghodoussipour S, Minervini A, Mari A, Lambertini L, Ghoreifi A, Nativ OF, Gonzalgo ML, Sidhom D, Sundaram CP, Ben-David R, Eraky A, Mehrazin R, Yoshida T, Kinoshita H, Dehghanmanshadi A, Rais-Bahrami S, Meagher MF, Puri D, Derweesh IH, Moghaddam FS, Djaladat H, Bertolo R, Autorino R, and Antonelli A. Radical nephroureterectomy vs kidney sparing surgery for upper tract urothelial carcinoma in solitary kidney patients: a multi-institutional analysis of the ROBUUST 2.0 registry. *World J Urol* 2025;43(1):534. PMID: 40897892. Full Text

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PURPOSE: Radical nephroureterectomy (RNU) for upper tract urothelial carcinoma (UTUC) in solitary kidney patients is a rare and underreported scenario. This study aims to compare the outcomes of UTUC solitary kidney patients becoming anephric after RNU to those of patients undergoing kidney-sparing surgery (KSS). METHODS: Data from patients with a solitary kidney were retrieved from the ROBUUST 2.0 database, a global, multicenter registry containing data on patients who underwent curative surgery for UTUC. Baseline patient demographics, disease characteristics, and surgical features were compared between RNU and KSS. Kaplan-Meier methods were used to estimate recurrence-free survival (RFS), metastasis-free survival (MFS), cancer-specific survival (CSS), and overall survival (OS) in patients undergoing RNU, with 3-year and 5-year cutoffs applied. RESULTS: Thirty-nine patients (76.5%) underwent RNU, whereas 12 (23.5%) underwent KSS. Despite a comparable preoperative renal function, the distribution of CKD stages differed significantly between the groups ($p = 0.019$). Despite a similar rate of postoperative complications, patients undergoing RNU experienced a significantly higher median LOS ($p < 0.001$). Among RNU patients, OS was 83.9%, CSS was 96.9%, RFS was 71.8%, and MFS was 84.4% at the 3-year follow-up. After 5 years post-surgery, OS was 73.4%, CSS was 83.1%, RFS was 59.9%, and MFS was 78.5% in the same cohort. CONCLUSIONS: UTUC solitary kidney patients undergoing RNU or KSS face a substantial perioperative burden. Despite these challenges, our cohort demonstrated favorable oncological outcomes comparable to those reported in the existing literature.

Urology
Ficarra V, Romito I, Sorce G, Maravigna D, De Stefano A, Mottrie A, **Abdollah F**, Viganò S, Stabile A, Salonia A, Giannarini G, Crocerossa F, Gandaglia G, Montorsi F, and Rossanese M. Comparison of Single- and Multiport Robot-assisted Approaches in Prostate and Renal Surgery: A Systematic Review and Meta-analysis. *Eur Urol* 2025; Epub ahead of print. PMID: 41016915. Full Text

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BACKGROUND AND OBJECTIVE: The aim of this systematic review with meta-analysis was to assess the perioperative, functional, and oncological outcomes of single-port (SP) robotic procedures in the surgical management of prostate and renal diseases. METHODS: A systematic review was conducted using the MEDLINE and Scopus databases, covering literature published up to December 2024. Studies were included if these compared SP versus multiport (MP) approaches in robot-assisted procedures, specifically radical prostatectomy (RARP), simple prostatectomy (RASP), partial nephrectomy (RAPN), radical nephrectomy (RARN), and pyeloplasty (RAP; PROSPERO registration number: CRD42025616519). Perioperative outcomes were assessed across all procedures. Functional and oncological outcomes were analysed specifically in patients undergoing RARP, while warm ischaemia time (WIT), off-clamp rates, and positive surgical margin rates were evaluated in those undergoing RAPN. KEY FINDINGS AND LIMITATIONS: A total of 26, three, nine, one, and two studies evaluated RARP, RASP, RAPN, RARN, and RAP, respectively. Compared with MP-RARP, SP-RARP was associated with lower estimated blood loss (standardised mean difference [SMD] = 0.51; 95% confidence interval [CI]: 0.16-0.87), shorter length of stay (SMD = 1.12; 95% CI: 0.63-1.62), and reduced postoperative pain (SMD = 0.12; 95% CI: 0.04-0.35). The only difference between SP- and MP-RASP was represented by the use of a higher morphine milligram equivalent in the MP group (SMD = 0.59; 95% CI: 0.01-1.16). In patients undergoing RAPN, SP was associated with a significantly higher WIT than MP (SMD = -0.32; 95% CI: -0.58 to -0.06). However, the length of hospital stay (SMD = 0.31; 95% CI: 0.03-0.59) and pain score on postoperative day 1 (SMD = 0.22; 95% CI: 0.01-0.43) were significantly in favour of SP-RAPN. Limitations were the lack of randomised trials, and the across-study heterogeneity in surgical techniques and outcome definitions. CONCLUSIONS AND CLINICAL IMPLICATIONS: Compared with the MP approach, SP robotic surgery offers advantages in terms of reduced postoperative pain and hospital stay. In patients undergoing RARP, functional and oncological outcomes were comparable between the two approaches. In patients undergoing RAPN, the SP approach was associated with a longer WIT.

Urology

Moghaddam FS, Ghoreifi A, Sayyid RK, Wu Z, **Abdollah F**, Antonelli A, Eun DD, Guo S, Hung AJ, Ma L, Margulis V, Matin SF, Mehrazin R, Porter J, Potretzke A, Pradere B, Roupret M, Seisen T, Shariat SF, Simone G, Stein RJ, Wang L, Wu J, Xylinas E, Yao L, Zargar H, Autorino R, Cacciamani GE, and Djaladat H. A structured training curriculum for robot-assisted radical nephroureterectomy: a Delphi consensus study. *BJU Int* 2025; Epub ahead of print. PMID: 40960222. Full Text

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OBJECTIVES: To develop an internationally validated, structured robot-assisted radical nephroureterectomy (RARNU) training programme through expert consensus. MATERIALS AND METHODS: A RARNU-specific questionnaire was developed/adapted from previously published, validated questionnaires for robot-assisted urological procedures. This included five key domains and 11 surgical steps. In all, 30 upper tract urothelial carcinoma experts were invited to participate. A two-stage modified Delphi approach was employed. Consensus was defined as ≥80% agreement. Modifications and additional statements were proposed during the second round following qualitative/quantitative feedback from the initial round. RESULTS: Response rates for the first and second Delphi rounds were 80% (24/30) and 92% (22/24), respectively. All agreed that adoption of a standardised training curriculum can improve clinical outcomes during the RARNU learning curve. There was ≥92% agreement on all proposed RARNU steps. Five RARNU clinical modules of increasing complexity were defined using individual step difficulty and number of prior RARNU cases required, with ≥96% agreement among respondents. Respondents unanimously agreed that the final assessment should be based on a procedure-specific scale focusing on the hilar dissection, ureteric dissection, and bladder cuff excision steps. No consensus was reached for the annual minimum RARNU volume required for eligibility as a RARNU curriculum host centre. CONCLUSION: This is the first structured training curriculum for RARNU using international expert consensus. This will help guide surgical educators and trainees toward independent completion of a full RARNU.

## Conference Abstracts

Cardiology/Cardiovascular Research

**Steenson K**, **Grimshaw C**, Paarmann K, and **Kerrigan DJ**. Feasibility Project To Assess the Use Of An AI-supported Phase 3 Cardiac Rehabilitation Program. *J Cardiopulm Rehabil Prev* 2025;45(5):E49. Full Text

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Introduction: Phase 3 cardiac rehabilitation (CR) programs are typically utilized as a strategy to help patients maintain the health gains achieved during phase 2 CR. However, due to many barriers for both patients and CR facilities, only a small percentage of individuals participate in these hospital-based programs. Home-based CR offers a promising convenient alternative, that can eliminate many common barriers to patients (e.g. transportation, limited class times) as well as facilities (limited space and staff). Purpose: To evaluate the feasibility of a home-based, virtual CR digital platform (KENTO Health, INC) following participation in CR. Primary outcomes were weekly engagement in the platform and synchronized coach visits. Secondary outcomes assessed the program's impact on QoL, depressive symptoms, and physical activity at 60 days. Design: Single-center, open-label, non-randomized, prospective pilot study. Methods: Eligible patients who had completed or were unable to continue their Phase 2 CR were consented and enrolled into the pilot study where they were given a tablet preloaded with the Kento Health application (KHapp) and an activity tracker (Garmin). The intervention consisted of a 12-week hybrid Phase 3 CR program featuring synchronous coaching, continuous physiologic monitoring (i.e. heart rate and steps), and AI-personalized educational content. Patients completed questionnaires online at the beginning of the study and at 60-days. The questionnaires given were the Patient Health Questionnaire-9 (PHQ-9), Dartmouth COOP, Godin Leisure-Time Exercise Questionnaire, and Net Promoter Score (NPS). A paired samples test was used to compare changes over time with an alpha level set at < 0.05 (SPSS 22.0 IBM). Results: 20 out of 24 patients who were enrolled and consented completed the initial and 60-day questionnaires. Average age was 69 + 12, with 45% female and 71% Black. The percentage of subjects that attended weekly coach visits was 79%. Satisfaction of the program at 60-days, as measured by the NPS, was 96%. Patient reported quality of life (QOL), as measured by the Dartmouth COOP total score was maintained [21 + 5 to 19 + 5 (p = 0.135)] 60 days after completion of CR. The Dartmouth COOP subscale score regarding 'how would you rate your health compared to 4 weeks ago' was improved (p = 0.025). Physical activity levels and self-reported depression were also maintained based on the Godin (p = 0.973) and PHQ (p = 0.283) scores, respectively. Conclusions: This pilot study supports the feasibility of a home-based virtual Phase 3 CR program delivered synchronously with weekly coach visits and AI driven education. Improvement in patient reported health at 60 days was observed. Further research is warranted to explore home-based, virtual programs as a strategy to improve outcomes in patients who participate in CR..

Diagnostic Radiology

**Fana M**, **Choudhury O**, **Chebl A**, **Latack K**, **Schultz L**, **Albanna A**, **Reardon T**, **Iqbal Z**, **Kole M**, and **Marin H**. The Rapid Occluded Vessel Etiology Score: A Novel Algorithm to Identify Acute Atherosclerotic Large Vessel Occlusions of the Middle Cerebral Artery. *Stroke* 2025;56. Full Text

M. Fana, Henry Ford Health, Detroit, MI, United States

Introduction: Mechanical thrombectomy (MT) devices were fundamentally designed for the treatment of cardioembolic (CE) strokes despite that 10-20% of large vessel occlusions (LVO) are caused by large artery atherosclerosis (LAA), which may not respond comparably. Therefore, the differentiation between LAA and non-LAA LVO may be critical for selecting the ideal MT technique. Here, we construct an algorithm for use in the emergent setting pre-operatively to differentiate between LAA and non-LAA LVO using clinical and radiographic features. Methods: Using our prospectively collected stroke database we identified all middle cerebral artery (MCA) occlusions treated with MT with confirmed etiology as either LAA or non-LAA (CE, cryptogenic) according to TOAST criteria. Stroke risk factors and CT angiography (CTA) of the head and neck features were compared between LAA and non-LAA etiologies in a univariate analysis. An algorithm was then constructed using these variables in a multivariable logistic regression

with corresponding score estimates for each variable to assess how well the model distinguished between LAA and non-LAA groups. The sensitivity and specificity were computed for each sum score to identify the ideal cut-off point for differentiating LAA from non-LAA LVOs. Results: Final analysis included 33 LAA, 207 CE, and 120 cryptogenic strokes. Patients presenting with LAA LVOs were significantly less likely to have atrial fibrillation (9.1% vs 53.8%; p<0.0001), EF<35% (9.1% vs 27.8%; p=0.0208) and more likely to present with progressive or fluctuating symptoms (21.2% vs 4.6%; p=0.0018), intracranial multi-vessel atherosclerotic disease on CTA (84.8% vs 37%; p<0.0001), tapered appearance of occlusion with associated collaterals (60.6% vs 0.9%; p<0.0001), and ICA bulb plaque with high-risk features (87.9% vs 37.6%; p<0.0001) (Table 1). The AUC was 0.9650 (95% CI=0.9332, 0.9968) and the highest combination of sensitivity and specificity (97% and 88%, respectively) was associated with a cut-off score of 9 (Tables 2 and 3). Conclusion: Our scoring system reliably differentiates between non-LAA and LAA LVO with high sensitivity and specificity based on 6 clinical and radiographic features. This will need to be validated with an external patient dataset and then in a prospective study. .

Emergency Medicine

Aboul-Nour H, Jumah A, **Albanna A**, Mohamed G, Alsrouji O, **Schultz L**, **Latack K**, **Miller J**, Uddin K, **Gunaga S**, **Muir J**, **Chebl A**, and **Ramadan AR**. Abstract WP225: Fibrinogen Depletion and The Risk of Intracerebral Hemorrhage following Mechanical Thrombectomy. *Stroke* 2025;56(Suppl_1). Full Text

A. Jumah, Emory University Hospital, Troy, MI, United States

Background: Intravenous thrombolysis (IVT) and mechanical thrombectomy (MT) are the standard of care for select stroke patients with acute large vessel occlusion (LVO). Fibrinogen levels may drop after IVT, and a significant decrease in fibrinogen is associated with an increased risk of intracranial hemorrhage (ICH). Our Pilot study aimed to explore the relationship between fibrinogen levels and the development of ICH in MT-treated patients and whether bridging with IVT further increases that risk. Methods: This is a prospective pilot study that enrolled adults presenting to our center with a diagnosis of LVO stroke and eligible to receive MT with or without IVT between April 2020 and May 2023. All patients consented to enrollment. Results: Forty-one patients were enrolled. Median age was 68 years [IQR 56-79], 58.5% were females and 56.1% were black. Nineteen patients (46.3%) were treated with MT+IVT, and 22 (53.6%) were treated with MT only. There was no difference in baseline characters between both groups. Baseline fibrinogen levels were similar between MT+IVT and MT-only groups [391 vs 352 mg/dL, p=0.4]. Post MT, the MT+IVT group had lower fibrinogen levels compared to the MT-only group [224 vs 303 mg/dL, p<0.001]. Similarly, there was a significant drop in fibrinogen levels between baseline and follow-up in the MT+IVT vs MT-only group [106 vs 39.5 mg/dL, p=0.001]. Eight patients (19.5%) developed ICH; 5 (26.3%) in the MT+IVT group and 3 (13.6%) in the MT-only group. No significant differences were seen in baseline, follow-up, or change in fibrinogen levels between patients who developed ICH and those who did not. However, there was a significantly lower follow-up fibrinogen levels between patients who suffered an ICH in the MT+IVT arm compared to those without ICH in the MT arm (200 vs 301 mg/dL, p=0.006). There was also a negative correlation between the drop in fibrinogen levels and the number of MT passes (Spearman CC -0.33, p=0.03). Conclusion: This pilot study's preliminary data show that fibrinogen depletion contributes to hemorrhagic transformation in MT-treated patients. This suggests that fibrinogen monitoring in patients undergoing MT after IVT may help identify patients with an increased risk of ICH. Larger studies areneeded to explore the cost-effectiveness of monitoring fibrinogen in patients undergoing bridging therapy and the benefit of repleting fibrinogen in this patient population.

Gastroenterology

Harrison JE, **Jafri SM**, Vemulapalli R, Mitchell G, Wolin D, Zografos L, Yang M, Jackson L, Wang J, Henderson J, Boules M, and Kumpf V. Beyond the diagnosis: The socioeconomic burden of SBS patients dependent on parenteral support. *Clin Nutr ESPEN* 2025;69:990-991. Full Text

Rationale: Short bowel syndrome (SBS) is a debilitating condition, often requiring long-term parenteral support (PS), that can significantly impact patients' health, employment, and daily functioning. This study assessed the socioeconomic burden of SBS. Methods: A noninterventional, cross-sectional, online survey capturing employment status, caregiver dependence, healthcare utilization (hospitalization/emergency department [ED] visits), and quality of life (QoL) was conducted in the US and Europe among patients

(≥18 years) diagnosed with SBS on parenteral support. QoL was assessed with the Short Form 36 Health Survey, Acute Version 2 (SF-36v2), which measured SBS/treatment impact on patient functioning; norm-based scores were compared with the US general population mean of 50.0. Results: 91 patients completed the survey (mean age: 50.4 years; 58.2% female, 69.1% White). Patients were receiving total parenteral nutrition (TPN; 90.1%) and/or IV hydration (73.6%) and glucagon-like peptide-2 analog therapy (24.2%). SBS impacted employment: 22.0% of patients were employed and 25.3% were permanently disabled. Among all patients, 57.3% missed ≥1 day of work/school/daily tasks in the past week and 25.8% missed ≥4 days. High healthcare utilization: 27.5% were hospitalized for SBS-related complications in the past 6 months and 41.8% had ED visits. 76.9% relied on informal caregiving, averaging 17.9 hours/week. Poor QoL: patients with SBS had notably lower functioning across all daily/work activity-related domains (SF-36v2 score range, 36.8-42.2) compared with the general population mean of 50. SF-36v2 Physical and Social Functioning scores were 41.9 and 38.6, respectively. Conclusion: SBS imposes a severe socioeconomic burden (disability, missed work, caregiver need, hospital/ED visits, and diminished QoL), underscoring a critical need for improved treatments and support systems to reduce this burden and enhance patient outcomes. Disclosure of Interest: J. Harrison Other: Volunteer for Girls With Guts, S.-M. Jafri Consultant for: Intercept, Ironwood, AbbVie, Gilead, Takeda, and Ipsen, R. Vemulapalli Other: CME Faculty for Novus Medical Education, G. Mitchell Other: Employee of Ironwood and may hold shares and/or stock options in the company., D. Wolin Other: Full-time employee of RTI Health Solutions, an independent nonprofit research organization, which was retained by Ironwood to conduct the research that is the subject of this abstract. Their compensation is unconnected to the studies on which they work., L. Zografos Other: Full-time employee of RTI Health Solutions, an independent nonprofit research organization, which was retained by Ironwood to conduct the research that is the subject of this abstract. Their compensation is unconnected to the studies on which they work., M. Yang Other: Employee of Ironwood and may hold shares and/or stock options in the company., L. Jackson Other: Full-time employee of RTI Health Solutions, an independent nonprofit research organization, which was retained by Ironwood to conduct the research that is the subject of this abstract. Their compensation is unconnected to the studies on which they work., J. Wang Other: Full-time employee of RTI Health Solutions, an independent nonprofit research organization, which was retained by Ironwood to conduct the research that is the subject of this abstract. Their compensation is unconnected to the studies on which they work., J. Henderson Other: Employee of Ironwood and may hold shares and/or stock options in the company., M. Boules Other: Employee of Ironwood and may hold shares and/or stock options in the company., V. Kumpf Consultant for: Ironwood, Baxter Healthcare, and Fresenius Kabi

Gastroenterology

**Jafri SM**, Harrison JE, Kumpf V, Mitchell G, Wolin D, Zografos L, Yang M, Jackson L, Wang J, Henderson J, Boules M, and Vemulapalli R. Reducing parenteral support: patient and healthcare professional preferences for potential new short bowel syndrome therapies. *Clin Nutr ESPEN* 2025;69:898-899. Full Text

Rationale: Understanding patient and healthcare provider (HCP) preferences for treatment and outcome attributes in patients with short bowel syndrome (SBS) dependent on parenteral support (PS) can inform management strategies and therapeutic advancements. Methods: A noninterventional, cross-sectional, online survey evaluating potential new treatment and outcome attributes was conducted in the US and Europe in patients with SBS on parenteral support (≥18 years at diagnosis) and HCPs with ≥2 years of SBS experience managing ≥1 patient. Results: Responses were collected from 91 patients and 336 HCPs. Patients' mean age was 50.4 years (58.2% female; 69.1% White). Patients were on total parenteral nutrition (TPN; 90.1%) and/or IV hydration (73.6%) and glucagon-like peptide-2 analog therapy (24.2%); 42.3% of HCPs were physicians. Among patients, outcome attributes rated as very important included minimizing TPN (70.3%), IV hydration/nutrition (64.8%), and side effects (68.1%). Most (67.0%) considered a days/week TPN decrease meaningful, including a 1–2 days/week decrease (33.0%). 63.3% rated minimizing injection frequency as very important. For HCPs, among attributes rated as very important, top priorities were reducing TPN central venous access need/related risks (73.5%), hospitalizations (72.8%), and injection frequency (63.4%). Reducing TPN was meaningful to 95.8% of HCPs, including a 1–2 days/week decrease (44.3%). Conclusion: Patients highly rated reducing TPN dependence/associated risks, with even a 1 day/week TPN reduction considered meaningful, and decreasing injection frequency for potential new SBS therapies. HCPs valued reducing central venous

access need/related risks, hospitalizations, and injection frequency. These findings highlight critical unmet needs in SBS management and the importance of therapies that reduce PS burden and side effects, leading to improved patient outcomes. Disclosure of Interest: S.-M. Jafri Consultant for: Intercept, Ironwood, AbbVie, Gilead, Takeda, and Ipsen, J. Harrison Other: Volunteer for Girls With Guts, V. Kumpf Consultant for: Ironwood, Baxter Healthcare, and Fresenius Kabi, G. Mitchell Other: Employee of Ironwood and may hold shares and/or stock options in the company., D. Wolin Other: Full-time employee of RTI Health Solutions, an independent nonprofit research organization, which was retained by Ironwood to conduct the research that is the subject of this abstract. Their compensation is unconnected to the studies on which they work., L. Zografos Other: Full-time employee of RTI Health Solutions, an independent nonprofit research organization, which was retained by Ironwood to conduct the research that is the subject of this abstract. Their compensation is unconnected to the studies on which they work., M. Yang Other: Employee of Ironwood and may hold shares and/or stock options in the company., L. Jackson Other: Full-time employee of RTI Health Solutions, an independent nonprofit research organization, which was retained by Ironwood to conduct the research that is the subject of this abstract. Their compensation is unconnected to the studies on which they work., J. Wang Other: Full-time employee of RTI Health Solutions, an independent nonprofit research organization, which was retained by Ironwood to conduct the research that is the subject of this abstract. Their compensation is unconnected to the studies on which they work., J. Henderson Other: Employee of Ironwood and may hold shares and/or stock options in the company., M. Boules Other: Employee of Ironwood and may hold shares and/or stock options in the company., R. Vemulapalli Other: CME Faculty for Novus Medical Education

Gastroenterology
**Singh B**, **Alluri S**, and **Ramanan S**. Complications of TPN in cirrhotic population. *Gut* 2025;74(Suppl_3):A235-A235. Full Text

Henry Ford Jackson, Jackson, MI USA
Henry Ford Detroit, Detroit, MI USA

Background This retrospective study seeks to illuminate complications in cirrhotic patients receiving TPN. TPN is generally started in patients with cirrhosis due to moderate to severe malnutrition. TPN-associated decompensation can be Serious and even progress to the liver. In our study, we look for complications due to decompensation and its contribution to overall mortality. Methods A retrospective chart review was conducted of all adults (18 years or older) at our center (2014-2024) with a history of Cirrhosis while on TPN. Data on basic patient demographics, indication for TPN, Duration of TPN therapy, changes in TPN formulation, and mortality were collected. Results In the study, a total of 12/107 patients had cirrhosis at the time of TPN initiation. Mortality was seen in 9/12 cirrhotics as compared to 43/95 non-cirrhotics. 4/12 cirrhotics had line infection, 0/12 had line clots, 7/12 had worsening ascite. A statistically significant difference in mortality was not observed. The association between cirrhosis and time from peak LFT to death was significant with p- 0.025 in which cirrhotics had a longer time between peaking LFT with 240 days compared to 70.55 days in non-cirrhotic. Conclusions Our findings suggest that TPN is associated with decompensation with ascites being the most common complication likely in the setting of volume overload. However, mortality is not significantly associated with pre-existing cirrhosis, rather cirrhosis had a larger difference between peak value and death. This can indicate that cirrhotic decompensation generally occurs slowly over time whereas non-cirrhotic generally die of liver failure which has a short course till death. The size of the study is extremely small and the external validity of the data can be questionable. This underscores the need for further research to identify an association between cirrhosis and TPN..

Gastroenterology
**Singh B**, **Alluri S**, **Ramanan S**, and **Bern M**. Patterns of transaminase elevation in patients on TPN and association with mortality. *Gut* 2025;74(Suppl_3):A232-A233. Full Text

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Henry Ford Detroit, Detroit, MI USA

Background There are three primary types of parenteral nutrition- associated liver disease: steatosis- benign, although can progress to cirrhosis in patients receiving long-term PN, cholestasis- serious and can progress to cirrhosis and liver failure, and gallbladder sludge/stones. Risk Factors included excess calories or lipids. Our study aims to study different patterns of transaminase elevation, determine If the cholestatic or hepatocellular pattern is more predominant, and finally if a certain kind of elevation has a higher mortality risk. Methods A retrospective chart review was conducted of all adults at our center between 2014-2024, who had a history of elevated liver enzymes while on TPN. Data on indication for TPN, prior history of liver disease, pattern of injury, workup obtained, use of growth factors, and mortality was collected. Results A total of 111 patients with elevated liver enzymes were included. 63 (56.7%) patients had a history of liver disease with the most common indications for TPN being prolonged malnutrition in 41 (36.9%) patients, and short gut syndrome in 39 (35.1%). Mortality occurred in 52 (46.8%) patients. There was no association between the elevation of AST and mortality, p-0.422, the mean time of death from the peak is 38.56 days in the population with transient (< 30 days duration) and 301.69 days in the population with persistent elevation (> 30 days). There was a statistically significant association of ALT with mortality with p- 0.022, with a mean time to mortality of 63.83 days and 328.1 days. There was a statistical association between ALP and mortality with p- 0.034, with a mean time to mortality in 70.8 days and 328.1 days. As for bilirubin, there is no association and the duration to death is 70.8 days and 190.8 days. Further people with TPN change had a higher association with p-0.007, with a mean time to death of 31.79 in the change group versus 36 days in the no change group. Most changes in TPN were associated with ALP and T bili elevation with p- 0.028 and .036 respectively. Conclusions Results indicate ALT elevation is more strongly associated with mortality followed by ALP. The pattern of liver injury more predominant was cholestatic leading to TPN change and further mortality..

Gastroenterology

Winkler MF, Harrison JE, Vemulapalli R, Kumpf V, Mitchell G, Wolin D, Zografos L, Yang M, Jackson L, Wang J, Henderson J, Boules M, and **Jafri SM**. Unseen burden: Emotional, financial and occupational impacts on caregivers of patients with short bowel syndrome. *Clin Nutr ESPEN* 2025;69:991. Full Text

Rationale: Short bowel syndrome (SBS) is a complex condition often requiring parenteral support (PS), leading to significant caregiver burden. This study assessed the multidimensional impacts of caregiving. Methods: A noninterventional, cross-sectional, online survey was conducted in the US and Europe among caregivers (≥18 years) of patients with SBS. The SF-12 Health Survey version 2 (SF-12v2) assessed health-related quality of life, and the Kingston Caregiver Stress Scale (KCSS) measured caregiver burden. SF-12v2 norm-based scores were compared with a US population-based mean score of 50.0. Results: 66 caregivers participated (US, n=45; Europe, n=21); most were White (62.3%), female (57.6%), and ≥45 years-old (56.1%). They were commonly a spouse/partner (39.4%), child (33.3%), or parent (15.1%); 51.5% provided care ≥25 hours/week, including errands (86.4%), appointments (84.8%), home healthcare (81.8%), and PS (78.8%). Caregivers reported moderate stress (mean KCSS, 20.2). Over 25% experienced moderate to extreme financial stress, with most (70.6%) caregiving ≥25 hours/week. 40 caregivers were unemployed. In the past 7 days, 53.8% of employed caregivers reported caregiver-related absenteeism and 92.0% reported impaired work productivity; impairment was highest for those who spent ≥25 hours caregiving. SF-12v2 physical (54.0) and social (49.2) domain scores were comparable to the general population; role–emotional (47.2) domain scores were lower. Conclusion: Caregivers of patients with SBS dependent on PS experience a substantial emotional, financial, and professional burden. Caregivers in this study, especially those who provided care ≥25 hours/week, reported substantial unemployment and financial stress. Most employed caregivers reported impaired work productivity and absenteeism. These findings emphasize the urgent need for support to alleviate caregiver burden and improve their well-being. Disclosure of Interest: M. Winkler Consultant for: Ironwood and Takeda Pharmaceutical, J. Harrison Other: Volunteer for Girls With Guts, R. Vemulapalli Other: CME Faculty for Novus Medical Education, V. Kumpf Consultant for: Ironwood, Baxter Healthcare, and Fresenius Kabi, G. Mitchell Other: Employee of Ironwood and may hold shares and/or stock options in the company., D. Wolin Other: Full-time employee of RTI Health Solutions, an independent nonprofit research organization, which was retained by Ironwood to conduct the research that is the subject of this abstract. Their compensation is unconnected to the studies on which they work., L. Zografos Other: Full-time employee of RTI Health Solutions, an independent nonprofit research organization, which was retained by Ironwood to conduct the research that is the subject of this abstract. Their compensation is

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Gastroenterology
Younossi Z, Yilmaz Y, Yu M-L, El-Kassas M, Fernández MIC, Eguchi Y, Papatheodoridis G, Wong VW-S, Duseja AK, Singal AK, Hamid SS, Bugianesi E, Isakov V, Romero-Gómez M, Chan W-K, Alswat KA, Fan J, and **Gordon SC**. FRI-030 In patients with metabolic dysfunction-associated steatotic liver disease, sleep disturbance is highly prevalent and associated with a profound impairment of health-related quality of life. *J Hepatol* 2025;82:S680-S681. Full Text

Background and aims: Metabolic dysfunctional-associated steatotic liver disease (MASLD) patients have impaired health-related quality of life and other patient-reported outcomes (PROs) which can be exacerbated by comorbidities, including sleep disorders. Our aim was to assess the prevalence of sleep disturbance and its association with PROs in MASLD. Method: Patients with MASLD were prospectively enrolled into the Global NAFLD/MASLD Registry™ (GNR). Clinical and PROs (FACIT-F, CLDQ-MASH, and WPAI) data were analyzed by the presence of sleep disturbance (defined as CLDQ-MASH Sleep score of <4on a 1-7 scale). Results: 5342 MASLD patients from 17 countries in the GNR were included: mean (SD) age 53 (13) years, 48% male and 60% obese, 41% had type 2 diabetes (T2D), 46% hypertension, 43% hyperlipidemia, 15% with advanced fibrosis (by biopsy or FIB-4 or transient elastography), 20% depression, 52% clinically overt fatigue, 32% abdominal pain, and 20% sleep apnea. Prevalence of sleep disturb¬ance among MASLD was 34%. MASLD patients and sleep disturbance were more commonly female (63% vs. 46%), with more components of metabolic syndrome (obesity 65% vs. 57%, T2D 47% vs. 37%, hypertension 54% vs. 42%, hyperlipidemia 51% vs. 39%), non-hepatic comorbidities (anxiety 52% vs. 24%, depression 31% vs. 13%, clinically overt fatigue 60% vs. 48%) and sleep apnea (26% vs. 16%) than those without sleep disturbance (all $p < 0.01$). In logistic regression model, presence of sleep disturbance in MASLD was associated with older age, female sex, history of anxiety, depression, clinically overt fatigue, abdominal pain, smoking, lack of regular exercise, and presence of significant pruritus (all $p<0.01$). In MASLD patients with sleep disturbance, PRO scores in all domains of CLdQ-MASH and FACIT-F were lower (up to -25% of a score range size), and work productivity impairment was higher (mean [SD] 0.30 [0.33] vs. 0.11 [0.23]) (all $p < 0.0001$). In particular, the presence of sleep disturbance was strongly associated with lower fatigue scores of CLDQ-MASH and FACIT-F (more fatigue) and with lower pruritus scores (more pruritus) of CLDQ-MASH (effect size -17% to -23%, all $p< 0.0001$). In multiple regression analysis, sleep disturbance was independently associated with lower PRO scores in all domains of CLDQ-MASH, FACIT-F, and WPAI (beta up to -15%). Other independent predictors of lower PRO scores in MASLD included age, female sex, comorbidities (metabolic syndrome components, psychiatric disorders, clinically overt fatigue, and sleep apnea), advanced fibrosis, smoking, and lack of regular exercise ( $p < 0.05$). Conclusion: Sleep disturbance is highly prevalent in patients with MASLD. It is associated with fatigue and pruritus, non-hepatic comorbidities, lifestyle factors, and substantial impairment in HRQL and work productivity. Patients with MASLD should be assessed for sleep disturbances and advised accordingly.

Internal Medicine
**Jaiswal V**, **Savaliya M**, **Shama N**, **Jaiswal A**, **Munnangi P**, Mashkoor Y, **Zulfiqar A**, Rajak K, Halder A, Ang SP, Younas A, Hanif M, and Biswas M. Effectiveness and safety of apixaban vs. aspirin for primary prevention of stroke and bleeding risk among patients with atrial fibrillation: A Meta-analysis of randomized controlled trials including ARTESIA trial. *Stroke* 2025;56. Full Text

V. Jaiswal, Henry Ford Jackson Hospital, Jackson, MI, United States

Background: Atrial fibrillation is a common arrhythmia that increases the risk of stroke. However, treatment of such patients with oral anticoagulants when compared with aspirin is not well established with uncertain benefits. Objective: We analyzed available study level data comparing Apixaban and Aspirin for efficacy and safety among atrial fibrillation patients. Methods: We performed a systematic literature search on PubMed, EMBASE, and ClinicalTrials.gov for relevant randomized controlled trials (RCTs) from inspection until August 10th, 2024, without any language restrictions. Odds ratios (OR) and 95% confidence intervals (CI) were pooled using a random-effect model, and a p-value of <0.05 was considered statistically significant. Results: A total of 3 RCTs with 14,224 patients were included (7,129 in apixaban and 7095 in the aspirin group) in the analysis. The mean age of the patients in apixaban and the aspirin groups was 72.4 and 72.8 years, respectively. Pooled analysis of primary and secondary endpoints showed that apixaban significantly reduced the risk of stroke or systemic embolism by 47% (OR, 0.53(95%CI: 0.38-0.75), P<0.001), stroke by 44% (OR, 0.56(95%CI: 0.44-0.70), P<0.001), and ischemic stroke by 51% (OR, 0.49(95%CI: 0.29-0.81), P=0.01) when compared with aspirin. However, the risk of major bleeding (OR, 1.03(95%CI: 0.69-1.53), P=0.88), myocardialinfarction (OR, 0.97(95%CI: 0.76-1.23), P=0.78), and all-cause mortality (OR, 0.97(95%CI: 0.80-1.17), P=0.72) was comparable when compared with the aspirin group of patients. Conclusion: In this comprehensive analysis of randomized controlled trials data, the use of apixaban was associated with reduction in stroke or systemic embolism, and ischemic stroke, when compared with aspirin therapy. Major bleeding risk, and all cause mortality was comparable between both groups of patients.

Internal Medicine

Jaiswal V, **Shama N**, Jaiswal A, Patel N, Rajak K, Kalra K, Ang SP, Sawhney A, Danisha F, Shrestha A, and Hanif M. Effectiveness and safety of direct oral anticoagulation vs. warfarin for primary prevention of stroke and bleeding risk among patients with atrial fibrillation. *Stroke* 2025;56. Full Text

V. Jaiswal, JCCR Cardiology Research, Jaunpur, India

Background: Atrial fibrillation (AF) patients carry a high risk of stroke, and treatment related bleeding complications. Evidence for the safety and efficacy of anticoagulation remains sparse with conflicting results. Objective: We sought to investigate the effectiveness and safety of direct oral anticoagulant (DOAC) versus warfarin in atrial fibrillation patients. Methods: We performed a systematic literature search on PubMed, EMBASE, and ClinicalTrials.gov for relevant randomized controlled trials (RCTs) from inspection until July 30th, 2024, without any language restrictions. Odds ratios (OR) and 95% confidence intervals (CI) were pooled using a random-effect model, and a p-value of <0.05 was considered statistically significant. Results: A total of 7 RCTs with 79,001 patients were included (46069 in DOAC and 32932 in the warfarin group) in the analysis. The mean age of the patients in DOAC and the warfarin groups was 72.8 and 72.9 years, respectively. Pooled analysis of primary and secondary endpoints showed that DOAC significantly reduced the risk of stroke or systemic embolism by 18% (OR, 0.82(95%CI: 0.75-0.91), P<0.01), stroke by 19% (OR, 0.81(95%CI: 0.68-0.97), P=0.02), and hemorrhagic stroke by 57% (OR, 0.43(95%CI: 0.33-0.56), P<0.01) when compared with warfarin. However, the risk of ischemic stroke (OR, 0.96(95%CI: 0.78-1.18), P=0.69), major bleeding (OR, 0.84(95%CI: 0.67-1.06), P=0.14) and myocardial infarction (OR, 1.07(95%CI: 0.89-1.28), P=0.45) was comparable between DOAC and the warfarin group of patients. The use of DOACs was associated with lower odds of all-cause mortality (OR, 0.91(95%CI: 0.85-0.97), P<0.01) when compared with the warfarin group of patients. Conclusion: In this comprehensive analysis of randomized controlled trials data, the use of DOACs was associated with reduction in stroke or systemic embolism, hemorrhagic stroke, and all cause mortality, compared with warfarin therapy. Major bleeding risk was comparable between both groups of patients.

Internal Medicine

**Singh B**, **Alluri S**, and **Ramanan S**. Complications of TPN in cirrhotic population. *Gut* 2025;74(Suppl_3):A235-A235. Full Text

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Background This retrospective study seeks to illuminate complications in cirrhotic patients receiving TPN. TPN is generally started in patients with cirrhosis due to moderate to severe malnutrition. TPN-associated decompensation can be Serious and even progress to the liver. In our study, we look for complications due to decompensation and its contribution to overall mortality. Methods A retrospective chart review was conducted of all adults (18 years or older) at our center (2014-2024) with a history of Cirrhosis while on TPN. Data on basic patient demographics, indication for TPN, Duration of TPN therapy, changes in TPN formulation, and mortality were collected. Results In the study, a total of 12/107 patients had cirrhosis at the time of TPN initiation. Mortality was seen in 9/12 cirrhotics as compared to 43/95 non-cirrhotics. 4/12 cirrhotics had line infection, 0/12 had line clots, 7/12 had worsening ascite. A statistically significant difference in mortality was not observed. The association between cirrhosis and time from peak LFT to death was significant with p- 0.025 in which cirrhotics had a longer time between peaking LFT with 240 days compared to 70.55 days in non-cirrhotic. Conclusions Our findings suggest that TPN is associated with decompensation with ascites being the most common complication likely in the setting of volume overload. However, mortality is not significantly associated with pre-existing cirrhosis, rather cirrhosis had a larger difference between peak value and death. This can indicate that cirrhotic decompensation generally occurs slowly over time whereas non-cirrhotic generally die of liver failure which has a short course till death. The size of the study is extremely small and the external validity of the data can be questionable. This underscores the need for further research to identify an association between cirrhosis and TPN..

Internal Medicine
**Singh B**, **Alluri S**, **Ramanan S**, and **Bern M**. Patterns of transaminase elevation in patients on TPN and association with mortality. *Gut* 2025;74(Suppl_3):A232-A233. Full Text

Henry Ford Jackson Hlth, Detroit, MI USA
Henry Ford Detroit, Detroit, MI USA

Background There are three primary types of parenteral nutrition- associated liver disease: steatosis- benign, although can progress to cirrhosis in patients receiving long-term PN, cholestasis- serious and can progress to cirrhosis and liver failure, and gallbladder sludge/stones. Risk Factors included excess calories or lipids. Our study aims to study different patterns of transaminase elevation, determine If the cholestatic or hepatocellular pattern is more predominant, and finally if a certain kind of elevation has a higher mortality risk. Methods A retrospective chart review was conducted of all adults at our center between 2014-2024, who had a history of elevated liver enzymes while on TPN. Data on indication for TPN, prior history of liver disease, pattern of injury, workup obtained, use of growth factors, and mortality was collected. Results A total of 111 patients with elevated liver enzymes were included. 63 (56.7%) patients had a history of liver disease with the most common indications for TPN being prolonged malnutrition in 41 (36.9%) patients, and short gut syndrome in 39 (35.1%). Mortality occurred in 52 (46.8%) patients. There was no association between the elevation of AST and mortality, p-0.422, the mean time of death from the peak is 38.56 days in the population with transient (< 30 days duration) and 301.69 days in the population with persistent elevation (> 30 days). There was a statistically significant association of ALT with mortality with p- 0.022, with a mean time to mortality of 63.83 days and 328.1 days. There was a statistical association between ALP and mortality with p- 0.034, with a mean time to mortality in 70.8 days and 328.1 days. As for bilirubin, there is no association and the duration to death is 70.8 days and 190.8 days. Further people with TPN change had a higher association with p-0.007, with a mean time to death of 31.79 in the change group versus 36 days in the no change group. Most changes in TPN were associated with ALP and T bili elevation with p- 0.028 and .036 respectively. Conclusions Results indicate ALT elevation is more strongly associated with mortality followed by ALP. The pattern of liver injury more predominant was cholestatic leading to TPN change and further mortality..

Neurology
Aboul-Nour H, Jumah A, **Albanna A**, Mohamed G, Alsrouji O, **Schultz L**, **Latack K**, **Miller J**, Uddin K, **Gunaga S**, **Muir J**, **Chebl A**, and **Ramadan AR**. Abstract WP225: Fibrinogen Depletion and The Risk of Intracerebral Hemorrhage following Mechanical Thrombectomy. *Stroke* 2025;56(Suppl_1). Full Text

A. Jumah, Emory University Hospital, Troy, MI, United States

Background: Intravenous thrombolysis (IVT) and mechanical thrombectomy (MT) are the standard of care for select stroke patients with acute large vessel occlusion (LVO). Fibrinogen levels may drop after IVT, and a significant decrease in fibrinogen is associated with an increased risk of intracranial hemorrhage (ICH). Our Pilot study aimed to explore the relationship between fibrinogen levels and the development of ICH in MT-treated patients and whether bridging with IVT further increases that risk. Methods: This is a prospective pilot study that enrolled adults presenting to our center with a diagnosis of LVO stroke and eligible to receive MT with or without IVT between April 2020 and May 2023. All patients consented to enrollment. Results: Forty-one patients were enrolled. Median age was 68 years [IQR 56-79], 58.5% were females and 56.1% were black. Nineteen patients (46.3%) were treated with MT+IVT, and 22 (53.6%) were treated with MT only. There was no difference in baseline characters between both groups. Baseline fibrinogen levels were similar between MT+IVT and MT-only groups [391 vs 352 mg/dL, p=0.4]. Post MT, the MT+IVT group had lower fibrinogen levels compared to the MT-only group [224 vs 303 mg/dL, p<0.001]. Similarly, there was a significant drop in fibrinogen levels between baseline and follow-up in the MT+IVT vs MT-only group [106 vs 39.5 mg/dL, p=0.001]. Eight patients (19.5%) developed ICH; 5 (26.3%) in the MT+IVT group and 3 (13.6%) in the MT-only group. No significant differences were seen in baseline, follow-up, or change in fibrinogen levels between patients who developed ICH and those who did not. However, there was a significantly lower follow-up fibrinogen levels between patients who suffered an ICH in the MT+IVT arm compared to those without ICH in the MT arm (200 vs 301 mg/dL, p=0.006). There was also a negative correlation between the drop in fibrinogen levels and the number of MT passes (Spearman CC -0.33, p=0.03). Conclusion: This pilot study's preliminary data show that fibrinogen depletion contributes to hemorrhagic transformation in MT-treated patients. This suggests that fibrinogen monitoring in patients undergoing MT after IVT may help identify patients with an increased risk of ICH. Larger studies areneeded to explore the cost-effectiveness of monitoring fibrinogen in patients undergoing bridging therapy and the benefit of repleting fibrinogen in this patient population.

Neurology

Bang OY, Son JP, Kim EH, and **Chopp M**. Clinical scale MSC-derived extracellular vesicles enhance poststroke neuroplasticity in a non-human primate model of stroke. *Stroke* 2025;56. Full Text

O.Y. Bang, Samsung Medical Center, Seoul, South Korea

Introduction: Stroke is a leading cause of death and disability. The therapeutic potential of mesenchymal stem cell-derived extracellular vesicles (MSC-EVs) has shown considerable promise in rodent models of stroke. However, the therapeutic efficacy and safety of clinical-scale MSC-EVs for ischemic stroke are not well elucidated, especially in non-human primates. Methods: We developed a scalable production method for MSC-EVs using a 3D bioprocessing platform. EVs were isolated with filter and tangential flow filtration and characterized through electron microscopy, nanoparticle tracking analysis, nanoflow cytometry analysis, proteomic and lipodomic analysis using mass spectrometry, and RNA sequencing. We determined the appropriate dosage and frequency of intravenous administration of EVs in a mouse stroke model. We then confirmed the efficacy of EVs in a marmoset model of stroke. Improvement in behavioral tests and MRI-based neuroplasticity were compared between the control and EV groups through blind evaluation. The proteome profiles of the infarcted hemisphere were also evaluated. Results: EV products showed suitable lot-to-lot consistent. In a mouse stroke model, intravenous administration of a dose of 6 x 108 EVs for five days resulted in the smallest infarct volume and improvement in motor function, with no significant toxicity observed at the tested dosages in the preclinical toxicity studies. Intravenous administration of an equivalent dose (3.5 x 109 EVs for five days) in a marmoset model of stroke improved motor functions and anatomical connectivity on diffusion tensor imaging and reduced infarct volume. Proteomics analyses of the infarcted region indicated that EV treatment promoted neurogenesis and synapse function-related protein expression. Conclusions: This study is the first to demonstrate that a clinical-scale EV product is safe and significantly enhances functions recovery and neuroplasticity in a non-human primate model of stroke, offering a promising treatment for human stroke.

Neurology

**Chebl A**. Long-term Outcomes of Total endovascular Reconstruction of Symptomatic Internal Carotid Artery Chronic Total Occlusions: An 18-year Experience. *Stroke* 2025;56. Full Text

A. Chebl, Henry Ford Health System, Bingham Farms, MI, United States

Background: Chronic total internal carotid artery occlusion (CTO) can be associated with a high (22- 25%) annual risk of stroke with limited therapeutic options. Total endovascular reconstruction (TER) is increasingly feasible but mid-term and long-term outcomes have not been reported. Methods: Data from all patients treated with carotid CTO treated with TER over the past 18years were collected in a database. Patients were selected based on the presence of angiographically proven symptomatic carotid occlusion, adequate landing zone and concurrent impairment of cerebrovascular reserve or recurrent ischemia despite maximal medical therapy. They were treated via a femoral approach using conventional CTO techniques with balloon expandable and/or self-expanding stents. Neurological evaluation of NIHSS, mRankin and carotid U/S were performed at discharge, 30days, and all subsequent follow-up. All TIA, stroke, death, and MI were recorded during follow-up. Angiographic follow-up was performed between 6-12months when possible. Results: Twenty-six symptomatic patients with a mean age of 65±7.8years were treated. Technical success was achieved in 22/26 (85%) on first attempt and in 3/4 on second attempt for total success rate of 25/26(96%). Total 30-day stroke/death/MI was 6.9% (2 ICH, both in first 3 years of experience). There were no recurrent events during 15.2±9.8months (median 12) of follow-up. Restenosis was found in 5/26 (19.2%) of patients; 2/5 were in unstented segments of the ICA. There was one case of asymptomatic carotid occlusion at 7months. The median mRS dropped from 2 to 1 at follow-up. Conclusion: TER is feasible in most patients with carotid CTO and is associated with a 30-day event rate lower than reported for STA-MCA bypass surgery. It is associated with good long-term stroke reduction despite a 19.2% risk of restenosis. Carotid re-occlusion is rare. Randomized trials are needed to validate this approach.

Neurology

**Chebl A**, **Zhang J**, **Aldilaimi A**, **Teng H**, **Li YF**, **Chopp M**, and **Zhang ZG**. Plasma small extracellular vesicles derived from patients with cerebral aneurysms impair cerebral endothelial permeability and promote angiogenesis. *Stroke* 2025;56. Full Text

A. Chebl, Henry Ford Health System, Detroit, MI, United States

Background: Small extracellular vesicles (sEVs) from blood samples of patients with cerebral aneurysms (CA) have been used as a biomarker for CA. However, biological function of sEVs in CA has not been studied. We tested the hypothesis that plasma sEVs from patients with CA impair cerebral endothelial cell (CEC) function. Methods: Plasma sEVs were isolated using ultracentrifugation from venous and arterial blood of patients with CA undergoing endovascular treatment. Size and marker proteins of sEVs were characterized. Human CECs were treated with sEVs at 1x10 particles/ml. The effects of sEVs on CEC permeability and angiogenesis were measured by trans-endothelial and tube formation assays, respectively. One-way ANOVA was used for statistical analysis. Results: Ten patients, 6 with non-ruptured CA and 4 with ruptured CA, ranging in age from 51-88 years old were studied. There were no significant differences in sEV sizes and protein markers between non-ruptured and ruptured CA (141 ± 6 nm vs 144 ± 2 nm). The permeability assay showed that compared to controls, sEVs derived from arterial samples (asEVs) from ruptured and non-ruptured CA significantly increased CEC leakage (116 ± 7 and 119 ± 14 vs 101 ± 6 control, respectively, $p<0.05$). The angiogenic assay showed that venous sEVs (vsEVs), but not asEVs, of non-ruptured CA, significantly ($p<0.05$) increased vascular branches (14 ± 6 vs 6 ± 3 control), however, both vsEVs and asEVs of ruptured CA robustly increased the branch numbers (13 ± 7, and 13 ± 5 vs 6 ± 3 control, respectively, $p<0.05$). Conclusions: Increased CEC permeability and vascular branches are highly related to blood brain barrier (BBB) damage and angiogenesis, respectively. Thus, our data suggest that sEVs from CA could damage the BBB and promote angiogenesis, which provides new insights into the role of sEVs in mediating CA progression. .

Neurology

**Fana M**, **Choudhury O**, **Chebl A**, **Latack K**, **Schultz L**, **Albanna A**, **Reardon T**, **Iqbal Z**, **Kole M**, and **Marin H**. The Rapid Occluded Vessel Etiology Score: A Novel Algorithm to Identify Acute Atherosclerotic Large Vessel Occlusions of the Middle Cerebral Artery. *Stroke* 2025;56. Full Text

M. Fana, Henry Ford Health, Detroit, MI, United States

Introduction: Mechanical thrombectomy (MT) devices were fundamentally designed for the treatment of cardioembolic (CE) strokes despite that 10-20% of large vessel occlusions (LVO) are caused by large artery atherosclerosis (LAA), which may not respond comparably. Therefore, the differentiation between LAA and non-LAA LVO may be critical for selecting the ideal MT technique. Here, we construct an algorithm for use in the emergent setting pre-operatively to differentiate between LAA and non-LAA LVO using clinical and radiographic features. Methods: Using our prospectively collected stroke database we identified all middle cerebral artery (MCA) occlusions treated with MT with confirmed etiology as either LAA or non-LAA (CE, cryptogenic) according to TOAST criteria. Stroke risk factors and CT angiography (CTA) of the head and neck features were compared between LAA and non-LAA etiologies in a univariate analysis. An algorithm was then constructed using these variables in a multivariable logistic regression with corresponding score estimates for each variable to assess how well the model distinguished between LAA and non-LAA groups. The sensitivity and specificity were computed for each sum score to identify the ideal cut-off point for differentiating LAA from non-LAA LVOs. Results: Final analysis included 33 LAA, 207 CE, and 120 cryptogenic strokes. Patients presenting with LAA LVOs were significantly less likely to have atrial fibrillation (9.1% vs 53.8%; p<0.0001), EF<35% (9.1% vs 27.8%; p=0.0208) and more likely to present with progressive or fluctuating symptoms (21.2% vs 4.6%; p=0.0018), intracranial multi-vessel atherosclerotic disease on CTA (84.8% vs 37%; p<0.0001), tapered appearance of occlusion with associated collaterals (60.6% vs 0.9%; p<0.0001), and ICA bulb plaque with high-risk features (87.9% vs 37.6%; p<0.0001) (Table 1). The AUC was 0.9650 (95% CI=0.9332, 0.9968) and the highest combination of sensitivity and specificity (97% and 88%, respectively) was associated with a cut-off score of 9 (Tables 2 and 3). Conclusion: Our scoring system reliably differentiates between non-LAA and LAA LVO with high sensitivity and specificity based on 6 clinical and radiographic features. This will need to be validated with an external patient dataset and then in a prospective study.

Neurology

**Gao HJ**, **Zacharek A**, **Powell B**, **Mccann M**, **Zhang ZG**, **Chopp M**, and **Liu XS**. Suppression of microRNA-145 alleviates the vascular cognitive impairment in a multiple microinfarction model. *Stroke* 2025;56. Full Text

H. Gao, Henry Ford Hospital, Detroit, MI, United States

Background: Vascular cognitive impairment (VCI) is the second most frequent subtype of dementia following Alzheimer's disease. However, the underlying mechanism has not been fully understood and there is no effective treatment for VCI. MicroRNAs (miRNAs) play critical roles in the pathologies of cerebral ischemia and dementia. This study aims to identify key miRNAs that may mediate cognitive outcomes using multiple microinfarction (MMI), a VCI model. Methods: MMI was induced by the administration of cholesterol crystals (70-100μm) into the internal carotid artery. Male Wistar rats (10-12 month) subjected to MMI or sham operation were euthanized 28 days after MMI (n=8/group). Total RNAs were isolated from the striatal tissues and miRNA-sequencing was performed. AAV-PHP.Eb carrying miR-145-5p sponge was delivered by the Intracerebroventricular injection at 2 days prior to MMI to knockdown miR-145-5p. The mNSS (modified Neurological Severity Score) and cognition tests were examined at 2 weeks after MMI. Results: MiRNA-sequencing analysis showed that compared to sham rats, MMI significantly up- and down-regulated 4 and 9 miRNAs respectively. Bioinformatics analysis revealed that these miRNAs were highly associated with the oligodendrocytes/myelination (miR-210 and miR-125), BBB (miR-665 and miR-29), and inflammation (miR-322), etc. Amongst them, miR-145 was the top upregulated miRNA in the striatum after MMI. In situ hybridization demonstrated that miR-145 expression was highly upregulated in the smooth muscle cells, which was negatively correlated with the decrease of contraction marker of smooth muscle cells (SMCs). Treatment of MMI rats with AAV-miR-145 sponge significantly reduced sensorimotor deficits assayed by lower mNSS score. Furthermore, MMI rats administered AAV-miR-145 spent less time on the closed arm in the EPM (AAV-miR-145 VS control AAV: 182±28 VS 263±9 (s), P=0.01) and showed less freezing time in the OFT (AAV-miR-145 VS control AAV: 205±9 VS 246±11 (s), P=0.015), compared with those treated with control AAV. These data indicate that inhibition of miR-145 reduces depression-like behavior and cognitive deficit induced by MMI. Conclusion: Our results uncovered the deregulated miRNAs associated with myelination, white matter and vascular

damage after MMI. Also, our data suggest that miR-145 could be a potential therapeutic target by the regulation of SMCs against VCI. Thus, our data provides new insights into the molecular mechanisms underlying VCI.

Neurology
Gener M, and **Zeidman L**. Small Fiber Neuropathy with Ganglioside Antibody: A Case Report (P7-11.004). *Neurology* 2025;104(7_Supplement_1). Full Text

M. Gener, Michigan State University College of Human Medicine, United States

Objective: To report a case of small fiber neuropathy associated with an elevated GD1a antibody titer and treatment with intravenous immunoglobulin (IVIG) Background: Cryptogenic small fiber neuropathy (SFN) is a vexing clinical problem often with limited treatment options besides symptomatic control. Immune SFN typically presents with acute or subacute onset, non-length dependent pathology, female gender, and often association with various autoantibodies. A number of immune mechanisms have been proposed, but the role of autoantibodies is controversial. Previous studies have shown an association between SFN and TS-HDS, FGFR- 3, Plexin D1, and other autoantibodies, and the role of these antibodies in identifying immunotherapy-responsive SFN is currently under investigation. Other reports have shown responsiveness to IVIG, steroids, or plasmapheresis in SFN related to sarcoidosis, Sjogren syndrome, vasculitis, and post-COVID SFN. Design/Methods: NA Results: A 58-year-old female reported a subacute onset of lower extremity pain, numbness and tingling. On examination the patient's Utah Early Neuropathy Scale (UENS) score was 12/42. Patient-reported questionnaires revealed the following: SFNRasch Overall Disability Scale (SFN-RODS)=58/64, SFN-Symptom Inventory Questionnaire (SFN-SIQ)=11/39, SFN-Screening List (SFN-SL)=18/84 (>11 sensitive for SFN). EMG was normal, but sweat gland nerve fiber density was low in 2 sites, and QSART was abnormal in her distal leg. IgM-GD1a antibodies were present at a titer of 7000 (normal <2000); no other neuropathy cause was identified. After 6 months of IVIG treatment the UENS score was 1/42, SFN-RODS was 61/64, and SFNSIQ was 13/39. The patient opted to discontinue IVIG treatment as symptoms had improved. Conclusions: This case of SFN with elevated GD1a autoantibody, and subjective and objective improvement on IVIG, highlights the importance of checking for autoantibodies in SFN. Anti-GD1a may be a useful biomarker in screening and managing patients with immune-mediated SFN and may be useful to predict response to immunotherapy, but further studies are needed.

Neurology
**Grover K**, Gandhi K, Cloutier M, Coteur G, Zhdanava M, El Khoury AC, Boonmak P, Cai Q, Tardif-Samson A, Ait-Tihyaty M, Wang Y, Choudhry Z, and Silvestri NJ. Real-world Treatment Patterns Among Patients with Generalized Myasthenia Gravis (P6-11.027). *Neurology* 2025;104(7_Supplement_1). Full Text

K. Grover, Henry Ford Health System, Detroit, MI, United States

Objective: To evaluate real-world treatment patterns and myasthenia gravis (MG)-related clinical events among patients with generalized MG (gMG) in the US. Background: gMG is a rare chronic autoimmune condition. Conventional treatments include acetylcholinesterase inhibitors (AChEI), corticosteroids, and non-steroidal immunosuppressants. Newly approved targeted therapies include neonatal Fc receptor (FcRn) and complement-5 (C5) inhibitors. Knowledge of real-world treatment patterns with currently available therapies and MG-related clinical events is limited. Design/Methods: Adults with gMG were identified from the Komodo Research Database (01/2017-09/2023). Index date was the first MG diagnosis by a neurologist. Baseline (12-months pre-index) demographic characteristics, follow-up (≥12 months post-index) treatment patterns, including first 5 observed treatment episodes, MG exacerbations and crises were described. Results: 6,195 patients were included (mean age: 61.1 years; female: 49.1%; mean follow-up: 32.7 months). Among those receiving treatments, from the first episode (n=5,652) to the fifth episode (n=2,107): AChEI use declined from 81.1% to 58.5%; corticosteroid use fluctuated between 48.2-63.2%, and use of the following treatments increased: any non-steroidal immunosuppressants (11.8% to 41.8%), any immunoglobulin (6.3% to 15.6%), FcRn inhibitors (0.1% to 2.7%), and C5 inhibitors (0.2% to 2.9%). Mean time from index date to FcRn initiation was 20.7 months and to C5

inhibitors initiation 15.8 months. Post-index, 48.8% and 3.1% of patients had MG exacerbation or crisis, respectively. Exacerbations and crises were most common 1-year post-index (41.5%), but declined over time (20.3%, 18.0%, and 14.4% in the second, third, and fourth year, respectively). Conclusions: Conventional treatments were an initial treatment strategy for most patients in this cohort, while immunoglobulin and targeted treatments were generally used later. This, combined with the high rates of exacerbation and crisis during the first year, highlights an unmet need for treatment strategies that provide stable and sustained disease control earlier in the disease course when managing patients with gMG.

Neurology
Jumah A, **Mohamedelkhair A**, **Elfaham A**, Batista S, Ma TW, Ngo S, **Mohn D**, **Vismara T**, **Reardon T**, Chughtai F, Sanchez GJS, Vilardo M, Camerotte R, and **Ramadan AR**. Predicting Stroke in Patients with Infective Endocarditis: A Comprehensive Systematic Review and Meta-Analysis of Risk Factors. *Stroke* 2025;56. Full Text

A. Jumah, Emory University, Atlanta, GA, United States

Introduction: Neurological complications in patients with infective endocarditis (IE), such as ischemic and hemorrhagic stroke, are well-described, serious complications of IE; however, predicting which patients are most likely to experience stroke remains uncertain. The objective of this systematic review was to identify the factors associated with risk of stroke in patients hospitalized with IE. Methods: A systematic search of Ovid MEDLINE, EMBASE, and Web of Science was conducted between January 1990 and to July 2024. Articles evaluating risk of acute ischemic stroke (AIS) and/or intracranial hemorrhage (ICH) in patients with IE were included. Meta-analysis was feasible for only some predictive factors due to study heterogeneity. (PROSPERO protocol CRD42024571058). Results: Of 3558 studies identified, 35 were included: The review included 9 prospective and 26 retrospective cohort studies. Staphylococcus aureus infection (odds ratio, 3.05 [95% CI, 1.96-4.73]; I =77.2%; 9 studies) and 1 mm longer in vegetation size, on average (odds ratio, 1.26 [95% CI, 1.02-1.55]; I =90.1%; 3 studies) were associated with a higher risk of AIS, adjusting for other covariates. Due to high heterogeneity among the studies, a meta-analysis was not feasible for the other predictive factors. High intensity signals on transcranial doppler, and comorbidities such as hypertension, atrial fibrillation, and hyperlipidemia were also found to have a higher risk of AIS. Risk of ICH was heightened by thrombocytopenia, mycotic aneurysms, prior ICH and/or AIS, and cerebral microbleeds. Conclusion: Physicians need to monitor numerous, diverse features of patients hospitalized with IE to mitigate the risk of ensuing stroke. While the causative microorganism, echocardiographic and neuroimaging findingsmay be particularly informative, underlying comorbidities and various laboratory values may also contribute to predicting IE-associated ischemic and hemorrhagic stroke.

Neurology
Ladha P, Amatya S, Kagzi Y, Savaliya R, Akkuş S, **Xu J**, Lulla D, and Sriwastava S. Pregnancy Outcomes in Neuromyelitis Optica Spectrum Disorder: A Meta-Analysis of Pharmacotherapeutic Agents (P11-8.020). *Neurology* 2025;104(7_Supplement_1). Full Text

P. Ladha, BJ Government Medical College, Pune, India

Objective: To analyze the evidence on outcomes of pregnancies in Neuromyelitis Optica Spectrum Disorder(NMOSD) treated with different pharmacotherapeutics. Background: Pregnancies with NMOSD present a complex scenario. Both the disease and pharmacological agents (PA) used in management have significant implications for maternal and fetal well-being. Design/Methods: A comprehensive analysis using different models, including a random-effects model, and separate analyses for specific drugs like rituximab, tocilizumab, and eculizumab was conducted. The analysis involved examining continuous variables, encompassing pregnancy age, full-term and preterm pregnancies, premature delivery, spontaneous abortion, elective termination with and without birth defects, stillbirth, and live births with birth defects. Additionally, meta-analysis was performed to assess pregnancy outcomes in NMOSD patients undergoing treatment with different PA. We excluded ravulizumab due to the limited number of studies. Results: In our meta-analysis of 31 studies investigating pregnancy outcomes in NMOSD treated

with rituximab, tocilizumab, and eculizumab, we observed majority pregnancies resulted in full-term births (70.8%) with 19.5% preterm deliveries and 10.3% miscarriages. Ectopic pregnancies were rare (0.2%). Rituximab, tocilizumab, and eculizumab demonstrated varying rates of full-term births (67.6%, 63.1%, and 80.7%, respectively) and preterm deliveries (11.7%, 6.9%, and 39.4%, respectively). Birth defects were infrequent across all treatments(2.2% with rituximab, 1.9% with tocilizumab, and 0.1% with eculizumab). These findings underscore the overall safety of these medications during pregnancy in NMOSD, emphasizing the need for tailored management strategies and vigilant monitoring. Conclusions: Overall considerations from the study and existing guidelines help us conclude that although there is not enough data on the primary treatments of NMO in pregnancy and lactation, the existing literature supports informed decision-making based upon the risk-benefit ratio with careful monitoring of fetus and infants exposed to the medications. This highlights the need for more data to be gathered as NMOSD often affects females of childbearing age-group.

Neurology
**Liu XS**, **Chopp M**, **Fan BY**, **Wang XL**, **Cui X**, **Powell B**, **Mccann M**, **Landschoot-Ward J**, and **Zhang ZG**. Gut-derived extracellular vesicles promote neurovascular damage and cognitive impairment in diabetic mice. *Stroke* 2025;56. Full Text

X. Liu, Henry Ford Hospital, Detroit, MI, United States

Background and Purpose: Gut microbiota dysfunction is associated with diabetic cognitive impairment (DCI). However, the mechanisms underlying the interaction of gut microbiota dysbiosis and DCI remain poorly understood. We tested the hypothesis that extracellular vesicles generated by diabetic gut microbiota exacerbate DCI by promoting the impairment of cerebral vascular function. Methods: Gut-EVs from the stools of male non-diabetic dm (dm-gut-EVs) and diabetic (db/db mice) with DCI (db-gut-EVs) mice at 20 weeks of age (20W) were isolated and characterized by means of ultracentrifugation and 16S rRNA sequencing, respectively. Given that db/db mice develop cognitive deficits at 20W, prediabetic db/db mice at 8 weeks of age (8W) were treated with gut-EVs at a dose of 1x10 particles/injection intravenously twice a week for 12 weeks. Cognitive performance was assessed using a battery of behavioral tests. Results: 16S rRNA analysis revealed significant alterations in the microbiota composition of db-gut-EVs derived from 20W db/db mice with DCI compared to dm-gut-EVs (n=5/group). Db/db mice treated with db-gut-EVs extracted at 20W, but not with dm-gut-EVs, exhibited a significant decline in learning and memory function, as assayed by the Novel object recognition, Social recognition memory, and Morris water maze assay, starting at 16W and worsening at 20W, compared to db/db mice treated with saline (n=10/group). Additionally, db/db mice treated with db-gut-EVs exhibited increased cerebral vascular thrombosis (18±2 vs 11±2 Fibrin+ vessels/mm in saline, $p<0.05$, n=5/group), whereas db/db mice treated with dm-gut-EVs showed a reduction of thrombosis (5±0.5 Fibrin+ vessels/mm , $p<0.05$). In vitro, treatment of human cerebral endothelial cells (hCECs) with db-gut-EVs significantly ($p<0.05$) upregulated pro-coagulation and inflammatory proteins, including plasminogen activator inhibitor-1 (PAI1), tissue factor (TF), NF-κB, and intercellular adhesion molecule 1 (ICAM-1), while reducing tight junction protein ZO-1 expression.Conclusions: Our findings indicate that db-gut-EVs promote DCI by inducing cerebral vascular damage, and underscore a major role for gut microbiota-brain communication in the development of DCI.

Neurology
Medalla M, Zhou YX, Mojica C, McCann R, Pessina M, Zeldich E, **Xin HQ**, Rosene D, and Moore T. Mesenchymal-derived extracellular vesicles mediate shifts in microglial phenotypes in functional recovery in a monkey model of cortical injury. *Stroke* 2025;56. Full Text

M. Medalla, Boston University, Sch Of Med, Boston, MA, United States

Mesenchymal stem cells (MSCs) have recently received attention as an intervention to reverse or slow neurodegenerative, stroke and injury-related changes in the aging brain as they suppress inflammation and facilitate tissue repair. In support of this idea, we have shown that extracellular vesicles (EVs) derived from bone marrow MSCs enhance recovery of motor function of the hand following cortical injury in aged female rhesus monkeys. Specifically, EV-treated treated monkeys (n=5) exhibited full recovery of fine

motor function by 3-5 weeks post-injury while vehicle monkeys (n=5) reached a plateau short of full recovery by 8-12 weeks postinjury. Post-mortem analyses of perilesional brain tissue from the same monkeys, revealed multifaceted cellular effects of EVs including downregulating inflammatory microglial phenotypes, dampening neuronal hyperexcitability, and enhancing neuronal and myelin plasticity. To explore the relationship between these processes and functional recovery, we utilized multi-labeling immunohistochemistry (IHC) and high-resolution confocal microscopy to assess microglia phenotypes, neuronal synaptic marker expression and microglianeuronal interactions in perilesional cortex. To assess these markers, semi-quantitative stereology in Neurolucida and particle analysis in ImageJ were utilized. Results show that MSC-EV treatment decreased the densities of pro-inflammatory hypertrophic microglia expressing LN3+, a marker for MHC II receptors, upregulated with immune activation. Conversely, MSC-EV treatment and functional recovery was significantly correlated with increased proportion of hypertrophic microglia expressing the key complement pathway protein C1q, a phenotype associated with enhanced debris-clearance and repair after degeneration. Interestingly this EV-associated increase in C1q+ hypertrophic microglia was correlated with decreased putatively damaged synapses tagged with C1q and greater synaptic marker expression in perilesional cortex. These data suggest that MSC-EVs promote a shift from pro- to anti-inflammatory repair microenvironment, via enhancement of debris clearance after injury. These findings demonstrate the efficacy of MSC-EVs as a therapeutic, likely acting to reduce inflammatory cascades, facilitate repair and rebalance neuronal synaptic connections to support recovery after cortical injury. .

Neurology

Yaghi S, Wu M, Shu L, Stipanovich A, Heldner M, **Goldstein E**, Kvernland A, Raz E, Hakim A, Radojewski P, Mordasini P, Antonenko K, Almiri W, de Havenon A, Prabhakaran S, Liebeskind D, Nguyen T, and Furie K. What Drives Early Recurrence in Intracranial Atherosclerosis: A Multicenter Study. *Stroke* 2025;56. Full Text

S. Yaghi, Brown University, Providence, RI, United States

Background: Intracranial Atherosclerosis carries a high recurrence rate. Single center studies have shown that impaired distal perfusion is a driver of early recurrence. In this study, we aim to identify predictors of 30-day ischemic stroke recurrence in a multicenter cohort. Methods: This is a pooled analysis of individual patient data from four comprehensive stroke centers of hospitalized patients with symptomatic intracranial arterial stenosis (50-99%) of the intracranial ICA and proximal middle cerebral artery (M1 or proximal M2). The study outcome was recurrent ischemic stroke by day 30. We compared baseline demographics (age, sex, race, ethnicity), vascular risk factors (hypertension, hyperlipidemia, diabetes, atrial fibrillation), NIHSS score, last known well to arrival, home medications (aspirin, anticoagulation), imaging variables (prior infarct in territory, degree of stenosis, perfusion delay volume, borderzone infarct pattern), and in-hospital treatments (thrombolysis, dual antiplatelet therapy, statin, permissive hypertension). Variables with $p<0.1$ on univariate analyses were included in a Cox regression model to identify important outcome predictors. Missing data was imputed as absent for categorical variables and at the median for continuous variables. Results: We identified 274 patients hospitalized with symptomatic intracranial stenosis who met the inclusion criteria; 70 patients (25.5%) had a recurrent ischemic stroke within 30 days. In unadjusted Cox regression models, predictors of early recurrence were mismatch volume of 25 ml or greater at T max of 6 seconds (HR 2.19 95% CI 1.37-3.51, p = 0.001), 70-99% (vs. 50-69%) stenosis (HR 3.34 95% CI 1.05- 10.60, p = 0.041), diabetes (HR 1.60 95% CI 1.0-2.57, p = 0.048), home aspirin (HR 1.77, 95% CI 1.06-2.95, p = 0.029), and home statin (HR 1.73 95% CI 1.04-2.89, p = 0.039). In adjusted Cox regression, the only predictors of 30-day recurrence were T max 6 mismatch volume 25 mL or more (adjusted HR 2.14 95% CI 1.27-3.61, p = 0.004), and 70-99% (vs. 50-69%) stenosis (adjusted HR 3.37 95% CI 1.05-10.84, p = 0.041). Conclusions: One in four medically treated patients with proximal anterior circulation symptomatic ICAS have a recurrent stroke within 30 days with impaired distal perfusion being an important driver of recurrence. Studies are needed to validate these findings and test reperfusion strategies in those with impaired perfusion.

Neurology

**Zhang L**, **Teng H**, **Luo H**, **Powell B**, Taketo M, **Chopp M**, and **Zhang ZG**. The activation of β-catenin in cerebral endothelial cells alleviates neurovascular damage after ischemic stroke. *Stroke* 2025;56. Full Text

L. Zhang, Henry Ford Hospital, Detroit, MI, United States

Background: Stroke induced disruption of the blood-brain barrier (BBB) exacerbates neurovascular damage. Emerging data show that deficiency of endothelial β-catenin contributes to stroke-induced BBB disruption and hemorrhagic brain injury. However, whether activation of β-catenin in cerebral endothelial cells (CECs) alleviates stroke induced neurovascular damage is unknown. Using transgenic mice with CEC specific activation of β-catenin, the present study investigated whether enhancement of CEC β-catenin activity reduces neurovascular damage after stroke. Methods: A transgenic mouse line with inducible CEC specific expression of a stable β-catenin mutant (CEC-Ctnnb1 mice) was generated by crossing Slco1c1-Cre mouse with Ctnnb1 mouse. Tamoxifen (TAM) was injected for 5 days to active Cre recombinase. Western blot was performed to verify β-catenin activation in the adult CEC-Ctnnb1 and their wild-type (WT) littermates (n=6/group) after termination of TAM. Male CEC-Ctnnb1 and WT mice treated with TAM were subjected to permanent middle cerebral artery occlusion (MCAO, n=10/group). Neurological function was evaluated with modified neurological severity score and foot-fault test at 1 and 7 days after MCAO. Brain tissues were processed for evaluations on infarct volume, gross hemorrhage, vascular leakage, and tight junction protein expression. Results: Immunohistochemistry and Western blot analyses revealed nuclear β-catenin expression specifically in the CECs of CEC-Ctnnb1 mice, but not in the WT mice, which was associated with significant elevation of β-catenin regulated the tight junction proteins, claudin 5 and ZO-1 by ~2 fold, compared to the WT mice. The ischemic CEC-Ctnnb1 mice exhibited significantly reduced infarct volume (16±5% vs 25±6% in WT), which was associated with a robust reduction of neurological deficits by 35% and 53% at 1 and 7 days after MCAO, respectively. Compared to the WT ischemic mice, ischemic CEC-Ctnnb1 mice exhibited significant increases of vascular claudin-5 by 45% and ZO-1 by 31%, which were associated with a significant reduction of extravascular fibrin deposition (5±1/mm vs 8±1/mm in WT). However, the incidence of gross hemorrhage was not different between the groups.Conclusions: The activation of β-catenin in CECs attenuates ischemic brain damage by alleviating stroke induced cerebrovascular disruption. Thus, targeting endothelial β-catenin signal may be a promising strategy for treatment of acute ischemic stroke.

Neurosurgery

Bheemireddy S, Gajjar A, Abe M, Custozzo A, Lipp S, Ringer A, Essibayi M, Altschul D, Goren O, Oliver J, **Reese J**, **Entezami P**, Chaudry I, Manos S, Sagues E, Gudino A, Samaniego E, Kuhn A, Singh J, Puri A, Roy J, El Naamani K, Gooch M, Jaikumar V, Siddiqui A, Boulos A, Dalfino J, and Paul A. MULTI-CENTER STUDY OF ASSOCIATION BETWEEN SOCIOECONOMIC STATUS AND TREATMENT OF RUPTURED CEREBRAL ANEURYSMS COMPARED TO UNRUPTURED CEREBRAL ANEURYSMS: INSIGHTS FROM 4,580 PATIENTS USING THE AREA DEPRIVATION INDEX. *J Neurointerv Surg* 2025;17:A92-A93. Full Text

A. Gajjar, Albany Medical College, Albany, NY, United States

Background Socioeconomic status influences health outcomes, including cerebrovascular diseases. Patients from socioeconomically deprived areas may present with more severe conditions due to delayed access to care. This study evaluates the association between neighborhood-level deprivation, measured by the Area Deprivation Index (ADI), and the treatment of RIAs (ruptured intracranial aneurysms) compared to unruptured intracranial aneurysms (UIAs) across multiple centers. Methods This retrospective cohort study analyzed data from 4,580 patients treated for cerebral aneurysms at nine U.S. comprehensive stroke centers between 2018 and 2024. Patients were stratified by national ADI quintiles based on their residential addresses. Multivariable logistic regression was used to examine the relationship between ADI and aneurysm rupture, adjusting for demographic and clinical covariates. Results Of 4,580 total patients, 1,217 (26.6%) presented with RIAs. Univariate analysis showed an upward trend between RIA presentation and higher ADI quintiles (OR = 1.162, 95% CI = 1.109-1.218, $p<0.0001$). Multivariable analysis confirmed ADI as an independent predictor of RIA presentation (OR = 1.131, 95% CI = 1.075-1.189, $p<0.0001$), after adjusting for age, sex, smoking history, and race.

Conclusions Socioeconomic deprivation independently predicts treatment of RIAs compared to the treatment of UIAs. These findings highlight disparities in aneurysm detection and management, emphasizing the need for targeted preventive care and accessible screening programs to mitigate the impact of socioeconomic disadvantage on cerebral aneurysm outcomes.

Neurosurgery

**Fana M**, **Choudhury O**, **Chebl A**, **Latack K**, **Schultz L**, **Albanna A**, **Reardon T**, **Iqbal Z**, **Kole M**, and **Marin H**. The Rapid Occluded Vessel Etiology Score: A Novel Algorithm to Identify Acute Atherosclerotic Large Vessel Occlusions of the Middle Cerebral Artery. *Stroke* 2025;56. Full Text

M. Fana, Henry Ford Health, Detroit, MI, United States

Introduction: Mechanical thrombectomy (MT) devices were fundamentally designed for the treatment of cardioembolic (CE) strokes despite that 10-20% of large vessel occlusions (LVO) are caused by large artery atherosclerosis (LAA), which may not respond comparably. Therefore, the differentiation between LAA and non-LAA LVO may be critical for selecting the ideal MT technique. Here, we construct an algorithm for use in the emergent setting pre-operatively to differentiate between LAA and non-LAA LVO using clinical and radiographic features. Methods: Using our prospectively collected stroke database we identified all middle cerebral artery (MCA) occlusions treated with MT with confirmed etiology as either LAA or non-LAA (CE, cryptogenic) according to TOAST criteria. Stroke risk factors and CT angiography (CTA) of the head and neck features were compared between LAA and non-LAA etiologies in a univariate analysis. An algorithm was then constructed using these variables in a multivariable logistic regression with corresponding score estimates for each variable to assess how well the model distinguished between LAA and non-LAA groups. The sensitivity and specificity were computed for each sum score to identify the ideal cut-off point for differentiating LAA from non-LAA LVOs. Results: Final analysis included 33 LAA, 207 CE, and 120 cryptogenic strokes. Patients presenting with LAA LVOs were significantly less likely to have atrial fibrillation (9.1% vs 53.8%; p<0.0001), EF<35% (9.1% vs 27.8%; p=0.0208) and more likely to present with progressive or fluctuating symptoms (21.2% vs 4.6%; p=0.0018), intracranial multi-vessel atherosclerotic disease on CTA (84.8% vs 37%; p<0.0001), tapered appearance of occlusion with associated collaterals (60.6% vs 0.9%; p<0.0001), and ICA bulb plaque with high-risk features (87.9% vs 37.6%; p<0.0001) (Table 1). The AUC was 0.9650 (95% CI=0.9332, 0.9968) and the highest combination of sensitivity and specificity (97% and 88%, respectively) was associated with a cut-off score of 9 (Tables 2 and 3). Conclusion: Our scoring system reliably differentiates between non-LAA and LAA LVO with high sensitivity and specificity based on 6 clinical and radiographic features. This will need to be validated with an external patient dataset and then in a prospective study. .

Obstetrics, Gynecology and Women's Health Services

**Kheil M**, **Kim S**, **Pezzillo M**, **Sharba N**, **Gracyzk K**, **Al-Juburi S**, and **Luck A**. URETHRAL DIVERTICULUM: PREVALENCE & PRESENTATION IN THE AFRICAN AMERICAN POPULATION. *Neurourol Urodyn* 2025;44:S101-S102. Full Text

[Kheil, Mira; Kim, Shihyun; Pezzillo, Michael; Luck, Ali] Henry Ford Hlth, Detroit, MI USA; [Sharba, Nora; Gracyzk, Kendal; Al-Juburi, Saleh] Wayne State Univ, SOM, Detroit, MI 48202 USA

Introduction: It has historically been alluded to that the prevalence of UD is higher in black women compared to white women. However, data has been inconsistent. We aim to investigate differences in prevalence, presentation, and outcomes across different races. Methods: Retrospective chart review was performed for 88 patients with UD diagnosis from 2014-2024. Demographic and clinical data was collected, including age, race, BMI, medical comorbidities, surgical history, date of UD diagnosis, presenting symptom, management, and follow up. Statistical analysis was performed using fisher's exact tests and chi-squared tests with significance defined as p-value < 0.05. Results: Out of 88 patients with UD, 50 (58.1%) are black, 32 are white (37.2%) and 4 (4.7%) belong to other races. There were no statistical differences in basic demographic characteristics including age, number of vaginal deliveries, BMI, HTN or history of prior pelvic surgery. Black patients were more likely to have DM (42% in black vs 15.6% in white, 0% in others, p 0.008). Most black (44%) and white (43.8%) patients were diagnosed by MRI; most patients of other races were diagnosed by physical exam (50%) with no statistical differences

among the three groups (p = 0.177). The most common presenting symptom was voiding dysfunction in all 3 groups (66%, 50%, 75%, respectively p = 0.266). More black patients underwent surgical management compared to patients of white & other races (58%, 50%, 50% respectively); however, this was not statistically significant (p = 0.515). No significant differences were noted in surgical complications (LUTS, fistula, UI) (p > 0.05), resolution of primary sx (p = 0.777), or recurrence (> 0.999) among different races. Conclusions: Although the prevalence of UD might be higher in the black community, there appears to be no statistically significant differences in presentation, management or clinical outcomes of the disease.

Pharmacy

Yahia A, Mahmood A, **Pifer J**, and White M. 579 Incidence of Acute Kidney Injury with Hydroxocobalamin Administration. *J Burn Care Res* 2025;46(Supplement_1):S163-S163. Full Text

A. Yahia, Detroit Receiving Hospital Burn Center, United States

Introduction: Hydroxocobalamin is frequently administered to patients with inhalation injuries. Recent literature has raised concerns about its potential association with an increased risk of acute kidney injury (AKI). This study aims to investigate the incidence of AKI following Methods: of data from a single adult Burn Center, including patients with confirmed inhalation injuries and/or those treated with hydroxocobalamin between January 1, 2013, and January 1, 2023. The primary outcome was the incidence of AKI, classified using KDIGO criteria, within 7 days of hospital admission. Secondary outcomes included the incidence and timing of renal replacement therapy, 28-day all-cause mor-tality, and lactate clearance up to 72 hours post-admission. In the hydroxocobalamin group, safety endpoints included the incidence and severity of AKI within 7 days of administration and the cause of AKI.Results: 167 in the hydroxocobalamin group and 145 in the control group. Baseline characteristics were not matched, with the hydroxocobalamin group being more critically ill and the control group having more chronic illness. There was no statistically significant difference in the incidence of AKI within 7 days of hospital admission between those who re-ceived hydroxocobalamin and those who did not (38.9% vs. 32.4%, p=0.345). Secondary outcomes showed a lower 28-day mortality rate in the control group (7.1% vs. 18.9%, p=0.029). Lactate clearance was also significantly higher in the control group (median 2.09, IQR 1.29-2.6) compared to the hydroxocobalamin group (median 3.05, IQR 1.56-5.72, p=0.00056), though patients in the hydroxocobalamin group had higher initial lactate levels within the first 24 hours. The incidence of renal replacement therapy for AKI was higher in the hydroxocobalamin group compared to controls (21.4% vs. 6.3%, p=0.071).Conclusions: This study did not find a statistically significant association between hydroxocobalamin use and AKI in were noted, including the lack of matched baseline charac-teristics, as critically ill patients were more likely to receive to determine whether hydroxocobalamin contributes to AKI, the extent of AKI (e.g., requiring renal replacement therapy), and to clarify potential risks and benefits when groups are appropriately matched.Applicability of Research to Practice: Despite concerns in the literature about the potential risk of AKI with hydroxocobalamin, this large retrospective study did not find a significant increase in AKI incidence associated with its use. However, further prospective studies are needed to defini-tively assess its impact on renal function and to explore the potential clinical benefits and risks.

Public Health Sciences

Aboul-Nour H, Jumah A, **Albanna A**, Mohamed G, Alsrouji O, **Schultz L**, **Latack K**, **Miller J**, Uddin K, **Gunaga S**, **Muir J**, **Chebl A**, and **Ramadan AR**. Abstract WP225: Fibrinogen Depletion and The Risk of Intracerebral Hemorrhage following Mechanical Thrombectomy. *Stroke* 2025;56(Suppl_1). Full Text

A. Jumah, Emory University Hospital, Troy, MI, United States

Background: Intravenous thrombolysis (IVT) and mechanical thrombectomy (MT) are the standard of care for select stroke patients with acute large vessel occlusion (LVO). Fibrinogen levels may drop after IVT, and a significant decrease in fibrinogen is associated with an increased risk of intracranial hemorrhage (ICH). Our Pilot study aimed to explore the relationship between fibrinogen levels and the development of ICH in MT-treated patients and whether bridging with IVT further increases that risk. Methods: This is a prospective pilot study that enrolled adults presenting to our center with a diagnosis of LVO stroke and

eligible to receive MT with or without IVT between April 2020 and May 2023. All patients consented to enrollment. Results: Forty-one patients were enrolled. Median age was 68 years [IQR 56-79], 58.5% were females and 56.1% were black. Nineteen patients (46.3%) were treated with MT+IVT, and 22 (53.6%) were treated with MT only. There was no difference in baseline characters between both groups. Baseline fibrinogen levels were similar between MT+IVT and MT-only groups [391 vs 352 mg/dL, p=0.4]. Post MT, the MT+IVT group had lower fibrinogen levels compared to the MT-only group [224 vs 303 mg/dL, p<0.001]. Similarly, there was a significant drop in fibrinogen levels between baseline and follow-up in the MT+IVT vs MT-only group [106 vs 39.5 mg/dL, p=0.001]. Eight patients (19.5%) developed ICH; 5 (26.3%) in the MT+IVT group and 3 (13.6%) in the MT-only group. No significant differences were seen in baseline, follow-up, or change in fibrinogen levels between patients who developed ICH and those who did not. However, there was a significantly lower follow-up fibrinogen levels between patients who suffered an ICH in the MT+IVT arm compared to those without ICH in the MT arm (200 vs 301 mg/dL, p=0.006). There was also a negative correlation between the drop in fibrinogen levels and the number of MT passes (Spearman CC -0.33, p=0.03). Conclusion: This pilot study's preliminary data show that fibrinogen depletion contributes to hemorrhagic transformation in MT-treated patients. This suggests that fibrinogen monitoring in patients undergoing MT after IVT may help identify patients with an increased risk of ICH. Larger studies areneeded to explore the cost-effectiveness of monitoring fibrinogen in patients undergoing bridging therapy and the benefit of repleting fibrinogen in this patient population.

Public Health Sciences

**Fana M**, **Choudhury O**, **Chebl A**, **Latack K**, **Schultz L**, **Albanna A**, **Reardon T**, **Iqbal Z**, **Kole M**, and **Marin H**. The Rapid Occluded Vessel Etiology Score: A Novel Algorithm to Identify Acute Atherosclerotic Large Vessel Occlusions of the Middle Cerebral Artery. *Stroke* 2025;56. Full Text

M. Fana, Henry Ford Health, Detroit, MI, United States

Introduction: Mechanical thrombectomy (MT) devices were fundamentally designed for the treatment of cardioembolic (CE) strokes despite that 10-20% of large vessel occlusions (LVO) are caused by large artery atherosclerosis (LAA), which may not respond comparably. Therefore, the differentiation between LAA and non-LAA LVO may be critical for selecting the ideal MT technique. Here, we construct an algorithm for use in the emergent setting pre-operatively to differentiate between LAA and non-LAA LVO using clinical and radiographic features. Methods: Using our prospectively collected stroke database we identified all middle cerebral artery (MCA) occlusions treated with MT with confirmed etiology as either LAA or non-LAA (CE, cryptogenic) according to TOAST criteria. Stroke risk factors and CT angiography (CTA) of the head and neck features were compared between LAA and non-LAA etiologies in a univariate analysis. An algorithm was then constructed using these variables in a multivariable logistic regression with corresponding score estimates for each variable to assess how well the model distinguished between LAA and non-LAA groups. The sensitivity and specificity were computed for each sum score to identify the ideal cut-off point for differentiating LAA from non-LAA LVOs. Results: Final analysis included 33 LAA, 207 CE, and 120 cryptogenic strokes. Patients presenting with LAA LVOs were significantly less likely to have atrial fibrillation (9.1% vs 53.8%; p<0.0001), EF<35% (9.1% vs 27.8%; p=0.0208) and more likely to present with progressive or fluctuating symptoms (21.2% vs 4.6%; p=0.0018), intracranial multi-vessel atherosclerotic disease on CTA (84.8% vs 37%; p<0.0001), tapered appearance of occlusion with associated collaterals (60.6% vs 0.9%; p<0.0001), and ICA bulb plaque with high-risk features (87.9% vs 37.6%; p<0.0001) (Table 1). The AUC was 0.9650 (95% CI=0.9332, 0.9968) and the highest combination of sensitivity and specificity (97% and 88%, respectively) was associated with a cut-off score of 9 (Tables 2 and 3). Conclusion: Our scoring system reliably differentiates between non-LAA and LAA LVO with high sensitivity and specificity based on 6 clinical and radiographic features. This will need to be validated with an external patient dataset and then in a prospective study. .

Public Health Sciences

Gorman M, Eigl BJ, Usmani N, Pollak M, Bouchard M, Thoms J, Kim JO, Elangovan A, **Ghosh S**, Wang Y, Vigneault E, Peacock M, Fleshner N, Campbell H, Vincent F, So A, Cury FL, Quon H, Carlson R, Lambert C, Klotz L, Chi KN, Brundage M, and Courneya KS. Hormone Changes Associated with Metformin Treatment in Prostate Cancer Patients Initiating Androgen Deprivation Therapy: A Correlative Analysis of the Randomized, Placebo-Controlled Prime Study. *Radiother Oncol* 2025;210:S6. Full Text

Purpose: To determine if prostate cancer (PCa) patients (pts) receiving androgen deprivation therapy (ADT) will have predictable changes in laboratory biomarkers associated with metabolic syndrome and type II diabetes, that can be mitigated with Metformin. Materials and Methods: PRIME is Phase III multicentre double-blind, randomized controlled trial in which 166 normoglycemic pts with PCa receiving at least 9 months ADT were randomized 2:1 to receive metformin 850 mg or placebo BID orally for 18 months (NCT03031821). For this correlative analysis, 47 pts from the metformin arm and 32 pts from the placebo arm underwent optional serum collection and analysis. Fasting (F) and post-prandial (PP) serum samples of the following analytes were collected at baseline, 9, and 12 months: IGF, IGFBP1, IGFBP2, IGFBP3, IGFBP7, leptin, adiponectin, GDF15, insulin, C-peptide, GLP-1, and IL-6. Two-tailed paired t-tests were used to determine if significant changes in laboratory values were evident in pts receiving metformin versus placebo; paired t-tests were conducted to evaluate analytes between timepoints for the metformin and placebo groups separately. Results: Mean leptin values increased markedly in the placebo group and significantly less in the metformin group at 9-months F ($p=4.98x10-5$), 12-months F ($p=9.20x10-4$), 9-months PP ($p=5.37x10-6$), and 12-months PP ($p=4.02x10-4$). Mean IGFBP1 values increased more with metformin compared to placebo at all time-points (all $p\leq0.05$). Mean IL-6 values decreased with metformin compared to placebo at 9-months F ($p=0.06$), 12-months F ($p=0.04$), 9-months PP ($p=0.04$), and 12-months PP ($p=0.03$). C-peptide and GLP-1 showed statistically significant changes with metformin versus placebo only at 9-months F. Some favourable but insignificant trends in mean changes were observed at other time points with C-peptide, GLP-1, insulin, adiponectin, and IGFBP2. No significant changes were observed in other analytes. Conclusions: This study demonstrates that metformin can mitigate changes induced by ADT in biomarkers (leptin, IGFBP1, IL-6) associated with an increased risk of type 2 diabetes and metabolic syndrome. Additionally, the attenuated increase in leptin with metformin signals a potential for improved PCa outcomes, as high leptin values have been correlated with aggressive disease and worse prognosis.

Public Health Sciences

Usmani N, Elangovan A, Courneya K, Ademola A, Lu S, **Ghosh S**, Kim J, Thoms J, Bouchard M, Peacock M, Fleshner N, Campbell H, Vigneault E, Vincent F, So A, Cury F, Quon H, Carlson R, Lambert C, Klotz L, Chi K, Brundage M, Pollak M, and Eigl B. Association of Exercise with Developing Metabolic Syndrome in Prostate Cancer Patients on Androgen Deprivation Therapy: A Secondary Analysis of a Randomized Controlled Trial. *Radiother Oncol* 2025;210:S29. Full Text

Purpose: To determine if prostate cancer (PCa) patients on androgen deprivation therapy (ADT) have lower odds of developing metabolic syndrome (MS) if they were meeting exercise guidelines. Materials and Methods: This is an exploratory analysis of a Phase III multicentre double blind, randomized controlled trial where normoglycemic men with prostate cancer planned for at least 9 months ADT were randomized 2:1 to receive metformin 850 mg or placebo BID orally for 18 months (NCT03031821; The PRIME study). At baseline, all study participants were provided a copy of the Canadian Physical Activity Guideline. At baseline and 12 months, participants completed the modified Godin Leisure Time Exercise Questionnaire which was used to calculate whether they were meeting the aerobic and strength exercise guidelines. The associations between meeting the exercise guidelines and the development of MS at 12 months was analyzed as the primary outcome using logistic regression. The associations between meeting the exercise guidelines and body weight (BW), waist circumference (WC), and hemoglobin A1C (HbA1c) were analyzed as secondary outcomes. Results: At baseline, 87/90 (96.6%) and 45/45 (100%) patients in the metformin and placebo arms completed the exercise questionnaires. At baseline, aerobic exercise guidelines were met by 26/87 (29.9%) and 12/45 (26.7%) patients in the metformin and placebo arms, respectively. Strength exercise guidelines at baseline were met by 40/87 (46%) and 14/45 (31.1%) in the metformin and placebo arms. At 12 months, aerobic exercise guidelines were met by 31/84 (36.9%) and 17/42 (40.5%) patients in the metformin and placebo arms, respectively. Strength exercise guidelines at 12 months were met by 22/84 (26.2%) and 13/42 (30.9%) in the metformin and placebo arms. The association of exercise (either strength or aerobic) with the outcome (MS) was not modified by the intervention (metformin versus placebo), or vice versa, on testing for interactions. Proportion of patients with MS in the metformin and placebo arms were 37/87 (42.5%) versus 26/45 (57.8%) at baseline and 44/83 (51.0%) versus 25/44 (56.8%) at 12 months, respectively. The likelihood of developing MS at 12 months was significantly reduced in the patients meeting aerobic exercise guidelines [odds ratio 0.38

(95% CI: 0.18 - 0.79); p=0.01], but not in those who met the strength exercise guidelines. Significant reductions in BW [-7.13 (95% CI -13.46 – -0.79); p<0.03] and WC [-6.88 (95% CI -11.61 – -2.15); p<0.001] were associated with meeting the strength exercise guidelines. Significant reductions in WC [-6.37 (95% CI -1.72 – -2.02); p<0.001] and HbA1c [-0.16 (95% CI -0.29 – -0.02); p=0.02] were associated with meeting the aerobic exercise guidelines. Conclusions: This exploratory analysis shows favourable differences in MS, BW, WC, and HbA1c at 12 months in PCa patients on ADT who meet exercise guidelines. These efficacy signals warrant confirmation as a primary analysis in future.

Radiation Oncology

**Ghanem AI**, Khanmohammadi R, **Verdecchia K**, **Hall R**, **Elshaikh M**, **Movsas B**, **Bagher-Ebadian H**, Chetty I, Ghassemi MM, and **Thind K**. Late Radiotherapy-related Toxicity Extraction From Clinical Notes Using Large Language Models for Definitively Treated Prostate Cancer Patients. *Am J Clin Oncol* 2025;48(8):S22. Full Text

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Background: For definitively treated prostate cancer, it is very hard to keep track of late radiotherapy (RT)-related toxicities because patients usually seek management beyond radiation oncology years after the radiotherapy course. Thus, reporting these toxicities entitles a complex timeconsuming process going through a huge number of followup notes of different specialties over a long duration. Large Language Models (LLM) represent a major advancement in the field of Artificial intelligence, capable of extracting clinically relevant information from electronic medical records.1,2 Objectives: We sought to automate the extraction of late RT-related toxicity symptoms from clinical notes for prostate cancer patients using LLM, utilizing a teacherstudent architecture. Methods: For a cohort of 177 localized prostate cancer patients treated definitively with 78 to 79.2 Gy +/- androgen deprivation therapy between 2013 and 2020 we identified 1133 clinical notes beyond 6 months after RT conclusion. For validation (434 notes), radiation oncologists manually captured late RT toxicities and relevant symptoms focusing on twelve genitourinary/gastrointestinal domains: cystitis, urgency, urinary obstruction, dysuria, hematuria, nocturia, secondary malignancy (urothelial carcinoma), incontinence, stricture, proctitis, rectal bleeding and erectile dysfunction. For the LLM model optimization, 699 notes were utilized: 294 single and 375 with multiple symptoms/ note with a median of 5/note. The Mixtral-8x7B student model was utilized which initially extracts toxicity symptoms, which are then refined by the GPT-4 teacher model over 16 rounds and 5 epochs, based on the student's performance and rationale. The process involves the student ranking concepts as positive, negative, or neutral and justifying the ranking, with the teacher model evaluating and improving the prompts based on this analysis. Using the validation set as a reference, we employed accuracy to assess the student model refinement, and we also calculated precision, recall and F1 scores to evaluate the performance of the refined prompts compared with the initial forms. Results: For single-symptom notes (n= 294), overall average accuracy for toxicity symptom extraction reached 0.71 postrefinements with final precision, recall and F1 scores of 0.82, 0.71 and 0.73, respectively, as depicted in Table 1. 'Urgency,' 'Urothelial Carcinoma,' and 'Stricture' reached the perfect accuracy (score=1) postrefinements with excellent precision, followed by 'Urinary Obstruction' (score= 0.8). Initial model performed optimally with no improvements for 'Dysuria,' 'Incontinence,' and 'Hematuria.' Scores were relatively lower for multiple symptoms notes (n= 375), with best accuracy for 'Hematuria,' 0.76; 'Urothelial Carcinoma,' 0.7 and 'Dysuria,' 0.62, with best improvements noted for 'Urothelial Carcinoma,' 0.05 to 0.7 and 'Rectal Bleeding,' 0.16 to 0.57. Compared with initial performance, improvements ranged between 16% and 30% for the assessment metrics for single-symptom and multi-symptom (Table 1). The incremental improvement of each symptom, across all note types, for each epoch achieved a final accuracy of 72% to 97% (Fig. 1 left), with overall average (SD) accuracy of 84 (72 to 96) % (Fig. 1 right). Description: A clear trend of improvement is observed in nearly all symptoms as the number of epochs increases, illustrating the efficacy of our prompt refinement process. Conclusions: Using our developing in-house novel student-teacher LLM with incremental self-improvements, we were able to achieve clinically meaningful results with a robust potential to accurately automate the process of late RT-related toxicity extraction for prostate cancer patients without compromises for patient privacy. We are in the process of leveraging the validity of this model by including more patients' data with longer follow-up, and we hope to expand the scope to encompass RT-toxicity grading and management.

Surgery

Dhanda U, Alameddine D, Schultz KS, Tran L, Silva D, Slade MD, **Kabbani LS**, Guzman RJ, Leeds IL, and Ochoa Chaar CI. Beyond DAPT for PAD: Dual Antithrombotic Pathway Inhibition Reduces Limb Events and Proves Cost-effective. *J Vasc Surg* 2025;82(4):e103-e104. Full Text

Introduction and Objectives: Antithrombotic therapy is essential for medical management of patients with peripheral arterial disease to prevent major adverse limb events and major adverse cardiovascular events. Although dual antiplatelet therapy (DAPT = aspirin + clopidogrel) has been widely studied, emerging evidence suggests that combining factor Xa inhibitors with clopidogrel may offer additional mitigation as it provides dual antithrombotic pathway inhibition (DAPI). This study aims to evaluate the outcomes and the cost-effectiveness of patients treated with DAPI compared with DAPT after lower extremity revascularization (LER). Methods: A retrospective review of patients who underwent open and endovascular LER in a tertiary center was performed. The characteristics of patients treated with DAPT and DAPI were compared after propensity matching (4:1). Cost-effectiveness was assessed using cost ($) and quality-adjusted life year (QALY) modeled for 5 years after LER. The incremental cost-effectiveness ratio (cost per QALY gained) was derived with a willingness-to-pay threshold of $150,000 per QALY. Results: A total of 987 patients underwent LER, most discharged on DAPT (95.5%) and only 5.6% (N = 55) on DAPI. Patients discharged on DAPI were significantly older (80 vs 72, P < .001), more likely to have congestive heart failure (27% vs 13%, P = .003), and more likely to be treated for chronic limb-threatening ischemia (62% vs 44%, P = .011). After matching, the Kaplan-Meier analysis demonstrated that patients treated with DAPI had significantly higher major adverse limb event-free survival, but there was no difference in major adverse cardiovascular event-free survival (Fig 1). DAPI was more expensive ($73,826 vs $39,548) but provided additional QALYs (4.64 vs 3.51) and was cost-effective with an incremental cost-effectiveness ratio of $30,331 per QALY compared with DAPT (decision tree in Fig 2). Conclusions: DAPI after LER is used in a relatively older patient cohort with increased comorbidities. In this patient population, DAPI seems to be associated with better outcomes than DAPT and is a cost-effective strategy for antithrombotic therapy. [Formula presented] [Formula presented]

Surgery

**Halabi M**, **Chamseddine H**, **Shepard A**, **Nypaver T**, **Weaver M**, **Boules T**, and **Kabbani L**. Outcomes of carotid artery stenting for nonatherosclerotic disease. *Eur J Vasc Endovasc Surg* 2025;70(3):e39-e40. Full Text

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Objective: This study aims to evaluate and compare the outcomes of transcarotid artery revascularization (TCAR) and transfemoral carotid artery stenting (tfCAS) in patients with nonatherosclerotic carotid diseases, including dissection, trauma, and fibromuscular dysplasia. Methods: Patients who underwent TCAR and tfCAS for nonatherosclerotic carotid diseases between 2016 and 2024 were identified in the Vascular Quality Initiative (VQI) database. Patients were classified into TCAR or tfCAS based on the procedure performed. Baseline characteristics, demographics, and operative details were collected. Primary outcomes included stroke, death, and major adverse cardiovascular events (MACE), which was defined as the composite of stroke, myocardial infarction, and death. Secondary outcomes included perioperative complications. Descriptive statistics, univariable comparisons, and multivariable logistic regression analyses were performed to evaluate the association between procedure type and outcomes. A two-tailed P value of <.05 was considered statistically significant. Results: Six hundred seventy six patients were identified (tfCAS, n = 503; TCAR, n = 173). TCAR patients were older (64 ± 14 years vs 56 ± 16 years; P < .001), and had higher rates of hypertension (74% vs 60.4%; P = .001) and coronary artery disease (34.1% vs 22.2%; P = .002). Dissection was the most common etiology (TCAR, 77.5%; tfCAS, 77.9%), followed by fibromuscular dysplasia (TCAR, 14.5%; tfCAS, 10.5%) then trauma (TCAR, 8.1%; tfCAS, 11.5%). Intraoperatively, TCAR patients had shorter fluoroscopy times (5 minutes vs 18.25 minutes; P < .001) and required less radiocontrast (30 mL vs 95 mL; P < .001), but had slightly longer procedure times (75.5 minutes vs 69 minutes; P = .055). When analyzed by procedure type, TCAR was associated with significantly lower rates of MACE (1.2% vs 7%; P = .004) and stroke/death (1.2% vs

6.4%; P = .007) compared with tfCAS. Furthermore, when stratified by symptomatic status, TCAR consistently had lower rates of MACE and stroke/death. On multivariate analysis, TCAR was independently associated with a significantly lower risk of MACE (odds ratio, 0.09; 95% confidence interval, 0.01-0.74; P = .025) and stroke/death (odds ratio, 0.11; 95% confidence interval, 0.01-0.95; P = .045). Conclusions: TCAR was associated with superior perioperative outcomes compared with tfCAS in the treatment of nonatherosclerotic carotid diseases. These findings highlight TCAR's potential to be a safer and more effective treatment option for this challenging patient population.

Surgery

Jones O, Magyar CTJ, **Rajendran L**, Aceituno L, Li Z, Choi W, and Sapisochin G. Liver transplantation or hepatic arterial infusion for unresectable colorectal liver metastases: A meta-analysis of reconstructed single-arm survival data. *Ann Oncol* 2025;36:2. Full Text

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